ETHIOPIAN MEDICAL JOURNAL

ISSN0014-1755

APRIL 2021 VOLUME 59 NUMBER 2

This April 2021 issue is dedicated for Dr. Worknesh Ayele

ETHIOPIAN MEDICAL ASSOCIATION
P.O. Box 3472, Addis Ababa, Ethiopia
Tel. No. 251-15533742
www.emjema.org
emjeditor2018@gmail.com
Fax: 251-1-5533742
Addis Ababa, Ethiopia

Dr. Abraham Assefa, previous board member of the editorial board member of EMJ has been awarded the prestigious African Union Kwame Nkrumah Continental Award for the Scientific Excellence for Life and Earth Sciences Category of the 2020 Edition.

The African Union Kwame Nkrumah Continental Award for Scientific Excellence (AUKNASE) is a three-level award: national, regional, and continental, to recognize African men and women in science who have distinguished themselves through their contribution to research and training for the continent's development.

The Editorial Board members of EMJ congratulate Dr. Abraham Assefa for his outstanding achievement.

The Ethiopian Medical Journal is the official quarterly publication of the Ethiopian Medical Association. It is devoted to the advancement and dissemination of knowledge pertaining to medicine in Ethiopia and other developing countries.

SHORT BIOGRAPHY OF DR. WORKENESH AYELE MOLTOTAL

The late Dr. Workenesh Ayele Moltotal was an outstanding scientist who received her Bachelor of Science in Biology from the Baylor University (Waco, Texas, USA), Master of Science in Pharmacology from the University of Houston (Houston, Texas, USA), and PhD degree in Virology from the University of Amsterdam, the Netherlands. She began her career at the Anderson Cancer Center (Houston, Texas, USA) as a research assistant and later joined the former Pasteur Institute (currently the Ethiopian Public Health Institute) in Addis Ababa working as a laboratory scientist in virology research. She was the principal scientist who played a key role in leading the establishment of the national laboratory for influenza and other emerging/re-emerging epidemic-prone viral infections at the institute.

Dr. Workenesh provided professional services in various capacities at Jimma University and the School of Medical Laboratory Technology at Addis Ababa University. She provided training on Research Methodology to students in Medical Laboratory, Public Health Laboratory Methods and Biosafety to residents of the Ethiopian Field Epidemiology Training Program (EFETP) at the School of Public Health, Addis Ababa University. She also provided training at the African Regional Capacity Building Network (ARCAN) for HIV/AIDS Prevention, Treatment and Care, and the St. Paul's Hospital Millennium Medical College. Since 2014, she served as the Director of Research and Compliance Coordinator at ECUSTA Higher Learning Institute in Addis Ababa.

Over the years, Dr. Workenesh served on a number of key national technical advisory committees and taskforces supporting the Ministries of Health and Science and Technology. She was a member of several professional associations, national and international, including the Ethiopian Public Health Association (EPHA), American Society of Microbiology (ASM), Organization for Women in Science for the Developing World, and Society of Ethiopian Women in Science and Technology. She was a member of the Ethiopian Academy of Sciences and served as Secretary of the Executive Committee of the Society of Ethiopian Women in Science and Technology.

Dr. Worknesh was an active member of the Editorial Board of the Ethiopian Medical Journal (EMJ) since 2016. She peer-reviewed and copy-edited hundreds of manuscripts. She was loved and respected by other members of the Board for her dedication to science, her honesty, and critical thinking as well as her considerate approaches to supporting young researchers to publish quality papers. She is missed by all her colleagues at the EMJ and Ethiopian Medical Association (EMA), and all those who happen to have worked with her at various institutions and organizations. Considering Dr. Worknesh's exceptional contribution to our journal and to hear field of specialty, the Editorial Board of EMJ have decided to dedicate the April 2021 issue of our journal in her memory. Dr. Worknesh will continue to be remembered for her dedication and exceptional contributions.

ETHIOPIAN MEDICAL JOURNAL
April 2021

EDITORIAL

ORIGINAL ARTICLES

SYSTEMATIC REVIEW

REVIEW ARTICLE

CASE REPORT

Mirkuzie Woldie. *Ethiop Med J, 2021, Vol. 59, No. 2*

EDITORIAL

PAY ATTENTION TO SOCIAL DETERMINANTS OF HEALTH: COVID-19 TAKES US BACK TO THE BASICS

Mirkuzie Woldie (M.D, M.P.H)

The World Health Organization (WHO) declared the coronavirus disease (COVID-19) as a global pandemic on March 11, 2020 (1). Since then the virus has affected almost every country on the globe with more than 124 million infected and 2,735,707 died as of March 24, 2021 (2). Different regions and countries of the world have witnessed sharp increases in the number of infected and died of the pandemic at different points in time.

The effort to curb the pandemic have proved to be a very challenging task all over the world. Its impact has been all rounded affecting economic, social, and political realm of life(3-5); not to mention its influence on health systems and how they operate(6).

The current pandemic has made it clear that addressing social determinants of health and disease in the population remains a key (7). The basics of public health intervention for population health promotion and disease prevention are proved relevant more than ever. Although this is an established fact several years ago, the current order of things in the globe has failed to address what matters most when it comes to population health. COVID-19 has revealed the current degree of social and economic inequity which immensely impacts the baseline health condition of people and how their body reacts to threats such as COVID-19 infection.

Several reports have demonstrated that populations across the world have witnessed significant damage to the health of already disadvantaged segments. An article by Global Alliance for Tax Justice stated: "The effects of the coronavirus are being felt disproportionately by the poor and the working class and the COVID-19 disruption is playing out along the lines of class, gender and wealth (8)." A press release of the United Nations (UN) suggested that there is an urgent need for "efforts towards more resilient, inclusive and sustainable economies and societies (9)."

Physical distancing, hand hygiene, face masking, vaccination campaigns and hospital care for those affected with severe disease are all important measures to halt the pandemic. However, the broader implications of what was observed in the globe should be well attended: we have to pause and figure out how to address the root causes of ill health in the global population.

The April Issue of EMJ is dedicated to the late Dr. Worknesh Ayele who served as a member of the EMJ Editorial Board for several years. This issue features articles on a range of topics with an opening relevant to the current global challenge, COVID-19.

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[1]Ministry of Health, Addis Ababa, Ethiopia.
[2]Fenot Project, Harvard T.H. Chan School of Public Health, Addis Ababa, Ethiopia.
*Corresponding Author E-mail: mirkuzie@yahoo.com

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Saleem Z, Shaikh H, Ramzan Z, Bhatia MR, Tabassum U, Majeed MM. *Ethiop Med J, 2021, Vol. 59, No. 2*

ORIGINAL ARTICLE

A COMPARATIVE STUDY TO EVALUATE COVID-19 RELATED ANXIETY AND FEAR AMONG PHYSICIANS AND DENTISTS

Salim Z, MDS [1], Shaikh H, FCPS [1], Ramzan Z, FCPS [2], Bhatia MR, FCPS[3], Tabassum U, FCPS[2], Majeed MM, MDS [4*]

ABSTRACT

Introduction: *Worse mental health outcomes appear to be related to COVID-19 as the virus is perceived as severe. Pakistan, being a developing country, had an immense burden on health care due to COVID-19. Healthcare professionals dedicatedly performing their duties carry a high risk of getting infected. Our study aimed to analyze the fear and anxiety among Pakistani physicians and dentists and also highlight the factors causing it.*

Methodology: *It was an online survey-based cross-sectional study. Fear and anxiety among physicians and dentists were observed with the help of previously validated fear of coronavirus-19 scale (FCV-19s) and Coronavirus Anxiety Scale (CAS). Data was analyzed on SPSS 21. Chi-square test, Independent sample t-test and Pearson correlation tests were applied.*

Results: *The study included 267 dentists and 220 physicians. Results demonstrated that severe fear (27.422 ± 4.455) and anxiety (14.80 ± 2.88) among the participants. Significantly higher levels of anxiety were found in dentists ($t_{(427.809)} = -2.498$, $P=0.013$. Females showed significantly higher fear and anxiety scores as compared to males ($p< 0.05$). A strong and significant positive correlation between Fear and Anxiety was established ($r=0.798$, $p<0.0001$).*

Conclusion: *COVID-19 poses a major challenge to the mental health of Healthcare professionals . A considerable proportion of our participants showed high values for fear and anxiety. Psychological help or support should be offered to all Healthcare professionals with importance on effective coping tactics.*

Keyword: *Dentists, Physicians, Anxiety, Fear, COVID-19*

INTRODUCTION

The global community came mindful of an outbreak of a novel coronavirus pathology called COVID-19, which is thought to originate in Hubei province in December 2019. It was declared a public health emergency of international concern by the World Health Organization (WHO) in January 2020, and it was soon characterized as a pandemic by the WHO in March 2020 (1-3).

Worse mental health outcomes appear to be related to COVID-19, as the virus is perceived to be severe. Myths and unfiltered non-scientific information amidst the pandemic largely concern the population, which has an impact on mental health (4, 5). Moreover, measures taken by the governments globally to contain the virus including lockdown, social distancing, closure of schools, remote work, and quarantine has further spread negativity. Meanwhile, healthcare professionals (HCPs) are still performing their duties and providing care to patients in a highly stressful environment (6-9).

Furthermore, psychological issues including anxiety, fear, depression etc. are common among the HCPs due to the direct exposure and interaction with the patients or suspected individuals (10). Moreover, a significant element for HCPs is the fear that relates to COVID-19 exposure and subsequent worry of transmitting the infection to their families (11, 12). Uncertainty about several elements related to disease like the mood of transmission, an infection transmitted by asymptomatic and pre-symptomatic patients, also contribute to stress among HCPs (13).

Past quantitative researches have demonstrated that HCPs interacting with patients infected with COVID-19 are at higher risk of mental health issues like stress, depression, anxiety, and insomnia (14). Moreover, frontline HCPs who have no experience of infectious pathologies face additional challenges while adjusting to a new work environment during the current pandemic (15).

[1]Department of Oral and Maxillofacial Surgery, Dow University of Health Sciences, Karachi, Pakistan.
[2]Department of Psychiatry, Dow University of Health Sciences, Karachi, Pakistan.
[3] Department of Psychiatry,People's University of Medical and Health Sciences, Nawabshah, Pakistan.
[4]Department of Oral Biology, Altamash Institute of Dental Medicine, Karachi, Pakistan.
*Corresponding Author E-mail: mmansoormajeed@gmail.com

To overcome the negative effects on mental health and contain the spread of COVID-19, it is important to consider unfavorable psychological issues and take appropriate measures at an initial stage (16, 17). The well-being of HCPs during the current pandemic necessitates just not them being sufficient but also maximum efficiency for providing profound care to the patients over burdened volume (11).

Previous studies conducted in Pakistan targeted COVID-19 knowledge, attitudes, practices, and anxiety among physicians, dentists, nurses, and pharmacists, or the general public (18-20).

This study aimed to evaluate and compare the fear and dysfunctional anxiety related to COVID-19 among the two main pillars of healthcare i.e., physicians and dentists, serving in Pakistan.

MATERIAL AND METHODS

Study Design: This was an online survey-based cross -sectional study. This study was conducted during the period of lockdown in May 2020.

Sampling: To find out the required sample, Rao soft (www.raosoft.com) was used. Considering the HCPs population 125 000, 95% confidence interval, 5% margin of error, the calculated sample size was 383. To cover inconsistencies and discrepancies, an additional 25% (n=96) was added. So the sample size of 479 was found sufficient for the current study.

Study Population: In this study, participant were the physicians and dentists with minimum qualification of Bachelor of Medicine & Bachelor of Surgery (MBBS) for physicians or Bachelors of Dental Surgery (BDS) for dentists respectively and more than 1 year of experience. Retired and non-practicing physicians and dentists were excluded. The investigators approached participants through their personnel contacts as per convenience snowball technique and also recruited through different social media platforms.

Questionnaire Design

To check the fear and anxiety among the physicians and dentists of Pakistan we used previously validated scales. Fear of Coronavirus Scale (FSC-19S) (21) and Coronavirus Anxiety scale (CAS) (22).

The FCV-19S is 7 items measured on five points Likert Scale. The FCV-19S is ranging between 7 and 35, the greater the score, the higher the fear. The CAS is a 5 item scale ranging between 4 and 20 and with a cut-off score of ≥ 9.

The scale discriminates between those with dysfunctional anxiety and non-anxiety.

After thorough literature search and discussion and a pilot study, the survey instrument of this study was finalized. The first part of the survey instrument comprises of the demographic data, including age, gender, specialty, city, and country of residence. The second part had questions from FCV-19S and CAS.

The reliability coefficient of the survey instrument for the current study was computed using SPPS V.21 (Cronbach's $\alpha = 0.884$) which is considered good.

Ethics: Data collection using an online questionnaire was conducted after ethical clearance was granted by the Ethics and review committee of Altamash Institute of Dental Medicine, Karachi, Pakistan.

Statistical Analysis: Sociodemographic data were reported as percentages and frequency. The independent sample t-test was performed to observe the difference in scores among dentists & physicians and between males and females for fear and anxiety. The linear correlation between fear and anxiety was evaluated using Pearson's correlation test. Multiple linear regression analysis was applied to observe the relationship of sociodemographic variables with anxiety and fear scores. A P-value of less than 0.05 was considered significant.

RESULTS

For the current study, data of 512 participants were collected. After sorting out due to some discrepancies, the data of 483 participants were analyzed. Significantly higher number of dentists, females and participants individuals under 30 years participated ($p<0.05$) **(Table 1).**

In Table II, the measures of central tendencies along with skewness and Kurtosis of each item of FCV-19S has been reported. The total mean score of FCV -19S was 27.422 ± *4.455 which is towards the higher side. . No statistically significant difference was observed between physicians and dentists* ($t_{(485)} = -0.952$, $p>0.05$). However, the mean fear score of dentists ($\bar{X} = 27.59 \pm 4.209$) *was found slightly higher as compared to the physicians* ($\bar{X} = 27.20 \pm 4.737$) ***(Table 2)***

Table 1: Demographic Characteristics, Pakistan, May 2020

Character	Frequency	Percentage	X2	p-value
Total	487	100.0		
Category				
Physicians	220	45.2%	4.536	0.033
Dentists	267	54.8%		
Gender				
Male	184	37.8%	29.078	<0.001
Female	303	62.2%		
Age Group				
Up to 30	268	55.0%		
31-40	135	37.7%		
41-50	36	7.4%	462.743	<0.001
51-60	22	4.5%		
61+	26	5.3%		

Table 2: Fear among the Physicians and Dentists, Pakistan, May 2020

FCV-19S Items	Category	MIN	MAX	Mean	SD	Kurtosis	Skewness	T-score	P-Value
I am most afraid of coronavirus-19.	Physicians	1	5	4.04	0.893	1.083	-1.012	-0.569	0.570
	Dentists	1	5	4.09	0.856	0.838	-0.927		
It makes me uncomfortable to think about coronavirus-19. **	Physicians	1	5	3.83	0.910	0.558	-0.751	-2.258	0.024**
	Dentists	1	5	4.01	0.882	1.381	-1.015		
My hands become clammy when I think about coronavirus-19.	Physicians	1	5	4.03	0.953	1.040	-1.119	-0.534	0.594
	Dentists	1	5	4.07	0.828	1.004	-0.901		
I am afraid of losing my life because of coronavirus-19.	Physicians	1	5	3.41	1.045	-0.287	-0.361	0.373	0.709
	Dentists	1	5	3.38	1.038	-0.592	-0.199		
When watching news and stories about coronavirus-19 on social media, I become nervous or anxious	Physicians	1	5	3.68	1.037	0.018	-0.718	-1.894	0.059
	Dentists	1	5	3.85	0.897	0.379	-0.740		
I cannot sleep because I'm worrying about getting coronavirus-19.	Physicians	1	5	4.01	0.912	1.339	-1.113	-1.212	0.226
	Dentists	1	5	4.10	0.830	0.678	-0.875		
My heart races or palpitates when I think about getting coronavirus-19	Physicians	1	5	4.20	0.799	0.697	-0.873	1.500	0.134
	Dentists	1	5	4.09	0.871	0.831	-0.966		
COVID-19 FEAR	Physicians	11	35	27.20	4.737	0.758	-0.884	-0.952	0.341
	Dentists	11	35	27.59	4.209	1.250	-0.836		
	Total	11	35	27.42	4.455	1.030	-0.877		

The total mean score of CAS was 14.80 ± 2.88 which is far beyond the cut off value of ≥9. Based on the cut-off score of ≥9.0 in the COVID-19 Anxiety Scale, 474 (97.3%) individuals were found to have dysfunctional levels of anxiety **(Figure 1).** We observed that dentists showed higher mean scores of anxiety in all the 5 items of CAS. We further analysed the difference between physicians and dentists for the total score of CAS. As per independent sample t-test, we found a significant t value ($t_{(427.809)}$ = -2.498, p=0.013).

It indicates that anxiety among the dentists is significantly higher than physicians. The analysis further revealed that dentists exhibited higher anxiety score ($\bar{x}$ =15.03 ± 2.722) as compared to physicians ($\bar{x}$ =14.47 ± 3.129) **(Table 3).**

Pearson's correlation analysis revealed there is a strong and significantly positive correlation between Fear and Anxiety (r=0.798, p<0.0001).

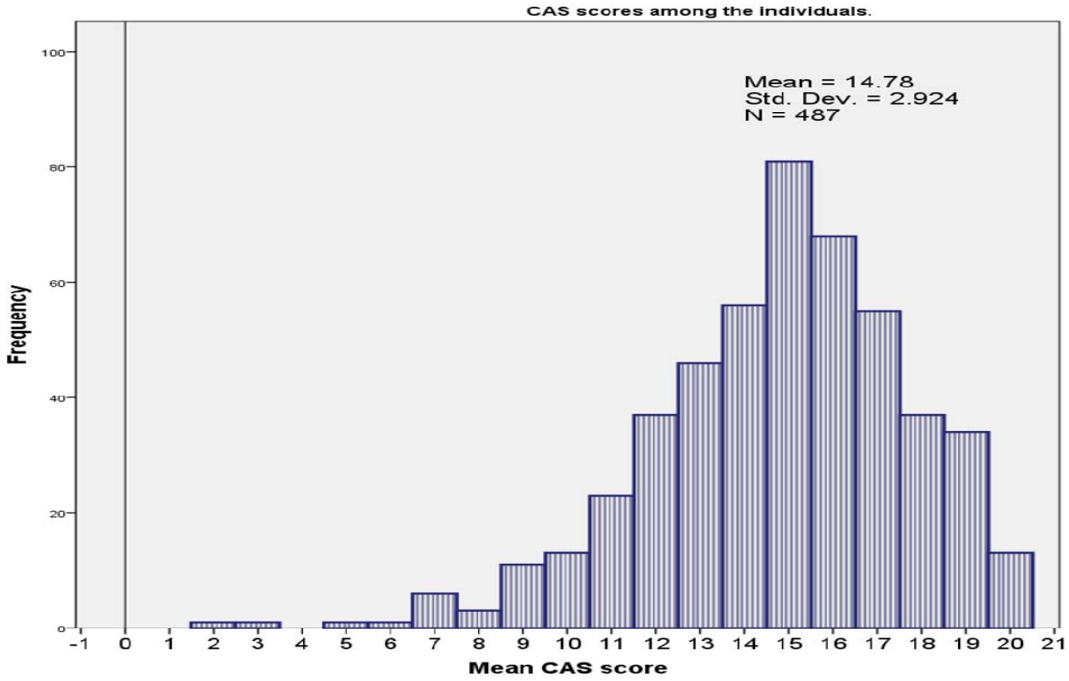

Figure 1: Histogram showing the mean Coronavirus anxiety score of the participants, Pakistan, May 2020

Table 3: ANXIETY among the Physicians and Dentists. Pakistan, May 2020

CAS Items	Category	MIN	MAX	Mean	SD	Kurtosis	Skewness	T-score	P-Value
I felt dizzy, lightheaded, or faint, when I read or listened to news about the coronavirus.	Physicians	0	4	2.61	1.074	-0.373	-0.577	-3.146	0.002*
	Dentists	0	4	2.89	0.833	-0.192	-0.494		
I had trouble falling or staying asleep because I was thinking about the coronavirus.	Physicians	0	4	3.05	0.913	1.437	-1.154	-1.135	0.257
	Dentists	0	4	3.14	0.785	0.926	-0.860		
I felt paralyzed or frozen when I thought about or was exposed to information about the coronavirus.	Physicians	0	4	3.00	0.860	1.024	-0.869	-2.101	0.036*
	Dentists	1	4	3.16	0.774	0.577	-0.819		
I lost interest in eating when I thought about or was exposed to information about the coronavirus.	Physicians	0	4	2.44	1.034	-0.549	-0.340	-.246	0.805
	Dentists	0	4	2.46	1.059	-1.022	-0.174		
I felt nauseous or had stomach problems when I thought about or was exposed to information about the coronavirus	Physicians	1	4	3.35	0.793	0.625	-1.088	-1.692	0.091
	Dentists	0	4	3.46	0.689	2.346	-1.316		
COVID19 ANXIETY Total Scores	Physicians	2	20	14.44	3.13	1.404	-0.958	-2.498	0.013*
	Dentists	7	20	15.10	2.62	-0.176	-0.226		
	Total	2	20	14.80	2.88	1.028	-0.705		

To check the association of sociodemographic variables (gender, age, and profession) on anxiety and fear scores, multiple linear regression analysis was applied.

The results demonstrated that gender has a highly significant association with anxiety and fear scores with p-value < 0.001 **(Table 4).**

Table 4: Multiple linear regression analysis of fear score and sociodemographic variables, Pakistan, May 2020

FEAR				**Anxiety**			
Adjusted R2	SEE	F	P-value	Adjusted R2	SEE	F	P-value
0.033	4.38	6.536	<0.001	0.028	2.841	5.685	0.001
Coefficients							
Variables	β	SEE	P-value	β	SEE	P-value	
(Constant)	24.343	1.175	<0.001	12.485	0.762	<0.001	
Age	0.026	0.203	0.899	.037	0.132	0.781	
Gender	1.826	447	<0.001	.903	0.290	0.002	
Profession	045	.0 426	0.916	.513	0.276	0.064	
Gender has a statistically significant association on the outcome variable (p<0.05).				Gender has a statistically significant association on the outcome variable (p<0.05).			
R= 0.198 showing a positive linear relationship				R= 0.185 showing a positive linear relationship			
3.3% of the variance of dependent variables is explained by the independent variable.				2.8% of the variance of dependent variables is explained by the independent variable.			

In our study, we evaluated the fear and anxiety score among male and females participants. A significant difference has been observed. As per independent sample t-test Females showed higher fear ($t_{304.034}$ = -4.126, p <0.001) and anxiety ($t_{319.555}$= -3.469, p =0.004).

Mean fear and anxiety score among gender is also significantly different (p<0.05) (**Figure 2).** In the current study, we found that HCPs below 30 years of age are more anxious and afraid of COVID-19.

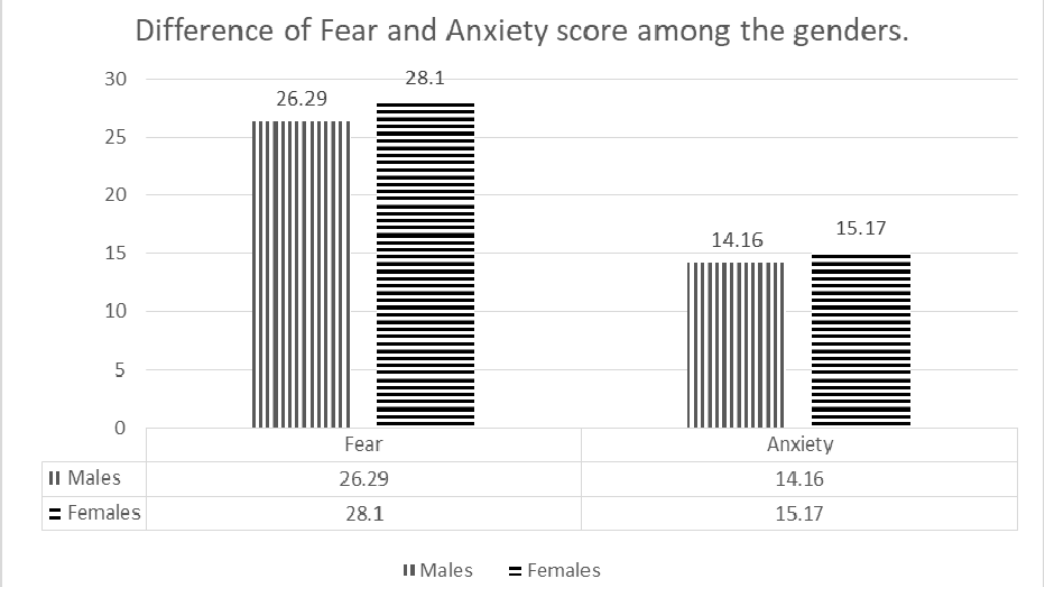

Figure 2: Fear and Anxiety score among male and female genders Pakistan, May 2020

DISCUSSION

The current pandemic has caused an immense strain on government, organization, and individuals (23, 24). According to the latest report (3rd August 2020) by the WHO, around 1.8 million cases have been reported globally with over 680000 deaths (25). In Pakistan 278,305 confirmed cases and 5,951 deaths due to COVID-19 has been reported (26). This has caused stress among the general public as well as health care professionals who are devotedly performing their duties despite the uncertainty about several factors related to the disease, including its infectivity, mode of transmission, and no available treatment option. Overall, the disease has put a burden on the country's healthcare system along with the strain on the country's economy by imposing lockdown and promoting social distancing, which has caused pay cuts and even unemployment in various regions. Pakistan is a developing country with limited health care facilities (27) and due to COVID-19 is experiencing various negative impacts.

Along with the general population, considering the mental health stability of HCPs is important so that maximum effort from them is achieved during the current situation when they are in need of the most for the well-being of their patients. Needless to say, all HCPs are playing their part to the best in overcoming the disease burden currently. However, in this study, we evaluated anxiety and fear specifically among dentists and physicians. Whether having previous experience of infection control or not, physicians and dentists are dealing with patients on a regular basis. Due to the potential of transmission despite being asymptomatic, dentists and physicians are taking all necessary precautions for all patients regardless of reporting no history for COVID-19 symptoms.

In the current study, we found that the mean fear score among the HCPs is towards the higher side. This coincides with the results of a cross-sectional study evaluating the psychological status of the healthcare workforce in China. (28). Another survey-based cross-sectional study carried out in Wuhan recorded the mental health status of health care professionals. The study reported symptoms of unstable mental health status among health care professionals, with 50.4% of participants reported depression, 44.6% anxiety, 34% insomnia and 71.5% reported distress (29). Similar results were also recorded in a study conducted in Pakistan, stated that 72.3% and 90.1% of HCPs suffering from moderate to extremely severe depression and stress, respectively. In the current study majority of the HCPs have specified disturbed sleep due to COVID-19, which is in accordance with the previous study (30).

Moreover, studies have testified that HCPs are in a state of fear and anxiety due to the contagious nature of this virus (3, 31). Correspondingly in the current study, we have observed similar findings. A recent study conducted in China demonstrated that more than 70% of HCPs reported moderate to severe fear and 22.6% of medical staff showed mild to moderate anxiety whereas 2.9% had severe anxiety (28).

In the current study we used Coronavirus Anxiety Scale to measure anxiety, based on the cutoff score of CAS, we found that more than 90% of the Physicians and Dentists of Pakistan have dysfunctional levels of anxiety. Likewise, a previous study conducted in Pakistan reported 85.7% HCPs who suffered from moderate to extremely severe anxiety, and 90.1% reported moderate to extreme stress levels. One study found similar results in Saudia Arabia where 31.5% showed mild, 36.1 had medium and 32.3% demonstrated a high level of anxiety(32). We also observed that fear and anxiety have a significant and strong positive correlation.

In the current study, dentists demonstrated more fear and significantly higher levels of anxiety as compared to the physician. Similar findings are also observed in previous studies conducted on HCPs, reported higher fear among the dentists as compared to physicians (12). Furthermore, different reports of the spread of this contagious disease due to dental procedure that generates aerosols as well as confined spaces of the dental surgery are also worrisome for the dental fraternity (33, 34).

Moreover, studies have reported anxiety among dentists due to the closure of dental clinics, institutes and hospitals during the pandemic and dentists suffered a lot of financial crises (35). Studies have documented that dental professionals are more prone to infections because of the aerosols generating procedures and confined environment of the dental offices (36, 37). In different studies, primarily focusing the fear among dentists during the current crisis revealed that fear of being infected from the patient or colleague, transmission of infection to family members, economic and financial insurgencies, panic and anxiety of getting quarantined, etc. are the major factors causing fear among the dentists (1, 31, 38). The major contributing factors to fear and anxiety among dentists in our study include lack of health facilities in our country, the undesirable effect of the disease on the economy, the thought of when the disease would get eradicated, and transmitting the disease to others. These contributing factors nearly matched the contributing factors mentioned in other literature (1, 39).

In our study, we observed significantly higher fear and anxiety among females as compared to males. In agreement with our findings, previous studies have also shown higher levels of anxiety among women (40) and female doctors (41,42).

The factors that significantly contributed to the increase in psychological pressure according to a previously conducted study included isolation ward duties, upsetting about getting infected, insufficient protective equipment, the thought that the current pandemic would never get under control, frustration related to unsatisfactory outcomes on work, and isolation away from loved ones (28, 29). Another study including participants from Pakistan and a few from the UK listed down the factors contributing to fear. The factors included family members getting an infection (79.7%), the rapid spread of disease (63%), complications of the disease (60.3%), becoming a carrier (28.8%), and missing the diagnosis (27.9%) (3).

A statistical test was run to observe the relations between anxiety and sociodemographic variables including, age, gender, and profession of the participants. The result demonstrated that there is a significant association between anxiety and fear score with gender. Female dentists and physicians demonstrating more anxiety and fear as compared to males.

Good mental health is essential for the well-being of the physicians and dentists during the current pandemic for maximum efficiency and to contain the virus. To combat the fear related to COVID-19 among physicians and dentists, several factors that lead to anxiety and fear should be considered and measures need to be taken to assure the healthcare providers.

The psychological issues due to COVID-19 among the physicians and dentist should be taken serious and longitudinal studies should be performed to document the prevalence of depression, disconnectedness, Sleep disturbances, psychoses, anxiety, fear, obsession, panic etc.

The strength of this study is that the data was collected from more than 35 cities from all the provinces of Pakistan. The limitation of this study is that due to the countrywide lockdown, only online data was gathered and those physicians and dentists who are not tech-savvy didn't participate, so results may not be generalized and may have source bias effects. Moreover, the findings of this study are based on self-reported data, and the participants may misjudge the answers in a way that they consider is socially acceptable rather than reporting authentic or honest answers.

Conclusion

Our study concludes the presence of severe fear and anxiety among Physicians and dentists. To obtain good mental health among dentists and physicians, factors that contribute to fear and anxiety should be considered and measures need to be taken to combat it.

Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

Funding

None

Authors' Contribution

SZ: Initial draft writing, literature search, data collection and final approval of the manuscript. **SH:** Data collection, write up, Critical revision and final approval of the manuscript. **RZ:** Study Concept and design and critically revised and approved the final draft of the manuscript. **TU:** Data collection, write up, tables and figure and final approval of the manuscript. **BMR:** Data collection, statistical work and final approval of the manuscript. **MMM:** Conceived the study, supervised the project and is responsible for the integrity of the research. Comprehensively contributed to Data collection, statistical work, writing of the manuscript and critically revised and approved the final draft of the manuscript.

ACKNOWLEGMENT

We acknowledge the support of the ethic and review committee of Altamash Institute of Dental Medicine, Karachi, Pakistan. We would like to thanks all the respected participants for their participation and support at every step of the research.

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Makram Tbini, Habib Jaafoura, Ezer Chebil, Ines Riahi, Rim Lahiani, Mamia Bensalah. *Ethiop Med J, 2021, Vol. 59, No. 2*

ORIGINAL ARTICLE

CORRELATION BETWEEN PARATHYROID ADENOMA VOLUME AND BIOCHEMICAL PARAMETERS

Makram Tbini, MD[1*], Habib Jaafoura, MD[1], Ezer Chebil, MD[1], Ines Riahi, MD1, Rim Lahiani, MD[1], Mamia Bensalah, MD[1]

ABSTRACT

Introduction: *Predicting the size of the parathyroid adenoma may be useful for the surgeon, hence assessing the correlation between the biochemical parameters and the dimensions of the parathyroid adenoma is important.*
Materials and methods: *A retrospective study was conducted using 6-year (2012-2017) data on patients operated on for parathyroid adenoma and who had records on biochemical assessment. The volume of the adenoma was estimated using its measured dimensions and a mathematical formula.*
Results: *Thirty five patients including 30 women and 5 men were operated for parathyroid adenoma. The mean age was 54 years. A correlation between the volume of the parathyroid adenoma and the values of preoperative PTH, calcium and phosphorus as well as the postoperative PTH were found. However, there was no correlation with intraoperative PTH or postoperative calcium.*
Conclusion: *Biochemical parameters can predict the size of a parathyroid adenoma.*
Keywords: *Parathyroid Adenoma, Calcium, Phosphorus, Parathormone, Parathyroidectomy, Volume*

INTRODUCTION

Primary hyperparathyroidism is a common endocrinopathy affecting calcium metabolism characterized by hypercalcemia with excessive secretion of parathormone (PTH) by one (80% of the cases) or multiple parathyroid glands (1). It may be secondary to parathyroid carcinoma in less than 1% of the cases or may be part of multiple endocrine neoplasia (MEN I or II) (2).

Curative treatment is surgery and is based on a bilateral neck exploration of the parathyroid glands but this method is increasingly supplanted by minimally invasive approach under local anesthesia (3). This selective approach requires a precise pre-operative topographic diagnosis associating functional imaging with 99mTc-MIBI scintigraphy and structural imaging such as cervical ultrasonography (4).

However, the sensitivity of ultrasonography decreases for small parathyroid adenomas (4) ; hence the interest of finding parameters that makes it possible to predict the volume of the adenoma.The aim of this work is to find a correlation between parathyroid adenoma volume and biochemical parameters.

MATERIALS AND METHODS

A retrospective study was performed at the Head and neck department of Charles Nicolle Hospital over a 6-year period (2012-2017) including all patients operated in the department for parathyroid adenoma; these patients had a pre- and post-operative biochemical assessment and imaging by 99mTc-MIBI scintigraphy and cervical ultrasonography.

Criteria for non-inclusion were double adenoma, parathyroid hyperplasia and parathyroid carcinoma. Patients with renal impairment or associated malignancy have been also excluded. Data collection was carried out through patient records (clinical, biochemical histopathological and radiological informations).

Biochemical parameters studied were preoperative blood calcium and phosphorus, preoperative PTH, intraoperative PTH measured 10 minutes after adenoma excision, and postoperative PTH and calcium a year after surgery.

[1] Head and neck surgery department, Charles Nicolle Hospital, Tunis, Tunisia.
*Corresponding Author E-mail: makramtb@yahoo.com

These biochemical parameters were measured by ABBOTT ARCHITECT. Parathyroid adenoma volume was estimated according to a mathematical formula: Volume = (4/3) * π * a * b * c with a, b and c are the dimensions of the adenoma measured by an anatomopathologist and π = 3.14159.

Data were collected and analyzed using the Statistical Package for the Social Sciences (SPSS) program version 20 designed for Windows. Quantitative variables were expressed with mean and standard deviation. Correlation study was performed by the Pearson chi-square test. Difference was considered significant if $p < 0.05$.

RESULTS

During this study period, 35 patients were operated for parathyroid adenoma including 30 women and 5 men. The average age was 54 years old.

The discovery of hyperparathyroidism was secondary to bone pain in 19 cases, renal lithiasis in 10 cases, brown tumor in 2 cases and incidentally in 4 cases.

The location of the adenoma was inferior in 88% of the cases (right inferior in 16 cases and left inferior in 15 cases) and right superior in 4 cases. The mean volume of the adenoma was 23.34 cm3 (1.05-87.96).

Means of the biochemical parameters as well as the standard deviations are detailed in Table 1.

A correlation between parathyroid adenoma volume and the preoperative values of PTH, calcemia and phosphoremia as well as the postoperative PTH were found. However, no correlation was found with postoperative calcium or intraoperative PTH (Table 2).

Table 1: Values (mean and standard deviation) of measured biochemical parameters, Charles Nicolle Hospital, 2012-17

	Mean	Standard deviation
Preoperative calcium (mmol/L)	2.8118	0.23357
Preoperative Phosphorus (mmol/L)	0.7650	0.24638
Preoperative PTH	961.6314	1174.10444
Intraoperative PTH	89.5697	105.94757
Postoperative PTH	138.5467	184.86847
Postoperative calcium (mmol/L)	2.2866	0.14345

Table 2: Correlation between calculated parathyroid adenoma volume and measured biochemical parameters, Charles Nicolle Hospital, 2012-17.

	Correlation coefficient	P
Preoperative calcium	0.426	0.012
Preoperative Phosphorus	-0.641	0.001
Preoperative PTH	0.358	0.035
Intraoperative PTH	0.322	0.068
Postoperative PTH	-0.325	0.069
Postoperative calcium	0.407	0.026

DISCUSSION

Primary hyperparathyroidism is a common pathology treated surgically since Felix Mandl in 1925 performed the first parathyroidectomy (5). This surgical management involves a bilateral cervical exploration of the 4 parathyroid glands.

Nevertheless, the improvement of surgical and imaging techniques induces a shift from standard exploration to a minimally invasive approach under local anesthesia with smaller incision, and shorter recovery time but with a higher risk of recurrence or persistence and the need for precise localization of the adenoma by preoperative imaging (6).

The combination of 99mTc-MIBI scintigraphy and cervical ultrasonography is an optimal first-line imaging strategy to localize the adenoma, but the sensitivity of ultrasound decreases for small parathyroid adenomas, hence the interest in finding parameters that allow to predict the volume of the adenoma (4).

Several studies have sought a correlation between the preoperative biochemical parameters and the volume or weight of the adenoma; which has been confirmed by some (7-12) ; and rejected by others (13-16).

The lack of correlation in some studies may be explained by the non-exclusion of patients with parathyroid hyperplasia, parathyroid carcinoma, double adenoma or renal failure (8).

In addition, Ozbey reported that the weight of parathyroid adenoma was significantly higher in patients with low levels of vitamin D which could give heterogeneous groups (17).

As for Hwang-Bo, he found that this correlation can be influenced by the presence of cystic lesions, hemorrhage and necrosis within the adenoma (13). In addition, Stern found a correlation between the percentage of primary cells in the adenoma and its weight (10).

Indeed, most parathyroid adenomas are composed mainly of chief cells but other subtypes of parathyroid adenoma may exist such as oxyphil cells, clear cells or lipoadenoma (18).

Conclusion

Biochemical parameters can help to predict the size of a parathyroid adenoma. Therefore, surgeon may know if s/he will deal with a small or large adenoma which can be useful in minimally invasive approach.

Ethical considerations

This is a retrospective study using data collected routinely for any patient hospitalized for primary hyperparathyroidism. These data were used anonymously. Ethical approval was not required.

ACKNOWLEDGMENT

We would like to thank our health care providers who were involved in the care of patients with this disease.

Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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Endale Tefera, Ali Dawed, Hayat Ahmed, Etsegenet Gedlu. *Ethiop Med J, 2021, Vol. 59, No. 2*

ORIGINAL ARTICLE

CARDIAC AUSCULTATION SKILLS AMONG PEDIATRIC RESIDENTS

Endale Tefera, MD[1], Ali Dawed, MD[2], Hayat Ahmed, MD[3*], Etsegenet Gedlu, MD[3]

ABSTRACT

Background*: Recent studies from different settings have demonstrated suboptimal proficiency in cardiac auscultation skills among pediatrics and internal medicine residents.*
Objectives*: This study reports proficiency in cardiac auscultation skills among a sample of residents in the Department of Pediatrics & Child Health, School of Medicine, Addis Ababa University.*
Methods*: Findings of five pediatric cardiac conditions: ventricular septal defect, atrial septal defect, patent ductus arteriosus, pulmonary valve stenosis and aortic valve regurgitation were selected and programmed on mannequins. After obtaining consent, residents were asked to auscultate the mannequins and write down their findings.*
Results: Twenty-nine residents participated in the study. Seventeen (58.6%) were in their 1st year of training, 7 (24.1%) were in their 2nd year of training and 5 (17.3%) were in their 3rd year. The mean percentage score for all residents and all cardiac lesions was 31 ± 13% (range, 21 – 71%). Ventricular Septal Defect was the most accurately identified lesion with a mean score of 70 ± 24% (range, 0 – 100%). Aortic regurgitation was the least accurately identified lesion with a mean score of 21 ± 20% (range, 0 – 67%). Year 3 residents significantly outperformed year I residents in accurately identifying findings of Atrial Septal Defect (p= .006). The overall mean rank scores for all cardiac lesions combined by year of residency were 13.24, 12.21 and 24.90, for year I, II, and III residents, respectively. Year III residents had significantly better overall mean rank score.
Conclusion*: Auscultation skills among pediatric residents were suboptimal. Therefore, these skills may need to be reinforced and continuously evaluated in our pediatric residency training programs.*
Key words*: cardiac auscultation skills, physical examination, residency training programs, Ethiopia*

INTRODUCTION

Physical examination is one of the most important skills in medical education that contributes considerably to physician-patient interaction and is also an important contributor to accurate clinical diagnosis (1,2). Bedside teaching is the most important track towards proficiency in medical history taking and physical examination including cardiac auscultation (3,4). However, owing to several factors, bedside teaching has progressively deteriorated (4).

Along with it, cardiac auscultation skills have also deteriorated, with some putting the blame on extreme reliance on technology, declining bedside teaching due to various reasons, and faulty training of teachers (5-9). Recent studies from different settings have demonstrated suboptimal proficiency in cardiac auscultation skills (5,10,11). Even though there are studies that evaluated auscultation skills in residents recruited to different clinical specialty programs in other parts of the world, there are no studies at least to our knowledge that evaluated proficiency in this important skill, in pediatric residency programs in sub-Saharan settings.

There are a number of challenges and gaps, specific to our situation and similar Sub-Saharan settings. Prior to the availability of mannequins, teaching aids available for this purpose in the low-income countries were scarce. The number of trained cardiologists and dedicated cardiology training units in many of the medical schools is limited. These and other related factors may contribute to suboptimal proficiency, not just to auscultation skills but clinical skills in general.

At the same time, our practice mainly relies on history taking and thorough physical examination to arrive at a logical diagnosis, as imaging and laboratory facilities are not always readily available.

This study reports proficiency in cardiac auscultation skills among a sample of residents in the Department of Pediatrics & Child Health, School of Medicine, Addis Ababa University, Addis Ababa, Ethiopia.

[1]Department of Pediatrics & Adolescent Health, Division of Cardiology, Faculty of Medicine, University of Botswana, Gaborone, Botswana. [2]Division of Pediatric Cardiology, Children's Heart Fund Cardiac Center, Addis Ababa, Ethiopia. [3]Department of Pediatrics & Child Health, Unit of Pediatric Cardiology, School of Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia.
*Corresponding Author E-mail: hayuethio@yahoo.com

METHODS

Study design and setting

This is a cross-sectional study that was conducted in the Simulation Unit of School of Medicine, Addis Ababa University, using programmed mannequins. The study period was between January 18 and 30, 2016.

Study participants

There were total of 62 residents (33 in year 1, 18 in year 2 and 11 in year 3) in the department though not all were available at the same point in time, owing to assignments out of the main hospital and being on annual and research leave absences. The population of residents is generally a finite population and if we calculated a sample size and adjust it with finite population correction factor (as we are sampling >5% of the population without replacement), a sample of 29 may not be so small (12). Those who were available at the time of the study were asked for consent.

Data collection tools and procedures

A senior Pediatric cardiologist (consultant) from outside the university hospital, who was not involved in the mentorship of residents, conducted the assessment. Those who consented were asked to perform cardiac auscultation on PAT Basic Pediatric Auscultation Trainer (Simulaids, Inc, NY, USA) and Physiko Physical Assessment Model (Kyoto Kagaku, Kyoto, Japan). These are mannequins with computer programmed simulated murmurs, with the murmurs localized to the specific locations on the precordium of the mannequin, where corresponding real-time murmurs on a patient's precordium would have been auscultated.

Auscultation findings of five common pediatric cardiac conditions: ventricular septal defect (VSD), atrial septal defect (ASD), patent ductus arteriosus (PDA), pulmonary valve stenosis (PS) and aortic valve regurgitation (AR) were selected and programmed on the mannequins. The consultant explained the procedure for the auscultation to the participants. Participants would have considered the mannequins as simulated patients and all steps and findings would be reported as in a real patient. Each participant was given 3 minutes for each simulated cardiac lesion. Study participants were asked to auscultate and write the type of murmur they heard, timing of the murmur, location and other associated auscultation findings and make logical conclusions as to the diagnosis of the cardiac lesions.

Scoring

A score of 1 was given for each key finding that a participant had identified correctly with the total score adding up to 14. The scoring system is shown in table 1.

Statistical analysis

Data were entered into SPSS version 20 (IBM Corp. Armonk, NY, USA) and analyzed. Numerical variables were reported as mean ± standard deviation. Kruskal-Wallis test followed by post hoc pairwise comparison was used to compare mean rank scores between residents by year of postgraduate training. This nonparametric test was selected due to the small sample size and non-normal distribution of the data. Statistical significance was set at.05.

RESULTS

A total of 29 residents participated in the study. Out of the 29 residents, 17 (58.6%) were in their 1st year of training, 7 (24.1%) were in their 2nd year of training and 5 (17.3%) were in their 3rd/final year of training. The mean percentage score for all residents and all cardiac lesions was 31 ± 13% (range, 21 – 71%). VSD was the most accurately identified lesion with a mean score of 70 ± 24% (range, 0 – 100%). Aortic regurgitation was the least accurately identified lesion, with a mean score of 21 ± 20% (range, 0 – 67%). The most correctly picked auscultation finding was pan-systolic murmur of VSD whereas only two participants picked splitting of the second heart sound in ASD. None of the participants picked Austin flint murmur in aortic regurgitation. Mean scores for each of the cardiac lesions by year of postgraduate training are shown in figure 1.

Year 3 residents significantly outperformed year I residents in accurately identifying findings of ASD ($p= .006$). The overall mean rank scores for all cardiac lesions combined by year of residency were 13.24, 12.21 and 24.90, for year I, II, and III residents, respectively. Accordingly, year III residents performed significantly better on the overall rank score compared to year I and II residents, ($p= .013$ and $p= .022$, respectively). There was no statistically significant difference detected in the mean rank score between year I and year II residents either in the individual cardiac lesions or the overall score. The comparative performances of the 3 groups of residents by individual cardiac lesions and overall mean rank scores are shown in table 2.

Table 1: The key findings scored for each lesion and corresponding scores

Diagnosis	Features (score)
Ventricular Septal Defect (VSD)	Pansystolic murmur on the left lower sternal border (1) Correct diagnosis (1)
Atrial Septal Defect (ASD)	Fixed split of S2 (1) Systolic ejection murmur at the left upper sternal border (1) Mid-diastolic rumble at tricuspid area (1) Correct diagnosis (1)
Patent Ductus Arteriosus (PDA)	Continuous/machinery murmur at left upper sternal border/left in-fraclavicular area (1) Correct diagnosis (1)
Pulmonary valve Stenosis (PS)	Systolic ejection click (1) Systolic ejection murmur at left upper sternal border (1) Correct diagnosis (1)
Aortic regurgitation (12)	Diastolic murmur over the left 3rd intercostal space (1) Austin-flint murmur at apex (1) Correct diagnosis (1)

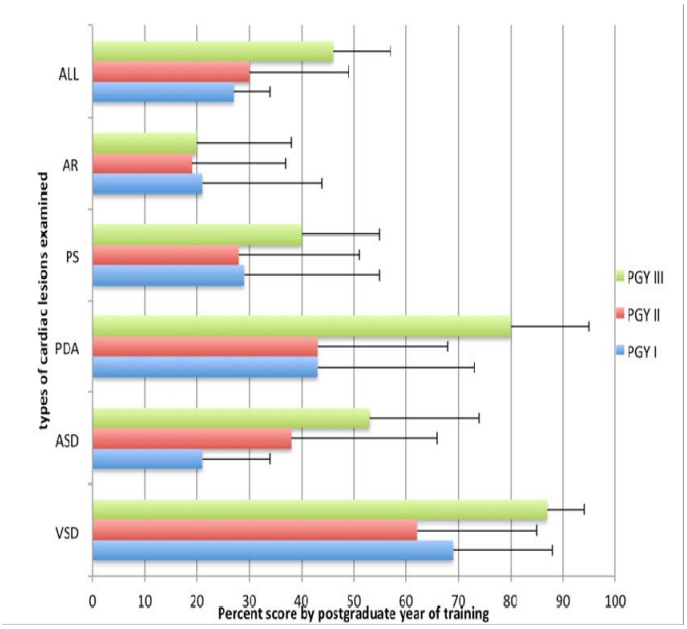

Figure 1: Mean performance scores for residents by post-graduate year of training and type of cardiac lesion

VSD-ventricular septal defect; ASD-atrial septal defect; PDA-patent ductus arteriosus; PS-pulmonary valve stenosis; AR-aortic valve regurgitation; PGY-postgraduate year

Table 2: Comparative performance of resident groups by postgraduate year of training and cardiac lesions examined

Cardiac lesions examined	Postgraduate year	Mean rank score	p-value
Ventricular septal defect (VSD)	I	14.97	
	II	12.07	.307
	III	19.20	
Atrial septal defect (ASD)	I	12.47	.008*
	II	14.00	
	III	25.00	
	Pairwise comparison	I – II	1.000
		I – III	.006*
		II – III	.054
Patent ductus arteriosus (PDA)	I	13.26	.071
	II	14.00	
	III	22.30	
Pulmonary valve stenosis (PS)	I	14.18	.484
	II	14.43	
	III	18.60	
Aortic regurgitation (12)	I	15.09	
	II	14.71	.994
	III	15.10	
Overall mean rank score	I	13.24	
	II	12.21	.010
	III	24.90	
	Pairwise comparison	I – II	
			1.00
		I – III	.013*
		II – III	.022*

*Statistically significant difference in mean rank score at α=0.05

DISCUSSION

The overall score achieved for skills in cardiac auscultation in our group of Pediatric residents is remarkably suboptimal. Though several studies from different corners of the world have shown similar findings (5,10,11,13-15), the implication of our study results is worrying due to the peculiarities pertaining to Sub-Saharan settings. In the developed world, the widespread availability of echocardiography may to some extent, compensate for the deficiency in physical examination skills. However, in resource-limited settings, like in Sub-Saharan Africa, echocardiography is usually unavailable or available only in teaching institutions or bigger public or private hospitals. Trained manpower performing echocardiography is also generally scarce. Once residents complete their training and are assigned to regional or district hospitals, their access to echocardiography is limited. Under many circumstances, patient evaluation, diagnosis and management is solely based on thorough history and physical examination. Therefore, there is no substitute to high-level proficiency in physical examination, including cardiac auscultation skills in most settings in Sub-Saharan Africa, including Ethiopia.

When compared with other studies, the results of our study are more or less similar to studies conducted elsewhere, though there were important differences in sample size and methodology. A study by Gaskin et al involving pediatric and combined pediatric/internal medicine residents, evaluated auscultation skills in 47 of 64 residents on 5 different cardiac lesions (pulmonary stenosis with ejection click, VSD, ASD, PDA and combined aortic stenosis/regurgitation) programmed on a mannequin. The overall accuracy of diagnosis was at 33% whereas the mean score for the lesions was a little above 11 out of possible 19 (10).

The St Claire et al study that compared auscultation skills among internal medicine residents on 3 simulated auscultation findings (mitral regurgitation, mitral stenosis and aortic regurgitation), showed an overall accuracy of 52% (15) but this study is different from our study in an important way, the type of the lesions tested, being the outstanding one. One of the largest studies by Mangione et al (13) recruited 453 internal medicine and family medicine residents and 88 medical students testing them on 12 different cardiac findings. The residents recognized only about 20% of the findings correctly.

The performances of all the three groups of residents in detecting key features of VSD and PDA were better, compared to the other lesions. This is not surprising, as these were the most common lesions with loud murmurs that practitioners encounter in pediatric practice.

In our study, year III residents performed comparatively better in identifying ASD features and in the overall mean rank score. This is in contrast to some other studies that reported year of training had no significant difference in the performance scores (10). This could be explained by the fact that all of the year III residents in our study have had their cardiology rotations.

One finding of interest is that even in those who detected the major murmurs and associated lesions correctly, most of them failed to look for other clues that would help differentiate some of the lesions from other lesions with similar findings. Those included mid systolic click of pulmonary valve stenosis, wide and fixed splitting of second heart sound and tricuspid mid diastolic murmurs that were associated with large ASDs and Austin flint murmur of aortic regurgitation. That may probably be due to the tendency of requesting echocardiograms once a murmur was detected without bothering to conduct further analysis.

Our study findings may serve as a stepping-stone to continuously assess and improve not only cardiac auscultation skills but also other physical examination skills in residency programs. Lots of opportunities exist for residents to improve their examination skills. Those may include the same simulation facilities on which our study was conducted, self-directed auscultation teaching programs (16,17) and other pertinent innovations. A good level of proficiency in cardiac auscultation skills may decrease unnecessary echocardiographic referrals besides helping timely and accurate diagnosis. Therefore, cardiac auscultation skill among general pediatricians should be reinforced, as they are the highest-level physicians caring for children with congenital and acquired heart diseases in many cases. There is no better opportunity than residency training programs as the skills can be assisted by feedback from experienced mentors and echocardiography.

Limitations of the study

Finally, our study had important limitations. First of all, the relative representation of the 2nd year and more significantly, the 3rd year residents was small due to consent issues. Related to the small number of participants in the 2nd and 3rd year groups, the distribution of scores is not expected to follow normality. Due to this limitation, our comparative statistics was worked out with non-parametric tests, making the comparison less accurate.

Secondly, those who consent to such skill studies may probably be those who are more self-confident in their proficiency in the skill under study, which may create bias as to the representativeness of the sample. Thirdly, there could be important differences with the auscultation findings on a Mannequin and a real patient. Findings in a real patient have many variations and complexity, whereas Mannequins are programmed on a more distinct finding.

Conclusion

Cardiac auscultation skills among pediatric residents in our study were suboptimal. Though the proficiency got better as the training year advanced in some cases, the overall assessment showed markedly low scores. Therefore, cardiac auscultation skills will need to be reinforced and evaluated in our pediatric residency training programs, as pediatricians are the highest-level physicians caring for children with congenital and acquired heart diseases in many cases.

In terms of acquiring the basic skill and thought framework, simulations play an important role as they are being used in high-income countries for basic medical education. With all its limitations, we still believe that our study laid a foundation and a framework for well-designed studies. Future studies may be designed as interventional studies, where the initial evaluation is followed by interventional measures and assessment of the impact.

ACKNOWLEDGEMENTS

We would like to thank Sr. Liyuwork Abebe and the School of Medicine for allowing us to use the Simulation Unit for this study. We are also grateful to all study participants for consenting to participate in this study.

Competing of interest

All authors declare no conflict of interest related to the study or publication of this manuscript.

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Atalel Fentahun Awedew, Bedemariam Tadesse Amsalu, Woldemariam Beka Belay, Dawit Zerihun Yalewu. *Ethiop Med J, 2021, Vol. 59, No. 2*

ORIGINAL ARTICLE

MAGNITUDE AND MANAGEMENT OUTCOME PREDICTORS OF MECHANICAL LARGE BOWEL OBSTRUCTION

Atalel Fentahun Awedew, MD[1], Bedemariam Tadesse Amsalu, MD, MPH[2], Woldemariam Beka Belay, MD[2], Dawit Zerihun Yalewu, MD[2]

ABSTRACT

Background*: Mechanical large bowel obstruction (MLBO) contributes a sizable portion of surgical emergency admissions.*

Objective*: To determine the magnitude of Mechanical large bowel obstruction and outcome predictors for morbidity and mortality in Debre Tabor General Hospital Northcentral Ethiopia, 2020.*

Method*: The study was conducted at Debre Tabor General hospital- located at Debre Tabor city in South Gondar Zone, Amhara regional state in Northcentral Ethiopia. A hospital-based retrospective study was employed. All patients from age 15years and above whom presented with clinical or/and radiological diagnosis of mechanical large bowel obstruction from Jan1, 2016-Dec31, 2019 at Debre Tabor General Hospital were included. Data were collected with a pre-tested and structured questionnaire which was developed by the English language after review different literature. The final collected data checked manually its consistency, and coded and entered to SPSS version 23 for processing and analysis. Normal distribution of quantitative values was presented as mean ± standard deviation and skewed quantitative values were presented median ± Interquartile range. A cross-tabulation analysis was employed.*

Result*: Mechanical large bowel obstruction (MLBO) was accounted for 33.1 %(N=135) of mechanical bowel obstruction. Almost all mechanical bowel obstruction cases were male (N=129, 95.6%) and rural residents (N=123, 91.1%). The age ranged from 19-88years with mean and median ages were 56.56(SD=±14.58) and 58 (IQR±18) respectively. The leading etiologies of mechanical large bowel obstruction were sigmoid volvulus (N=124, 91.9%) and colorectal cancer (N=7, 5.2%). The pattern of bowel viability 65.2 %(N=88) was a simple bowel obstruction and 34.8% (N=47) was a gangrenous bowel obstruction. The overall complication rate was 21.5 %(N=29) and the mortality rate was 8.9 %(N=12*

Conclusion: *Large bowel obstruction commonly occurred in males and elders. Sigmoid volvulus was a leading etiology of large bowel obstruction.*

Keywords*: Large bowel obstruction, Ethiopia, Sigmoid volvulus*

INTRODUCTION

Mechanical Large Bowel Obstruction (MLBO) constitutes approximately 25% of mechanical bowel obstruction in the western (1) and accounting for approximately 15-36.5% in the developing world (2-7). It is accounting for approximately 2-4% of surgical admissions (8). Colorectal carcinoma, colonic volvulus, and diverticulitis covered more than 90% of mechanical large bowel obstruction (MLBO) in the western (9).

Colorectal cancer has been contributed to 60% of large bowel obstruction (10). Colorectal cancer is the third most prevalent large bowel malignancy worldwide in both morbidity and mortality following breast and lung cancer in females and prostatic and lung cancer males (15).

The incidence and mortality decreased through time (15) but the predicated colorectal cancer worldwide will be 2•5 million new cases in 2035 due to the increase of the population size (16). Colorectal cancer has been accounted for 10% morbidity and 9% mortality worldwide (17). Approximately, 20% of colorectal cancer patients present with malignant large bowel (9), and 7-29% presented with acute bowel obstruction (8).

Colonic volvulus and diverticular disease are accounting 30% of Mechanical Large Bowel Obstruction in western (10). Colonic volvulus refers to the torsion of the bowel around its mesentery. In Western sigmoid volvulus is accounting nearly 60-75%, cecal volvulus nearly 25-30% and Transverse colon volvulus is extremely rare and accounts for 5% of all cases of colonic volvulus (8).

[1]Addis Ababa University, Department of Surgery.
[2]Debre Tabor University, Department of Surgery.
*Corresponding Author E-mail: fentahunatalel27@gmail.com

Sigmoid volvulus is a common cause of large bowel obstruction in the volvulus belt area which covers regions of South Asia Middle East, South America, and Africa.

This may due to their stable food of higher fiber diet those results in redundant and long sigmoid volvulus (11). Sigmoid volvulus is the third cause of large bowel obstruction in developed countries. (12). It accounts for 3.4% of large bowel obstruction following cancer and diverticular disease in the USA (13). In contrast to this, sigmoid volvulus is much higher in volvulus belt countries; Ethiopia, Brazil, India, Nigeria, and Iran where sigmoid volvulus has been handled 50% to 85% of large bowel obstruction (11, 14, 23). Another rare cause of large bowel obstruction is including fecal impaction, Ischemia, Inflammatory bowel disease, and intussusception (8).

METHODS AND MATERIAL

Study area and period

The study was conducted at Debre Tabor General hospital- located at Debre Tabor city in South Gondar Zone, Amhara regional state in Northcentral Ethiopia. It is one of the oldest hospitals in the country and gives service for approximately 80,000 outpatients and 900 patients each year from the catchment area of population 3.5milion. Medical chart review included from Jan1, 2016-Dec31, 2019.

Study Design

A hospital-based retrospective cross-sectional study was employed. All patients from age 15years and above who presented with clinical or/and radiological diagnosis of mechanical large bowel obstruction from Jan1, 2016-Dec31, 2019 at Debre Tabor General Hospital were included in the study whereas below 15years of age and functional obstruction were excluded from the study.

Data collection and analysis

Data was collected by a pre-tested and structured questionnaire which was developed in the English language after review different literature. The structured questionnaire contained demography, clinical presentation and duration of illness, causes, diagnosis, intraoperative finding, procedures, postop complications, and outcome of large bowel obstruction. The final collected data checked manually for its consistency, and coded and entered to SPSS version 23 for processing and analysis Normal distribution was evaluated with the Q-Q plot test and histogram diagram. Normal distribution of quantitative values was presented as mean ± standard deviation and skewed quantitative values were presented median ± Interquartile range.

A cross-tabulation analysis was employed.

Ethical consideration

The Ethical issue was approved by the Ethical Review Committee of Debretabor University. Data collection was started after obtaining permission from Debre Tabor hospital. All information obtained from patients' medical charts was kept confidential.

RESULT

During the study period, there were 408 bowel obstruction admissions. Mechanical Large bowel Obstruction (MLBO) was accounted for 33.1 %(135) of mechanical bowel obstruction. Almost all mechanical bowel obstructions were males (N=129, 95.6%) and rural residents (N=123, 91.1%). The age ranged from 19-88years and the peak age ranged from 56-65. The mean and median ages were 56.56(SD=±14.58) and 58(IQR±18) respectively (Table 1).

The clinical presentations were abdominal pain 99.3%, failure to pass faces/flatus 95.6%, and abdominal distention 83.7%, vomiting 47.4%, and rectal bleeding 3.7%. The most common clinical findings were abdominal tenderness 96.2%, visible peristalsis 68.9%, and Hypo/hyper bowel sound 64.4 %(Table 2). The overall mean of hospital stay was 8.65 (SD±4.8) days and the median was 8 (IQR±5) days. The mean of hospital stay for elective admission was 10.98(SD±4.33) days and the median was 11 (IQR±5) days. The mean of hospital stay for emergency admission (excluding death and Leave against medical advice) was 8.25 (SD±4.16) days and the median was 8 (IQR±2) days.

The leading etiologies of mechanical large bowel obstruction were sigmoid volvulus (N=124, 91.9%) and colorectal cancer (N=7, 5.2%). The pattern of bowel viability 65.2 %(N=88) was a simple obstruction and 34.8% (N=47) was gangrenous obstruction. The overall complication rate was 21.5 % (N=29) and the mortality rate was 8.9 %(N=12). Wound infection 27.58% and anastomosis leak and wound dehiscence 17.24% were the most common complications. (Table 3).

Table1: The Demographic and Characteristics of the Patients with Mechanical Large Bowel Obstruction, Debre Tabor Hospital, Northcentral Ethiopia, 2020.

Item		Frequency	Percent (%)
Age	15-25	4	3.0
	26-35	8	5.9
N=135	36-45	19	14.1
	46-55	30	22.2
	56-65	40	29.6
	>66	34	25.2
	Total	135	100.0
Sex	M	129	95.6
N=135	Female	6	4.4
	Total	135	100.0
Residence	Rural	123	91.1
N=135	Urban	12	8.9
	Total	135	100.0

Table2: The Clinical presentation of Patients with Mechanical Large Bowel Obstruction, Debre Tabor Hospital, Northcentral Ethiopia, 2020

Item		Frequency	Percent
Clinical Symptoms	Abdominal Pain	134	99.3
	Vomiting	64	47.4
	Abdominal Distention	113	83.7
	Constipation	129	95.6
	Rectal bleeding	5	3.7
Clinical Sign	Drainage Vital sign	22	16.3
	Abdominal Tenderness	125	92.6
	Hypo/Hyperactive bowel sound	87	64.4
	Visible peristalsis	93	68.9
Duration of Illness	<48hr	84	62.2
N=135	48-72hr	22	16.3
	72-96hr	15	11.1
	>96hr	14	10.4
	Total	135	100.0
Mode of presentation	Elective	46	34.1
N=135	Emergency	89	65.9

Cross tabulation analysis showed that complications was less common in male 20.9%% vs. 33.3%, (p= 0.384, OR for male=0.529), rural resident 19.5% vs. 41.7% (P=0.084, OR of rural=0.339), Simple LBO 13.6%% vs. 36.2%%, $\chi 2$ (1, N=135) = 8.857, p =0.003, OR Simple LBO=0.279). Hospital stay >7days 20.0%vs. 22.2% $\chi 2$ (1, N=135) = 0.096, p =0.757, OR of Hospital stay <=7days =1.143), Sigmoid volvulus=20.2%vs. colorectal cancer 42.9% vs. colocolonic intussusception=100% ($\chi 2$ (4, N=135) = 6.259, p =0.181), Resection and primary anastomosis 17% vs. stoma 50% $\chi 2$ (2, N=135) = 16.024, p <0.001. Multiple variable repressions were morbidity rate done for residency, bowel viability, etiology and surgical procedure but there is no statistical significance. Cross tabulation analysis showed that mortality rate was less common in male 8.5% vs. 16.7% (p= 0.434, OR for male=0.446), age >50 years 7.9% vs.10.9% (p=0.387, OR of age</=50years =1.429), rural resident 8.1% vs.

Table3: The Pattern, Etiology and Outcome of Patients with Mechanical Large Bowel Obstruction, Debre Tabor Hospital, Northcentral Ethiopia, 2020

Item		Frequency	Percent
LBO N=135	Simple LBO	88	65.2
	Gangrenous LBO	47	34.8
Etiology of LBO N=135	Sigmoid Volvulus	124	91.9
	Colorectal Cancer	7	5.2
	Intussusception	1	.7
	Cecal volvulus	2	1.5
	Angagliomegacolon	1	.7
Outcome	Improved	100	74.1
	complicated and Improved	17	12.6
	leave against medical advice	6	4.4
	Death	12	8.9
	Total	135	100
Complicated case (N=29)	Wound Infection	8	27.58
	Anastomosis Leak	5	17.24
	Fistula	1	3.45
	Paralytic illness	1	3.45
	others	2	6.89
	Death	12	41.38

16.1% (P=0.289, OR of rural=0.442), Hospital stay >7days 2.5%vs. 16.2%p=0.005, OR of Hospital stay <=7days =7.8),Simple LBO 3.4%% vs. 19.1%%, (p=0.004, OR of Simple LBO=0.149). Sigmoid volvulus=6.5%, colorectal cancer 42.9%%, colocolonic intussusception=100% ($\chi 2$ (4, N=135) = 12.1, p =0.017), Resection and primary anastomosis 3% vs. stoma 37.5% $\chi 2$ (2, N=135) = 22.286, p <0.001. Multiple variable repressions for mortality rate were done for bowel viability, etiology, hospital stay and surgical procedure but there is no statistical significance.

DISCUSSION

We found that mechanical large bowel obstruction contributed to a sizable proportion of surgical emergency visits and admissions. We found that mechanical large bowel obstruction (MLBO) was accounted for 33.1 % of bowel obstruction. It constitutes 25% of mechanical bowel obstruction in the western world (1) and accounting for approximately 15-36.5% in the developing world (2-7).

We found that the most common etiologies of mechanical large bowel obstruction were sigmoid volvulus 91.9% and colorectal cancer 5.2%. Colorectal carcinoma, colonic volvulus, and diverticulitis covered more than 90% of Mechanical Large Bowel Obstruction (MLBO) in the western (9). Colorectal cancer is accounting 60%, and colonic volvulus and diverticular disease are accounting 30% of mechanical large bowel obstruction in the western (10).

Sigmoid volvulus is the third cause of LBO in developed countries (12). It accounts for 3.4 % of large bowel obstruction following cancer and diverticular disease in the USA (13). A study conducted in the different countries reported that sigmoid volvulus constituted for large bowel obstruction approximately 58.62- 73% in Ethiopia, (18-19), 53.57% in Somalia (20), 72% in Nigeria (21), and 52% in India (22). Sigmoid volvulus is a common cause of large bowel obstruction in the Volvulus belt, which covers regions of the Middle East, South America, Africa, and South Asia (23) where low incidence of colorectal cancer. This may due to their stable food of higher fiber diet those results in redundant and long sigmoid volvulus (11).

Most large bowel obstruction occurs in the elderly. A report from New Orleans, 77% of the patient were over 50s years of age (24). Byrne1960 reported that with 94 percent being over fifty and 48 percent over seventy (25). Reports from different countries revealed that the mean age of occurrence of large bowel obstruction varied; 51(SD ±13.53) with a range between 28 – 78 years in India (22) and median age 49yeas with age range 20-80years in Nigeria (21). This study found that male predominance (95.6%), the mean and median age were 56.56(SD=±14.58) and 58(IQR±18) respectively with age range 19-88years.

This finding is similar to findings in developing countries (21-22) but lowered age from developed countries (24-25). This difference may be mainly the etiology of large bowel obstruction where sigmoid volvulus for developing countries and colorectal cancer for developed countries.

Our study finding noted that the mean and median of elective hospital stay were 10.98(SD±4.33) and (IQR±5) days respectively while mean and median of emergency hospital stay(excluding death and Leave against medical advice) were 8.25 (SD±4.16) and 8 (IQR±2) days respectively. As compared to a study conducted in India stated that the average hospital stay was 14.52 +/- 4 days, which is higher than our study finding. The elective admission stayed longer may be due to bowel preparation and cancellation. The mortality rate of large bowel obstruction varied from geography to geography due to the health-seeking behavior of the community and the availability of health service delivery institutions. The mortality rate reported 12% in a study done by AZ Sule et al. (2011) (21) and 24% in a study by A. Bansod et al. (2013) (22).

Our study showed the overall complication rate was 21.5 % and the mortality rate was 8.9 %.

Conclusion

Large bowel obstruction commonly occurred in the male and elderly population. Sigmoid volvulus was a leading etiology of large bowel obstruction.

Competing of Interest

Authors declared that no conflict of interest.

ACKNOWLEDGMENT

First and most, thanks our Almighty GOD for helping us from beginning to finishing. Then, we would like to express our deep gratitude to Debre Tabor General Hospital staff providing valuable information, invaluable care and support to do this research. Finally, we express our deep gratitude to staffs at school of medicine of Debre Tabor University-whom give valuable and constructive comments

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Yeshambel Agumas Ambelie, Getu Degu Alene, Damen Hailemariam Gebrekiros. *Ethiop Med J, 2021, Vol. 59, No. 2*

ORIGINAL ARTICLE

FRAMEWORK FOR BUILDING AND MEASURING WORKFORCE'S COMPETENCE TO LEAD, MANAGE AND GOVERN THE HEALTH DELIVERY SYSTEM

Yeshambel Agumas Ambelie, PhD[1*], Getu Degu Alene, PhD[2], Damen Hailemariam Gebrekiros, MD, PhD[3]

ABSTRACT

Introduction: *Currently, there is a promising signal that health systems authorities look forward to producing competent workforce in leading, managing and governing the health delivery system. However, constructing reliable and locally validated framework in this arena has been overlooked in Ethiopia.*
Objective: *To model a reliable and valid framework for building and measuring the health workforce's competence to lead, manage and govern the health delivery system in Ethiopia.*
Methods*: A cross-sectional survey was conducted in three zones of Amhara regional state. Eight-hundred-thirteen participants were recruited from 32 health facilities. The data were collected using a structured self-rated questionnaire. Factor analysis, composite reliability and average variance extraction were applied. Factor analysis was unlocked to assemble the relationship among latent factors extracted, items rated and error variances observed. Latent factors labeled, items rated and error variances observed were assembled to develop a competence building and measuring framework. Its reliability and validity were tested using composite reliability and average variance extraction, respectively.*
Results: *A four-factor framework was resulted. The factors extracted were labeled as compliance with principles, strategic sensitivity, system building, and contextual thoughtfulness. These explained 68.434% of the total variability. Composite reliability and average variance extraction for all factors were .807 and greater, and .512 and greater, respectively.*
Conclusions: *The current study provides a four-factor framework for building and measuring the health workforce's competence to lead, manage and govern the health delivery system. This framework has implications for training, evaluation, and research.*
Keywords: *Competence, Health workforce, Lead, manage and govern, Factor analysis, Latent factors*

INTRODUCTION

The health workforce who are competent to lead, manage and govern the health delivery system improve health outcomes (1-5). Such a competence supports them to balance people's needs, workloads and organizations' requirements simultaneously (6). Thus, a continuous deal to find a tool for building and measuring the workforce's competence to lead, manage and govern the health delivery system is important (7, 8). The reason that supports the need for continuous dealing is the rhetoric that has been told as the three paths are separated and reserved to a gifted group of people.

Currently, there is a promising signal that health systems authorities look forward to producing competent workforce in leading, managing and governing the health delivery system (4, 9). It is more inspiring when one sees such a signal among authorities working in low and middle-income countries' health systems. Usually, such ecosystems are characterized by epidemiological, economic, social, demographic, political and technological turbulences within rising public expectations.

These have sought the formulation of new designs and frameworks regarding the workforce's competence to lead, manage and govern the health systems.

Though limited, studies reported that there was a significant duplication among the functions (practices) of the three paths (2, 3). Such duplications might be emanated from the absence of a parsimonious and meaningful framework for building and measuring competence to lead, manage and govern the health delivery system.

Moreover, constructing locally validated and reliable framework in this arena has been overlooked in Ethiopia. This, in turn, might make the health system workforce exhausted and unstable. However, this has unique importance to Ethiopia due to four reasons: (i) It has ancient vellum scriptures that have been written both in Geez and Amharic languages; (ii) It has ancient history of nation building; (iii) There is increased decentralization and raised public expectations; and (iv) This country is resource-limited.

[1]Department of Health Service Management and Health Economics, School of Public Health, Bahir Dar University, Ethiopia. [2]Department of Biostatistics and Epidemiology, School of Public Health, Bahir Dar University, Ethiopia. [3]Department of Health Service Management and Health Economics, School of Public Health, Addis Ababa University, Ethiopia.
*Corresponding Author E-mail: tgyesh@gmail.com / Yeshambel.Agumas@bdu.edu.et

Hence, the contest and promise of this research is to bring it a burning matter in both civil services and academic spheres. Consequently, the results of this study can enhance the ability of policymakers, program planners, implementers and researchers in renewing a framework for building and measuring competence to lead, manage and govern the health delivery system in light of the indigenous ecological, social and economic realities.

METHODS AND MATERIALS

Study design and participants

A cross-sectional study was conducted. Eight hundred thirteen participants were included in the current study. These were selected from 32 healthcare organizations located in three zones of Amhara regional state.

Data collection

Data were collected using a structured self-rated multi -item questionnaire. Twenty-six items that had the potential to model a framework for building and measuring competence to lead, manage and govern the health delivery system were adapted from the Ethiopian hospital leadership, management, and governance implementation checklist; management and organizational sustainability tool; pact organizational capacity assessment tool, and the WHO health governance assessment tool. From the 26 items: ten, eight and another eight items were on leading, managing and governing practices respectively. All items were rated with a five-point Likert scale. The test stimuli (psychometric properties) of the questionnaire was refined through rigorous debriefing sessions. In this process, five specialists of health service management, of whom three were from civil service and two from the academic spheres were involved.

Data analysis

Data were entered using epi-demographic information version 7 and analyzed using statistical package for social science version 20. Different data analysis techniques such as descriptive, exploratory factor, composite reliability, and average variance extraction were employed. Descriptive statistics was used to summarize the information about the socio-demographic characteristics of the participants, and the central tendency of the rated items. Factor analysis was unlocked to assemble the relationship among latent factors extracted and labeled, items rated, and error variances observed.

A latent factor was an unobserved variable or a theoretical construct that typically could not be directly measured, but it was assumed to cause the observed scores on the item.

An item was the direct measured variable. Error variance was the portion of the factor that could not be predicted from the remaining latent factors. About five data to model fit indices of factor analysis were tested: inter-correlation of .3 and greater; Kaiser-Meyer-Olkin test of overall measure of sampling adequacy of .5 and greater with Bartlett's test of sphericity ($P<.05$); intra-item consistency of .7 and greater, total variance explained of 60% and greater and communality of .5 and greater (10-12). The communality represented a proportion of each item's variance that had been explained by the latent factors (11, 13).

Considering the communalities indicated, particularly at the off brackets in the last column of Table 3, two items: (i) set annual and strategic organizational plan (communality = .470), and (ii) allocate adequate resources for work (communality = .498) were violated the statistically recommended cutoff point. Accordingly, a series of factor analysis was run until all the items remained in the model had a communality of .5 and greater. This was done by removing a single item with a minimum value at a time (rule of thumb).

Thus, the first iteration was done by removing an item that is set annual and strategic organizational plan. The output showed that allocate adequate resources for work again violated the rule (communality = .481). By trimming it, the second iteration was run. At this point, the outputs indicated, particularly, within the brackets in the last column of Table 3 showed that the remained items had communality .5 and greater. At this stage, the original 26-item dataset was reduced to a 24-item dataset. With this dataset, factor analysis was iterated, and another four items: (i) provide appropriate feedback to other organization members, (ii) look for best practices in the last 12 months, (iii) match deeds to words, and (iv) develop a structure that provides accountability and authority were removed due to violating the rule of complex structure. Meaning, any factor has not been resided on more than one item with factor loadings of .4 and greater (10). It showed that the dataset that satisfied the requirements of factor analysis was reduced to a 20-item dataset.

Using this dataset, latent factors were extracted using principal axis factoring method with varimax rotation and a cut point of eigenvalue greater than 1. Meanwhile, to make the extracted factors more meaningful, they were labeled by considering the contents (scientific and empirical domains) of the items clustered within each factor (13-15).

Following this, the framework for building and measuring the health workforce's competence to lead, manage and govern the health delivery system was modeled by assembling latent factors labeled, items rated and error variances observed.

Finally, Composite Reliability (CR) and Average Variance Extraction (AVE) were calculated to test the reliability and validity of the framework respectively (16, 17). CR was calculated from the squared sum of factor loadings divided by the squared sum of factor loadings and the sum of error variances (18). To reaffirm the reliability, the CR was triangulated with the total variance explained.

AVE was calculated from the sum of factor loading squared divided by the sum of factor loading squared and the sum of error variances (19). The square root of AVE was also calculated to confirm the presence of validity by comparing each value with factor correlations. The squared root value for each factor had been greater than most of the correlation coefficients of items clustered within it, confirmed the presence of validity.

Moreover, correlations were also tested whether they were significantly different from zero, which supported the presence of convergent validity or the higher number of times that the item highly correlated within its factor compared with the items of the other factors that indicated the presence divergent validity. The percent of variability that the items shared was determined by squaring the correlations between items and multiplied by 100. The rule was that items should relate more strongly to their factor than to another factor.

Ethical approval

Ethical clearance with a protocol record 090/18-04 was secured from Bahir Dar University. Each participant provided consent, and end-to-end anonymous response was kept. Additionally, this work can also be found as a preprint on research square (20).

RESULTS

Basic characteristics of participants

Table 1 displays basic characteristics of the study participants. Overall, eight hundred thirteen participants were included. Regarding sex, 396 (48.7%) were females. In relation to responsibility, 582 (71.6%) were service owners.

Table 1 Basic characteristics of participants (n = 813), Ethiopia, 2020

Variables	Categories	Frequency	Percent
Sex	Male	417	51.3
	Female	396	48.7
Age	<= 24 years	124	15.3
	25-29 years	334	41.1
	30-34 years	256	31.5
	>34 years	99	12.2
Educational level	Diploma and less	363	44.6
	First degree	411	50.6
	Second degree and above	39	4.8
Responsibility	Head of office	61	7.5
	Process owner	35	4.3
	Unit coordinator	135	16.6
	Service owners	582	71.6
Year of service	<2 years	209	25.7
	2-4 years	222	27.3
	5-8 years	283	34.8
	>8 years	99	12.2

Indices tests

Table 2 indicates the means *($\bar{x}$)*, standard deviations (s), and correlations (r) of measuring items. The means and standard deviations were included to show simply the overall trend of the data set that is to display how the data were spread around it. Other ways, it did not provide evidence for a nuanced decision.

As indicated in the table, the maximum and minimum mean scores were recorded for the items: determine key priorities for action (3.38+1.097), and describe the outcomes related to the allocated resources (2.76+1.231).

Table 2 Means, Standard Deviations and correlations of items (n = 813), Ethiopia, 2020

Item	$\bar{x}$	S	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
1	3.35	1.103	1																									
2	3.36	1.076	.679	1																								
3	3.11	1.168	.548	.644	1																							
4	3.33	1.103	.542	.619	.545	1																						
5	3.38	1.097	.540	.595	.529	.752	1																					
6	2.86	1.197	.432	.473	.563	.496	.494	1																				
7	2.97	1.214	.444	.474	.493	.547	.541	.725	1																			
8	3.25	1.161	.485	.527	.426	.591	.549	.439	.507	1																		
9	3.04	1.197	.392	.442	.472	.528	.481	.514	.504	.676	1																	
10	3.00	1.160	.387	.448	.496	.541	.506	.534	.561	.624	.716	1																
11	3.32	1.165	.413	.394	.369	.506	.523	.369	.380	.434	.455	.490	1															
12	3.04	1.172	.328	.364	.379	.416	.419	.459	.412	.434	.500	.521	.531	1														
13	3.06	1.111	.409	.414	.402	.470	.446	.491	.465	.455	.535	.523	.549	.626	1													
14	3.24	1.126	.449	.500	.456	.516	.521	.473	.467	.430	.447	.449	.531	.499	.665	1												
15	3.16	1.091	.469	.479	.424	.493	.512	.433	.430	.484	.490	.495	.541	.496	.670	.687	1											
16	3.22	1.097	.455	.459	.402	.507	.529	.406	.422	.476	.465	.470	.554	.502	.637	.673	.758	1										
17	3.20	1.136	.470	.466	.450	.537	.501	.394	.443	.455	.449	.506	.518	.402	.538	.598	.634	.657	1									
18	3.19	1.125	.453	.513	.481	.508	.507	.480	.467	.454	.452	.493	.534	.491	.584	.605	.640	.633	.713	1								
19	3.24	1.230	.428	.475	.360	.540	.510	.321	.349	.470	.393	.410	.454	.338	.413	.487	.525	.507	.580	.572	1							
20	2.95	1.171	.374	.464	.471	.466	.474	.479	.481	.379	.473	.479	.401	.412	.519	.534	.544	.551	.526	.602	.579	1						
21	2.86	1.160	.426	.487	.463	.497	.462	.495	.481	.405	.454	.486	.481	.490	.535	.537	.517	.542	.555	.613	.565	.687	1					
22	2.96	1.162	.412	.462	.407	.513	.544	.440	.503	.416	.426	.471	.490	.431	.516	.542	.546	.547	.560	.603	.564	.666	.753	1				
23	3.10	1.240	.466	.488	.427	.580	.577	.381	.435	.471	.422	.413	.506	.394	.490	.565	.531	.551	.551	.557	.580	.584	.663	.721	1			
24	2.97	1.223	.427	.460	.423	.547	.541	.446	.452	.462	.427	.447	.488	.441	.509	.556	.500	.538	.537	.615	.567	.602	.703	.720	.812	1		
25	3.07	1.284	.439	.449	.358	.558	.535	.365	.423	.477	.437	.444	.452	.353	.462	.524	.513	.518	.547	.538	.637	.532	.621	.649	.722	.731	1	
26	2.76	1.231	.388	.396	.395	.516	.501	.423	.459	.421	.439	.456	.422	.413	.444	.494	.461	.482	.505	.567	.558	.588	.657	.667	.681	.729	.756	1

Note: The numbers from 1 to 26 represented: 1 = Identify client and stakeholder needs and priorities; 2 = Recognize trends, opportunities, and risks; 3 = Look for best practices in the last 12 months; 4 = Articulate the organization's mission, strategy and vision; 5 = Determine key priorities for action; 6 = Enlist stakeholders to commit resources; 7 = Unite mobilized resources to reach organizational vision; 8 = Match deeds to words; 9 = Show trust and confidence and acknowledge contributions; 10 = Model of creativity, innovation and learning; 11 = Set annual and strategic organizational plan; 12 = Allocate adequate resources for work; 13 = Develop a structure that provide accountability and authority; 14 = Considers the organizational lines of authority for delegation; 15 = Integrate work structures and work flow; 16 = Coordinate practices with other staff's programs; 17 = Monitor their achievements against the plan, and take lessons; 18 = Provide appropriate feedback to other organization members; 19 = Uphold ethical and moral integrity to serve the public interest; 20 = Establish a consultation mechanism to heard public voice; 21 = Ensure participation of key stakeholders; 22 = Establish alliances for joint action at all levels; 23 = Oversee a shared direction to achieve organizational mission; 24 = Advocate organizational mission and vision to stakeholders; 25 = Use resources in a way that maximizes the public well-being; and 26 = Describe the outcomes related to the allocated resources.

The inter-correlations presented on the off-diagonal part of the table ranged from .328 to .812. When each correlation was squared and multiplied by 100, it determined the percentage of variability that the respective two variables shared. For example, when the coefficient .328 that is the coefficient between item "12" (row) and item "1" (column) is squared, it becomes .108, and when multiplied by 100, it is 10.8%. This showed that the two items shared 10.8% of the variability of each other.

Table 3 presents the internal consistency (alpha value) and communality of each item. The MSA for items, which were displayed on the off-diagonal part of the table were .936 and greater. Also, the overall MSA with Bartlett's test of sphericity (P<.001) was .962.

Table 3: Internal consistencies and communalities of items (n = 813), Ethiopia, 2020

Item	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Communality
1	.960																										.571(.577)
2	-.375	.948																									.690(.704)
3	-.135	-.293	.960																								.526(.526)
4	-.002	-.143	-.068	.965																							.659(.659)
5	-.057	-.084	-.064	-.418	.961																						.622(.622)
6	-.038	.012	-.197	-.008	-.050	.936																					.566(.560)
7	-.046	.004	.032	-.081	-.073	-.504	.943																				.574(.580)
8	-.090	-.125	.083	-.093	-.046	.054	-.121	.954																			.525(.527)
9	.031	.027	-.071	-.041	.028	-.091	.039	-.364	.948																		.613(.623)
10	.076	.014	-.102	-.039	-.014	-.031	-.122	-.175	-.353	.961																	.650(.658)
11	-.071	.074	.022	-.053	-.126	.039	.034	.040	-.039	-.101	.977																.470 (-)
12	.039	-.001	-.010	.017	-.035	-.066	.027	-.042	-.055	-.108	-.185	.963															.498(-)
13	-.044	.047	.049	-.038	.086	-.062	-.017	.021	-.109	-.024	-.078	-.280	.966														.675(.624)
14	.041	-.093	-.040	-.004	-.025	-.056	-.038	.049	.020	.062	-.057	-.031	-.228	.979													.632(.633)
15	-.052	-.015	.005	.055	-.018	-.024	.041	-.036	-.025	-.030	-.026	.001	-.188	-.185	.965												.733(.757)
16	-.032	.023	.051	.003	-.082	.041	.020	-.062	.011	.036	-.069	-.059	-.079	-.144	-.365	.968											.719(.723)
17	-.080	.079	-.070	-.086	.048	.087	-.058	.034	.002	-.119	-.033	.095	.004	-.084	-.062	-.186	.963										.602(.608)
18	.037	-.104	-.041	.051	.009	-.067	.012	-.018	.047	.020	-.083	-.058	-.057	-.014	-.105	-.042	-.356	.969									.633(.635)
19	-.018	-.055	.076	-.102	-.034	.032	.097	-.132	.052	.023	-.066	.018	.079	-.002	-.074	.047	-.139	-.086	.968								.538(.531)
20	.080	-.039	-.095	.054	-.020	-.031	-.061	.126	-.119	-.039	.112	.059	-.060	-.018	-.041	-.094	.050	-.091	-.228	.967							.562(.572)
21	-.016	-.079	-.041	-.009	.159	-.102	.023	.063	-.005	-.023	-.039	-.120	-.023	.024	.062	-.035	-.038	-.023	-.066	-.205	.968						.678(.672)
22	.030	-.019	.074	.061	-.123	.059	-.127	.044	.038	-.043	-.036	.021	-.018	.021	-.066	.023	-.034	-.030	-.001	-.154	-.322	.970					.707(.706)
23	-.041	-.008	-.046	-.071	-.061	.101	-.004	-.053	-.011	.107	-.077	.044	.002	-.063	-.034	-.013	-.038	.098	-.004	-.038	-.039	-.184	.961				.740(.744)
24	.021	.029	.001	-.005	-.009	-.090	.061	-.064	.058	-.002	-.004	-.039	-.027	-.035	.098	-.018	.056	-.155	.027	-.019	-.122	-.095	-.438	.959			.769(.773)
25	-.039	-.027	.092	-.043	-.021	.043	-.009	-.029	-.035	-.026	.015	.104	-.035	-.033	-.050	-.002	-.052	.073	-.220	.091	-.035	-.026	-.140	-.170	.959		.691(.690)
26	-.017	.115	-.037	-.032	-.012	-.006	-.048	.039	-.042	-.027	.053	-.082	.070	-.010	.043	.010	.036	-.102	-.014	-.086	-.086	-.078	-.042	-.163	-.396	.964	.700(.700)

Note: - The numbers from 1 to 26 represented the same items explained in the footnote of Table 2.
-The KMO test of overall MSA with Bartlett's test of sphericity was .962 (P<.001)

Factor extraction

Table 4 displays the variance explained by the initial solution, extracted factors and rotated factors. In all the three sections of the table, the total column reports the amount of variance, or the eigenvalue in the original items accounted for by each factor. The percent of variance column contained the percent of total variance accounted for by each factor. Finally, the cumulative percent column contained the cumulative percentage of variance accounted for by the current and preceding factors.

The first section of Table 4 indicates the initial eigenvalues or the variances of the factors. For the initial solution, there were as many factors as items. In correlation analysis, items were standardized, to mean that each item had a variance of 1, and sum of the eigenvalues equals the number of factors. Accordingly, the first four factors accounted for 68.434% of total variance.

The second section of Table 4 presents the extraction sums of squared loadings. The number of rows in this section of the table correspond to the number of factors retained. In the current case, four factors were retained; thus, there were only four rows in this section of the table.

The values in this section of the table were calculated in the same way as the values in the initial eigenvalue section, except that here the values were based on the common variance. These values were lower than the values in the initial eigenvalue section because they were based on common variance, which is always smaller than the total variance.

The third section of table 4 shows rotation sums of squared loadings. The values in this section of the table represent the distribution of the variance after rotation. The rotation maximized the variance of each of the factors, so the total amount of variance accounted for was redistributed over the four extracted factors.

For example, before rotation factor 1 accounted for considerable level of variance than the other three that is 52.612% compared to 6.596%, 5.070% and 4.156% move from factor 2 to factor 4, but when rotated, it accounted for only 20.572%, compared to 15.771%, 13.798 and 12.716% respectively.

Table 4: Total variance explained by the initial solution, extracted factors and rotated factor (n = 813), Ethiopia, 2020.

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	13.679	52.612	52.612	13.316	51.214	51.214	5.349	20.572	20.572
2	1.715	6.596	59.208	1.357	5.221	56.435	4.100	15.771	36.343
3	1.318	5.070	64.278	.963	3.705	60.140	3.587	13.798	50.141
4	1.081	4.156	68.434	.706	2.717	62.857	3.306	12.716	62.857
5	.927	3.564	71.999						
6	.702	2.698	74.697						
7	.622	2.391	77.088						
8	.559	2.148	79.237						
9	.491	1.887	81.124						
10	.462	1.778	82.902						
11	.442	1.700	84.602						
12	.396	1.522	86.124						
13	.361	1.389	87.513						
14	.338	1.299	88.812						
15	.313	1.203	90.015						
16	.303	1.167	91.182						
17	.283	1.090	92.272						
18	.278	1.069	93.341						
19	.262	1.009	94.350						
20	.257	.989	95.339						
21	.241	.926	96.265						
22	.223	.858	97.123						
23	.207	.798	97.921						
24	.196	.753	98.673						
25	.187	.717	99.391						
26	.158	.609	100.000						

Note: The numbers from 1 to 26 represented the same items explained in the footnote of Table 2.

Factor loadings

Table 5 provides factor loadings and communality values of the 20-item dataset. In this table, unless the coefficients .4 and less were suppressed to emphasize that which factor was highly loaded on a specific item, other ways all the factors had a loading on each item. Perhaps, if each loadings was displayed, it could be supportive to check the communality of each item manually (11), which was displayed in the last column of the table. Likewise, unless factor loadings were sorted by size, other ways the table could also be presented differently.

Table 5: Factor loadings and communalities of items (n = 813), Ethiopia, 2020

Factor		1	2	3	4	Communality
1	Advocate organizational mission and vision to stakeholders.	.787				.775
	Oversee a shared direction to achieve organizational mission.	.746				.756
	Describe the outcomes related to the allocated resources.	.745				.694
	Use resources in a way that maximizes the public well-being.	.722				.699
	Establish alliances for joint action at all levels.	.710				.709
	Ensure the participation of key stakeholders.	.677				.686
	Establish a consultation mechanism to heard public voice.	.554				.588
	Uphold ethical and moral integrity to serve the public interest.	.535				.536
2	Enlist stakeholders to commit resources.		.712			.639
	Unite mobilized resources to reach organizational vision.		.695			.652
	Model of creativity, innovation, and learning.		.624			.585
	Show trust and confidence and acknowledge contributions.		.577			.527
3	Integrate work structures and workflow.			.747		.766
	Coordinate practices with other staff`s programs.			.724		.742
	Considers the organizational lines of authority for delegation.			.569		.608
	Monitor their achievements against the plan, and take lessons.			.546		.595
4	Recognize trends, opportunities, and risks.				.648	.626
	Articulate the organization's mission, strategy, and vision.				.630	.693
	Identify client and stakeholder needs and priorities.				.611	.542
	Determine key priorities for action.				.605	.653

Factor labeling

The four latent factors extracted were labeled considering the contents, scientific and empirical domains, of the items clustered within each factor (13-15). Correspondingly, factors 1, 2, 3 and 4 were labeled as compliance with principles, strategic sensitivity, system building, and contextual thoughtfulness respectively (detailed in the discussion section).

A four-factor framework

Figure 1 indicates the four-factor framework for building and measuring the health workforce's competence to lead, manage and govern the health delivery system.

The lines radiated from each latent factor towards the item represent the degree of correlation of each item with the corresponding factor. The lines reflected against each item symbolize the error variance. These variances were calculated from one minus communality (values indicated in the last column of Table 5).

The higher error variance (.5 and greater) indicated that an item might not belong to any factor. Observing the figure from left to right, the lines rayed from competence to lead, manage and govern the health delivery system denote the latent factors extracted.

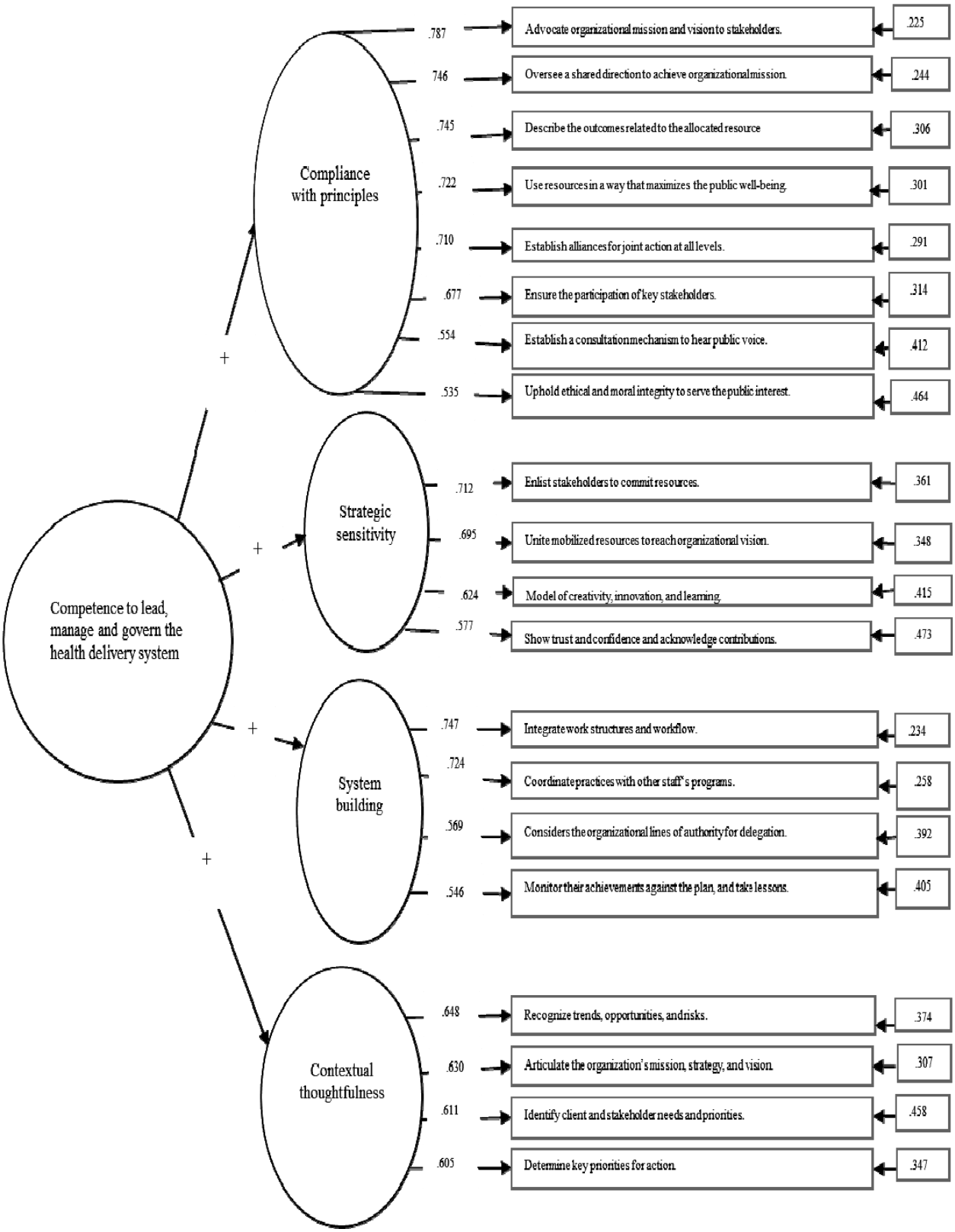

Figure 1: Framework for building and measuring competence to lead, manage and govern the health delivery system, Ethiopia, 2020.

Reliability and validity test

Table 6 presents the CR, and AVE of each factor. The CR for compliance with principles, strategic sensitivity, system building and contextual thoughtfulness were .921, .810, .838 and .807, respectively. The AVE for respective factors were .598, .517, .569 and .512.

Table 6: CR and AVE of the factors indicated on the four-factor model (n = 813), Ethiopia, 2020

Parameters	Factors			
	Compliance with princi-	Strategic sensitivity	System building	Contextual thoughtfulness
Sum of factor loadings	5.476	2.608	2.586	2.494
Squared sum of factor loadings	29.987	6.802	6.687	6.220
Sum of squared factor loadings	3.807	1.712	1.704	1.556
Sum of error variance	2.557	1.597	1.289	1.486
CR	.921	.810	.838	.807
AVE	.598	.517	.569	.512
√AVE	.773	.719	.775	.716

Note: Squared factor loadings and sum of error variances were calculated by using estimates indicated in Figure 1.

DISCUSSION

The current four-factor framework for building and measuring competence to lead, manage and govern the health delivery system is developed by assembling latent factors extracted, items rated, and error variances observed. To make this framework more meaningful the four latent factors extracted are labeled based on the contents that the factor loadings reflect (13-15).

The eight items clustered within the first factor reflect compliance with organizational principles. The word compliance describes the act of acquiescing with a set of rules, and the other word principle explains an accepted rule of action. Hence, compliance with principles refers to the ability to act with an accepted set of rules.

The four items loaded within the second-factor talk about strategic sensitivity. The terms strategic and sensitivity describe mindfulness and strong attention, about mission and vision, respectively. Thus, strategic sensitivity is defined as the intensity of mindfulness and attention towards mission and vision (21).

The other four items clustered within the third factor explain system building. System means a group of interdependent components that form a unified whole (22), and building refers to improving interactions among the components. Consequently, system building symbolizes the ongoing process of improving interaction among the components.

The remaining four items gathered within the last factor denote contextual thoughtfulness. The term contextual and thoughtfulness refer to state of exploring conditions regarding environment and deliberate thinking before doing something respectively. Thus, contextual thoughtfulness represents deliberate thinking in exploring conditions regarding the environment.

Groups of items assembled in the four-factor framework are nicely loaded. However, these values could be interpreted with important cautions. In one way, a high value for CR does not imply that the framework is unidimensional due to that CR is not a statistical test (18). On the other way, a high AVE value does not tell solely that the variance is due to the construct (16, 17, 19, 23). Thus, the CR values could be supported by the total variance explained that reaffirms the unidimensionality of the model when the total variance for the first factor is quite larger than the next factor. Similarly, AVE values need triangulation with the correlation coefficients. Convergent validity implies that all within-construct correlations are significantly different from zero and of approximately the same magnitude. Divergent validity is satisfied if the cross-correlations are high, uniform and lower than the within-construct correlations.

Generally, the scientific reliability and empirical scalability of this framework is revealed through three key actions. (i) Taking representative items from leading, managing and governing functions.

(ii) Unlocking a theoretically reasonable analysis technique that is factor analysis. (iii) Conducting CR and AVE to test its reliability and validity. The above listed actions could give confidence to the health system authorities to build and measure competence of the health workforce to lead, manage and govern the health delivery system using the current framework (2, 7, 24, 25). Note that since this research is a pioneer, additional testing and refinement are important next steps for its application in various settings.

Generally, the current study has important implications for policymaking, planning, implementing and researching in the context of the low and middle-income countries' health systems. In this regard, health authorities who lead, manage and govern the health delivery system in such countries and who wish to achieve better results could consider a contextualized capacity-building model.

Concussion

The current study provides a four-factor framework for building and measuring the health workforce's competence to lead, manage and govern the health delivery system. It acquires its name from the four latent factors extracted. These include compliance with principles, strategic sensitivity, system building, and contextual thoughtfulness. The framework can provide foundations for future training, evaluation, and research. Feature research needs to examine the framework at both individual and organizational levels.

ACKNOWLEDGMENTS

Our special thanks and sincere appreciation go to the study participants, data collectors, and data supervisors, for their valuable contribution. Our gratitude also extends to Bahir Dar University for funding this study.

Conflict of interests

All the authors declare that they have no both financial and non-financial competing interests.

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Lucy Eriba, Oseiwe Oboh, Peter Agbonrofo, Omorodion Irowa, Jamil Jatto, Amina Okhakhu, Vincent Odigie.
Ethiop Med J, 2021, Vol. 59, No. 2

ORIGINAL ARTICLE

PATTERN OF POST-TREATMENT METASTATIC SUBSITES IN BREAST CANCER PATIENTS IN A TERTIARY HEALTHCARE CENTRE IN NIGERIA

Lucy Eriba, MD[1], Oseiwe Oboh, MD[1], Peter Agbonrofo, MD[2*], Omorodion Irowa, MD[2], Jamil Jatto, MD[1], Amina Okhakhu, MD[3], Vincent Odigie, MD[4]

ABSTRACT

Introduction: *Managing breast carcinoma in Nigeria is challenging as a large proportion of these patients present at advanced stage of their disease. Our study aims at determining the pattern of post-treatment metastasis in the University of Benin Teaching hospital.*
Methods: *A retrospective review of records of breast cancer patients seen over a five-year period (January 2013 to December 2017) was conducted. Relevant information was extracted and analyzed with statistical package for social science software 21.*
Results: *A total of 292 patients with carcinoma of the breast were seen at the University of Benin Teaching Hospital. Metastases developed in 113(38.7%) patients post-treatment with taxane-based therapy within 2 years. Majority of patients were aged 30-59years (77.4%). Moderately differentiated carcinoma was the main histologic diagnosis (62.8%). The pattern of metastases was commonly to the loco-regional sites (39.5%), bone (16.9%), lungs (10.6%), brain (6.3%) and liver (4.4%) while multiple sites were (15.0%) and of these, 51.3% developed the metastasis within 10 – 12months. Within a period of 2 years, 60.2% had stable disease.*
Conclusion: *Our study showed loco-regional site as the commonest metastatic sub-site in this region with bony metastasis being the commonest distant spread. These occur commonly within the first one year post-treatment. Careful evaluation of these sites during follow-up is advocated to ensure early detection and appropriate management. This study also showed a significant survival of patients at 2 years following taxane-based therapy. We therefore advocate that taxane-based therapy should be the main stay of treatment of breast cancer patients.*
Keywords: *Metastatic breast cancer; pattern of metastasis; breast; taxane.*

INTRODUCTION

Breast cancer is the most common cancer in women worldwide. It accounts for 12 percent of all cancers diagnosed yearly, and a major cause of cancer-related death in women worldwide (1).

Approximately 1.68 million new cases of breast cancer were diagnosed and 520,000 deaths from breast cancer recorded globally, in 2012 (1). The lifetime risk of developing invasive breast cancer is about 1 in 8 American women and 1 in 100 men (2).

In Nigeria, breast cancer accounts for 29.7% of 818 cancer cases seen annually. This makes it the most common cancer with a substantial increase in its incidence in recent times (3, 4).

Breast Cancer peaks a decade earlier in Nigerian women than in Caucasian women (5). This disease is aggressive and unpredictable in Blacks: some patients present with early stage disease and succumb to widespread metastasis within six months to one year; some patients survive longer despite presenting with advanced disease (5). There are disparities concerning breast cancer in blacks in contrast to the Caucasians with peculiar characteristics of breast cancer among blacks (6).

Breast cancer incidence in Nigeria is rising: 13.8-15.3 per 100,000 in 1992; 33.6 per 100,000 in 2000 (7). It was estimated that 7000 - 10,000 new cases would develop in 2005, and most of these patients presented with advanced disease (7, 8). A lot of advocacy and health enlightenment has been instituted, leading to an overall 5-year survival rate of 89% which is a dramatic improvement over the 63% rate recorded in early 1960s. The 5-year survival rate is dependent on the stages of breast cancer: 99% for localized disease; 85% for regionally advanced disease (spread to regional lymph nodes), and 26% for distant metastasis (stage 4) (9).

[1]Consultant Radio-oncologist, Department of Radiotherapy, University of Benin Teaching Hospital, Benin City, Nigeria.
[2]Lecturer/Consultant, Department of Surgery, University of Benin/ University of Benin Teaching Hospital, Benin City, Nigeria.
[3]Lecturer/Consultant, Department of Ear, Nose and Throat, University of Benin/ University of Benin Teaching Hospital, Benin City, Nigeria.
[4]Professor/Consultant, Department of Surgery, University of Benin/ University of Benin Teaching Hospital, Benin City, Nigeria.
*Corresponding Author E-mail: pagbonrofo@gmail.com, peter.agbonrofo@uniben.edu

There is paucity of data as regards metastatic sub-sites and time to metastasis in our locale hence the need to determine the pattern of metastatic sub-sites post-treatment- the aim of our study.

MATERIALS AND METHODS

This study was conducted at the Radiotherapy and Surgery Departments of University of Benin Teaching Hospital (UBTH) Benin, Edo State, the premier tertiary referral center in South-South Nigeria and it provides radiotherapy and surgical services for neighboring states. It was a retrospective review of all patients that had metastasis following treatment (post-treatment) for breast cancer between January 2013 and December 2017.

Post-treatment refers to all patients who had metastasis following modified radical mastectomy, taxane-based chemotherapy and External beam irradiation. All patients had 3 - 4 cycles of neo-adjuvant taxane-based chemotherapy and 4 – 6 cycles of adjuvant taxane-based chemotherapy. These were included in the study. Data obtained include the socio-demographics, menopausal status, parity of the patient, metastatic sub -sites and time to metastasis post-treatment.

All the patients had routine investigations as follows: Abdominopelvic Ultrasound, a Chest X-ray, Liver Function Test, a Bone Scan and Computerized Tomography scan as appropriate. Clinico-pathological features of the patients: site of the disease (left, right or both breast), Stage, Histological subtypes, Histological grade, Hormone receptor status, Metastatic sub sites, Status within two years following treatment

All the patients had late-stage disease.

Diagnosis of post-treatment metastatic lesions was made from clinical and radiological evaluation. Following diagnosis of post-treatment metastatic disease, triple negative patients received further adjuvant platinum-based chemotherapy while hormone receptor positive patients received hormonal therapy. Her2/Neu positive patients were managed with trastuzumab and cytotoxic chemotherapy where affordable, otherwise they received further cytotoxic chemotherapy alone.

The protocol of this study was in accordance with the World Medical Association Declaration of Helsinki.

The data obtained were analyzed using the IBM Corporation Statistical Package for the Social Sciences (SPSS) statistics for windows, version 21.0. Armonk, New York, United States of America.

RESULTS

Two hundred and Ninety-two patients were seen during the study. Of these, 113 (38.7 %) had metastatic disease post-treatment with taxane-based chemotherapy and external beam irradiation.
Peak age at presentation was 40-49 years (31.1%). (Figure 1)

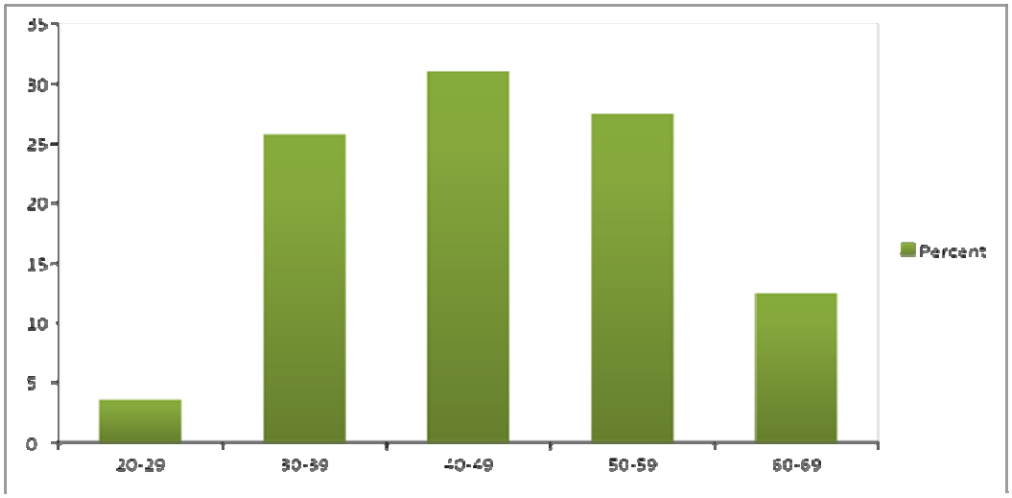

Figure 1: Age distribution of metastatic breast cancer patients, University of Benin Teaching Hospital, 2013-17.

Mean age at presentation was 44.51years. Most patients in this study were premenopausal (54.0%), multiparous (73.5%) with tertiary education (53.1%). (Table 1)

Table 1: Patients' characteristics, University of Benin Teaching Hospital, 2013-17.

Sex	Frequency	Percent
Male	1	0.9%
Female	112	99.1%
Menopausal status		
Premenopausal	61	54.0%
Postmenopausal	52	46.0%
Parity		
Nulliparity	15	13.3%
Primipara	7	6.2%
Multiparity	83	73.5%
Grandmultiparity	8	7.1%
Educational Status		
None	4	3.5%
Primary	12	10.6%
Secondary	37	32.7%
Tertiary	60	53.1%

Invasive ductal carcinoma of the breast was the commonest histologic variant, accounting for 95.6% of the metastatic disease. Most of these carcinomas were moderately differentiated (62.8%). (Table 2)

Table 2: Site of Cancer, histologic types and grade of differentiation, University of Benin Teaching Hospital, 2013-17.

Site of cancer	Frequency	Percent
Right breast	49	43.4%
Left breast	52	46.0%
Bilateral	12	10.5%
Histologic types		
Invasive Ductal Carcinoma	108	95.6%
Medullary Carcinoma	2	1.8%
Papillary Carcinoma	2	1.8%
Invasive Lobular Carcinoma	1	0.9%
Grade of differentiation		
Well differentiated	10	8.8%
Moderately differentiated	71	62.8%
Poorly differentiated	32	28.3%

The Immunohistochemistry report of the study participants were as follows: ER +ve 27.4% (31), PR +ve 7.0% (8), ER/PR +ve 34.5% (39) and Triple negative (ER +ve, PR +ve and Her2/neu +ve) 28.3% (32). Triple positive, Her2/neu positive only and PR +ve/ Her2/neu +ve were 0.9% (1) respectively. Cumulatively ER positivity was 61.9%.

Distant metastasis occurred in 60.7% of patients. Bone was the commonest distant site (16.9%). Ipsilateral axillary nodes were the commonest locoregional site (27.5%). Metastasis to multiple sites was found in 15.0% of patients in this study. (Figure 2)

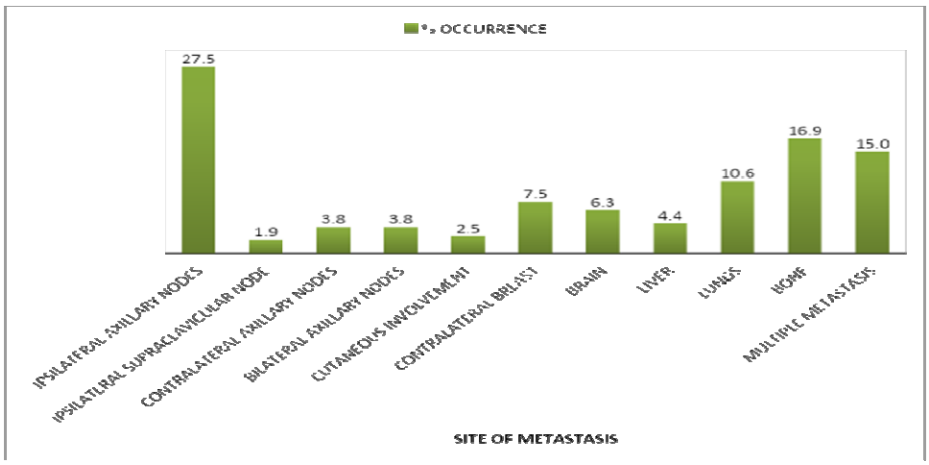

Figure 2: Pattern of metastasis, University of Benin Teaching Hospital, 2013-17

Most (51.3%) of the patients in this study, developed metastasis within 10-12 months while 28.3% developed metastasis within 22 – 24 months. (Figure 3)

Majority of the patients were alive at 2 years; 12.4% were disease free, 60.2% had stable disease while 7.0% died. (Fig 4)

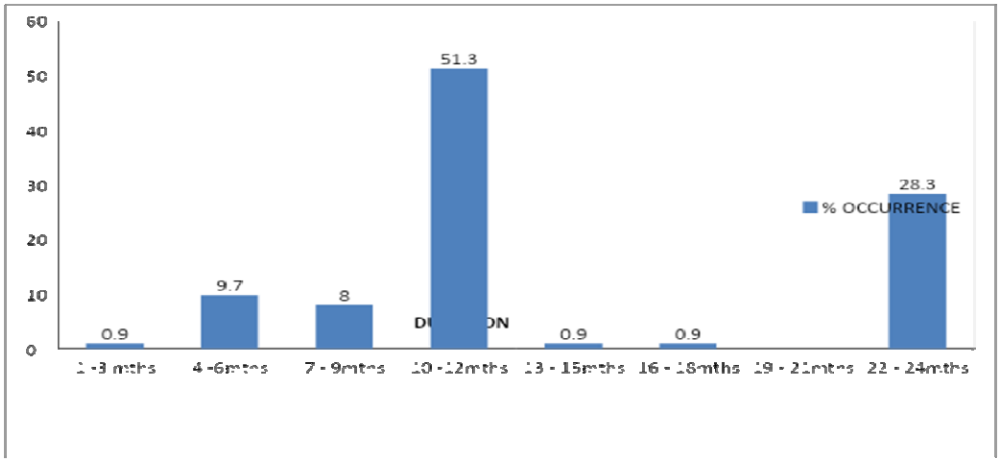

Figure 3: Time to metastasis, University of Benin Teaching Hospital, 2013-17

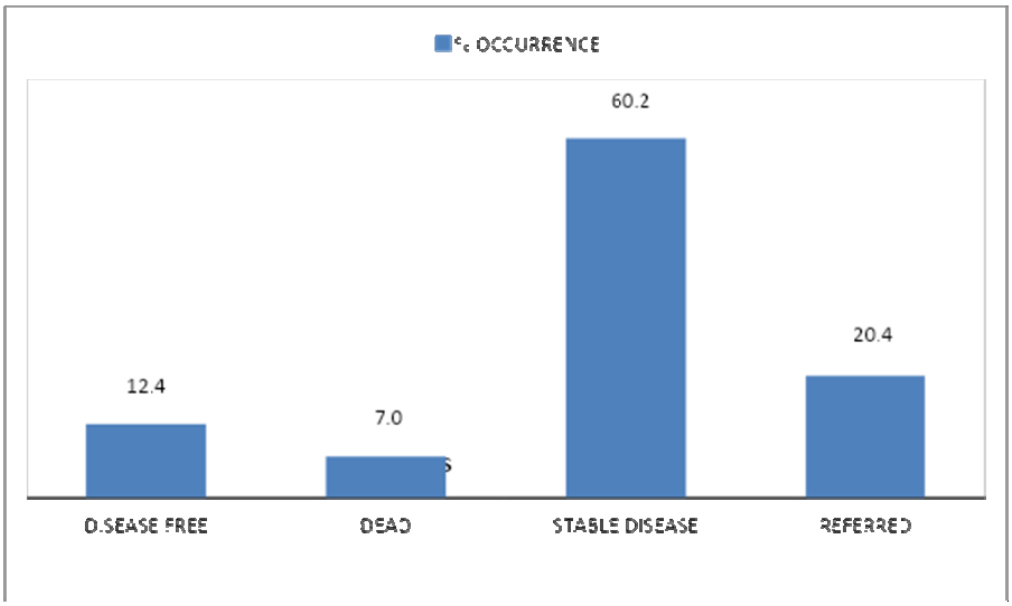

Figure 4: Status after two years, University of Benin Teaching Hospital, 2013-17

DISCUSSION

Breast cancer can metastasize to any part of the body and this was the cause of death in most of the patients with this disease (10). Our study showed that 113 (38.7%) of the patients seen within the study period had metastasis post treatment; this is higher than that reported by Thompson where 10 -15% had distant metastasis within 3 years of diagnosing the primary tumor (11). Most (53.8%) of our patients were between the ages of 30 and 50 years with mean age of 47 years. This is comparable to the works done by Adebamowo et al and Rahman GA et al; where most patients were young, pre- and peri-menopausal (12,13,14). Breast cancer in the young is known to be more aggressive, more likely to recur after treatment loco-regionally or at distant sites and associated with shorter disease free survival and higher mortality, than in older women. (15).

In our study, invasive ductal carcinoma of the breast was the commonest histologic variant and accounted for greater than 50% of the metastatic disease. Most of these carcinomas were moderately differentiated .This is in tandem with other studies that showed invasive ductal carcinoma of the breast as the most common histologic type (16, 17, 18). The histologic subtype and grade have a substantial influence on the development of metastasis and survival in patients with breast cancer (19). The pattern of immunohistochemistry in our study- estrogen positivity of 61.9% and triple negativity of 28.3% - is comparable to previous studies done in Nigeria (20, 21).

There is a high proportion of distant metastasis (60.7%) in this study and this is in contrast to reports by Ikpatt OFR et al (19) and Tesfamariam A et al (22) which showed a high proportion of loco-regional disease. In this study, bone was the commonest distant site (16.9%). Varying incidence of bone metastasis have been reported in Nigeria; Ketiku K documented 19.6% in Lagos and Elumelu TN et al reported 24.1% in Ibadan (23, 24).

In Zaria, Nigeria, 72.0% of all bone metastasis seen were primarily from Breast cancer (25).

Lung metastasis accounted for (10.6%), and liver (4.4%); which is lower than that found by Tesfamriam et al (22). In Ile Ife, Adesunkanmi et al, reported a higher incidence of lung metastasis (20.3%) (26), while in Uganda 42 % of their patients had lung metastases (27). These discrepancies may be due to difference in study designs.

In our study, brain metastasis accounted for 6.3%. Clegg-Lamptey JNA et al and Lee YT reported a comparable incidence of brain metastasis in their studies (28, 29). Brain CT scan, MRI or PET scan either singly or in combination are required for the diagnosis of brain metastasis. Most of our patients are unable to afford CT scan or MRI by the time they develop brain metastasis. Majority of these patients are terminally ill patients and require palliative care, thus, there is the need to weigh the cost against the benefit of these diagnostic tools.

Metastasis to multiple sites was found in 15.0% of patients in our study, this increases their risk of death from the disease. Most deaths from the disease are accounted for by distant metastasis rather than the primary tumor (30).

Most (51.3%) of the patients in this study, developed metastasis within 10-12 months, so a close follow up during this period is required for early detection of metastasis and appropriate treatment.

Majority of the patients were alive at 2 years; 12.4% were disease free while 60.2% had stable disease, 7.0% died but 20.4% were referred back to their primary physicians based on proximity to their place of abode and need for care by close relatives.

Taxane-based chemotherapy was used in this study and we recorded 60.2% of a stable disease at 2 years. Extended survival with taxane-based chemotherapy in metastatic breast cancer has been reported (31, 32).

Limitation of the study

Metastatic lesions were not subjected to pathological evaluation in this study. Diagnosis of metastasis was made based on clinical and radiological features of the lesions.

Follow up of patients was a challenge. Patients needed to be supported to get Taxane for completion of treatment.

Conclusion

The report of this study is a reflection of the disease pattern in this region where the commonest metastatic sub-sites is loco-regional with bony metastasis occurring as the commonest distant spread.

These occur commonly within the first one year post-treatment.
During follow up, these sites should be carefully evaluated to ensure early detection and appropriate management.

This study also showed a significant survival of patients at 2 years following taxane-based therapy. We therefore advocate that taxane-based therapy should be the main stay of treatment of breast cancer patients.

ACKNOWLEDGEMENT

The authors acknowledge the contributions of Okoduwa Kester in the manuscript preparation.

Conflict of interest

The authors declare that they have no conflicts of interest in this study.

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ORIGINAL ARTICLE

MAGNITUDE OF COMMUNITY ACQUIRED PNEUMONIA AMONG TREATED ADULTS IN TIKUR ANBESSA SPECIALIZED HOSPITAL: A RETROSPECTIVE STUDY

Tamene Abera Desissa MD[1*], Amsalu Bekele MD[1], Wondwossen Amogne, MD,PhD[1] , Yimtubezinash Woldeamanuel MD, PhD[2] , Daniel Asrat MD, PhD[2] , Tamrat Abebe PhD[2], Stephen Aston MD[3]

ABSTRACT

Introduction: *Pneumonia is a major cause of morbidity and mortality in children and adults in low-and middle-income countries . The aim of this study was to determine the magnitude of community acquired pneumonia among treated adults of 13 years and above at Tikur Anbessa Specialized Hospital.*

Methods: *This is a register based retrospective community acquired pneumonia study. The study period was from August 2017 to 2019 . Data were collected using a structured checklist for record review. Data analysis was conducted using SPSS.*

Results: *The magnitude of community acquired pneumonia was 1.19 % (104/8673; 95% CI: 0.97%,1.43%) of all patients managed as in patient. Fifty five (52.9%) of the community acquired pneumonia patients were male and 49(47.1%) were females. Indication for admission by CURB65 (Confusion, Bun, Respiratory rate, systolic blood pressure, age>65) criteria was only 28% (29/104). Patients were on IV antibiotics on the average for 8 days with average length of stay of 10.8 days before discharge. Anti-TB was started for 16 % (17/104). Sputum culture was done for only 8 % (8/104). Eighty six percent (89/104) survived to discharge and 14 % (15/104) died in the hospital. Readmission within 30 days was 10.5% (11/104)*

Conclusions: *Community acquired pneumonia encompasses only few of manged inpatients. Indication for admission based on severity score and outcomes were confounded by co comorbidities. Pulmonary TB was diagnosed in significant number of patients who present with clinical and radiological community acquired pneumonia patients.*

Keywords: *Community acquired pneumonia, Tikur Anbessa Specialized Hospital, Ethiopia*

INTRODUCTION

Community-acquired pneumonia (CAP) is commonly described as an acute infection of the lung parenchyma acquired in the community. It is most commonly caused by bacteria and is associated with clinical and/or radiological evidence of consolidation of part or parts of one or both lungs (1). CAP is associated with a considerable burden of disease in most regions of the world (2–7). As part of the burden of respiratory infections, CAP is well recognized to be a leading cause of death among the infectious diseases (6, 8).

Pneumonia is a major cause of morbidity and mortality in children and adults in low-and middle-income countries (LAMICs). In the last decade, there have been several advances and new interventions, resulting in a substantial reduction in pneumonia incidence and improved outcomes. Nevertheless, pneumonia remains the most common reason for adult hospitalization in sub-Saharan Africa, with an estimated 4 million episodes and 200 000 deaths each year (9).

There are a considerable number of risk factors for CAP that exists in populations all over the world, and most of these risk factors are associated with an impairment of host immune defense (7).

In addition to aging, the common risk factors in adults are smoking; the presence of various underlying comorbid conditions, including chronic cardio-respiratory, renal and hepatic conditions, and, at least in some regions of the world, concomitant human immunodeficiency virus (HIV) infection (7, 11-18).

But, little is known about the epidemiology, etiology and predictors of poor outcomes for CAP in Ethiopia. Thus, the main objectives of this study was to determine the proportion of admissions with CAP, indications and place of admission, etiology, treatment outcome and predictors of poor outcome at one of the oldest tertiary teaching hospital in Ethiopia.

[1]Department of Internal Medicine, College of Health Sciences,Addis Ababa University
[2]Department of Microbiology, Immunology & parasitology, Addis Ababa University .
[3]Academic Clinical Lecturer in Infectious Diseases, Institute of Infection and Global Health, University of Liverpool.
*Corresponding Author E-mail: tamansissa@yahoo.com

METHODS

Study Setting: The study was conducted at Tikur Anbessa Specialized Hospital (TASH). The hospital is tertiary hospital located in Addis Ababa, Ethiopia. The hospital is one of the oldest tertiary referral care centers. It has more than 700 inpatient beds and 18 common ICU beds. Department of Internal Medicine at TASH has 120 inpatient medical beds and six ICU beds. It has 18 intermediate ward beds and used to have emergency medical ward. Registers with CAP from all medical wards, intermediate, emergency and MICU were included in the study

Study design: The study design was a register based retrospective study on patients admitted to medical inpatients with clinician made diagnosis of CAP based on clinical and radiological evidence. Pneumonia diagnosis was made when a patient with acute presentation (symptom less than 2 week) with chest symptoms like cough, fever chest pain and difficulty of breathing with radiologic evidence of pneumonia like consolidation, lung infiltrate and pleural effusion and physician decided to treat as a case of community acquired pneumonia. The study period was from August 2017 to 2019. During the study period, data was collected using data abstraction form on indications (CURB65 score) and place of admission, comorbidities, treatments and their outcomes including death for each study subject admitted with CAP.

Study population: The source populations for this study were all patients admitted to the medical wards and MICU of Tikur Anbessa Specialized Hospital. The study populations were all CAP patients admitted and managed in the hospitals in the last two years. There were difficulties obtaining some charts of patients with the diagnosis of CAP.

Dependent variables: The dependent variable to be studied was proportion of CAP, indications for admission, place of admission, severity of disease, length of stay, treatment outcomes including discharge, readmission and death.

Independent Variables: The independent variables of this study were age, sex, severity scores and comorbidities.

Sample Size

Total of 104 patients with clinician and radiologic diagnosis of CAP from August 2017 to 2019 admitted to TASH inpatient was included in the analysis.

Sampling procedures: All admitted patients to the medical wards with diagnosis of CAP were selected to be included in the sample.

Data collection procedures: The sources of data for this study were the inpatient ward registers of the hospital. In the registers, clients' socio demographic, clinical and laboratory information, treatments being provided to the clients, the starting date and stopping date of treatment and the follow up status for each client were recorded and reviewed. Data were collected using a structured data extraction form for record review developed in English for this study from the registers and standard guidelines.

Data were collected by the primary investigator, the medical resident, in the hospital wards and card rooms. The developed checklist was pilot tested, and some amendments were made before it was used for the actual data collection. Incomplete data mainly with no radiological evidence were excluded.

Data Analysis

After the data have been collected, it was first checked daily for completeness after collection in the field and electronic data were captured by the principal investigator. For data analysis, SPSS version 25.0 was used. Descriptive statistics was generated for demographics of CAP population, descriptions of treatment, severity assessment and predictors of mortality were taken as significant at $P<0.05$ level of significance. Completion rates were described by subcategories of demographic and clinical characteristics. Independent variables that were significantly associated with treatment completion in bi-variate analysis were further examined in multivariate analysis using log-binomial regression.

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Ethical clearance was secured from the Ethical Clearance Committee of the Department of Internal Medicine, College of Health Sciences, Addis Ababa University, and Support letter from department has been obtained and submitted to the hospitals card room. To ensure the confidentiality, names and any other personal identifiers were not used during the data collection and analysis.

RESULTS

The magnitude of community acquired pneumonia was 1.19 % (104/8673; 95% CI: 0.97%,1.43%) of all patients managed as in patient. Fifty five (52.9%) of the community acquired pneumonia patients were male and 49(47.1%) were females. The mean age of CAP patients was 41.9 years with age ranging from 13 years to 79 years. All CAP patients were admitted through the emergency route.

Majority (55%) were admitted during day time. Common age group affected by CAP was from 30-64 years of age and age more than 64 years constitute 17%. Smoking rate among CAP patients was 4%. The mean duration of symptoms during presentation was 11 days. All patients had at least derangement in one vital sign during presentation. Common presenting symptoms include cough, fever, shortness of breath fatigability and weight loss. Age is associated with severity and outcome of CAP though confounded by comorbidities. Almost all CAP patients included in the analysis had at least one comorbidity.

Twenty four per cent of them had more than one comorbidity. The most common comorbidity seen in CAP patients admitted to TASH include, 27% cancer of any kind, 21% Heart failure, 17% Bronchiectasis, 11.5% Hypertension, 8.5% renal disease, 7% Asthma, 6% Chronic Obstructive Pulmonary Disease(COPD) and 6% Diabetes Miletus (DM) . Major established risk factors for development of CAP include presence of comorbidities of different types, previous TB, previous pneumonia, HIV and smoking (Table 1).

Table 1: Major risk factors for CAP among study participants in Tikur Anbessa Specilaized Hospital, August 2017-19

Risk factors	Frequency/Percentage (%)
Previous TB	18(17%)
Previous pneumonia	20(19%)
HIV/AIDS	9(8.6%)
Smoking	4(3.8%)
Comorbidity	104(100%)

The diagnosis of pneumonia was made using clinical parameter which includes acute symptoms less than 2 weeks and other alternative diagnosis ruled out and supportive radiologic finding. All patients had radiologic evidence of lung involvement and 45% (46/104) had evidence of pleural effusion.

Only 28% (29/104) of CAP patients had CURB65 score greater or equal to two needing admission. The decision of admission was determined by presence of comorbidity and other factors rather than severity. The majority of patients 97% of them were admitted to general ward and only few of them were directly admitted to ICU. All patients were started on antibiotics and the most commonly used antibiotic regimen was ceftriaxone and azithromycin 64/104(61.5%) followed by cefepime and vancomycin18/104(17%). The mean duration of IV antibiotics was 8 days.

Microbiological investigation was done for a significant number of cases, which included 8/104 (8%) sputum culture, 78/104(75%) blood Culture, 8/104(8%) sputum MTB/RIFXPERT and 1/104 (1%) sputum TB culture. All investigations were found in the patient charts and 2 sputum cultures grow streptococcus pneumonia, no growth of blood cultures, 4 patients were sputum MTB/ RIFXPERT positive but negative sputum TB culture.

Advanced interventions were needed for some patients. The intervention included invasive mechanical ventilation1/104(1%), inotropes/ vasopressor use 3/104(3%) and renal replacement therapy1/104(1 %). After admission and initiation of treatment, 17/104(16%) of them were found to have pulmonary tuberculosis and their treatment was changed clinically or bacteriologically, while 4/104(4%) developed pneumocystis pneumonia (PCP) clinically.

The treatment outcomes of patients treated for CAP in TASH showed that the majority (86%) of patients treated were discharged with improvement. From the total of patients discharged with improvement 10.5% were readmitted due to worsening of the symptoms. Further, the treatment outcome of 14% patients was death. The average length of stay before discharge was 11 days and the average length of stay before death was 10 days (Table 2).

Table 2: Treatmetn oucomes of patienst treated for CAP at Tikur Anbessa Specilaized Hospital, August 2017-19

Outcome Measurement	Frequency (%)
Survival to discharge	89(86%)
Death	15(14%)
Readmitted with 30 days	11(10.5%)
Average LOS before discharge	10.82 days
Average LOS before death	9.8 days

DISCUSSION

As part of the burden of respiratory infections, CAP is well recognized to be a leading cause of death among the infectious diseases (6, 8). A total of 104 patients with clinical suspected and radiologically confirmed patients with CAP were included.

The main findings were 1) relatively young patients having pneumonia; 2) limitation of CURB-65; 3) presence of comorbidly in all patients; 4) high mortality rate as compared to other countries (<8%) for CAP in the hospital; and 5) overlapping clinical symptom (TB,PCP,CAP).

This study clearly showed us, the proportion of CAP admissions were significantly lower than other studies done in this country and other African countries (19, 20). This shows us many things. First, in this study only patients with imaging confirmed cases were involved. Second, chart retrieving and documentation in our hospital was unacceptably poor (21). Third, even if CAP is still the cause of inpatient mortality according to FMOH, Ethiopia, cases might be managed at primary health care unit (22). CURB-65 severity score, even though very easy to use in our setting, it identified only 28 % of those admitted patients. It was calculated and some data were missing for blood urea nitrogen and correctly identified in 16% for complete data. This is explained by the young population with mean age of 42 years and at least one comorbid condition in all patients was not part of calculation (23).

This indicates that CURB-65 has limitation in Africa patients and difficult to generalize in this part of the region where the population pyramids showed younger one and few cross more than 65 year. Even though, 45% of the patients have associated pleural effusion, the mean duration of IV antibiotics was only 8 days. Probably this may be a reason for readmission of some of the patients. Further studies are needed to establish the duration of antibiotic therapy for adults with complications of CAP and adults with prolonged time to achieving clinical stability (25).

The hospital mortality rate of 14% found in this study was high compared to the 11% obtained in a study done at the same hospital, Ethiopia, 23 years ago (27). This is explained by the presence severe & multiple comorbidities. Compared to the same study (27), the comorbidity was much higher in this study (100% vs 38%). Again, this is explained by better inpatient care in this study. Thus, comorbidities were risk for disease acquisition and bad outcome (25).

In this study, there was a significant number of overlaps of CAP with Pulmonary TB which was identified and 16% of them started on anti-TB and 4% developed Pneumocystic pneumonia (PCP). In this part of the world, there is over lap of common lung infections (CAP, TB and PCP) up to 10%. This figure is high, probably mode of the patients were patients with chronic disease and at high risk to develop TB. (24)

Microbiologic diagnosis especially sputum culture was very low and bacteremic CAP not found. Even if doing sputum culture for CAP patient is not cost effective (25), in our setting it is quite worthy in two ways. First, the need to have national antimicrobiome (drug sensitivity patterns of common microorganisms) to facilitate appropriate drug selection, Second 7.8 % of patients were found to be smear positive pulmonary TB indicating similar clinical and radiological findings. It is clear that blood cultures should be obtained before antibiotic administration in all patients with CAP who are ill enough to be hospitalized and likelihood of having bacteremia. The IDSA and ATS have also recommended blood cultures for patients who are admitted to an ICU and have a cavitary lesion, leukopenia, active alcohol abuse, asplenia, a positive pneumococcal urinary antigen, or a pleural effusion (27). Furthermore, because the cause of pneumonia is not always found, assessment of clinical response to initial therapy is important, and blood cultures should be obtained in patients not responding to antibiotic therapy (28, 229).

The duration of antibiotics use was also prolonged as compared to the nation & international standards for CAP inpatient management and the antibiotic stewardship should be strengthen to prevent emergency of drug resistance (25).

Limitation

This study focused only on patients treated at one national specialized hospital, the Tikur Anbessa Specialized hospital located at the capital city of the country. The setups of the study hospital and the clinical status of patients treated at the study hospital might be different from patients with the same health problem but who were treated at other hospitals of Ethiopia. Moreover, data were collected from purposively selected patients treated for CAP which may limit generalizability of the result to the general population. Thus, the outcomes of this study may be generalized with caution.

Conclusion

The study revealed that there were many caveats in management of admitted CAP patients. Hence, having this as baseline data performing prospective multicentric longitudinal studies is recommended. The study also needs to look the clinical care from patient's perspective to make it complete.

ACKNOWLEDGEMENTS

We would like to thank the Department of Internal medicine, College of Health sciences, Addis Ababa University for giving me this opportunity and provide financial support to conduct this research.

We thank the NIHR Global Health Research Unit on Lung Health and TB in Africa at LSTM - "IMPALA" for helping to make this work possible.

In relation to IMPALA (grant number 16/136/35) specifically: IMPALA was commissioned by the National Institute of Health Research using Official Development Assistance (ODA) funding.

The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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ABSTRACT

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Comorbidity	104(100%)

The diagnosis of pneumonia was made using clinical parameter which includes acute symptoms less than 2 weeks and other alternative diagnosis ruled out and supportive radiologic finding. All patients had radiologic evidence of lung involvement and 45% (46/104) had evidence of pleural effusion.

Only 28% (29/104) of CAP patients had CURB65 score greater or equal to two needing admission. The decision of admission was determined by presence of comorbidity and other factors rather than severity. The majority of patients 97% of them were admitted to general ward and only few of them were directly admitted to ICU. All patients were started on antibiotics and the most commonly used antibiotic regimen was ceftriaxone and azithromycin 64/104(61.5%) followed by cefepime and vancomycin18/104(17%). The mean duration of IV antibiotics was 8 days.

Microbiological investigation was done for a significant number of cases, which included 8/104 (8%) sputum culture, 78/104(75%) blood Culture, 8/104(8%) sputum MTB/RIFXPERT and 1/104 (1%) sputum TB culture. All investigations were found in the patient charts and 2 sputum cultures grow streptococcus pneumonia, no growth of blood cultures, 4 patients were sputum MTB/ RIFXPERT positive but negative sputum TB culture.

Advanced interventions were needed for some patients. The intervention included invasive mechanical ventilation1/104(1%), inotropes/ vasopressor use 3/104(3%) and renal replacement therapy1/104(1 %). After admission and initiation of treatment, 17/104(16%) of them were found to have pulmonary tuberculosis and their treatment was changed clinically or bacteriologically, while 4/104(4%) developed pneumocystis pneumonia (PCP) clinically.

The treatment outcomes of patients treated for CAP in TASH showed that the majority (86%) of patients treated were discharged with improvement. From the total of patients discharged with improvement 10.5% were readmitted due to worsening of the symptoms. Further, the treatment outcome of 14% patients was death. The average length of stay before discharge was 11 days and the average length of stay before death was 10 days (Table 2).

Table 2: Treatmetn oucomes of patienst treated for CAP at Tikur Anbessa Specilaized Hospital, August 2017-19

Outcome Measurement	Frequency (%)
Survival to discharge	89(86%)
Death	15(14%)
Readmitted with 30 days	11(10.5%)
Average LOS before discharge	10.82 days
Average LOS before death	9.8 days

DISCUSSION

As part of the burden of respiratory infections, CAP is well recognized to be a leading cause of death among the infectious diseases (6, 8). A total of 104 patients with clinical suspected and radiologically confirmed patients with CAP were included.

The main findings were 1) relatively young patients having pneumonia; 2) limitation of CURB-65; 3) presence of comorbidly in all patients; 4) high mortality rate as compared to other countries (<8%) for CAP in the hospital; and 5) overlapping clinical symptom (TB,PCP,CAP).

This study clearly showed us, the proportion of CAP admissions were significantly lower than other studies done in this country and other African countries (19, 20). This shows us many things. First, in this study only patients with imaging confirmed cases were involved. Second, chart retrieving and documentation in our hospital was unacceptably poor (21). Third, even if CAP is still the cause of inpatient mortality according to FMOH, Ethiopia, cases might be managed at primary health care unit (22). CURB-65 severity score, even though very easy to use in our setting, it identified only 28 % of those admitted patients. It was calculated and some data were missing for blood urea nitrogen and correctly identified in 16% for complete data. This is explained by the young population with mean age of 42 years and at least one comorbid condition in all patients was not part of calculation (23).

This indicates that CURB-65 has limitation in Africa patients and difficult to generalize in this part of the region where the population pyramids showed younger one and few cross more than 65 year. Even though, 45% of the patients have associated pleural effusion, the mean duration of IV antibiotics was only 8 days. Probably this may be a reason for readmission of some of the patients. Further studies are needed to establish the duration of antibiotic therapy for adults with complications of CAP and adults with prolonged time to achieving clinical stability (25).

The hospital mortality rate of 14% found in this study was high compared to the 11% obtained in a study done at the same hospital, Ethiopia, 23 years ago (27). This is explained by the presence severe & multiple comorbidities. Compared to the same study (27), the comorbidity was much higher in this study (100% vs 38%). Again, this is explained by better inpatient care in this study. Thus, comorbidities were risk for disease acquisition and bad outcome (25).

In this study, there was a significant number of overlaps of CAP with Pulmonary TB which was identified and 16% of them started on anti-TB and 4% developed Pneumocystic pneumonia (PCP). In this part of the world, there is over lap of common lung infections (CAP, TB and PCP) up to 10%. This figure is high, probably mode of the patients were patients with chronic disease and at high risk to develop TB. (24)

Microbiologic diagnosis especially sputum culture was very low and bacteremic CAP not found. Even if doing sputum culture for CAP patient is not cost effective (25), in our setting it is quite worthy in two ways. First, the need to have national antimicrobiome (drug sensitivity patterns of common microorganisms) to facilitate appropriate drug selection, Second 7.8 % of patients were found to be smear positive pulmonary TB indicating similar clinical and radiological findings. It is clear that blood cultures should be obtained before antibiotic administration in all patients with CAP who are ill enough to be hospitalized and likelihood of having bacteremia. The IDSA and ATS have also recommended blood cultures for patients who are admitted to an ICU and have a cavitary lesion, leukopenia, active alcohol abuse, asplenia, a positive pneumococcal urinary antigen, or a pleural effusion (27). Furthermore, because the cause of pneumonia is not always found, assessment of clinical response to initial therapy is important, and blood cultures should be obtained in patients not responding to antibiotic therapy (28, 229).

The duration of antibiotics use was also prolonged as compared to the nation & international standards for CAP inpatient management and the antibiotic stewardship should be strengthen to prevent emergency of drug resistance (25).

Limitation

This study focused only on patients treated at one national specialized hospital, the Tikur Anbessa Specialized hospital located at the capital city of the country. The setups of the study hospital and the clinical status of patients treated at the study hospital might be different from patients with the same health problem but who were treated at other hospitals of Ethiopia. Moreover, data were collected from purposively selected patients treated for CAP which may limit generalizability of the result to the general population. Thus, the outcomes of this study may be generalized with caution.

Conclusion

The study revealed that there were many caveats in management of admitted CAP patients. Hence, having this as baseline data performing prospective multicentric longitudinal studies is recommended. The study also needs to look the clinical care from patient's perspective to make it complete.

ACKNOWLEDGEMENTS

We would like to thank the Department of Internal medicine, College of Health sciences, Addis Ababa University for giving me this opportunity and provide financial support to conduct this research.

We thank the NIHR Global Health Research Unit on Lung Health and TB in Africa at LSTM - "IMPALA" for helping to make this work possible.

In relation to IMPALA (grant number 16/136/35) specifically: IMPALA was commissioned by the National Institute of Health Research using Official Development Assistance (ODA) funding.

The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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Amsalu Bekel, Tewodros Haile, Amha Mekekasha, Oumer Fuad, Winters Muttamba, Levi Mugenyi, Wincey Katagira, George Nyale, Njira Lugogo, William Worodria, Hellen T. Aanyu, Moses Joloba, Corina de Jong, Fred Makumbi, Thys van der Molen, Jeremiah Chakaya,Bruce J Kirenga, Getenet Yimer. *Ethiop Med J, 2021, Vol. 59, No. 2*

ORIGINAL ARTICLE

CHARACTERIZATION OF ASTHMA AND ITS DETERMINANTS IN ETHIOPIA: PART OF THE AFRICAN SEVERE ASTHMA PROJECT

Amsalu Bekel MD[1], Tewodros Haile MD[1], Amha Mekekasha MD,MSC[1] Oumer Fuad MSC[1], Winters Muttamba MBChB, MPH[2], Levi Mugenyi PhD[2] Wincey Katagira MBChB, MMed[2], George Nyale MBChB, MMed[3], Njira Lugogo MD[4], William Worodria MBChB, MMed, PhD[5], Hellen T. Aanyu MBChB, MMed[5] Moses Joloba MBChB, MS, PhD[6], Corina de Jong PhD [7], Fred Makumbi PhD [8], Thys van der Molen MD, PhD[9], Jeremiah Chakaya MBChB, MMed[10], Bruce J Kirenga MBChB, MMed [2,11], Getenet Yimer MD,PhD[12]

ABSTRACT

Introduction: *Asthma is a major public health problem globally affecting 339 million people with 300,000 annual death. African Severe Asthma Program was a multi-country prospective cohort study designed to characterize severe asthma in three African countries, Ethiopia, Uganda and Kenya. In this study, we describe the baseline characteristics and disease severity among asthmatics enrolled in the Ethiopia site of African Severe Asthma Program.*

Methods: *Asthmatics seen at Tikur Anbessa Specialized Hospital from August 2016 to May 2018 were studied. Asthma was diagnosed based on symptoms and spirometry. Baseline demographic and clinical data were collected using a structured questionnaire. Standardized research tools were used to assess asthma severity, asthma control and asthma quality of life.*

Results: *A total of 419 asthmatic patients were enrolled in the study; the mean age for the group was 52 ± 8 years and 58.2 % were female. The majority of the participants, 365 (87.2%), had a prior diagnosis of asthma with a median (IQR) age at first diagnosis of 29 (IQR: 22 - 36) years. A family history of asthma was present in 149 (35.6%) subjects. Current or previous cigarette smoking was reported in 8.6% of the participants. Overall, 93.8% of the participants reported uncontrolled asthma symptoms (ACQ >1.5). More than half of the patients, had severe persistent asthma and 35% presented with one or more comorbidities.*

Conclusions*: In Ethiopia, asthmatics presenting to a tertiary care hospital were characterized as predominantly female with late onset disease, poor control, and associated comorbidities.*

Key Words: *Asthma, Characteristics, determinants and Severe*

INTRODUCTION

Asthma is a common chronic disease that is estimated to affect as many as 339 million people worldwide and cause over 300,000 deaths each year(1). In addition, according to the 2015 Global Burden of Diseases Report on Asthma, 22 million disability-adjusted life years (DALYs) are annually lost to asthma (2). In Africa, the prevalence of asthma is approximately 119 million or 13.8% of the population. The rates are higher in urban compared to rural areas and are increasing over time (3), possibly reflecting greater exposure to environmental risk factors, increased cigarette smoking, and a more westernized affluent lifestyle (4-8)

Globally, 5-10% of patients have severe disease (9-11). However, control of asthma (usually defined as minimal or no symptoms, normal activities and sleep, and optimal pulmonary function) may be achieved in the majority of patients (12-14).

Lack of asthma control may be due to a number of factors including an incorrect diagnosis, under treatment, ongoing exposure to sensitizing agents, and an unresponsive underlying inflammatory process (15-18).

Finally, various comorbid conditions are increasingly recognized as frequent contributors to uncontrolled asthma. The identification of comorbidities is now recognized as an integral part of the core management of asthma (15, 16).

In Ethiopia, 2.5 million adults and children (2.3% of the population) have asthma (19) and an increasing prevalence of disease has resulted in significant public health challenges (20-22). Little is still known about the characteristics of these asthmatics and the control and severity of their asthma, which is information important to lessen the country's burden of disease.

[1]Addis Ababa University, College of Health Sciences, Addis Ababa, Ethiopia. [2]Makerere University Lung Institute, Kampala Uganda. [3]Kenyatta National Hospital, Nairobi Kenya. [4]Department of Internal Medicine, Michigan Medicine, University of Michigan. [5]Mulago Hospital, Kampala Uganda. [6]Department of Medical Microbiology, Makerere University, Kampala Uganda. [8]School of Public Health, Makerere University, Kampala Uganda, [9]GRIAC-Primary Care, department of General Practice and Elderly Care, University of Groningen, University Medical Center Groningen (UMCG), The Netherlands. [10]Kenya association of Physicians against TB and Lung Diseases (KAPTLD), Nairobi Kenya. [11]Department of Medicine, Makerere University, Kampala Uganda. [12]Global One Health initiative, Office of International Affairs, The Ohio State University, Addis Ababa, Ethiopia .

*Corresponding Author E-mail: amsalubekele2016@gmail.com

This study was undertaken to describe the baseline characteristics, disease control, and severity among asthmatics enrolled in the Ethiopian site of the African Severe Asthma Program (ASAP), a multi-country prospective cohort study designed to characterize severe asthma in three African countries, Ethiopia, Uganda and Kenya.

METHODS

Study design and setting: This study was a prospective observational cohort study designed to investigate the prevalence, determinants, and impact of severe asthma in Ethiopia as part of ASAP (23). All enrolled asthmatics were recruited from chest clinic of Tikur Anbessa Specialized Hospital (TASH), the largest public tertiary medical center in Ethiopia.

Study participants:
Asthmatics were required to have at least one of the following: 1) more than one characteristic respiratory symptom, 2) physician diagnosed asthma, 3) use of asthma medications with improvement in symptoms, 4) history of wheezing in the past 12 months, and 5) pre-bronchodilator Forced Expiratory Volume in One second (FEV_1) ratio <0.70% and bronchodilator reversibility ≥12% and ≥200 mL (3). The diagnosis of asthma was confirmed by an expert pulmonologist. All asthmatics presenting to TASH over the age of 12 years were recruited. Subjects were excluded for the following reasons: 1).

contra-indications to spirometry testing, 2) a known diagnosis of an alternative lung disease (e.g. chronic obstructive pulmonary disease (COPD), bronchiectasis, pulmonary fibrosis and tuberculosis (TB), 3) age over 70 years, 4) pregnancy determined by self-reported last menstrual period, and fixed airflow obstruction on spirometry as defined as post-bronchodilator FEV_1/FVC ratio <0.70. Eligible patients were consecutively enrolled until the sample size was attained. Subjects were seen monthly for the first six months and then at 9 and 12 months. GINA based stepwise therapy was utilized to adjust treatment; all asthma medications were provided by the project. The study enrolled participants from August 2016 to May 2018.

Questionnaires: All eligible patients who provided written informed consent underwent a respiratory focused clinical evaluation using a pre-developed case report form (CRF) to collect data on socio-demographics, respiratory symptoms, vital signs, respiratory system signs, exposures to indoor and outdoor pollutants, known asthma triggers, tobacco smoking, psychosocial issues, and comorbidities (allergies, GERD). Asthma control was assessed using the Asthma Control Questionnaire (ACQ) (24), while the National Heart, Lung and Blood Institute (NHLBI) Expert Panel Report (EPR3) guidelines (25), were used for asthma severity grading.

Depression was assessed and graded using the Patient Health Questinnaire-9 PHQ-9) (26) and quality of life was assessed using the Asthma Quality of Life Questionnaire (AQoL) (27). We also assessed work and activity impairment with the Work Productivity and Activity Impairment Due to Asthma tool (WPAI: asthma) (28).

Spirometry: Spirometry was performed according to American Thoracic Society/European Respiratory Society(ATS/ERS)guidelines (29) using a Pneumotrac® spirometer with Spirotrac® V software (Vitalograph Ltd., Buckingham, United Kingdom). To achieve uniformity, we used the National Health and Nutrition Examination Survey (NHANES) references values for %predicted FEV_1 and %predicted FVC as there are no appropriate African reference values to date (30). Pre- and post-bronchodilator spirometry was performed for only those with FEV_1 ratio <0.70. We used 4 doses of inhaled salbutamol (400mcg) separated by one minute and repeated spirometry after 15 minutes.

Skin prick test (SPT): SPT was performed by trained nurse and interpreted according to published international guidelines (31). Common aero- and food allergens were preselected based on their published occurrence in African settings and included; house dust mite mix, soy bean, Blomia Tropicalis, Bermuda Grass(Cynodon Dactylon), Mold Mix IV, Aspergillus Fumigatus, dog epithelia (Canis Fam), cat epithelia (Felis Domesticus), German cockroach (Blat Germ), egg white, cow milk, and peanut (Arachys Hypogaea)(32).

Definitions
Uncontrolled asthma was defined as an ACQ score of ≥1.5 (24). Asthma exacerbation was defined according to the ATS/ERS definition as "events characterized by a change from the patient's previous status" (33). We considered only exacerbations that required a patient to either visit a health facility or to be hospitalized (i.e. moderate to severe exacerbations) as recommended by the ATS/ERS guidelines (33,34). Allergic sensitization was defined as having at least one positive allergen on the ASAP allergen panel of 12 allergens as previously defined in other studies (35) Depression was graded by the PHQ-9 Questionnaire as follows: 0-4 none, 5-9 mild, 10-14 moderate, 15-19 moderately severe, 20-27 severe (26). Moderate to severe depression included everyone with scores ≥10.

Statistical analysis
Descriptive statistics were used to summarize enrolled patients' characteristics. For categorical variables, we present frequencies and percentages. For continuous variables, median and the interquartile ranges are presented. All analyses were done using STATA version 14 software

Ethical considerations

Ethics approval was obtained from College of Health Sciences Institutional review board (IRB) at Addis Ababa University, Ethiopia. All patients provided a written informed consent. Patients below 18 years provided assent while their parents/legal guardians gave written consent.

RESULTS

There were a total of 419 asthmatics enrolled in the study. Socio-demographic characteristics are shown in Table 1. The mean ± SD age for the group was 52 ± 8 years with a range of 15-70 years. Subjects 55-64 years of age (28.2%) were most affected followed by those 45-54 years, 26.3%; the least affected age group included participants less than 25 years of age, 4.1%.

The majority of subjects were female 244 (58.2%). Most were married 280 (66.9%) with 56 (13.4%) widowed and 42 (10.1%) single. The majority, 365 (87.2%) had a prior diagnosis of asthma with the median (IQR) age at first asthma diagnosis being 29(22-36) years. A family history of asthma was present in 149 (35.6%) of subjects.

Current and previous history of smoking was reported by 36 (8.6%) participants and secondhand smoking was reported by 23 (5.5%) subjects. A majority of study participants 304 (72.6%) had a history of biomass exposure.

Table 1: Socio-demographic characteristics of study participants, Tikur Anbessa Specialized Hospital, 2016-18

Socio-demographic Characteristics	Frequency (%)
Age in Year	
<15	6 (1.4)
15-24	11 (2.6)
25-34	31 (7.4)
35-44	70 (16.7)
45-54	110 (26.3)
55-64	118 (28.2)
65+	73 (17.4)
Mean Age	52 Years
Median age of onset of asthma(IQR)	29(22 - 36) years
Gender	
Male	175 (41.8)
Female	244 (58.2%)
Marital status	
Single	42 (10.1)
Married	279 (66.91)
Divorced	32 (7.8)
Widowed	56 (13.4)
Family History of Asthma	
Yes	149(35.6)
No	255(61.0)
I don't know	14(3.4)
Smoking History	
Current /Former smoker	36(8.6%)
Second hand smoke	23(5.5)
Never Smoked	381(91.4)
Biomass Exposure history	
Yes	304(72.6)
No	115(27.5)

The majority of the patients 243 (58.0%) had severe persistent asthma; 134 (32.0%) had moderate persistent asthma, 36 (0.6%) had mild persistent asthma, and 5 (1.2%) had mild intermittent asthma (Figure 1). Approximately 90% of study subjects had moderate to severe asthma. The most common respiratory symptoms were cough (189, 45.1%) and wheeze (158, 37.7%). On average, study participants used systemic steroids for asthma control three times per year and had at least one yearly exacerbation and emergency room visit. A large number of asthmatics, 196 (47.0%), had three or more exacerbations in one year; a smaller number, 103 (24.6%), had at least one hospital admission per year.

The number of asthma exacerbation was greater in the uncontrolled group than the controlled asthma group (P=0.007). Overall, 93.8% of the cohort reported uncontrolled asthma symptoms (ACQ >1.5) on study entry. Self-report of medication adherence was high in 67.7% of study participants, medium in 17.2%, and low in 15.1%. Despite this high adherence, 90 % of subjects had moderate to severe asthma. Allergy testing using skin prick was positive in only 19(6.9%) of the participants.

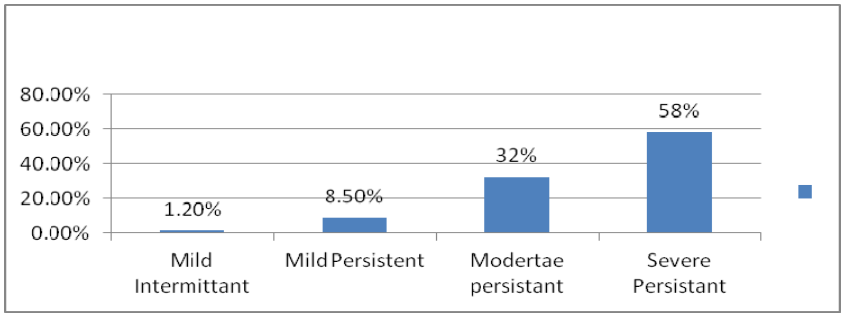

Figure 1: Asthma classification based on severity among study participants, Tikur Anbessa Specialized Hospital, 2016-18.

Medication use is shown in Table 2. Salbutamol MDI was the most common medication used (56.6%) followed by theophylline/aminophylline tablets (23.2%), oral steroids (22.7%), injectable steroids (13.4%), inhaled corticosteroid/long-acting beta agonist combination MDI (12.2%), inhaled steroid alone (Beclomethasone) (12.2%), Salbutamol tablets/syrup (11%).

A small number of subjects, 46 (11%) were not using any asthma medication despite their diagnosis. Poor asthma control was associated with use of salbutamol in any form (P=0.048) and use of theophylline as a controller medication (P=0.01).

Table 2: Asthma medications use among study participants, Tikur Anbessa Specialized Hospital, 2016-18

Medication use	**Frequency (%)**	
Currently on the following medications:	N = 419	100%
Salbutamol tabs/syrup	46	11.0
Salbutamol inhaler	237	56.6
Theophylline/Aminophylline tablets	97	23.2
Theophylline /Aminophylline injections	30	7.2
Nebulized salbutamol	2	0.5
Nebulized salbutamol/ipratropium	3	0.7
Nebulized steroid	2	0.5
Oral steroids such as prednisolone, dexamethasone	95	22.7
Injectable steroids such as hydrocortisone, dexamethasone	7	1.7
Inhaled steroids such as beclomethasone inhaler	51	12.2
Combination inhalers (steroids and long acting beta agonists)	56	13.4
Combination inhaler(salbutamol/ipratropium)	1	0.2
Leukotriene modifiers such as montelukast and zafirlukast	1	0.2
On systemic steroids (Oral & injectable steroids)	95	22.7
Not taking any asthma medication	46	11.0

Common asthma triggers are shown in Figure 2. Cold weather (88.1%), dust (86.6%), upper respiratory infections (82%), and strong smells and perfumes (70%) were the most frequently reported triggers. Exercise (59%), emotional situations (45.6%), cigarette smoke exposure (43%) and household pets were less often reported as triggers (3.34%)

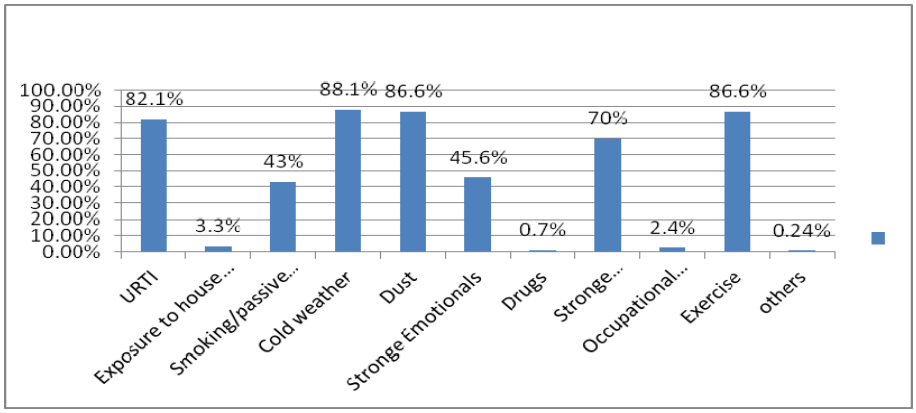

Figure 2: Reported common asthma triggers among study participants, Tikur Anbessa Specialized Hospital, 2016-18

A total of 147 (35%) of subjects had at least one comorbidity (Figure 3). Depression (86%) was the most common finding; minimal, mild, and moderate/severe depression were seen in 62.5%, 17%, and 4% subjects, respectively. Other less common comorbidities included: Hypertension (36%), obesity (10.7%), GERD (7.6%), rhinosinusitis (4.1%), and eczema/dermatitis (4.1%). The assessment of quality of life based on quality of life using Asthma Quality of Life Questionnaire (AQoL) was poor in uncontrolled asthma than controlled Asthma (P=0-000)

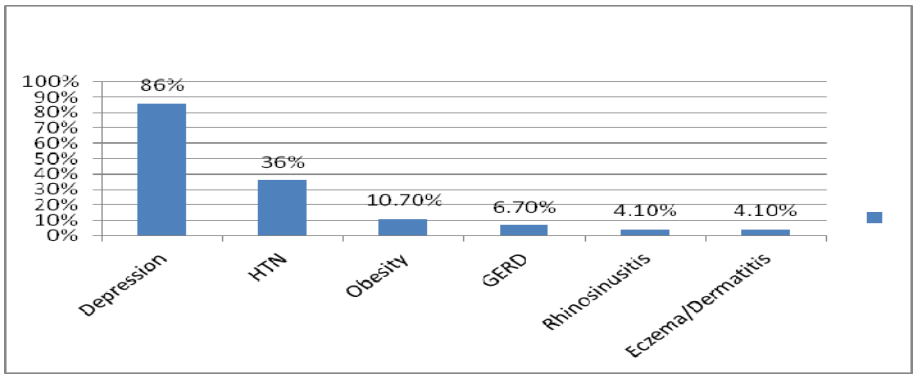

Figure 3: Comorbidities among study participants, Tikur Anbessa Specialized Hospital, 2016-18.

DISCUSSION

This study is the largest comprehensive evaluation of the characteristics of asthmatics living in Ethiopia. Spirometry was performed on all subjects and the diagnosis of asthma was confirmed using strict criteria. Many of our results are in concert with other published research. We found a predominance of older female asthmatics with late onset disease and infrequent atopy, as measured by skin prick testing. This can be explained by improved life expectancy, urbanization, increases rate of obesity and increased rate of air pollution in our population (34, 37) Studies from the United States and Europe have found similar findings; adult-onset asthma and adult-onset phenotypes were associated with factors such as female gender, obesity, occupational exposure, rhinitis, respiratory infections, smoking, stressful life events, and low level of lung function (38-41).

Asthmatics in this study appear to have more severe disease than reported in other studies from high resource countries (42-44).

A majority of the study patients (90%) had moderate to severe asthma and reported frequent respiratory symptoms, asthma exacerbations, use of systemic steroids, and hospital admissions.

In addition, 393 (93.8%) of the group reported uncontrolled asthma symptoms (ACQ >1) despite reporting high medication adherence. The number of asthma exacerbation was more in uncontrolled group than controlled asthma group (P=0.007). The percent of uncontrolled asthma was higher than in studies from high resources countries (45, 46) but in keeping with other research done in Africa (47-54-) and a smaller study done in Ethiopia (55).

This is also reflected by poor quality of life based on quality of life assessment using Asthma Quality of Life Questionnaire (AQoL) (P=0.000) Several factors may explain the observed disease severity and poor asthma control. In our study, short acting beta agonists served as the mainstay of treatment; only 25% were on proper controller medications. Poor asthma control was associated with use of salbutamol of any form and use of theophylline as a controller medication.

Previous studies done in Ethiopia found that the cost of inhaled corticosteroids and limited access to this class of medications played a critical role in undertreatment of asthma; our findings are in concert with those results (56-58). Also, improper inhaler technique, fear of inhaler use, and physician fear of unaffordability of inhaled ICS to prescribe for their patients may have also contributed to the observed poor asthma control (55-60). In addition, many of our asthmatics came to medical attention at a later stage of disease which reflects the health seeking behavior of the population in Ethiopia (61, 62). Development of national guidelines, additional education of patients and physicians on asthma and its proper management, and the availability and affordability of controller medications are necessary if asthma control is to improve in Ethiopia.

The prevalence of comorbidities in those with severe asthma was high in our study, as in others (63-65) and may also help explain the severity of disease seen. However, a more unique observation was the high rate of depression in our analysis, possibly reflecting impaired quality of life due to poor asthma control. Further investigations are needed to confirm this finding.

Unlike other studies, a history of rhinosinusitis and eczema was very low likely reflecting the infrequent presence of atopic asthma.

Conclusions

In Ethiopia, asthmatics presenting to a tertiary care hospital are characterized as predominantly female with late onset disease, a strong family history, minimal atopy, and limited exposure to cigarette smoke. In addition, there is a high percent of uncontrolled, moderate/severe disease associated with one or more comorbidities. Development of national guidelines, patient and physician education on asthma and its management, and increased availability and affordability of controller medications are urgently needed.

ACKNOWLEDGEMENTS

We are grateful to the patients who participated in African Severe Asthma Project (ASAP) study in Ethiopian. We would like to thank Tikur Anbessa Specialized Hospital, Addis Ababa University for allowing us to use the premises for the study. We would like to thank the study team and spirometry technicians for their hard work in data collection and pre and post lung function measurements. Last but not least we thank our funder, GSK Africa NCD Open Lab for sponsoring this project

Funding:

Funding was provided by GSK Africa NCD Open Lab.

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Gizachew Tadele Tiruneh, Tesega Mengistu Birhanu, Abdurahaman Seid, Mahteme Haile Workneh, Dareskedar Getie, Tenagnework Antefe Abebe, Ambanesh Necho Mulat, Taye Zeru Tadege, Bekele Belayhun, Gashaw Andargie, Kassahun Alemu Gelaye, Tadesse Awoke Ayele. *Ethiop Med J, 2021, Vol. 59, No. 2*

SYSTEMATIC REVIEW

NEONATAL MORTALITY IN NEONATAL INTENSIVE CARE UNIT HOSPITALS IN ETHIOPIA REMAINS HIGH: A SYSTEMATIC REVIEW AND META-ANALYSIS

Gizachew Tadele Tiruneh, MPH[1]*, Tesega Mengistu Birhanu, MPH[2], Abdurahaman Seid, MSc[3], Mahteme Haile Workneh, PhD[2], Dareskedar Getie, MPH[2], Tenagnework Antefe Abebe, MPH[2], Ambanesh Necho Mulat, MPH[4], Taye Zeru Tadege, MPH[2], Bekele Belayhun, PhD[5], Gashaw Andargie, PhD[6], Kassahun Alemu Gelaye, PhD[6], Tadesse Awoke Ayele, PhD[6]

ABSTRACT

Introduction : *In Ethiopia, the neonatal mortality rate has not shown significant changes over time and is among the world's highest. This review aimed to explore the pooled magnitude and determinates of neonatal mortality in neonatal intensive care unit hospitals in Ethiopia.*

Methods: *The research team retrieved global peer-reviewed journal articles available as electronic databases including PubMed, Popline, and Scopus databases. Random-effects meta-analysis model was used to pool the estimates of the magnitude of mortality among studies. The results were presented as the pooled estimates (odds ratio and proportion) with 95% confidence intervals, at less than 0.05 significant levels.*

Results: *In this review, ten studies were included with a total of 8,729 neonates. Of these, 1,779 (20.4%) neonates died in the neonatal intensive care unit. The pooled neonatal mortality rate was 19.0% (95% CI: 14.0-25.0). The neonatal mortality is three times higher among early age (OR: 2.80; 95% CI: 1.45-5.40) and preterm newborns (OR: 3.27; 95% CI: 2.12-5.07) than their counterparts. Early age of the newborn, prematurity, low birth weight, perinatal asphyxia, mode of delivery, hypothermia, late initiation of breastfeeding, and having antenatal care visits were the main determinants for neonatal mortality.*

Conclusion: *Neonatal mortality in the intensive care unit is high. It is unacceptably high amongst early and preterm neonates. Special care for preterm and early age newborns, timely initiation of breastfeeding, exclusive breastfeeding, and appropriate mode of delivery, essential obstetric and newborn care, and promoting antenatal visits are recommended to reduce neonatal mortality.*

Keywords: *neonatal mortality, neonatal intensive care unit, Ethiopia, determinants, risk factors,*

INTRODUCTION

The neonatal mortality rate (NMR) in sub-Saharan Africa is 29 per 1,000 live births accounting for 36 % of under-five mortalities with a slow decline over the past 25 years (i.e., 1990-2015). (1) In Ethiopia, neonatal mortality has declined from 61 to 28 deaths per 1,000 live births during the same period. (2, 3) Despite progress, the NMR is high and far from the sustainable development global targets to reduce NMR to 12 per 1,000 live births by 2030. (4, 5)

Until the 2010-2015 National Fourth Health Sector Development Plan, newborns received very little programmatic attention from Ethiopia's health system. Since then, newborn health is now one of the country's priorities. The country developed different strategies and programs to address newborn survival at health facility and community level, including integrated management of the neonatal and childhood illness, community-based neonatal care, newborn corner initiative, and neonatal intensive care unit (NICU). (6) Besides the national efforts of expanding NICU to improve newborn's survival in recent years, neonatal mortality is still persistently high with no significant change over the last decade. (7-9).

Evaluating the causes of neonatal morbidity and mortality is an essential step toward improving the quality of existing practices. Therefore, this study systematically evaluated the factors of neonatal mortality and pooled the magnitude of mortality in the NICU hospitals in Ethiopia.

METHODS

Inclusion and exclusion criteria

Observational studies, including cross-sectional, case-control/case-referent, cohort, case-cohort designs, reported at least one component of factors

[1]JSI Research & Training Institute, Inc./ The Last Ten Kilometers (L10K) Project, Addis Ababa, Ethiopia. [2]Amhara public health institute, Bahir Dar, Ethiopia . [3]Wollo University School of Public Health, Dessie, Ethiopia. [4]UNICEF, Bahir Dar, Ethiopia. [5]USAID Transform: Primary Health Care Project, Pathfinder International Ethiopia . [6]Institute of Public Health, College of Health Sciences, University of Gondar, Gondar, Ethiopia.
*Corresponding Author E-mail: gizt121@gmail.com

that affect neonatal mortality or magnitude of mortality and published in the English language since 2012, where the country plans to expand NICU in the hospitals, were included.

Commentaries, letters, duplicate studies, editorials, and studies written by different languages other than English were excluded from the review.

Search strategy

The research team systematically examined global peer-reviewed journal articles available as electronic databases, including PubMed, Popline, and Scopus databases. Search terms were identified as Condition, Context, Population, and Exposure themes and used in a variety of combinations for neonatal mortality, infant mortality, hospital, and determinant, associated, or risk factors, and Ethiopia. A search strategy presented as supplemental material.

Study selection procedure

The search returned 283 records after removing duplicates. The review authors independently screened the titles and abstracts yielded by the search against the inclusion criteria. Accordingly, 28 full articles were screened reading titles and abstracts. The final synthesis included ten papers (Figure 1).

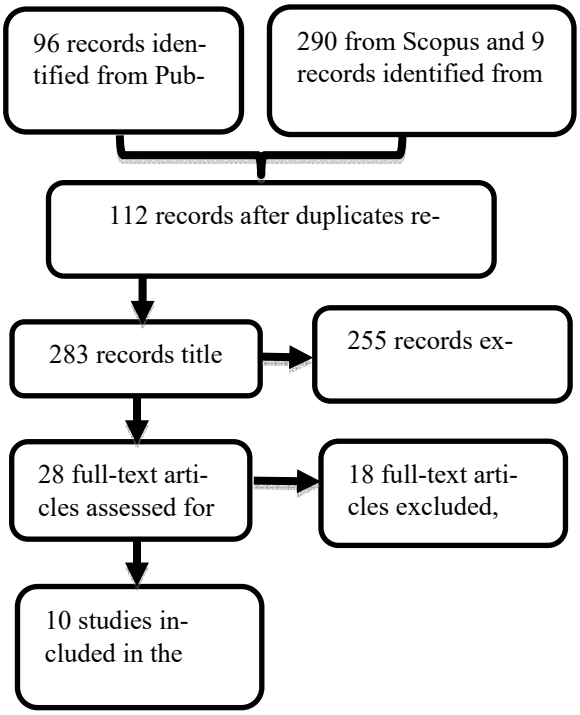


Figure 1: Study flow diagram

Critical appraisal

Authors independently reviewed each included study's methodological quality using the Joanna Briggs Institute (JBI) critical appraisal checklists for different study designs as appropriate. (10-12) To obtain an overall quality score, publications scored "1" point for each item fully met and "0" for none or very little information reported. Studies that scored 75% or more were categorized as high quality, scores in the range of 50-74% were ranked as a medium, and scores less than 50% were rated as poor. According to the JBI quality appraisal tool, six of the cohort studies scored high quality (81%). Likewise, the seven cross-sectional studies scored medium quality (72%) in which most studies lacked strategies to deal with confounding.

The standard review protocol, Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA) checklist, was followed to establish minimum information that should be included when reviewing and reporting. (13) Moreover, the protocol was registered at the International prospective register of systematic reviews (PROSPERO) with registration number CRD42019123195.

Data synthesis

A narrative synthesis was used to analyze and interpret the findings. A random-effects meta-analysis model was used to pool the estimates of the magnitude of mortality and determinant factors accounting for the variability among studies using Stata v15. (14) The results were presented as the pooled estimates (odds ratio (OR) and proportion) with 95% confidence intervals (CI), at less than 0.05 significant levels, and the estimates of Tau^2 and I^2 statistic for heterogeneity. We also investigated the presence of publication and other bias in the extracted data using a funnel plot and Stata's "*metabias*" command. (14, 15).

Assessment of heterogeneity

The *P*-value of the Chi-squared test of heterogeneity and the I^2 and Tau^2 statistics were examined for heterogeneity between the studies. We did a subgroup analysis to examine the pooled magnitude of mortality varied by administrative region, age of the neonate at admission, and gestational age at birth.

Moreover, sensitivity analysis was conducted to examine the effect of studies that are exclusively reported of the magnitude of mortality on early neonates, preterm and studies with a large sample.

RESULTS

Description of studies

Ten articles were included: four in Amhara, two in Addis Ababa, two in Oromia, one in Southern Nations, Nationalities, and Peoples' (SNNP), and one in the Somali region.

All studies were published from 2012 to 2019. Six of the studies identified employed hospital-based cohort designs; (16-21) the remaining four applied cross-sectional designs (22, 23) (Table 1).

Table 1: Characteristics of included studies

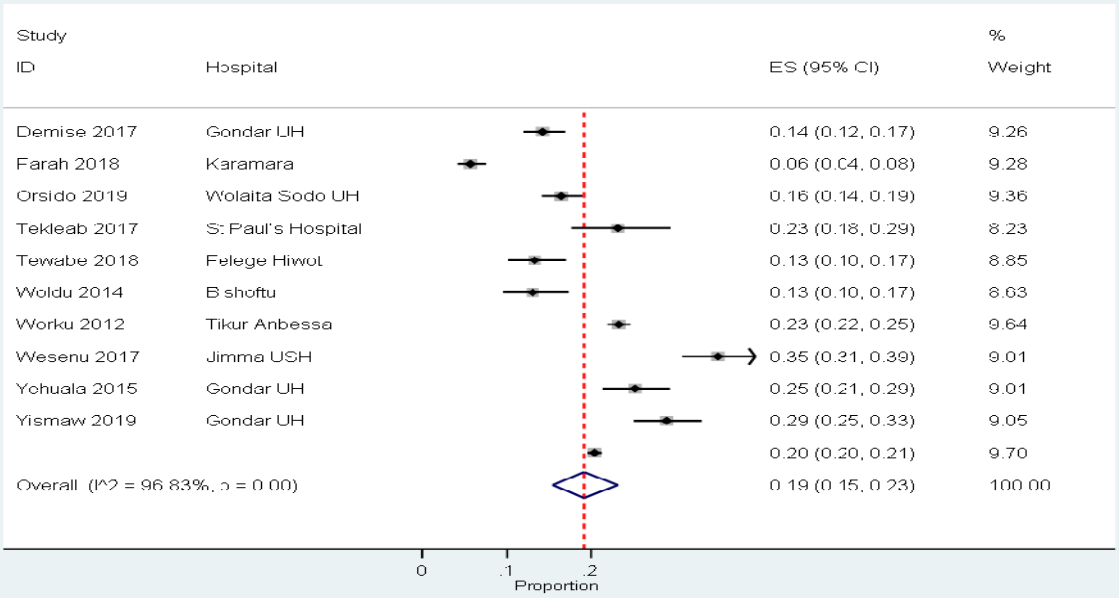
Study ID	Design	Objective	Region	Hospital	NICU capacity	Age of neonate	# of newborn deaths	Sample size	NMR (%)
Demise 2017	Cross-sectional	Identify the patterns of neonatal admission and factors associated with mortality	Amhara	Gondar University Hospital	A 32-beds NICU with 4 separate rooms (1 room for each of preterm babies, term babies, isolation room for communicable diseases, and for those who need KMC). It was staffed with 7 medical interns, 2 pediatric residents, 1 pediatrician, and 17 nurses	<28 days	110	769	14.3
Farah 2018	Retrospective cohort	Examine the trends of admission, specific causes and rate of neonatal mortality as well as predictors of neonatal mortality	Somali	Karamara General Hospital	A fully-functional 12-beds NICU that has 3 rooms (1 room for intensive care, 1 for kangaroo mother care, and another for septic neonates)	<28 days	45	792	5.7
Orsido 2019	Retrospective cohort	Describe the reasons for admission and the magnitude of mortality	SNNP	Wolaita Sodo University Hospital	A 20-beds NICU	<28 days	159	964	16.5
Tekleab 2017	Cross-sectional	Describe the reasons for admission and the magnitude of neonatal mortality	Addis Ababa	St Paul's Hospital Millennium Medical College	A fully-functional NICU providing services for 24-hours a day and nurses, intern doctors, pediatric resident doctors, and pediatricians were working in the unit.	<28 days	50	216	23.2
Tewabe 2018	Cross-sectional	Assess neonatal mortality rate	Amhara	Felege Hiwot General Hospital	The neonatal unit had 60 beds and staffed with 5 pediatricians and 20 nurses. About 6,300 neonates were seen annually	<28 days	52	391	13.3
Woldu 2014	Cross-sectional	Examine the risk factors, antimicrobial use pattern and clinical outcomes of neonatal sepsis	Oromia	Bishoftu General Hospital	NICU had 16 beds and staffed with 2 physicians, 3 nurses, and 2 cleaners. More than 1,000 of neonates admitted at NICUs annually	<28 days	40	306	13.1
Worku 2012	Prospective cohort	Assess the independent predictors of early neonatal mortality	Addis Ababa	Tikur Anbessa Specialized Hospital	It had 50 beds and it is the largest ICU in the country with a very high patient admission	<7 days	881	3789	23.3
Wesenu 2017	Retrospective cohort	Model survival probability of premature infants and identify risk factors	Oromia	Jimma University Specialized Hospital	No data Same as "Demise 2017"	<28 days & preterm	171	490	34.9
Yehuala 2015	Retrospective cohort	Compared survival of premature infants using the Cox proportional hazard model and the semi-parametric gamma frailty model and examine the risk factors of death	Amhara	Gondar University Hospital	Same as "Demise 2017"	<28 days & preterm	122	485	25.2
Yismaw 2019	Retrospective cohort	Assess time to death and predictors among preterm neonates	Amhara	Gondar University Hospital	The neonatology department had 1:5 nurse-patient and 1:10 physician-patient ratio for 24 h and seven days with 40 neonatal beds providing an outpatient and inpatient medical service for neonates	<28 days & preterm	149	516	28.9

The capacity of NICU in terms of bed-size and staffing varied from hospital to hospital. It ranged from16-beds NICU (24) to 50-beds NICU (18), and some hospitals had comprehensive neonatal care that included intensive care, kangaroo mother care (KMC), and isolation rooms. (16, 18-20, 22) It was staffed with medical interns, pediatric residents, physicians, and nurses.

Magnitude of neonatal mortality

In this review, ten studies involving 8,718 neonates with 1,779 (20.4%) neonatal deaths were included. As presented in Figure 2 below, the random effects pooled analysis showed that the neonatal mortality rate is 19.0% (95% CI:15.0-23.0).

Figure 2: Magnitude of Neonatal Mortality in Neonatal Intensive Care Unit



Sensitivity analysis

We conducted three different analyses by excluding studies on early neonates which is also a large sample, (18) on preterm, (19-21), and both preterm and early neonates. (18-21) Following the removal of a study on the early neonate, the overall pooled estimate was not changed. On the other hand, excluding studies on preterm neonates, the pooled estimate was decreased to 15% (95% CI: 0.10-0.21) without lowering heterogeneity between studies, and excluding both studies on preterm and early neonate, the NMR decreased to 14% (95% CI: 0.09-0.19) with reduced heterogeneity. As a result, we conducted a sub-group analysis for preterm and early neonates to compare the magnitude of mortality with their counterparts.

Sub-group analysis

Three different subgroup analyses were conducted to investigate whether the observed magnitude of mortality is consistent across regions, preterm and term neonates, early and late neonates.

Mortality by region

The subgroup analysis showed that NMR is significantly higher in Oromia than in other regions; likewise, NMR is significantly lower in other regions category (SNNP and Somali) (Table 2).

Preterm mortality

Six studies (16-18, 22, 23, 25) reported neonatal mortality disaggregated by gestational age, and the other three studies (19-21) were conducted among preterm neonates. Accordingly, mortality rates were compared among preterm and term/post-term neonates.

The pooled mortality by gestational age at birth indicated that preterm neonates had three times (OR: 3.27; 95% CI: 2.12-5.07) higher odds of death as compared to term and post-term neonates (Table 2).

Early neonatal mortality

One study (18) was conducted among early neonates. The other three studies (16, 17, 23) reported neonatal mortality disaggregated by neonatal age. We compared the neonatal mortality rate by age of the newborn at admission. As such, neonatal mortality is about three times (OR: 2.80; 95% CI: 1.45-5.40) higher among early age newborns than late age neonates (Table 2).

Table 2: Subgroup analysis for neonatal mortality by region, neonatal age, and gestational age

Predictor variables	# of studies	Random-effects model		Fixed-effects model		Test for heterogeneity		p-value for subgroup heterogeneity
		%	95% CI	%	95% CI	I2 (%)	p-value	
Overall	10	0.19	0.15-0.23	0.20	0.19-0.21	96.8	<0.01	NA
Region								
Amhara	4	0.20	0.13-0.28	0.20	0.18-0.21	97.1	<0.01	<0.01
Addis Ababa	2	0.23	0.22-0.25	0.23	0.22-0.25	.	.	
Oromia	2	0.26	0.23-0.29	0.26	0.23-0.29	.	.	
Other regions	2	0.11	0.10-0.13	0.11	0.10-0.13	.	.	
Gestational age								
Preterm	9	0.28	0.18-0.39	0.25	0.24-0.26	98.3	<0.01	<0.01
Term & post-term	6	0.09	0.06-0.13	0.11	0.10-0.12	91.6	<0.01	
Age of neonate								
Early	3	0.16	0.08-0.27	0.20	0.19-0.21	98.3	<0.01	<0.01
Late	4	0.06	0.05-0.09	0.06	0.05-0.09	.	.	

Determinants of neonatal mortality

In this review, many factors that could have influenced neonatal mortality were identified. As presented in Table 3, newborn age, gestational age, birth weight, perinatal asphyxia (PNA), mode of delivery, hypothermia, breastfeeding, and antenatal care (ANC) visit are the main determinants pooled from the studies.

Age of neonate: Early age of the newborn was significantly associated with neonatal mortality in three studies. (16, 17, 23)

Gestational age: Six studies, two studies among preterm neonates (19, 21), and four among all neonates (16, 18, 23, 25) reported gestational age as an independent predictor of neonatal mortality.

Perinatal Asphyxia: Four studies identified PNA as 2.51 times higher than neonates with no PNA (OR: 2.51; 95% CI: 1.85-3.40). Moreover, Demise et al. (22) report respiratory distress had 12.97 times higher odds of death (95% CI:5.37,31.30); Worku et al. (18) present a first minute APGAR of 3 or less was independently associated with NMR. Neonates who were resuscitated had two times higher risk of death than neonates who were not resuscitated (AHR: 2.28; 95% CI:1.54–3.38).

Mode of delivery: Demise et al (22) reports instrumental delivery increased risk of neonatal mortality as compared with vaginal delivery (AOR: 2.99; 95% CI: 1.08–8.31); while the same study presents cesarean delivery had 87% higher odds of death than normal deliveries but not statistically significant (AOR: 0.87; 95% CI: 0.46-1.64).

On the other hand, Orsido et al. (17) reported cesarean delivery had a 66% lower risk of death as compared with vaginal delivery (AHR:0.34; 95% CI:0.19–0.61).

Breastfeeding

A study by Orsido et al. (17) reports that neonates who were not breastfed within one hour of birth had a 2.6 times higher risk of death than their counterparts (AHR:2.62; 95% CI:1.60–4.30). Tewabe et al. (23) also identified late breastfeeding initiation and non-exclusive breastfeeding as independent neonatal mortality predictors.

Determinants of preterm mortality

Three studies reported determinants of preterm mortality among neonates admitted at NICU. (19-21) The leading causes of death were PNA, (19-21) hyaline membrane disease (HMD), (19, 21), and respiratory distress syndrome (RDS). (20, 21) Perinatal asphyxia (19-21) HMD, (19, 21) and RDS (20, 21), and prematurity (19, 21) were identified as the most determinant and statistically associated with the death of premature infants admitted to NICU (Table 4).

Table 3: Determinant factors for neonatal mortality among neonates admitted at NICU

Domain	Determinants	n	(%)	Measure	AOR/ AHR	95% CI		P-value	Study ID
Mode of delivery	Instrumental delivery	8	21.6	OR	2.99	1.07	8.31	<0.05	Demise 2017
	CS delivery	13	6.5	HR	0.34	0.19	0.61	<0.001	Orsido 2019
Hypothermia	Severe hypothermia	5	71.2	OR	10.45	1.04	104.7	<0.05	Demise 2017
	Temperature of neonate at admission (<35.5)	110	34.1	HR	1.58	1.06	2.34	<0.05	Orsido 2019
Sepsis	Early onset of neonatal sepsis	88	19.2	OR	2.66	1.16	6.11	<0.05	Demise 2017
	Late onset of neonatal sepsis	11	17.2	OR	13.51	2.64	69	<0.05	Demise 2017
Asphyxia	PNA (Yes)	33	34.4	OR	5.97	3.06	11.64	<0.05	Demise 2017
	PNA (Yes)	58	22.9	HR	1.81	1.24	2.63	<0.05	Orsido 2019
	PNA (Yes)	14	40.0	OR	5.817	1.61	21	<0.05	Tekleab 2017
	PNA (Yes)	174	30.6	OR	1.82	1.32	2.51	<0.001	Worku 2012
Respiratory Distress Syndrome (RDS)	RDS (Yes)	43	51.2	OR	12.97	5.37	31.3	<0.05	Demise 2017
Resuscitation	Neonate resuscitated (Yes)	122	27.2	HR	2.28	1.06	2.34	<0.05	Orsido 2019
APGAR score	APGAR score at 1st min (<=3)	185	39.7	OR	2.12	1.39	2.23	<0.001	Worku 2012
Length of stay (LOS)	Average LOS (>=8+)	9	4.5	OR				0.01	Farah 2018
	Average LOS (<=2)	22	9.5	OR	0.418	0.19	0.936	0.034	Farah 2018
Multiple pregnancy	Birth level (Multiple)	69	48.3	HR	1.8	1.1	2.94	<0.05	Orsido 2019
	Gestation (single)	723	22.0	OR	0.7	0.54	0.9	<0.05	Worku 2012
ANC visit	ANC (None)	80	48.2	HR	6.02	3.52	10.27	<0.001	Orsido 2019
	ANC (None)	106	34.1	OR	1.7	1.28	2.26	<0.001	Worku 2012
HMD	HMD (Yes)	31	66.0	HR	2.04	1.16	3.59	<0.05	Orsido 2019
Breastfeeding	Breastfeeding initiated (after 1 h)	137	30.8	HR	2.62	1.6	4.3	<0.001	Orsido 2019
	Late breastfeeding initiation time	33	22.0	OR	2.89	0.1	8.38	<0.05	Tewabe 2018
	Exclusive breastfeeding (No)	18	7.1	OR	6.77	3.04	15.07	<0.001	Tewabe 2018
Prematurity	Prematurity (Yes)	14	8.9	OR	0.492	0.25	0.957	0.037	Farah 2018
	Gestational age (GA) (less than the mean (36.6 wks.)			OR	0.683	0.59	0.795	<0.05	Tekleab 2017
	GA (<37 wks.)	21	33.3	OR	2.14	1	4.52	<0.05	Tewabe 2018
	GA (<32 wks.)	347	52.5	OR	10.46	5.39	20.31	<0.001	Worku 2012
	GA (32-37 wks.)	227	21.2	OR	3.6	1.39	6.69	<0.01	Worku 2012
	GA (37-42 wks.)	248	15.2	OR	2.05	1.16	3.364	<0.05	Worku 2012
Age of admission	Age of newborn at admission (early)	43	15.6	OR	0.39	0.16	0.97	<0.05	Tewabe 2018
	Age of newborn at admission (<= 1 day)	693	24.6	OR	2.53	1.66	3.85	<0.001	Worku 2012
	Age of newborn at admission (1-3 days)	158	18.6	OR	2.2	1.38	3.48	<0.001	Worku 2012
Length	Length (45-51 cm)	261	16.2	OR	0.58	0.4	0.85	<0.05	Worku 2012
Congenital anomaly	Congenital anomaly (any)	108	34.4	OR	2.02	1.33	2.51	<0.05	Worku 2012
Oxygen treatment	Oxygen treatment (Yes)	755	31.6	OR	2.65	1.89	3.72	<0.001	Worku 2012
Jaundice	Jaundice at admission (No)	745	27.4	OR	2.65	1.89	3.72	<0.001	Worku 2012
	Birth weight (<=1500 gm)	268	59.3	OR	9.64	3.32	27.97	<0.001	Worku 2012
Birth weight	Birth weight (1501-2449 gm)	281	21.6	OR	3.54	1.28	9.78	<0.05	Worku 2012
	Birth weight (2500-3999 gm)	241	15.5	OR	3.16	1.21	8.24	<0.05	Worku 2012
# of siblings	# of siblings (3+)	155	29.8	OR	2.04	1.15	3.64	<0.05	Worku 2012
Birth order	Birth order (2nd)	229	26.4	OR	1.79	1.28	2.51	<0.05	Worku 2012
Marital status	Marital status (not in marriage)	119	29.2	OR	1.55	1.2	2	<0.05	Worku 2012

Table 4: Determinant factors for preterm mortality among neonates admitted at NICU

Domain	Determinants	n	(%)	Measure	AOR/ AHR	95% CI		P-value	Study ID
ANC	ANC (Yes)	88	18.1	HR	0.5247	0.338	0.814	<0.05	Yehuala 2015
Gravidity	Gravidity (6-10)	17	3.5	HR	2.072	1.001	4.289	<0.05	Yehuala 2015
RDS	RDS (Yes)	54	31.8	HR	7.774	4.712	12.826	<0.001	Yehuala 2015
	RDS (Yes)	114	32.9	OR	3.287	2.033	5.315	<0.001	Wesenu 2017
HMD	HMD (Yes)	107	57.2	OR	2.636	1.597	4.352	<0.001	Wesenu 2017
	HMD (Yes)	39	26.0	HR	3.02	1.86	4.88	<0.001	Yismaw 2019
PNA	PNA (Yes)	46	31.0	HR	1.55	1.09	2.2	<0.05	Yismaw 2019
	PNA (Yes)	27	64.3	OR	2.479	1.239	4.959	<0.05	Wesenu 2017
	PNA (Yes)	63		HR	2.123	1.42	3.18	<0.001	Yehuala 2015
	Neonate cry immediately at birth (Yes)	385		HR	0.57	0.39	0.83	<0.05	Yismaw 2019
Jaundice	Jaundice (Yes)	10	7.0	HR	1.62	1.12	2.35	<0.05	Yismaw 2019
	Jaundice (Yes)	90	76.3	OR	2.737	1.718	4.361	<0.001	Wesenu 2017
Sepsis	Sepsis (Yes)	52	47.3	OR	2.072	1.242	3.459	<0.05	Wesenu 2017
GA	GA (30-32)	33	37.1	OR	0.336	0.138	0.822	<0.05	Wesenu 2017
	GA (32-34)	32	27.6	OR	0.241	0.099	0.589	<0.05	Wesenu 2017
	Small weight for GA at birth	109		HR	1.65	1.12	2.43	<0.05	Yismaw 2019
	GA			HR	0.82	0.74	0.91	<0.001	Yismaw 2019
Home delivery	Home delivery	23		HR	2.29	1.05	4.98	<0.05	Yismaw 2019
KMC	KMC (Yes)	68		HR	0.23	0.1	0.51	<0.001	Yismaw 2019
Hypoglycemia	Hypoglycemia (Yes)	112		HR	1.75	1.21	2.54	<0.001	Yismaw 2019
HIV status	HIV status (Positive)			HR	1.803	1.037	3.135	<0.05	Yehuala 2015
Anemia	Anemia (Yes)			HR	4.67	1.769	12.33	<0.05	Yehuala 2015
Breastfeeding	BF initiated (<1 h)			HR	0.102	0.045	0.233	<0.001	Yehuala 2015
	BF initiated (1-2 h)			HR	0.129	0.068	0.246	<0.001	Yehuala 2015
	BF initiated (>2 h)			HR	0.375	0.225	0.625	<0.001	Yehuala 2015
Temperature	Temperature			OR	0.811	0.683	0.964	<0.05	Wesenu 2017
Maternal illness	Maternal illness/disease (Yes)			HR	1.57	1.1	2.26	<0.05	Yismaw 2019
Type of pregnancy	Type of pregnancy (Single)	331		HR	2.35	1.58	3.5	<0.001	Yismaw 2019

Publication bias

The funnel plot appeared symmetrical, which suggests no evidence of small-study effects. The Egger's test also indicated the low possibility of publication bias (Coef. =-5.472; $p = 0.476$).

DISCUSSION

In this review, the pooled neonatal mortality rate was 19.0%. Early age of the newborn, prematurity, low birth weight, perinatal asphyxia, mode of delivery, hypothermia, late initiation of breastfeeding, and having antenatal care visits were the main determinants for neonatal mortality among neonates admitted to intensive care units.

Previous literature indicated that the overall mortality rate in NICU of developing countries ranged from 0.2% to 64.4%. (26) A wide variation in the mortality rates among NICUs was also reported in Brazil (9.5-48.1%), with an overall mortality rate for newborns admitted at nine NICU sites being 18.6% (27) which is comparable to our result. These higher rates of mortality could be associated with suboptimal NICU neonatal services across the country. (16, 22)

Our stratified analysis also showed that preterm neonates had three times higher odds of death than preterm and term and post-term neonates. Previous studies also documented a similar higher risk of death amongst preterm neonates in NICUs. (28-31) This is because preterm newborns had immaturity of immune systems and other body defense mechanisms that help control newborn infection and disease susceptibility. Other possible explanations for preterm neonates' high death rate might bs a delay in receiving adequate health care due to poor facilities and lack of medical supplies in Ethiopia.

In this review, gestational age or prematurity was related as a factor in neonatal mortality. The finding is also consistent with the systematic review in developing and developed countries. (26) It might be due to their intrinsic susceptibility to infection due to lack of immunologic competence, the lack of appropriate treatment modalities, such as mechanical ventilation, surfactant administration, parenteral nutrition, and delay in the initiation of health care services. (19, 25)
Perinatal asphyxia is identified as a risk factor for neonatal mortality. The reason might be the quality and access of emergency obstetric newborns and comprehensive emergency obstetric services are inadequate in a clinical setting. (17, 19) Training of health care workers to detect risk factors, fetal asphyxia during labor and delivery including neonatal resuscitation provision ,must be given. (25)

We observed that the mode of delivery showed a variation in the rate of neonatal mortality. Instrumental mode of delivery is identified as a risk factor for neonatal mortality. (22) On the other hand, the mode of delivery had a protective effect on the risk of neonatal mortality. (17, 27)

It might be related to the use of timely decisions rather than waiting for vaginal delivery. Delivering by cesarean section reduces the risk of death and complications that can come due to prolonged labor. (17) On the contrary, it is reported that the cesarean section had increased neonatal mortality, which could have resulted from the delay in decision making during prolonged labor, poor quality of operation procedure, and its prohibition effect on early breastfeeding initiation. (17, 22, 24)

Delayed breastfeeding after 1 hour of birth results in a higher risk of neonatal mortality than their counterpart. (17, 23) This indicates the sub-optimal practice of early initiation of breastfeeding despite its great importance in the reduction of neonate death. It is also important to consider the neonates who are sick who might not be able to suck breast milk instead of a healthier one. (17)

Neonates born from mothers who had no ANC visit are more likely to die compared to neonates born from mothers who have ANC follow-up. (17, 18, 22, 23) ANC visit saves the lives of babies by early detection and management of the problems related to the pregnancy by promoting and establishing good health. (17, 23)

As to authors' knowledge, the current systematic review and meta-analysis are the first of their kind to be conducted at the NICU hospitals of Ethiopia. The information obtained may improve knowledge on the cause of neonatal mortality at NICU to reduce neonatal mortality rates in Ethiopia. Nevertheless, the inclusion of only English language articles in the review is a limitation. Moreover, all the studies are based on facility-based records that are subject to information bias.

Conclusions

Neonatal mortality at NICU hospitals in Ethiopia is high. Subgroup analysis shows that the mortality rate is also higher among early and preterm neonates. Gestational age, mode of delivery, ANC follow-up, breastfeeding, hypothermia, age of the neonate, hypoglycemia, place of delivery, and low birth weight were among the factors identified for neonatal mortality rate at NICU hospital in Ethiopia. Almost all identified factors associated with neonatal mortality at NICU hospitals are preventable.

Therefore, special care for preterm and early age newborns, timely initiation of breastfeeding, exclusive breastfeeding, the appropriate mode of delivery, essential obstetric and newborn care, and promoting antenatal visits are recommended to reduce neonatal mortality. Moreover, the finding calls policymakers and program managers to focus on strengthening NICU services by revising the strategies set in place for optimal quality services and the prevention of risk factors with neonatal mortality at NICU hospital during, pregnancy, delivery, and postnatal period.

Abbreviations

NMR	neonatal mortality rate
AHR	adjusted hazard ratio
ANC	antenatal care
AOR	adjusted odds ratio
AP-GAR	Appearance, Pulse, Grimace, Activity, and Respiration
CI	confidence interval
GA	gestational age
HMD	hyaline membrane disease
JBI	Joanna Briggs Institute
KMC	kangaroo mother care
LOS	length of stay
NICU	neonatal intensive care unit
OR	odds ratio
PNA	perinatal asphyxia
PRISMA	Preferred Reporting Items for Systematic and Meta-Analysis
PROSPERO	International prospective register of systematic reviews
RDS	respiratory distress syndrome
SNNP	Southern Nations, Nationalities, and Peoples'

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing of interest

All contributing authors declare no conflicts of interest.

Funding

This article was prepared as part of systematic review and meta-analysis training provided to regional knowledge hub members. The training was financially supported by USAID Transform: Primary Health care, JSI/L10K project, and Amhara Public Health Institute. The funders had no role in study design, data extraction and analysis, decision to publish, or preparation of the manuscript.

ACKNOWLEDGMENTS

The authors would like to acknowledge the Transform Primary Health Care project and JSI Research, Training Institute Inc. /The Last Ten Kilometers Project, University of Gondar Institute of Public Health, and Amhara Public Health Institute (APHI), for their support to the successful accomplishment of this review. We also take this opportunity to thank Dr. Kassahun Alemu, and Dr. Tadesse Awoke for their hands-on systematic review training.

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Daniel Atlaw, Kenbon Seyoum, Habtamu Gezahegn. *Ethiop Med J, 2021, Vol. 59, No. 2*

ORIGINAL ARTICLE

PREVALENCE OF FEMALE GENITAL MUTILATION AMONG REPRODUCTIVE-AGE WOMEN IN ETHIOPIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

Daniel Atlaw, BSc, MSC [2*], Kenbon Seyoum, BSc,MSC[1], Habtamu Gezahegn, BSc,MSC, MPH [3]

ABSTRACT

Introduction: - *Female genital mutilation (FGM) is the most common harmful traditional practice in Africa characterized by partial or total removal of the female external genitalia for non-therapeutic reasons. Globally, FGM affects about 130 million women and girls. Female genital mutilation (FGM) is a harmful traditional practice that affects the physical and mental health of girls and women.*

Methods: - *Systematic Review and meta-analysis were conducted using the guideline of Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA). Both published and unpublished articles were searched. Articles were searched from different databases including PubMed, Popline, AJOL, EMBASE, and gray literature like Google Scholar and Google. Articles were searched using terms like "prevalence", "magnitude", "female genital cutting" "female genital mutilation", and "female circumcision". Joanna Briggs Institute (JBI) Critical Appraisal-Checklist for Analytical Cross-Sectional Studies was used to assess the quality of the included paper. Egger's test and I^2 statistics were used to assess Publication bias and heterogeneity respectively.*

Result and discussion: - *About thirteen studies with total participants of 7850 were included for systematic review and meta-analysis. The pooled prevalence of female genital mutilation among reproductive-age women in Ethiopia was 87.5%: 95% CI (84.25, 90.78). I^2 test statistics showed high heterogeneity (I^2 =94.4, p=0.000), and Egger's test was done to check for publication bias, but the test has revealed that there is no statistically significant publication bias (p-value=0.374).*

Conclusion: - *The pooled prevalence of female genital mutilation is high in Ethiopia. Subgroup analysis does not revealed significant differences among different regions found in the country.*

Key Words: *Female, Genital , Mutilation, Meta-analysis, Ethiopia*

INTRODUCTION

Female genital mutilation (FGM) is the most common harmful traditional practice in Africa and characterized by partial or total removal of the female external genitalia for non-therapeutic reasons (1). The type of FGM procedures varies not only across countries but also within countries, across ethnic groups, and within cultural communities (2). Female genital mutilation is practiced in variable forms among different communities. The most severe form is Pharaonic operation (infibulation) in which the clitoris is removed along with the labia minora and at least two-thirds of the labia majora (3). The procedure is performed using a blade or sharp materials by a religious leader, town elder, or a medical professional with limited training (4).

Globally, FGM affects about 130 million women and girls (5). About 84% of parents still have the intention to mutilate their daughters (6). The practice of FGM remains prevalent in East and West African countries (7) (8).

As many as 93% of girls in developing countries such as Yemen, Nigeria, and Sudan are mutilated (9). Female genital mutilation is most prevalent in north-eastern Africa countries where the prevalence varies from 97% in Egypt to 80% in Ethiopia (10). Female genital mutilation is documented to be widespread across Ethiopia and is believed to be widely practiced in the Somali region(11). Ethiopia is the second-ranked African country by the number of girls and women with FGM (23.8 million) next to Egypt (12).

As revealed by Ethiopia demographic health survey in 2016 the prevalence of FGM was 65%(13). Female genital mutilation is practiced Significantly in Oromo, Afar, Amhara, Somali, and Tigray ethnic groups (14). Female genital mutilation is abnormal practice which results in substantial physical, obstetrical and psychological effect on women and newborn during childbirth (15,16). The consequences can even include death as a result of shock, hemorrhage, or septicemia (17).

[1]Madda Walabu University Goba Referral Hospital, Department of Midwifery.
[2]Madda Walabu University Goba Referral Hospital, Department of Human Anatomy.
[3]Madda Walabu University Goba Referral Hospital, Department of Medical Physiology.
*Corresponding Author E-mail: danielatmwu@gmail.com

Further, FGM increases the risk of infectious disease transmission (18,19). In addition to the direct complication of FGM, it increases the woman's biological vulnerability to HIV transmission if exposed to the virus (17).

The National constitution, Criminal and Family laws, of Ethiopia, included articles that prohibit female genital mutilation. However, the existence of this law alone does not provide protection for women's undergoing female genital mutilation (20).

Despite the hard work done to combat FGM in Ethiopia (21), the magnitude is still very high (22). Female genital mutilation (FGM) is a harmful traditional practice that violates women's rights and threatens their health (23) in several ways, as they are subjected to different forms of FGM right from the date of their birth (24). Many governments in Africa have taken steps to eliminate the practice of FGM in their countries (25). Although female genital mutilation has serious complications, the prevalence of this problem is underestimated due to hidden practice in Africa (26). Even though, a high level of knowledge regarding the complications of FGM and a high level of awareness, FGM continues to be prevalent in Addis Ababa (27). The most frequently mentioned reasons for the practice include fear of being rejected by the community, preparing the girl for marriage, ensuring premarital virginity, and preventing marital fidelity (23).

There are different studies conducted in Ethiopia on female genital mutilation, but the finding of studies vary from 78.5% in the Bale Zone (28) to 98% in the Hababo Guduru district (12). Therefore this study aimed to determine the pooled prevalence of female genital mutilation among reproductive-age group women. This may imply the risk of complications during labor and delivery.

METHODS

Search strategy

The protocol of this systematic review and meta-analysis has been registered on Prospero with an identification number of CRD42019137284. A systematic review and meta-analysis were conducted using the guideline of Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA). The search for this review had included published and unpublished articles. Articles were searched from different databases including PubMed, Popline, AJOL, EMBASE, and gray literature like Google Scholar and Google. Articles were searched using terms like "prevalence", "magnitude", "female genital cutting" "female genital mutilation", and "female circumcision".

Quantitative studies conducted in different regions of Ethiopia were included in this systematic review and meta-analysis. Community and institutional-based cross-sectional studies were included for meta-analysis. Duplicates from different databases and google searches were removed using the endnote citation manager. Articles were screened by their title and abstracts for full-text evaluation. Only articles written in the English language from 2011 to 2019 were retrieved for review. Three authors conducted searching and screening procedures.

Joanna Briggs Institute (JBI) Critical Appraisal-Checklist for Analytical Cross-Sectional Studies was used to assess the quality of the included articles. The checklist has a maximum of 8 points with a score of 0, 1, and not applicable (table 1). Critical appraisal was done independently by two authors. Data were extracted using a Microsoft Excel worksheet. Author's name, year of publication, region, setting, design, sample, and prevalence of female genital mutilation were extracted. The extracted data were then imported to Stata software version 14 for analysis.

Egger's test and I^2 statistics were used to assess Publication bias and heterogeneity respectively. A P-value of less than 0.05 was used to declare the publication bias. I^2 test statistics result of 25%, 50%, 75%, and 100% was declared as little concern, concerning, very concerning, and substantial heterogeneity respectively. A random-effect model was used for meta-analysis. STATA version 14 was used to conduct analysis. A Forest plot was used to present the estimated prevalence at a 95% confidence interval. Prevalence of female genital mutilation was taken from the studies and standard error was calculated using the formula SE= $\sqrt{pq/n}$. The prevalence and the calculated standard error were entered into STATA version 14 to calculate the pooled prevalence at 95% CI. Subgroup analysis was conducted to evaluate differences among different regions within the country.

RESULT

A total of 402 studies were identified through the initial search for review. From 402 studies 187 articles were excluded as a result of duplication. About 215 articles screened based on their title and abstract to be included for full-text review. During title and abstract screening, 199 articles were excluded from the review because they are not quantitative and not from the Ethiopian community.

Therefore only 16 articles were undergone full-text review and from full-text review, about 3 articles have been excluded because their methodology is not clear and one of these studies was conducted on girls less than 15 years. Finally, 13 articles were included in the study (figure. 1).

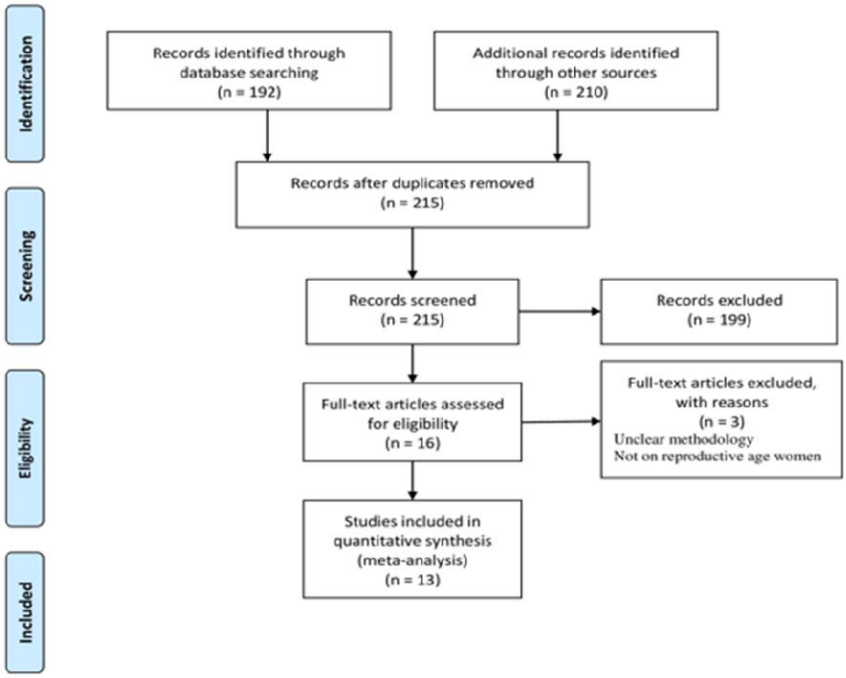

Figure 1: PRISMA flow chart of the overall phases of review on prevalence of FGM in Ethiopia.

Table 1: The methodological quality of included studies for review on prevalence of FGM among reproductive-age women in Ethiopia.

Author name	Criteria for inclusion in the sample clearly defined	Study subjects and the setting described in detail	Exposure measured in a valid and reliable way	Objective, standard criteria used for measurement of the condition	Confounding factors identified	Strategies to deal with confounding factors stated	Outcomes measured in a valid and reliable way	Appropriate statistical analysis used	Overall appraisal
Tamire et al (22)	0	1	1	1	N/A	N/A	1	1	5/8
Yerga et al (29)	0	1	1	1	N/A	N/A	1	1	5/8
Bogale et al (28)	0	1	1	1	N/A	N/A	1	1	5/8
Degefa et al (15)	0	1	1	1	N/A	N/A	1	1	5/8
Ejigu et al (8)	1	1	1	1	N/A	N/A	1	1	6/8
Teshoma et al (30)	0	1	1	1	N/A	N/A	1	1	5/8
Mitike et al (6)	0	1	1	1	N/A	N/A	0	Unclear	3/8
Muktar et al (26)	0	1	1	1	N/A	N/A	1	1	5/8
Shay et al (9)	0	0	0	1	N/A	N/A	0	1	2/8
Andualem et al (31)	0	1	1	1	N/A	N/A	1	1	5/8
Gabermariam et al (10)	0	1	1	1	N/A	N/A	1	1	5/8
Abate et al (32)	0	0	1	0	N/A	N/A	1	0	2/8
Gajaa et al (12)	1	1	1	1	N/A	N/A	1	1	6/8
Abdisa et al (33)	1	1	1	1	N/A	N/A	1	1	6/8
Abeya et al (34)	1	1	1	1	N/A	N/A	1	1	6/8
Moges et al (35)	1	1	1	1	N/A	N/A	1	1	6/8

The methodological quality of the studies was done using the JBI critical appraisal tool. The tool has eight items. Each item will be given a score of 0, 1, or not applicable. Based on JBI critical appraisal too1 studies were excluded from review (table. 1).

A total of 7,850 participants were included for review with an individual study sample size ranging from 235 studies conducted in the Amhara region (35) to 858 studies conducted in the Oromia region (29).

Four studies from the Oromia region, three studies from the Amhara region, three studies from Somali region, two studies from SNNP region and one study from Afar region were included in this review (table. 2). All studies included in this review were cross-sectional studies and most of the studies were community-based (table. 2).

Table 2: Summary characteristics of studies included for review on prevalence of FGM among reproductive age women in Ethiopia.

SN	Authors	year	Region	Setting	Design	sample	Prevalence
1	Tamire et al.	2013	SNNPR	High school	Cross-sectional	780	82.2
2	Bogale et al.	2014	Oromia	Community	Cross-sectional	634	78.5
3	Degefa et al.	2017	SNNPR	Hospital	Cross-sectional	395	92.2
4	Muktar et al.	2013	Somali	Community	Cross-sectional	323	90
5	Andualem et al.	2016	Amhara	Community	Cross-sectional	718	96
6	Gebremariam et al.	2016	Somali	School	Cross-sectional	679	82.6
7	Abdisa et al.	2017	Somali	Community	Cross-sectional	320	87.1
8	abeya et al.	2016	Afar	Community	Cross-sectional	792	90.8
9	Gaja et al.	2016	Oromia	Community	Cross-sectional	610	98
10	Moges et al.	2015	Amhara	Community	Cross-sectional	235	82.6
11	Yirga et al.	2012	Oromia	Community	Cross-sectional	858	92.3
12	Tashoma et al.	2016	Oromia	Community	Cross-sectional	842	79.5
13	Ejigu et al.	2014	Amhara	Community	Cross-sectional	664	85.4

Prevalence of female genital mutilation in Ethiopia

Studies included in this review were those studies conducted on the prevalence of female genital mutilation among women of reproductive age group. The pooled result of the study indicated about 87.5 % of women of reproductive age group undergone female genital mutilation in Ethiopia (figure. 2). I^2 test statistics showed high heterogeneity (I^2=94.4, $p < 0.001$) (figure. 2).

Subgroup analysis

Subgroup analysis was done to check prevalence among different regions of Ethiopia. It has showed almost similar prevalence of female genital mutilation among reproductive age group women in different regions with overall prevalence (figure. 3).

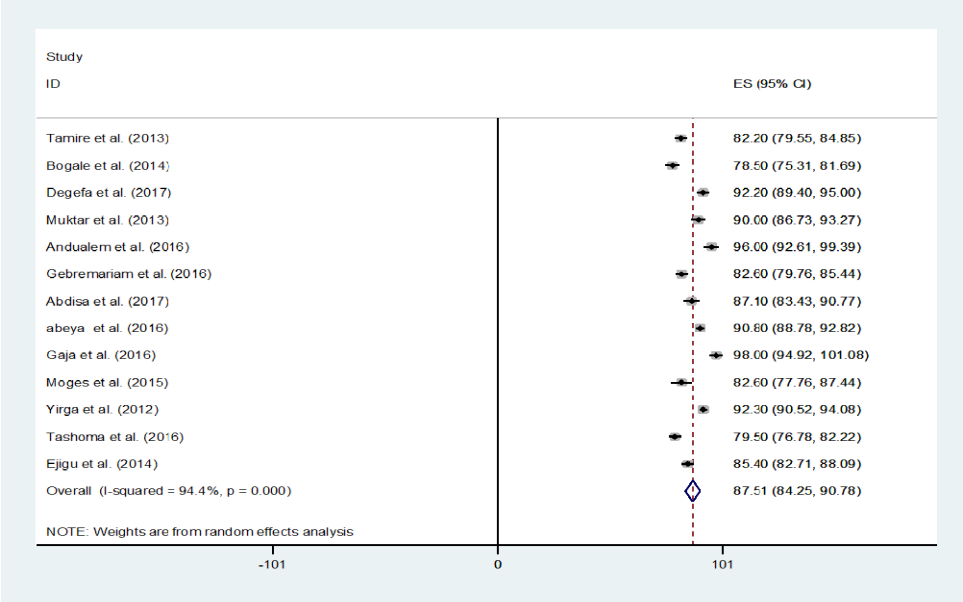

Figure 2: Forest plot displaying the pooled result of the prevalence of FGM among reproductive age Women in Ethiopia

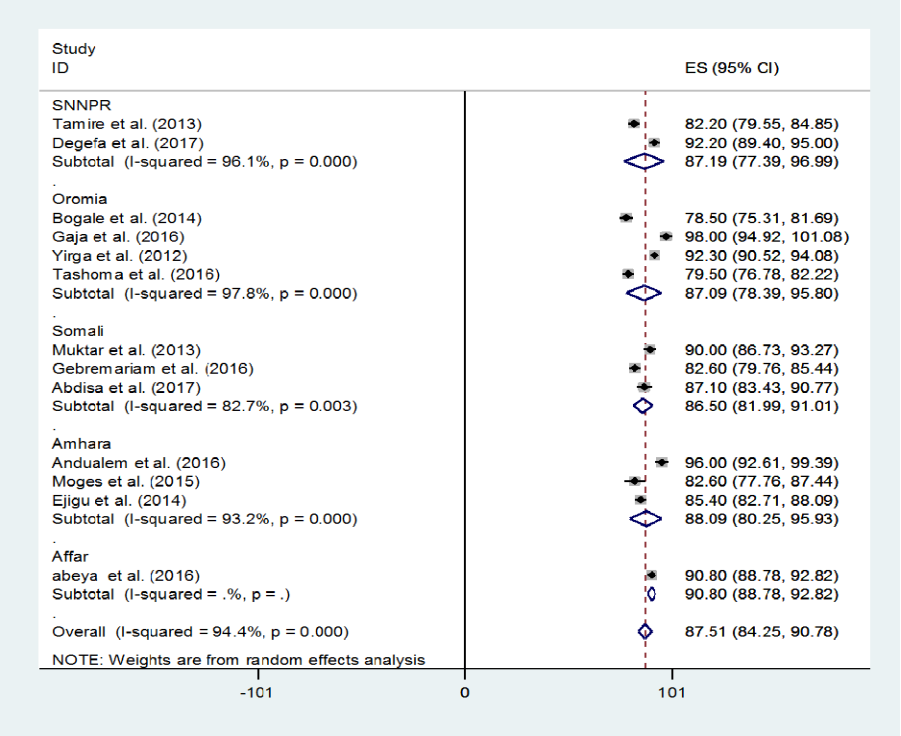

Figure 3: Forest plot displaying the pooled result of prevalence of FGM among reproductive age women in Ethiopia

Egger's test was done to check for publication bias, but the test has revealed that there is no statistical significant publication bias (p-value=0.374) (table 3).

Table 3: Egger's test for review on prevalence of FGM among reproductive age women in Ethiopia

Number of studies = 13 Root MSE = 4.246

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	94.31267	6.835173	13.80	0.000	79.26855	109.3568
bias	-4.528477	4.884428	-0.93	0.374	-15.27903	6.222077

Test of H0: no small-study effects P = 0.374

DISCUSSION

This systematic review and meta-analysis were done to determine the pooled prevalence of female genital mutilation among reproductive-age group women in Ethiopia with thirteen studies included from different regions of Ethiopia.

In this systematic review and meta-analysis, the pooled prevalence of female genital mutilation among reproductive-age group women in Ethiopia was 87.5%: 95% CI (84.25, 90.78). The current pooled prevalence of female genital mutilation among reproductive-age group women was higher than many African countries except Somalia and Djibouti(36). This finding is also higher than the 2016 annual report of WHO (37). This difference may be attributed to sociodemographic differences of the African community.

The subgroup analysis of this pooled prevalence has not shown difference among different regions of Ethiopia. This implies that being in a community of different culture and regions have no difference to towards the practice of female genital mutilation in Ethiopia.

The limitation of this systematic review and meta-analysis were lack of studies from some regions of the country, which might affect the pooled prevalence of female genital mutilation in Ethiopia.
The Strength of this review was comprehensive searching and strict following of PRISMA guideline.

Conclusion

This study has revealed that about nine in ten reproductive-age group women have mutilated in Ethiopia. Subgroup analysis among different regions of Ethiopia has not shown a significant difference. Therefore strengthening health education, creating awareness about the complication of female genital mutilation may play a great role to reduce the practice of female genital mutilation in Ethiopia.

ACKNOWLEDGMENTS

We sincerely thanks all the authors of original articles who have responded timely to our queries through emails.

Competing of interest

Authors declare no competing interests in this work.

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Seifu Megersa, Malede Berihun Yismaw, Minyahil Alebachew Woldu, Tamrat Assefa Tadesse. *Ethiop Med J, 2021, Vol. 59, No. 2*

REVIEW ARTICLE

COMPARISON OF AMPHOTERICIN B AND ITS COMBINATION WITH FLUCY TOSINE IN THE MANAGEMENT OF CRYPTOCOCCAL MENINGITIS: A REVIEW

Seifu Megersa Kumsa, MSc[1], Malede Berihun Yismaw, MSc[2], Minyahil Alebachew Woldu, MSc[1], Tamrat Assefa Tadesse, MSc[1]*

ABSTRACT

Cryptococcosis is a global invasive mycosis that is associated with high morbidity and mortality. With its profound propensity to locate within the central nervous system, which is frequently accompanying by fungal meningitis. Immunocompromised patients with cryptococcal meningitis should receive Amphotericin B deoxycholate 0.7–1.0 mg/kg/day intravenously plus Flucytosine 100 mg/kg/day divided into four doses for at least 2 weeks, followed by Fluconazole, 400 mg orally daily, for a minimum of 8 weeks OR Amphotericin B monotherapy for 10 weeks duration. Hence, the objective of this review was to compile evidence on the comparison of the effectiveness of Amphotericin alone and combined with Flucytosine in the management of cryptococcal meningitis. A literature review of research articles was done, by accessing electronic journals from MEDLINE, EMBASE, COCHRANE LIBRARY and PUBMED published from years 1979 to 2018. Findings of randomized clinical trials studies done in English and published documents were included in the review. The available evidence from the included studies finding supported that combining Amphotericin B with Flucytosine had better clinal improvement than AmB monotherapy. In all studies included Flucytosine addition resulted in better outcomes in cerebrospinal fluid yeast count, serologic evidence, clinical symptoms, survival rate, or occurrence of adverse drug events.

INTRODUCTION

Cryptococcal meningitis (CM) is an infection of the brain parenchyma and subarachnoid space by the encapsulated saprophytic yeast organism, *Cryptococcus neoformans* (1). In many areas where there is a high prevalence of human immunodeficiency virus (HIV), such as sub-Saharan Africa, it has become the leading fatal adult meningitis (2). Although healthy hosts can be infrequently affected, the disease occurs frequently in immunosuppressed individuals. In HIV -positive patients, autoimmune deficiency syndrome (AIDS-associated CM) typically affects individuals with a CD4 cell count <100 cells/mm3 (3).

Cryptococcal meningitis is a common opportunistic infection and AIDS-defining illness in patients with late-stage HIV infection, particularly in Southeast Asia and Southern and East Africa (4). Although the extensive availability of antiretroviral therapy (ART) has substantially reduced the worldwide prevalence of Cryptococcosis, it has still become a major problem in developing countries. Early diagnosis and treatment are the keys to treatment success (5). It was predicted that in 2014 there were over 220,000 new cases of CM globally resulting in more than 180,000 deaths and responsible for15% of all AIDS-related deaths (6), which contributes up to 20% of AIDS-related deaths in low- middle-income countries per annum (7).

Cryptococcal meningitis was a steadily fatal disease before the introduction of Amphotericin B (AmB). Flucytosine (5-FC) can also cure this infection, but secondary drug resistance and a low proportion of cures make this drug unattractive as a single agent. In vitro and in vivo evidence suggested that AmB and 5-FC were additive in their effects against cryptococcus prompted clinical trials of the combination (8).

Immunocompromised patients with CM should receive AmB 0.7–1.0 mg/kg/day intravenously plus 5-FC 100 mg/kg/day divided into four doses for at least 2 weeks, followed by Fluconazole (FLU) 400 mg orally daily for a minimum of 8 weeks (9). For a setting where 5-FC is unavailable, a combination of AmB and high-dose FLU 800–1200 mg per day is used as second-line induction treatment. The initial 2 weeks induction treatment should be followed by consolidation and maintenance phases of treatment with FLU (10).

AmB was the first effective therapy and, at doses of 0.3–0.5 mg/kg/day for 10 weeks, led to cure rates of over 50% in non-HIV-associated infection. It has concentration-dependent activity, and more recent trials at doses of 0.7 mg/kg/day have yielded improved results (4). AmB given for 4–6 weeks has been considered to be the gold standard for the initial treatment of CM in patients with HIV infection (11).

[1] Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia. [2]Department of Pharmacy, College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia
*Corresponding Author E-mail: ztamratassefa13@gmail.com

5-FC is the most common choice and is recommended in the CM treatment guidelines. However, this treatment has not been shown to reduce mortality, as compared with amphotericin B monotherapy. 5-FC is frequently unavailable where the disease burden is greatest, and concerns about cost and side effects have limited its use in resource-poor settings (7). Monotherapy with 5-FC commonly led to the development of resistance which is not a problem when it is combined with AmB. This combination has also been shown to have additive effects in both pre-clinical studies and clinical trials in non-HIV-associated and HIV-associated infections (4).

Although guidelines exist for the antifungal management of CM, recommendations are based on limited data from randomized controlled trials (RCTs), and in clinical practice, treatment is highly variable due to drug costs, availability, and ability to monitor and manage drug-related. A Cochrane review on treatment for HIV-associated cryptococcal meningitis was published in 2018 (12), but several clinical trials comparing new induction regimens in treating non-HIV associated had not been included. Therefore, this review aimed to compile evidence which compares AmB monotherapy versus a combination regimen of AmB with 5-FC as part of an induction regimen for cryptococcal meningitis.

METHODS

Search strategy and search terms

A systematic review of research articles from electronic journals including Medline, EMBASE, Cochrane Library, and PubMed was done, which were published from 1979 to 2018. The following keywords were used as search terms: cryptococcal meningitis, Cryptococcus neoformans, meningitis, amphotericin B, flucytosine, Amphotericin B with flucytosine, human immunodeficiency virus, and by connecting each of these keywords using Boolean operators.

Data extraction and Review system

We extracted key information by reference: including journal, title, author, volume in page numbers; objective: the study objective as stated by the authors; study design: randomized clinical trials; population: demographics of the participants in the study and outcome: results.

Earlier studies compared AmB and combined with 5-FC in treating CM, had been found to show variation in terms of outcomes, and also, they were conducted by different study designs. For this reason, in this review, we didn't compare and contrast each finding and the results were summarized according to the category of each separate study.

Inclusions and exclusion Criteria

Findings from RCTs articles, studies done in English, published from 1979 to 2018 were taken as inclusion criteria. However, journals with abstract only, and written in languages other than English were not included in the review.

Quality of review

Quality evaluation was performed in which each article received a summary quality measurement that corresponded with important attributes of the study, adapted from previous studies. These include research design, data analysis, measurement and validity, the strength of the study and, consistency or homogeneity of the findings across the studies.

Types of outcome measures

The primary treatment outcome measures in this review include cerebrospinal fluid (CSF) yeast count, serologic evidence, clinical symptoms, mortality, whereas drug-related adverse events and rate of fungal clearance were considered as secondary outcome measures.

RESULTS

A total of 76 journal articles were downloaded, of which 68 were excluded due to various reasons. Finally, 8 articles were selected for eligibility. The search and selection strategy is presented as a PRISMA flow chart in figure 1.

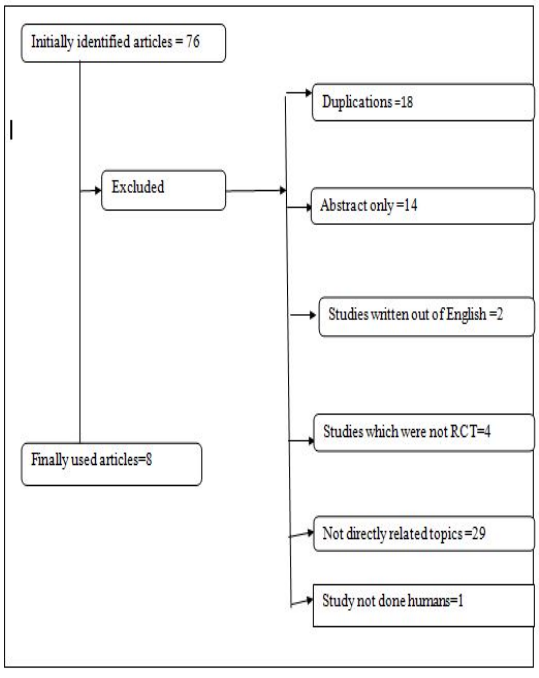

Figure 1: Flow chart showing selection process of articles in systematic review.

The review covered studies conducted to evaluate the efficacy of AmB versus AmB plus 5-FC after 14, 28, 42, and 70 days of treatment. Of the included studies, five of them compared AmB monotherapy versus AmB plus 5-FC, one study evaluated the efficacy of AmB monotherapy, another one study evaluated the efficacy of AmB plus 5-FC combination regimen and the rest one study compared AmB plus 5-FC combination regimens at different doses of AmB (Table 1).

Table 1: Comparison of Amphotericin and combined with Flucytosine in treatment of cryptococcal meningitis

Study	Name and dose of drugs	Sample size	Evaluation day	Primary outcomes	Improved patients (%)	Death (%)
(Day et al.,2013) (10)	AmB-1m/kg/day	99	14 days	CSF yeast count and clinical symptoms*	74 (74.75)	25 (25.3)
	AmB 1m/kg/day +5 -FC 100mg/kg/day	100	14 days		85 (85)	15(15)
(Dismukes, 1987) (8)	AmB-0.4mg/kg/day	27	70 days	CSF culture♠and clinical symptoms*	11(40.74)	5 (18.52)
	AmB-0.3mg/kg/ day+5-FC-150mg/ kg/day	24	42 days		16(66.67)	5 (20.83)
(Perfect et al., 2010) (13)	AmB-0.7mg/kg/ day+5-FC-100mg/ kg/day	30	70 days	CSF yeast count and serologic evidences	24(80)	6(20)
	AmB-1mg/kg/ day+5-FC-100mg/ kg/day	34	70 days		25(73.53)	8 (23.53)
(Jackson et al., 2012) (9)	AmB-0.3mg/kg/ day+5-FC-150mg/ kg/day	202	14 days	CSF culture♠ and clinical symptoms*	102(50.5)	11 (5.44)
	AmB-1m/kg/day	179	14 days		76(42.46)	10 (5.59)
(Molloy et al., 2018) (14)	AmB-1mg/kg/ day+5-FC-100mg/ kg/day	228	70 days	CSF yeast count, clinical symptoms*	157(68.8)	71 (31.2)
	AmB-1m/kg/day	229	70 days		138(60.2)	91 (39.7)
(Bicanic et al., 2008) (15)	AmB-1m/kg/day	48	70 days	CSF culture♠	32 (66.6)	16 (33.3)
(Dromer et al., 2008) (16)	AmB-1mg/kg/ day+5-FC-100mg/ kg/day	142	14 days	CSF culture♠	51 (36)	No report
	AmB-1m/kg/day	142	14 days	CSF culture♠	89 (63)	
(Loyse et al., 2012) (17)	AmB-0.7mg/kg/ day+5-FC-100mg/ kg/day	80	70 days	CSF culture♠	57(71.25)	23 (28.8)

**The clinical outcome was considered to be successful if fever, headache, and meningismus were improved or no worse*

♠- Mycological outcome was considered to be successful if CSF fungal culture was negative, CSF-cerebrospinal fluid, AmB-Amphotericin B,5-FC-Flucytosine

Outcomes-based on the evaluation period

On 2nd week

Day *et al.*, 2012 reported that there is no significant differences in survival rates across groups at day 14 (15 deaths in patients treated with AmB 1m/kg/day +5 -FC 100mg/kg/day vs 25 deaths in patients who took AmB-1m/kg/day; p=0.08) (10). Molloy *et al.*, 2018 also revealed that there were no significant differences in the proportions of patients with stable or improved symptoms (78% of the combination-therapy group and 83% of the AmB group, P=0.18), unchanged or improved (77% of the combination-therapy group and 74% of the AmB group, P=0.42), or combined mycological and clinical responses (50% of the combination-therapy group and 42% of the AmB group, p=0.12) (14).

Results from a cohort study with 208 HIV-positive and negative patients with meningoencephalitis clearly emphasized the success of therapy with AmB plus 5-FC for 14 days over any other induction regimen in persons with high fungal burden disease and abnormal neurological features, showing that there was a 26% failure rate in the combination group versus a 56% failure rate for other treatments (P <0.001) (13).

On 6th week

Dismukes *et al*., 1987 compared a combination of AmB and 5-FC versus AmB monotherapy in 66 patients. The result showed that 23 of 34 (68%) were cured or improved by combination, and 15 of 32 (47%) by AmB monotherapy (p>0.05). Similar results were also reported when courses not adhered to the protocol were excluded totally; 16 of 24 patients (67%) were cured or improved by the combination, and 11 of 27 (41%) by AmB alone (x^2=2.47, p> 0.05) (8).

At 10th week

Bicanic and Harrison, 2005 showed mortality rate was 24% (15 of 63 patients) at 10 weeks, with no difference between groups (AmB-0.7mg/kg/day+5-FC-100mg/kg/day vs. AmB-1mg/kg/day+5-FC-100mg/kg/day). They also illustrated that 68% and 60% of patients were alive at 6 months and 1 year, respectively and there was no difference in survival rates between the 2 groups at any time point (4). Day *et al.*, 2013 also exposed that by day 70, a total of 44 patients treated with amphotericin B monotherapy had died, as compared with 30 patients treated with AmB and 5-FC, in which treatment with a combination regimen is associated with a significantly reduced hazard of death by day 70 in the intention-to-treat analysis (hazard ratio, 0.61; 95% confidence interval (CI), 0.39 to 0.97; P=0.04) (10).

A study conducted by Molloy et al. also compared AmB plus 5-FC versus AmB plus FLU combination regimens for the management of CM. This study revealed that AmB plus 5-FC was superior to AmB plus FLU (71 deaths (31.1%) vs. 101 deaths (45.0%); hazard ratio for death at 10 weeks, 0.62; 95% confidence interval (CI), 0.45 to 0.84; P=0.002) (14).

DISCUSSION

Patients treated with combination of Amphotericin B with Flucytosine at doses of AmB-1m/kg/day+5-FC-100mg/kg/day and AmB-0.3mg/kg/day+5-FC-150mg/kg/day, after 14 days of initiating therapy, showed greater improvements, i.e. 85% and 50.5%, respectively (10,14) than those treated with AmB 1mg/kg/day alone, which was 42.46% (14).This finding aligns with guidelines of the Infectious Disease Society of America (14) which recommend the first choice for induction-phase treatment as: AmB (0.7 - 1.0 mg/kg/dose) plus 5-FC (100 mg/kg/day) (10). A regimen of 0.7 – 1.0 mg/kg q24h in combination with 5-FC for two weeks is currently recommended for induction therapy (18).

The rate of clearance of infection during the first 2 weeks of therapy was more rapid for group 2 (AmB-1mg/kg/day+5-FC-100mg/kg/day) than for group 1 (AmB-0.7mg/kg/day+5-FC 100mg/kg/day). The mean early fungicidal activity (SD) was -0.56 +/- 0.24 log cfu/mL of CSF per day for group 2 and -0.45 +/- 0.16 log cfu/mL of CSF per day for group 1 (15). Dromer *et al.*, 2008 reported that mycological failure at week 2 was significantly less frequent among patients treated with AmB+5-FC than AmB monotherapy, which was 20/86 (23%) vs. 47/100 (47%) (16).

It also revealed that with the same yield of sterilization for patients with meningoencephalitis, even those with abnormal neurology at baseline, the highest rate of mycological failure was observed for AmB alone. Mortality was lower in patients who were given AmB and 5- FC at the 3 months point but the overall reduction in mortality with the 5-FC combination group was not different (2).

Even though the combination regimen was given for only six weeks and monotherapy of AmB for 10 weeks, the combination cured or improved more patients (16 vs. 11), produced fewer failures or relapses (3 vs. 11), more rapid sterilization of CSF (p<0.001) and less nephrotoxicity (p<0.05) than did AmB monotherapy (19).

But, Molloy *et al.*, 2018 reported that 11 patients (2.9%) had toxic effects requiring the withdrawal of the study drug (6 receiving combination therapy and 5 receiving amphotericin B alone). Three patients had elevated serum creatinine values, two had nausea, two had hypokalemia, and one each had a rash, headache, hemolytic anemia, and a gastrointestinal hemorrhage (14).

Day *et al.*, 2013 also reported that by day 70, a total of 44 (total patients =99) patients treated with AmB monotherapy had died, while 30 patients treated with AmB plus 5-FC and 33 patients treated with AmB plus FLU. It revealed that treatment with AmB plus 5-FC was associated with a drastically reduced hazard of death by day 70 in the intention-to-treat analysis (hazard ratio, 0.61) (10). AmB plus 5-FC has also shown to be the most potent and advocated regimen for the induction phase (5).

The time to fungal clearance was significantly shorter in patients receiving AmB plus 5-FC than in those receiving AmB monotherapy, with more rapid rates of decline in the colony count (−0.42 log10 CFU per day vs. −0.31 log10 CFU per day) (10). However, on day 70, a visual deficit was reported in 16 of 46 assessed patients treated with AmB, as compared with 9 of 54 patients treated with AmB plus 5-FC. Neutropenia was more frequent among patients receiving AmB plus 5-FC than those receiving amphotericin B monotherapy (34% vs. 19%).

Surprisingly, a Phase II Randomized Controlled Trial conducted in Malawi showed that early fungicidal activity (EFA) for the triple combination of AmB plus FLU plus 5-FC was greater than for AmB plus FLU: -0.50 ± 0.15 log CFU/day vs. -0.38 ± 0.19 log CFU/day (p = 0.03); and greater than FLU plus 5-FC (-0.28 ± 0.17) or FLU alone (-0.11 ± 0.09). Combined analysis across steps revealed that addition of 5-FC plus AmB had significant, independent additive effects on EFA, with trends toward fewer early deaths with the addition of 5-FC (4/41 vs. 11/39, p = 0.05) and fewer deaths overall with the addition of AmB (13/39 vs. 20/40, p = 0.1) (20).

A retrospective cohort study done at Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China revealed that a combination of FLU plus 5-FC is promising in treating non-HIV- and non-transplant-associated CM patients who do not tolerate or are not suited for AmB plus 5-FC regimen. There is no significant differences in cryptococcus clearance (74.4% vs 70.2%, $P = 0.814$), treatment time (39 days, 20-69 days vs 21 days, 7-63 days, $P = 0.107$) and successful response rates (69.7% vs 72.3%, $P = 0.820$), but FLU plus 5-FC treatment had lower total adverse events (19.1% vs 90.7%, $P < 0.001$) (21).

Limitation of the review

This review excludes studies done in languages other than English and abstracts only pieces of the manuscripts. The literature review was done on the effectiveness of Amphotericin B alone and combining Amphotericin B with Flucytosine which has wide variations regarding strength. There was a lack of recent randomized clinical trials comparing the two regimens.

The cure rates we encountered also cannot be compared easily with various reports because the characteristics of patients affect the outcome.

Conclusion and Recommendations

Our review indicated that combining Amphotericin B with Flucytosine showed better sterilization of cerebrospinal fluid and improvement of clinical symptoms which leads to the conclusion that a combination regimen is better than Amphotericin B monotherapy of Cryptococcal meningitis. Further studies should be done to include studies done in languages other than English. A continuation arm of the interim analysis reports of some of the study should be incorporated to answer some of the above limitations to increase updated literature sources. Assessment of compliance with the prescribed drug therapy, which may have had an impact on effectiveness outcomes, should also be done.

Competing of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

ACKNOWLEDGMENTS

We would like to express our gratitude to College of Health Sciences, Addis Ababa University for allowing us to use required resources to prepare this review article.

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Tinsae Alemayehu, MD[1,2], Alan Karibian, MD[3], Demeke Mekonnen. *Ethiop Med J, 2021, Vol. 59, No. 2*

CASE REPORT

PEDIATRIC INFLAMMATORY MULTISYSTEM SYNDROME TEMPORALLY ASSOCIATED WITH SARS COV 2 (PIMS-TS): A CASE REPORT FROM ETHIOPIA AND A REVIEW OF LITERATURE

Tinsae Alemayehu, MD[1,2], Alan Karibian, MD[3], Demeke Mekonnen, MD[4]

ABSTRACT

Many thousands of children have so far been diagnosed with SARS-CoV-2 infection. An uncommon presentation of pediatric Coronavirus Disease COVID-19 is the Pediatric inflammatory multisystem syndrome temporally associated with SARS CoV 2 (PIMS-TS), also referred to as Multisystem Inflammatory Syndrome in Children (MIS-C). Though more than 35 countries have reported this syndrome, there have been very few reports from low- and middle-income countries, including Ethiopia. We are reporting the first child from Ethiopia affected by PIMS-TS and a review of the literature on its presentation, diagnosis, and management.

INTRODUCTION

The COVID-19 pandemic caused by the SARS-CoV-2 virus had led to more than 100 million cases worldwide one year after its onset in December 2019, claiming the lives of close to 2.5 million people (1). The first child diagnosed with COVID-19 was reported from Shenzhen, China, on 20th January 2020 (2). In March 2020, pediatricians in Europe began reporting children infected with SARS-CoV-2 and presenting with fever and multisystem inflammation (3). Even though hundreds of more cases have subsequently been diagnosed with this syndrome, now known as Pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) – very few has been reported from low- and middle-income countries (4). Its commonest presentations include fever, hypoxia and/or hypotension, less often abdominal pain, conjunctivitis, cough, diarrhea, headache, mucositis, lymph node swelling and rash (5). We are reporting here the first child from Ethiopia affected by PIMS-TS.

CASE PRESENTATION

A four years and eight months old boy presented with a high grade fever of five days. He also had a reddish-colored rash behind his right ear and trunk in the preceding few hours, which did not follow a contiguous spread. He also complained of poor appetite, intermittent mild abdominal, dysuria, groin pain, and intermittent cough. His parents reported red eyes and swollen lips, which started a day prior to the presentation. He had no runny nose.

He was vaccinated with a single dose of the Measles vaccine at nine months of age and was up-to-date for his age on the rest of his vaccines. An asymptomatic close contact (of a patient who tested positive for PCR of SARS-CoV-2 three weeks ago) had spent two nights with the boy and his family a fortnight ago. His parents reported no history of allergies to medication and food. He had received antipyretics, oral Amoxicillin for one day, and oral Cefpodoxime for three days for presumed acute pharyngitis but his symptoms failed to improve. He had no travel history outside of his hometown – Addis Ababa – a city 2400 meters above sea level in Ethiopia's central highlands – a malaria-free area.

On physical examination, his temperature was 36.3°C, pulse rate 160 beats per minute, respiratory rate 28 per minute, and blood pressure 80/40 mmHg. He had bilateral injected bulbar conjunctivae sparing the limbs, strawberry tongue, swollen erythematous and cracked lips, anterior cervical lymphadenopathy (largest having a diameter of 1.5 cm), erythematous palms with macules (blanching), and an erythematous maculopapular rash over the right posterior auricular region, right axilla, left leg as well as the trunk (Figure 1).

His admission lab work-up showed a white blood cell count of 11000/mm^3 with neutrophils of 9770/mm^3 and platelets of 111,000/mm^3. The rest of his complete blood count was within normal ranges for his age. His serum C-reactive protein (CRP) was elevated (118 mg/l). His urinalysis showed 1 – 2 white blood cells and 0 – 1 red blood cells per high power field with no proteins.

[1] American medical center, Addis Ababa, Ethiopia. [2] St. Paul's hospital millennium medical college, Addis Ababa, Ethiopia.[3] Suisse Clinic, Addis Ababa, Ethiopia.[4] St. Peter's referral hospital, Addis Ababa, Ethiopia.
*Corresponding Author E-mail: tigisttinsae@gmail.com

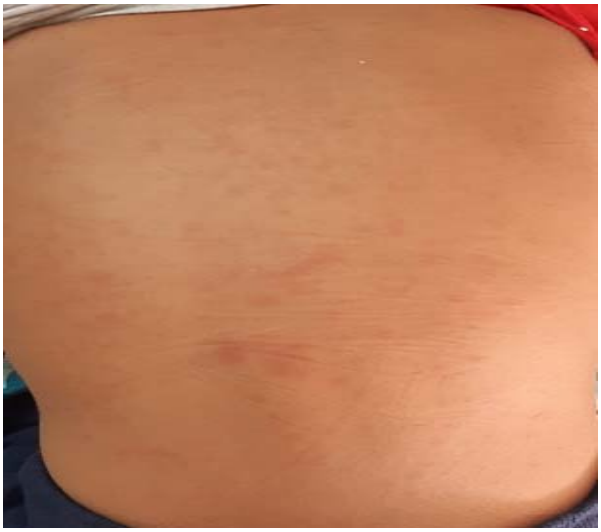

Figure 1: Erythematous maculopapular rash over the child's back

His serum urea nitrogen and creatinine were 15 mg/dl and 0.5 mg/dl, respectively, while liver enzymes were elevated two times (Alanine transaminase 85 U/l and Aspartate transaminase 98 U/l). His seromarkers for hepatitis B and C were negative, while his group A rapid streptococcal antigen test was negative. His serum albumin was 3.1 g /dl (normal: 3.8 – 5 g/dl).

His SARS-CoV-2 PCR (nasopharyngeal and oropharyngeal samples) was negative, while his SARS-CoV-2 specific IgM and IgG were positive. Echocardiography done at admission (day five of fever) showed acute mild mitral regurgitation with no evidence of coronary artery lesions and pericardial or myocardial abnormalities. His troponin could not be determined. His chest X-ray did not show any abnormalities. An abdominal ultrasound showed mild terminal thickening with enlarged mesenteric lymph nodes, the largest having central necrosis and measuring 0.88 cm x 1.27 cm.

He met the diagnostic criteria for Kawasaki disease (KD): fever of five days, bilateral injection of the bulbar conjunctivae with limbic sparing and without exudate, erythematous swollen cracked mouth and lips, strawberry tongue, erythematous maculopapular rash, palmar erythema, and anterior cervical lymphadenopathy. In addition, he had abdominal pain with ultrasound findings of ileitis and mesenteric lymphadenopathy, urethritis, neutrophilia and lymphopenia, abnormal inflammatory markers (elevated serum CRP, hypoalbuminemia) and positive SARS-CoV-2 specific serum IgM and IgG, which led to a final diagnosis of Pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS).

The boy was given a first dose of IV immunoglobulin (IVIG) infusion at 2 g/kg over 12 hours and also started on Aspirin per os (PO) at 40 mg/kg/day divided into four doses. He was given oral paracetamol for fever records of more than 37.8^{o}C. Nearly two days (44 hours) after completing his IVIG dose, he became afebrile and the redness of his eyes started to subside. The abdominal pain and dysuria also lessened. His rash started to fade after 60 hours IVIG completion and disappeared within the ensuing 24 hours. His pulse rate dropped to 105 beats per minute while his blood pressure elevated to 90/50 mmHg.

His serum CRP dropped to 50.4 mg/L after 24 hours of admission and to 5 mg/L by the 14th day of illness. A repeat echocardiography on his 14th day of illness showed very mild mitral regurgitation with normal coronary arteries. His liver enzymes normalized within 48 hours of starting treatment. On his 14th day, his complete blood count (CBC) abnormalities had corrected to normal ranges for age (absolute neutrophil count being 2190/mm^3 and platelets 332,000/mm^3). Though he did not require a second dose of IVIG, he continued taking aspirin at 4 mg/kg/day as a single dose after 48 hours lapsed without fever until six weeks after onset of illness. Echocardiography, CBC, and CRP done at the end of the sixth week of follow-up showed normal findings and aspirin was stopped.

DISCUSSION

The World Health Organization defines the PIMS-TS as seen in a patient aged 19 years or less with a fever of more than three days and two, or more of the following signs (6):

- Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet)
- Hypotension or shock
- Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including Echocardiographic findings or elevated Troponin/ NT-proBNP)
- Evidence of coagulopathy (by prothrombin time (PT), partial thromboplastin time (PTT), elevated D-dimers)
- Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)

This should be accompanied by elevated markers of inflammation such as erythrocyte sedimentation rate (ESR), CRP, or procalcitonin in the absence of an alternative diagnosis and evidence of COVID-19 (RT -PCR, antigen test or serology positive), or likely contact with patients with COVID-19. Our patient fulfilled the criteria through his fever, typical rash, echocardiographic evidence of valvulitis, abdominal pain, elevated CRP and serologic evidence of a recent COVID19 infection (positive SARS-CoV-2 specific immunoglobulin (Ig) M and IG (6) .

The proposed mechanisms for PIMS-TS are post-viremia aberrant immune response mediated by enhanced non-neutralizing IgG antibodies (7,8) and delayed and excess cytokine storm caused by a high SARS CoV 2 viral load leading to impaired types I and III interferon responses (7,9). Clinical signs of PIMS-TS resemble that of KD. In their review of 21 children with PIMS-TS, Toubiana et al. noted the fulfillment of diagnostic criteria for KD in all of their cases while Feldstein et al. reported overlapping features of KD with PIMS-TS in 43% of patients (10,14). In PIMS-TS with presentations mimicking KD, treatment with IVIG, and aspirin should be initiated (12). The mean age at presentation of PIMS-TS is eight years with males, and black children disproportionally affected. The commonest presentations are fever (99%), gastrointestinal (86%) and cardiovascular symptoms (80%). Children with isolated KD (not associated with SARS CoV 2) are younger with a peak age at presentation being 18 – 24 months, and manifest with myocarditis less frequently (< 5%) while gastrointestinal symptoms frequently occur in both PIMS-TS and KD (11,12).

The syndrome is postulated to be due to a post-viremia hyperinflammatory response and as such, a recent COVID19 diagnosis is more likely to be made with serologic tests rather than RT-PCR tests. A study from the United Kingdom (U.K.) showed that of a cohort of 78 children with PIMS-TS, only 17 tested positive for RT-PCR from nasopharyngeal and oropharyngeal samples while 33 and 35 respectively had positive IgM and IgG (8).

SARS-CoV-2 serologic tests show no cross-reactivity with other respiratory viruses and are better diagnostic tests for acute (positive IgM and IgG) and resolved (negative IgM and positive IgG) beyond five days of illness (13). Elevated inflammatory markers are a hallmark feature in PIMS-TS, with 92% of affected children having high ESR, C-reactive protein, or procalcitonin levels (14). While coronary aneurysms are a recognized complication of KD, they are infrequently seen in PIMS-TS.

Only three children of a total 58 presenting with PIMS-TS in the U.S. were found to have coronary aneurysms on Echocardiography (15).

A large proportion of children may need ICU care with mechanical ventilation rarely needed. Mortality due to PIMS-TS is rare, with death rates of 0 – 2.5% recorded among cohorts in Italy, the U.S., U.K., Switzerland, and France and average length of admission of 7 days (8,10,14-17).

The foundation of treatment for PIMS-TS is immune -modulation with IVIG being the preferred therapy among many reports (8,10,14-17). Other treatment options used with less frequency include corticosteroids, interleukin 6 inhibitors (Tocilizumab), interleukin 1 receptor antagonist (Anakinra) and anti-TNF inhibitors (Infliximab) (14-15, 18).

Our patient was successfully treated with IVIG alone with clinical and echocardiographic resolution and with his inflammatory markers subsiding to normal levels. He did not require respiratory support or inotropes. Accessing IVIG is difficult in Ethiopia and when available, it's expensive. Corticosteroids like Methylprednisolone were used in 31 – 80% of cohorts of PIMS-TS globally (8,10,14-17) and adding steroids to IVIG was associated with recovery of cardiac function in PIMS-TS according to one report (19). In the absence of alternatives, steroids alone should be used to treat PIMS-TS in addition to supportive care.

In conclusion, we are reporting the first case of Pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) from Ethiopia as a useful communication to manage similar cases amidst the ongoing COVID19 pandemic.

ACKNOWLEDGEMENT

The authors would like to thank their colleagues in their respective institutions for their valuable input in managing this child.

Competing of interest

The authors report no conflicts of interest.

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Shahana Zaman, Deb Dulal Debnath, Shaila Nabi, Muhammad Abdur Rahim, Mohammad Ullah, M Atahar Ali.
Ethiop Med J, 2021, Vol. 59, No. 2

CASE REPORT

CARDIAC INVOLVEMENT BY LYMPHOMA: REPORT OF A FATAL CASE

Shahana Zaman, FCPS[1], Deb Dulal Debnath, MD[1], Shaila Nabi, FCPS[1], Muhammad Abdur Rahim, FCPS[2], Mohammad Ullah, FCPS, MD[3], M Atahar Ali, FCPS, MD[1]

ABSTRACT

Lymphomas are one of the most common malignant neoplasms of the heart. Cardiac lymphomas may be primary but most of the cases are part of disseminated disease. A young Bangladeshi man, diagnosed with non-Hodgkin lymphoma and on chemotherapy, presented with features of heart failure. Initial evaluation revealed complete heart block with narrow QRS complexes and intra-cardiac mass lesion suggesting lymphomatous deposit. The patient expired while awaiting an endo-myocardial biopsy.
Key words: *cardiac lymphoma, complete heart block, non-Hodgkin lymphoma.*

INTRODUCTION

Lymphomas are one of the most common malignant cardiac neoplasms. Cardiac lymphomas may be primary or cardiac involvement may be a part of disseminated disease or metastatic in nature.(1,2) In most cases, cardiac lymphomas are diagnosed after death; ante-mortem diagnosis needs a high index of clinical suspicion. If patients with lymphoma present with features of cardiac outflow obstruction, heart failure, pericardial effusion, cardiac temponade, arrhythmia or conduction block, a thorough cardiac evaluation is mandatory. Patients with cardiac lymphoma receiving chemotherapy may be complicated by cardiac rupture and sudden death is not uncommon in such instances.(3) Here, we present a case of non-Hodgkin lymphoma complicated with cardiac involvement.

CASE REPORT

A 26-year-old Bangladeshi male patient, diagnosed with non-Hodgkin lymphoma, involving the cervical, axillary and inguinal lymph nodes, presented with one-week history of worsening oedema and breathlessness. He received 5 cycles of chemotherapy with initial clinical improvement before presenting to our facility.

The patient was dyspneic with a respiratory rate of 20/min and had ankle oedema. He had a surgical scar in left side of neck resulting from the previous lymph node biopsy and enlarged left supra-clavicular lymph node. His pulse was 60/min and blood pressure was 100/50 mm Hg. He had raised jugular venous pressure with intermittent cannon waves, left parasternal lift and palpable P2. Pulmonary component of 2nd heart sound was loud and there was a pan-systolic murmur (grade 3/6) in left para-sternal area. He had few bi-basal crepitations and 4-cm hepatomegaly below the costal margin. He had anaemia (haemoglobin 10.5 gm/dl) and high erythrocyte sedimentation rate (78 mm/1-h). Electrocardiogram revealed complete heart block with narrow QRS complexes (Figure 1). Chest radiograph revealed cardiomegaly and left lower lobe consolidation (Figure 2). Transthoracic echocardiography revealed a fixed non-homogenous intra-cardiac mass occupying right atrium adherent to inter-atrial and inter-ventricular septum encroaching the tricuspid valve (Figure 3a, 3b) with spontaneous echo-contrast in inferior vena cava, mild pulmonary hypertension, impaired right ventricular systolic function and mild pericardial effusion. Computed tomography (CT) scan revealed diffuse intra-cardiac mass involving right atrium, inter-atrial septum, inter-ventricular septum, superior vena cava and left innominate vein and thrombus in the left sub-clavian vein (Figure 4). Blood culture revealed no growth.

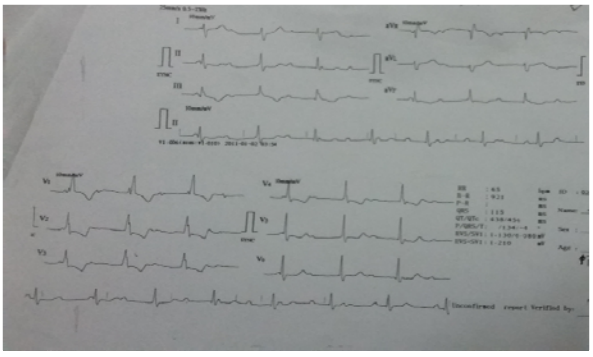


Figure 1: Electrocardiogram showing complete heart block with normal QRS complex, Bangladesh, 2020.

[1]Cardiology, NICVD, Dhaka, Bangladesh
[2]Nephrology, BIRDEM, Dhaka, Bangladesh
[3]Cardiology, SSMC, Dhaka, Bangladesh
*Corresponding Author E-mail: muradrahim23@gmail.com

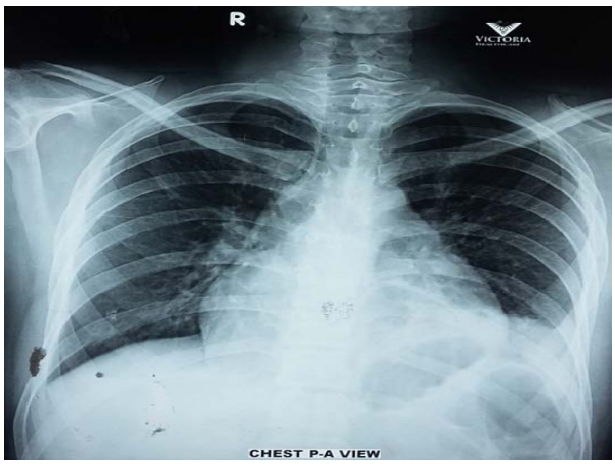
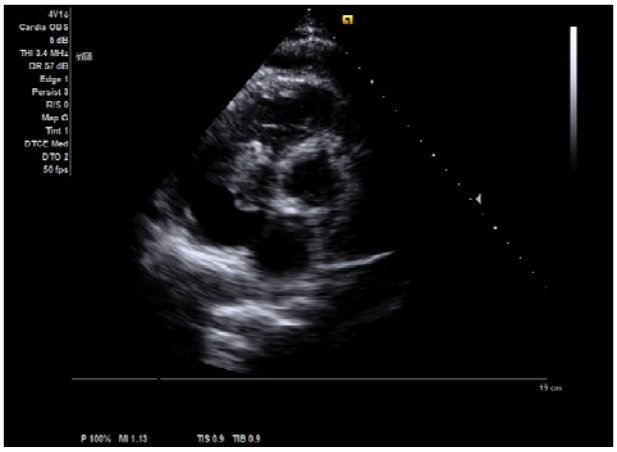


Figure 2: Chest x-ray posterior-anterior view showing enlarged cardiac shadow with left lower lobe consolidation, Bangladesh, 2020.



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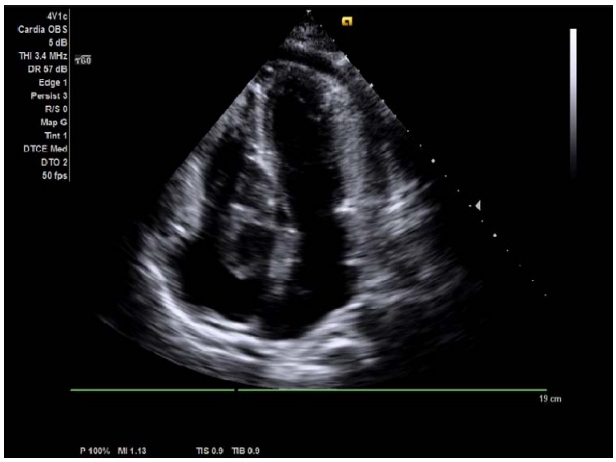

3b

Figure 3a, 3b: Transthoracic echocardiography showing fixed non-homogenous intra-cardiac mass occupying the right atrium adherent to inter-atrial and inter-ventricular septum encroaching the tricuspid valve, Bangladesh, 2020.

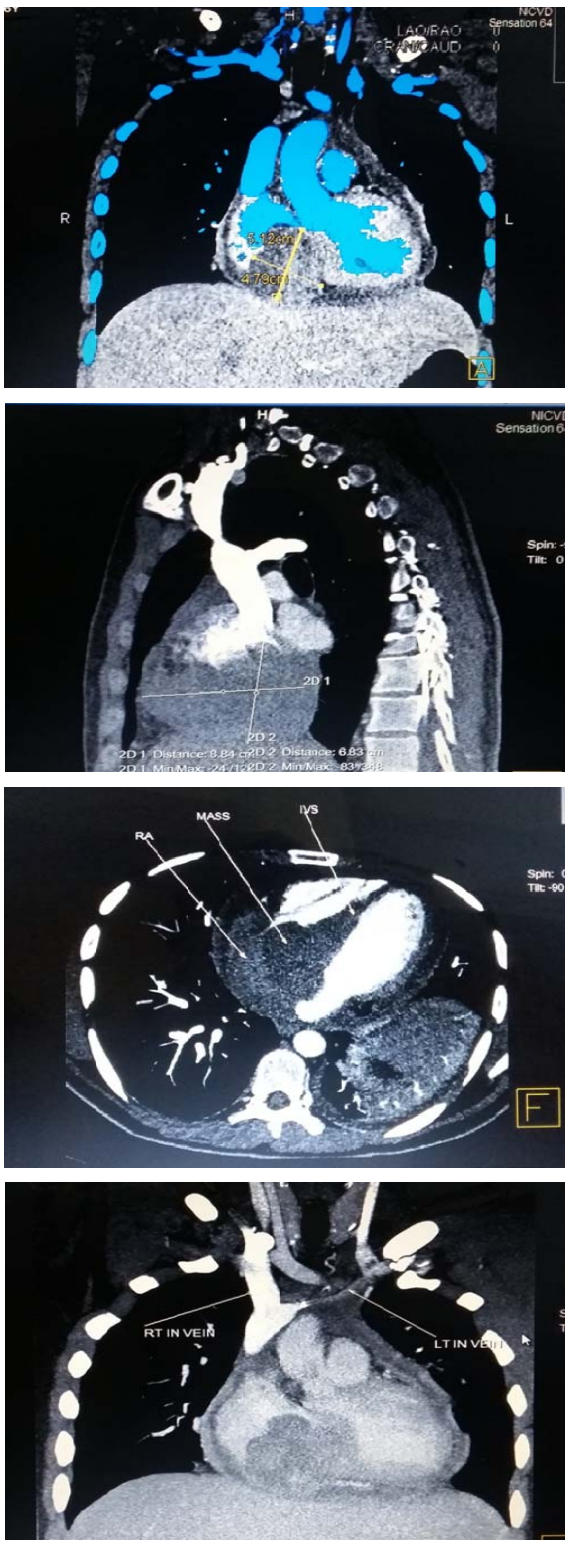

Figure 4: Computed tomography scan showing diffuse intra-cardiac mass involving the right atrium, inter-atrial septum, inter-ventricular septum, superior vena cava and left innominate vein and thrombus in the left sub-clavian vein, Bangladesh, 2020.

Considering the background diagnosis, the intra-cardiac mass was suspected as being cardiac involvement by the aforementioned non-Hodgkin lymphoma. Patient received treatment for cardiac failure along with anti-coagulation and consultation from surgical team was sought, but unfortunately, the patient succumbed to death while awaiting an endo-myocardial biopsy and subsequent cycle of chemotherapy.

DISCUSSION

Cardiac involvement in lymphoma is not uncommon; 18% of patients with non-Hodgkin lymphoma had autopsy evidence of cardiac involvement.(2,4) Improved imaging techniques including echocardiography, cardiac CT and magnetic resonance imaging (MRI) have increased the diagnosis in life.(1,2) Majority of these cases are part of a disseminated disease; primary cardiac lymphoma is rather rare, constitutes ~1% of primary cardiac tumours and is defined by the absence of extra-cardiac lesions.(1,5)

Clinical presentation of cardiac lymphoma depends up on the location and extent of cardiac involvement.[2] Patients may present with heart failure, features of outflow obstruction, pericardial effusion, myocardial infarction and arrhythmia.(1,2,5) Patients may have history of treated lymphoma or may have concurrent nodal and extra-nodal features.(1,2,4) Non-specific systemic features like fever and weigh loss are common.(1,2)

Chest imaging may reveal cardiomegaly, features of heart failure, pericardio-pleural effusions and mediastinal lymphadenopathy.(1,2,6) Electrocardiography may show arrhythmia (1,2,6) and conduction abnormality as was seen in the present case. Conduction defects may result from malignant infiltration in to the conductive tissues (2) or adverse chemotherapeutic effects.

Echocardiography including trans-oesophageal echocardiograhy may identify pericardial effusion, intra-cardiac lesion and extent.(1,2) Cardiac CT scan and MRI can delineate the nature and extent of lesion. (1,2,6) Positron emission topography (PET) scan can identify apparently unidentified lesions elsewhere. (1,6)

However, tissue diagnosis remains the gold standard for establishing the diagnosis and includes endo-myocardial biopsy, analysis of pericardial fluid and lymph node biopsy.(1,2,5,6) Immuno-phenotyping further refines the diagnosis.(5,6)

Patients with non-Hodgkin lymphoma merit evaluation for human immunodeficiency virus (HIV) status, staging CT and bone marrow study.(2,5,6)

There is no definite treatment protocol for cardiac lymphoma and chemotherapy remains the mainstay of treatment.(5) R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisolone) had resulted in remission in published case reports.(1) Arrhythmias may warrant temporary pacing and cardiac obstructive lesion may require surgery.(1,5)

Prognosis is variable, depends up on stage of disease, presence of arrythmia and quality of care.(1,2) Overall survival is in term of months.(5) Death may occur from life-threating arrhythmia, cardiac rupture and myocardial infarction.(3) The exact cause of death in our patient could not be evaluated as autopsy was not done.

In conclusion, a high index of suspicion for cardiac lymphoma is needed in appropriate clinical context, as early diagnosis and appropriate treatment may result in favourable outcome.

Consent: Informed consent was taken from father of the patient regarding publication of this case and accompanying images.

Competing interest: Nothing to declare.

ACKNOWLEDGMENTS

We express our acknowledgements to the Department of Radiology and the Department of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh for their supports during evaluation and management of the patient.

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Tinsae Alemayehu, Tewodros Yalew, Helen Mintesnot Dessalegn. *Ethiop Med J, 2021, Vol. 59, No. 2*

CASE REPORT

TRICHINELLA MYOPATHY IN A CHILD PRESENTING WITH A NECK MASS: CASE REPORT AND LITERATURE REVIEW

Tinsae Alemayehu, MD[1,2*], Tewodros Yalew , MD[3], Helen Mintesnot Dessalegn, MD[4]

ABSTRACT

Human Trichinellosis is a widely distributed tissue nematode infection. It is infrequently from Ethiopian children. We report on a twelve-year-old boy who presented with a left-sided neck swelling of three months and dysphagia of one-month duration. A muscular biopsy confirmed the presence of Trichinellosis and the child was treated with Albendazole for ten days. Children with dietary risk factors and presenting with chronic myositis should be evaluated for Trichinella infection as part of their work-up.
Keywords: *Children, Ethiopia, Myositis, Trichinellosis,*

INTRODUCTION

Human Trichinellosis is widespread globally. Any carnivorous animal can serve as the reservoir of Trichinella species. The predominant pathogen is Trichinella spiralis followed by Trichinella native, and Trichinella britovi. Eating raw meat is the leading risk factor for acquiring the infection. Following ingestion, larvae released from a gravid female enter circulation and preferentially disseminate to skeletal muscles. Though mostly asymptomatic, enteric and extra- gastrointestinal symptoms can follow heavy infections (2).

Outbreaks among humans had been described in Ethiopia (from soldiers in the Gojjam region and police officers in the Arsi region) in relation to the consumption of warthog meat in the 1980s and 1990s, with a total of 28 cases and a single mortality described (3, 4). We are reporting our case as Trichinellosis has not been described among children in Ethiopia and because its description is informative for child health practitioners to be on the lookout for the risk factors, presentation and treatment for Trichinella infections.

CASE PRESENTATION

A twelve-year-old boy presented to Tikur Anbessa Specialized Hospital with a left lateral neck mass of three months. It was pea-sized initially but progressively enlarged. As it was not associated with pain or warmth, his parents only sought medical care when he started experiencing dysphagia one month prior to presentation. He had no other body swellings. He had no fever, sweating, breathing difficulties, cough, a loss of appetite or weight. He lived in rural Southern Ethiopia with his diet comprising of legumes, fruits and intermittently raw beef. His past medical history was unremarkable. His family reported he had received all childhood vaccines. He had frequent exposure to cattle and sheep within the proximity of his household.

He was comfortable upon examination. His vital signs were within normal limits. He had a left posterior cervical triangle lymphadenopathy – non-matted, non-tender, mobile, and the largest spanning 2 cm. He also had a solitary large non-tender left lateral neck mass, with a smooth overlying surface and measuring 15 cm x 15 cm (Figure 1A).

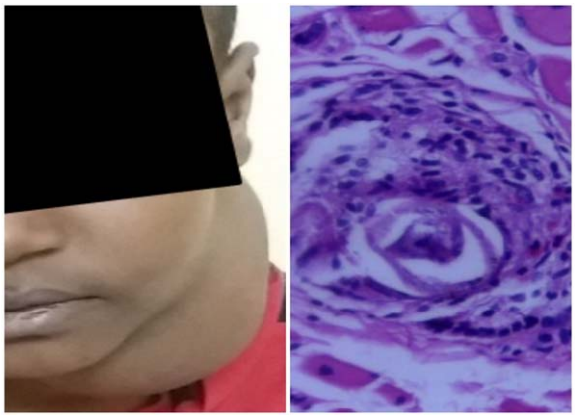

Figure 1A: Neck swelling of the child; Figure 1B: Histologic section from muscle biopsy

[1] American medical center, Specialty center for infectious diseases and travel medicine, Addis Ababa, Ethiopia.
[2] St. Paul's hospital and millennium medical college, Addis Ababa, Ethiopia.
[3] Department of Pathology, College of health sciences, Addis Ababa University, Addis Ababa, Ethiopia.
[4] Department of Pediatrics and child health, College of health sciences, Addis Ababa University, Addis Ababa, Ethiopia.
*Corresponding Author E-mail: tinsae.alemayehu@aau.edu.et

Serial hematologic work-ups showed WBC counts of 6000 – 7000/mm^3, absolute neutrophil counts of 3800 - 4300/mm^3, absolute lymphocyte counts of 1400 - 2200/mm^3, absolute eosinophil counts of 400 - 500/mm^3, normal basophil and monocyte counts; hemoglobin of 9.5 gm/dl, mean corpuscular volume of 63 fl and platelets of 415,000/mm^3. He had normal serum electrolytes, renal/liver function tests, serum LDH and uric acid levels. His chest x-ray was normal but a chest CT showed multiple homogeneously enhancing matted cervical (measuring 10.3 x 8.6 x 4.9 cm overall), bilateral axillary and mediastinal lymphadenopathies.

A bone marrow aspirate showed no abnormalities. The neck muscle biopsy confirmed multiple cystic larvae (*Trichinella*) within skeletal muscle along with epithelial granuloma and foreign body type multinucleated giant cells (Figure 1B) with a lymph node aspirate suggestive of a reactive lymphadenopathy. Stool microscopy was negative. He was treated with a ten day regimen of Albendazole. The child was subsequently lost from follow-up.

DISCUSSION CONCLUSIONS

After ingestion of infected meat, symptomatic Trichinellosis progresses through two phases: enteral and parenteral. The enteral phase is notable for watery diarrhea, abdominal discomfort, and vomiting. The third week of illness heralds the onset of the parenteral phase whereby adult worms produce larvae which encyst within striated cells (5).

Neck, extra-ocular, and masseter muscles are frequently affected. Myalgia, facial and peri-orbital edema, sub-conjunctival, and splinter hemorrhages can be seen due to inflammatory and allergic responses to invading larvae (6). Our patient experienced neck muscle swelling described in the literature mentioned above, while other extra-muscular manifestations were not seen. Pneumonia, encephalitis, or myocarditis cause most mortality in heavy infections (7). The stool examination is occasionally helpful in diagnosing enteric illness.

A biopsy from a tender swollen muscle, eosinophilia, elevated creatinine phosphokinase, positive IgM and IgG antibodies, or abnormal electromyography helps confirm *Trichinella* myositis (8). The diagnosis in our patient was settled using a muscular biopsy. A 10 – 15 day course of Albendazole or Mebendazole can help eradicate adult worms in the intestinal phase. There is no consensus on the pharmacologic management of parenteral illness. Steroids may be used in severe infections (9). Killing *Trichinella* larvae by cooking meat to temperatures of more than 55^{o}C (especially pertinent to prevent infections due to eating raw beef in Ethiopia) or freezing pork meat to temperatures of -15^{o}C or lower can help prevent infections (8).

Reports of Human Trichinellosis are scarce in Ethiopia. Human Trichinellosis has been reported from 4 sub-Saharan countries though high-risk activities like raw meat (bushpigs, warthogs, cattle) consumption are observed in many African communities (10). The same culinary practice is also the likely predisposition for our patient's presentation. Raw beef, in particular, is a commonly consumed dish among many societies in Ethiopia. His swollen body part is an anatomic location, which is frequently cited as affected by this tissue nematode. A high parasite burden may have contributed to the notably large muscular swelling.

In conclusion, Trichinellosis should be included in the work-up of children with dietary risk factors and chronic myositis. This case report highlights its presentation and management.

ACKNOWLEDGMENTS

We would like to thank our colleagues in our respective institutions and beyond for valuable input in this manuscript's preparation.

Competing of interest

The authors report they have no conflicts of interest.

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Editorial responsibilities

The Editor-in-Chief is responsible for deciding which articles submitted to the journal will be published. The decisions are made based exclusively on the manuscript's merit. They must be free from any racial, gender, sexual, religious, ethnic, or political bias. When making decisions the Editor-in-Chief is also guided by the editorial policy and legal provisions relating to defamation, copyright infringement and plagiarism.

Members of the Editorial Board including the Editor-in-Chief must hold no conflict of interest about the articles they consider for publication. Members who feel they might be perceived as being involved in such a conflict do not participate in the decision process for a manuscript.

The information and ideas presented in submitted manuscripts shall be kept confidential.

Editors and the editorial staff shall take all reasonable measures to ensure that the authors/reviewers remain anonymous during and after the evaluation process in accordance with the type of reviewing in use.

The Editorial Board is obliged to assist reviewers with additional information on the manuscript, including the results of checking manuscript for plagiarism.

Reviewers' responsibilities

Reviewers are required to provide the qualified and timely assessment of the scholarly merits of the manuscript. The reviewer takes special care of the real contribution and originality of the manuscript. The review must be fully objective, and the judgment of the reviewers must be clear and substantiated by arguments.

The reviewers assess manuscript for the compliance with the profile of the journal, the relevance of the investigated topic and applied methods, the scientific relevance of information presented in the manuscript, and the pres-

entation style. The review has a standard format. It is submitted through the online journal management system where it is stored permanently.

The reviewer must not be in a conflict of interest with the authors or funders of research. If such a conflict exists, the reviewer is obliged to promptly notify the Editor-in-Chief. The reviewer shall not accept for reviewing papers beyond the field of his/her full competence.

Reviewers should alert the Editor-in-Chief to any well-founded suspicions or the knowledge of possible violations of ethical standards by the authors. Reviewers should recognize relevant published works that have not been considered in the manuscript. They may recommend specific references for citation but shall not require citing papers published in the Ethiopian Medical Journal, or their own papers, unless it is justified.

The reviewers are expected to improve the quality of the manuscript through their suggestions. If they recommend correction of the manuscript prior to publication, they are obliged to specify the way this can be achieved. Any manuscript received for review must be treated as confidential document.

Ethical Considerations

Dealing with unethical behavior

Anyone may inform the Editor-in-Chief at any time of suspected unethical behavior or any type of misconduct by giving the necessary credible information/evidence to start an investigation.

- Editor-in-Chief makes the decision regarding the initiation of an investigation.
- During an investigation, any evidence should be treated as confidential and only made available to those strictly involved in the process.
- The accused will always be given the chance to respond to any charges made against them.

If it is judged at the end of the investigation that misconduct has occurred, then it will be classified as either minor or serious.

Minor misconduct (with no influence on the integrity of the paper and the journal, for example, when it comes to misunderstanding or wrong application of publishing standards) will be dealt with directly with authors and reviewers without involving any other parties. Outcomes include:

- Sending a warning letter to authors and/or reviewers.
- Publishing correction of a paper, e.g. when sources properly quoted in the text are omitted from the reference list.

Publishing an erratum, e.g. if the error was made by editorial staff.

In the case of major misconduct, the Editor-in-Chief may adopt different measures:

- Publication of a formal announcement or editorial describing the misconduct.
- Informing officially the author's/reviewer's affiliating institution.

The formal, announced retraction of publications from the journal in accordance with the Retraction Policy.

- A ban on submissions from an individual for a defined period.

Referring a case to a professional organization or legal authority for further investigation and action.

The above actions may be taken separately or jointly. If necessary, in the process of resolving the case relevant expert organizations, bodies, or individuals may be consulted.

When dealing with unethical behavior, the Editorial Board will rely on the guidelines and recommendations provided by the Committee on Publication Ethics (COPE).

Plagiarism prevention

The Ethiopian Medical Journal does not publish plagiarized papers. The Editorial Board has adopted the stance that plagiarism, where someone assumes another's ideas, words, or other creative expression as one's own, is a clear violation of scientific ethics. Plagiarism may also involve a violation of copyright law, punishable by legal action.

Plagiarism includes the following:

- Self-plagiarism, which is using one's own previous work in another context without citing that it was used previously
- Verbatim (word for word), or almost verbatim copying, or purposely paraphrasing portions of another author's work without clearly indicating the source or marking the copied fragment (for example, using quotation marks) in a way described under Authors' responsibilities;
- Copying equations, figures or tables from someone else's paper without properly citing the source and/or without permission from the original author or the copyright holder.

Any manuscript which shows obvious signs of plagiarism will be automatically rejected. In case plagiarism is discovered in a paper that has already been published by the journal, it will be retracted in accordance with the procedure described under Retraction policy, including blacklisting the author(s) .

To prevent plagiarism, the manuscripts are submitted to a plagiarism detection process. The results obtained are verified by the Editorial Board in accordance with the guidelines and recommendations of the Committee on Publication Ethics (COPE).

Retraction policy

Legal limitations of the publisher, copyright holder or author(s), infringements of professional ethical codes, such as multiple submissions, bogus claims of authorship, plagiarism, fraudulent use of data or any major misconduct require retraction of an article.

Occasionally, a retraction can be used to correct numerous serious errors, which cannot be covered by publishing corrections. A retraction may be published by the Editor-in-Chief, the author(s), or both parties consensually.

The retraction takes the form of a separate item listed in the contents and labeled as "Retraction".
The original article is retained unchanged, except for a watermark on the PDF indicating on each page that it is "retracted".

Open access

Open access policy

The Ethiopian Medical Journal is published under an Open Access license. All its content is available free of charge. Users can read, download, copy, distribute, print, search the full text of articles, as well as to establish HTML links to them, without having to seek the consent of the author or publisher.

The right to use content without consent does not release the users from the obligation to give the credit to the journal and its content in a manner described under Licensing.

Article processing charge

The Ethiopian Medical Journal does not charge authors or any third party for publication in its regular quarterly Issues. Both manuscript submission and processing services, and article publishing services are free of charge.
There are no hidden costs whatsoever.

GUIDELINES FOR AUTHORS

The *Ethiopian Medical Journal (EMJ)* is the official Journal of the Ethiopian Medical Association (EMA) devoted to the advancement and dissemination of knowledge pertaining to the broad field of medicine in Ethiopia and other developing countries. Prospective contributors to the Journal should take note of the instructions of Manuscript preparation and submission to EMJ as outlined below.

Article types acceptable by EMJ

Original Articles (*vide infra*) on experimental and observational studies with clinical relevance
Brief Communications
Case Series
Case Reports
Editorials, Review or Teaching Articles: by invitation of the Editorial Board.
Correspondences/Letters to the Editor
Monographs or set of articles on specific themes appearing in a Special Issues of the Journal
Book reviews
Perspectives,
Viewpoints
Hypothesis or discussion of an issue important to medical practice
Letter to the Editor
Commentaries
Advertisements
Obituaries

N.B. Articles are not acceptable if previously published or submitted elsewhere in print or electronic format, except in the form of abstracts in proceedings of conferences.

Content and format of articles:

Title: The title should be on a separate page. It should not have acronyms or abbreviations. The title should be descriptive and should `not exceed 20 words or 120 characters including space. The title page should include the name(s) and qualification of the author(s); the department or Institution to which the study/research is attributed and address of the corresponding Author. If the author has multiple affiliations only use the most preferred one.

1. Original Articles

2,500 words, excluding Abstracts, References, Figures and Tables. The manuscript of the Article, should appear under the following headings:

a) Abstract: The abstract of the Article is prepared on a separate paper, a maximum of 250 words; it should be structured under the titles: a) Background; b) Methods; c) Results; d) Conclusions. Briefly summarize the essential features of the article under above headings, respectively. Mention the problem being addressed in the study; how the study was conducted; the results and what the author(s) concluded from the results. Statistical method used can appear under Methods paragraph of the Abstract, but do not insert abbreviations or references in the Abstract section.

Keywords: Provide three to six key words, or short phrases at the end of abstract page. Use terms from medical subject heading of Index Medicus to assist in cross indexing the Article.

b) Introduction : Should provide a short background and context of the study and provide the rationale for doing the study. It should not be a detailed review of the subject and should not include conclusions from the paper.

c) **Patients or (Materials) and Methods:** should contain details to enable reproducibility of the study by others. This section must include a clear statement specifying that a free and informed consent of the subjects or their legal guardians was obtained. Corresponding author should submit a copy of institution review Board (IRB) clearance or letter of permission from the hospital or department (if IRB exempt) with the manuscript. For manuscripts on clinical trials, a copy of ethical approval letter from the concerned body should be submitted with the Manuscript. If confidential data is being used for publication (such as student grades, medical board data, or federal ethics board data), then appropriate support/ agreement letter should be included. Photos of patients should disguise the identity or must have obtained their written consent. Reference number for ethical approval given by ethics committee should be stated. In general, the section should include only information that was available at the time the plan or protocol for the study was being written; all information obtained during the study belongs in the Results section.

d) **Results:** This section should present the experimental or observational data in text, tables or figures. The data in Tables and Figures should not be described extensively in the text.

e) **Discussion:** The first paragraph should provide a summary of key finding that will then be discussed one by one in the paragraphs to follow. The discussion should focus on the interpretation and significance of the results of the study with comments that compare and describe their relation to the work of others (with references) to the topic. Do not repeat information of Results in this section. Make sure the limitations of the study are clearly stated.

f) **Tables and Figures:** These should not be more than six. Tables should be typed in triplicate on separate sheets and given serial Arabic numbers. Titles should be clearly place underneath Tables and above Figures. Unnecessary and lengthy tables and figures are discouraged. Same results should not be presented in more than one form (choose either figure or table). Units should appear in parentheses in captions but not in the body of the table. Statistical procedures, if not in common use, should be detailed in the METHODS section or supported by references. Legends for figures should be typed on separate sheets, not stapled to the figures. Three dimensional histograms are discouraged. Recognizable photographs of patients should be disguised. Authors should submit editable soft versions of the tables and figures.

g) **Acknowledgement:** Appropriate recognition of contributors to the research, not included under Authors should be mentioned here; also add a note about source of the financial support or research funding, when applicable.

h) **References**:

- The titles of journals should be abbreviated according to the style used for MEDLINE (www.ncbi.nlm.nih.gov/nlmcatalog/journals).
- References should be numbered consecutively in the order in which they are first mentioned in the text and identify references in text, tables, and legends by Arabic numerals in parentheses.
- Type the References on a separate sheet, double spaced and keyed to the text.
- Personal communications should be placed NOT in the list of references but in the text in parentheses, giving name, date and place where the information was gathered or the work carried out (e.g. personal communication, Alasebu Berhanu, MD, 1984, Gondar College of Medical Sciences). Unpublished data should also be referred to in the text.
- References with six or less authors should all be listed. If more than six names, list the first three, followed by et al.
- Listing of a reference to a journal should be according to the guidelines of the International Committee of Medical Journal Editors ("Vancouver Style') and should include authors' name(s) and initial(s) separated by commas, full title of the article, correctly abbreviated name of the journal, year, volume number and first and last page numbers.
- Reference to a book should contain author's or authors' name(s) and initials, title of chapter, names of editors, title or book, city and name of publisher, year, first and last page numbers.

The following examples demonstrate the acceptable reference styles.

Articles:

- Gilbert C, Foster A. Childhood blindness in the context of Vision 2020: the right to sight. *Bull World Health Org 2001;79:227-32*
- Teklu B. Disease patterns amongst civil servants in Addis Ababa: an analysis of outpatient visits to a Bank employee's clinic. *Ethiop Med J 1980;18:1-6*
- Tsega E, Mengesha B, Nordenfelt E, Hansen B-G; Lindberg J. Serological survey of human immuno-deficiency virus infection in Ethiopia. *Ethiop Med J 1988; 26(4): 179-84*
- Laird M, Deen M, Brooks S, et al. Telemedicine diagnosis of diabetic retinopathy and glaucoma by direct ophthalmoscopy (Abstract). *Invest Ophthalmol Vis Sci 1996; 37:104-5*

Books and chapters from books:

- Henderson JW. Orbital Tumors, 3rd ed. Raven Press New York, 1994. Pp 125-136.
- Clipard JP. Dry Eye disorders. In Albert DM, Jakobiec FA (Eds). Principles and Practice of Ophthal-mology. W.B Saunders: Philadelphia, PA 1994 pp257-76.

Website:

- David K Lynch; laser History: Masers and lasers. http://home.achilles.net/jtalbot/history/massers.htmAccessed 19/04/2001

2. **Brief Communication**

Short versions of Research and Applications articles, often describing focused approaches to solve a health problem, or prelnary evaluation of a novel system or methodology

- Word count: up to 2000 words
- Abstract up to 200 words; excluding: Abstract, Title, Tables/Figures and References
- Tables and Figures up to 5
- References (vide supra – Original Article)

3. **Case Series**

Minimum of three and maximum of 20 cases

- Up to 1,000 words; excluding: Abstract, Title, Tables/Figures and References
- Abstract of up to 200 words; structured; (vide supra)
- Statistical statements here are expressed as 5/8 (62.5%)
- Tables and Figures: no more than three
- References: maximum of 20

4. **Case Report**

Report on a rare case or uncommon manifestation of a disease of academic or practical significance

- Up to 750 words; excluding: Abstract, Title, Tables/Figures and References
- Abstract of up to 100 words; unstructured;
- Tables and Figures: no more than three
- References: maximum of 10

5. **Systematic review**

Review of the literature on topics of broad scientific interest and relevant to EMJ readers

- Abstract structured with headings as for an Original Article (*vide supra*)
- Text should follow the same format as what is required of an Original Article
- Word count: up to 8,000 words, excluding abstract, tables/Figures and references
- Structured abstract up to 250 words
- Tables and Figures up to 8

6. **Teaching Article**

A comprehensive treatise of a specific topic/subject, considered as relevant to clinical medicine and public health targeting EMJ readers

- By invitation of the Editorial Board; but an outline of proposal can be submitted
- Word limit of 8,000; excluding abstract, tables/Figures and references
- Unstructured Abstract up to 250 words

7. Editorial

- By invitation of the Editorial Board, but an editorial topic can be proposed and submitted
- Word limit of 1,000 words: excluding references and title; no Abstract
- References up to 15.

8. Perspectives

- By invitation of the Editorial board, but a topic can be proposed and submitted
- Word limit of 1,500
- References up to six

9. Obituaries

- By invitation of the Editorial board, but readers are welcome to suggest individuals (members of the EMA) to be featured.

Preparation of manuscripts

- Manuscripts must be prepared in English, the official language of the Journal.
- On a single separate sheet, there must be the title of the paper, with key words for indexing if required, and each author's full name and professional degrees, department where work was done, present address of any author if different from that where work was done, the name and full mailing address of the corresponding author, including email, and word count of the manuscript (excluding title page, abstract, references, figures and tables). Each table/figures/boxes or other illustrations, complete with title and footnotes, should be on a separate page.
- All pages should be numbered consecutively in the following order: Title page; Abstract and keywords page; main manuscript text pages; References pages; acknowledgment page; Figure-legends and Tables
- The Metric system of weights and measures must be used; temperature is indicated in degrees Centigrade.
- Generic names should be used for drugs, followed by propriety brand name; the manufacturer name in parenthesis, e.g. diazepam (Valium, Roche UK)
- Statistical estimates e.g. mean, median proportions and percentages should be given to one decimal place; standard deviations, odds ratios or relative risks and confidence intervals to two decimal places.
- Acronyms/Abbreviations should be used sparingly and must be given in full, at first mention in the text and at the head of Tables/foot of Figure, if used in tables/figures.eg. Blood Urea Nitrogen (BUN). Interstitial lung disease (ILD).
- Use the binomial nomenclature, reference to a bacterium must be given in full and underlined - underlining in typescript becomes italics in print (e.g. *Hemophilus influenzae)*, and later reference may show a capitalised initial for the genus (e.g. *H. influenzae)*
- In the text of an article, the first reference to any medical phrase must be given in full, with the initials following in parentheses, e.g., blood urea nitrogen (BUN); in later references, the initials may be used.
- Manuscripts for submission should be prepared in Microsoft Word document file format

Submission of manuscripts

- As part of the submission process, authors are required to check off their submission's compliance with journals requirements

- All manuscripts must be submitted to the Editor-in-Chief of the Journal with a statement signed by each author that the paper has not been published elsewhere in whole or in part and is not submitted elsewhere while offered to the *Ethiopian Medical Journal*. This does not refer to abstracts of oral communications at conferences/symposia or other proceedings.
- It is the author's responsibility to proof-read the typescript or off-print before submitting or re-submitting it to the Journal, and to ensure that the spelling and numerals in the text and tables are accurate.
- Authors should submit their work through the Ethiopian Medical Journal website; ema.emj@telecom.net.et.

Conflict of interest

Authors should disclose at the time of submission of manuscripts any conflict of interest, which refers to situations in which financial or other personal considerations may compromise, or have the appearance of compromising their professional judgment in conducting or reporting the research results They should declare that there is no conflict of interest to declare if there is none,

Manuscripts review procedures

The procedures for manuscripts review include:

- Within one week of receipt of a manuscript, the Editorial Board will review it in reference to (i) conformity with the Journal's "guidelines to authors (revised version available in all issues starting January 2020)", (ii) relevance of the article to the objectives of the *EMJ*, (iii) clarity of presentation, and (iv) plagiarism by using appropriate software
- The Editorial Board has three options: accept manuscripts for external review, return it to author for revision, or reject it. A manuscript not accepted by a board member is blindly reviewed by another board member. If not accepted by both, the manuscript is rejected by the Editorial Board. Decision will be made by the suggestion of a third Editorial Board member if the decisions of first two do not concur.
- Once accepted for external review, the Editorial Board identifies one (for brief communication, case reports, and teaching articles) or two (for original articles) reviewers with appropriate expertise. The reviewers will be asked to review and return manuscripts with their comments online within two weeks of their receipt. Reviewers have four options; accept, accept with major revision, accept with minor revision, or reject.
- A Manuscript accepted subject revision as suggested by reviewers will be returned to the corresponding author. Author(s) will be given four weeks to respond to reviewers' comments, make necessary changes, and return the manuscript to the Editorial Board. A Manuscript not returned within the specified time will be considered withdrawn by the author(s).
- Manuscripts with minor revisions will be cleared by the Editorial Board and accepted for publication. Those with major revisions will be returned to external reviewers and follow the procedures as outlined for the initial review.

General information

The Editorial Board reserves the right for final acceptance, rejection or editorial correction of papers submitted. However, authors are encouraged to write an appeal to the Editor-in-Chief for reconsideration of rejected manuscripts or any other complaints they might have.

Accepted papers are subject to Editorial revision as required and become the copy-right of the EMA Twenty-five reprints of published articles are supplied free to the first/corresponding author.

The Editorial Board welcomes comments on the guidelines from Journal readers.

Privacy statement

The names and email addresses entered in this journal site will be used exclusively for the stated purposes of this journal and will not be made available for any other purpose or to any other party.

Acknowledgment
We gratefully acknowledge the financial support of the U.S. Centers for Disease Control and Prevention (CDC) obtained through the CDC-EMA Cooperative Agreement No. 5U2GPS000834. We also warmly thank those who generously give donations to meet the Journal's cost.

THE ETHIOPIAN MEDICAL JOURNAL

The *Ethiopian Medical Journal*, founded in 1962, appears four times a year and is available from the Secretary, EMA House, Addis Ababa, or by mail P. O. Box 3472, Addis Ababa, Ethiopia. Request for previous issues is welcomed. For this and any other information, please contact us through:

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NOTICE TO MEMBERS OF THE ETHIOPIAN MEDICAL ASSOCIATION

If you are a paid–up member of EMA, and have not received your copy of EMJ, please notify the secretary, with the support of your ID card or letter from your hospital. Also, if you are transferred to a different hospital or institution, please return the following change of address form **PROMPTLY.**

NAME (in block) .....……..
FORMER ADDRESS: .....……..
P. O. BOX ..... CITY/TOWN .....
NEW ADDRESS .....……
INSTITUTION .....……
P. O. BOX ..... CITY/TOWN .....…..

Ethiopian Medical Association has scheduled its 57th Annual Medical Conference from April 22 - 23, 2021 under the theme “Ethiopian Health Care system readiness on COVID-19 response”.

This year’s Annual Medical Conference is going to be a hybrid event where our association will be taking comprehensive measures to adhere to WHO Guidelines to prevent the spread of COVID-19 infections.

The conference will be preceded by a blood donation event under the theme “Blood Should Circulate” and Continuing Medical Education (CME) sessions to be conducted virtually on 15th and 16th of April/2021 by both local and international collaborators.

We will then host our Medical Conference with invited participants on April 22-23/2021.Our events will be broadcasted via our zoom platform for registered members and Facebook live streaming for our Social Media followers. The conference will entail a closed Business meeting, Lifetime Merit award, Outstanding students’ award followed by, Panel discussions on selected topics and presentation of scientific papers.