ETHIOPIAN MEDICAL JOURNAL

JANUARY 2024 VOLUME 62 NUMBER 1 ISSN0014-1755

EMA
የኢትዮጵያ ሕክምና ማኅበር
ETHIOPIAN MEDICAL ASSOCIATION

ETHIOPIAN MEDICAL JOURNAL
P.O. Box 3472, Addis Ababa, Ethiopia
Tel. No. 251-15533742 Fax: 251-1-5533742
www.emjema.org

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.

ETHIOPIAN MEDICAL JOURNAL
January 2024

EDITORIAL

ORIGINAL ARTICLES

CASE REPORTS

CASE SERIES

Ethiopian Medical Journal 2024, 62 (1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420 Workicho

Editorial

Evidence-Informed Policy Making in the Ethiopian Health System: Opportunities and Challenges

Abdulhalik Workicho

[1]Fenot project, Harvard T.H. Chan School of Public Health

[*] Corresponding author: **abushra@hsph.harvard.edu, abdulhalikw@gmail.com**

Policy development is a complex and iterative process with multiple stages involving multiple stakeholders and demanding resources. In the health system, problems of various nature, often requiring evidence, trigger the policy development process. Evidence Informed Policy Making (EIPM) is believed to increase the credibility, effectiveness, efficiency, equity, trustworthiness, and acceptability of policies and interventions (1). It also facilitates a more efficient use of scarce resources in health care, reduces research waste, and improves transparency and accountability (2, 3). Hence, the interface between evidence and policy-making in the health system is becoming increasingly important. Ideally, the policy-making process would base on scientific evidence and through participating all stakeholders. But of course, scientific evidence is not the only consideration in policy decisions. Contrary to its depiction, the pathway to EIPM in the health system, in fact, in any other sector, is generally non-linear (4).

In most circumstances, including the health system, EIPM is implemented in a system that operates under a complex and dynamic environment that is challenged by uncertainty. It requires a collaborative effort between various stakeholders with divergent perspectives, capacity, interests, accountability, and power of influence (4, 5). In this process, the researchers and policymakers are the main actors. The former is engaged in leading the production of scientific knowledge while the policy maker owns and leads the process of EIPM to support decision-making. Engagement of policymakers through co-designing/co-creating the policy question and agreeing on the evidence generation process is a key aspect in the interaction between the two actors to translate the evidence into action. Therefore, it is required to use systematic approaches and iterative process so we can optimize the attributes of EIPM (1, 4-7). It is also important and necessary that the approaches we follow and the tools we use are comprehensive enough to account for diverse perspective and contexts. Moreover, they should allow flexibility in working in the complex, dynamic and unpredictable ecosystems of evidence and policy (1, 2, 4, 5). Failure to follow EIPM in the health system will result in implementing programs which are less effective and undesirable outcomes.

In the context of Ethiopia, since the implementation of the Health Sector Transformation Plan (HSTP) (8), the focus on using evidence in the policy making pathway has gained a momentum. With a recent revision of the HSTP in to Health Sector Medium Term Development and Investment Plan (HSDIP)(9), the use of evidence in program designing and implementation is also placed at the epicenter implementing all the nine strategic objectives. Furthermore, the Ministry of Health (MoH) recently has revised its organizational structure aiming to efficiently use resources and implement its programs. The restructuring has led to establishment of few new offices but more importantly organized related programs and departments together so they can optimize their implementation capacity. One of the structures newly established offices is the Policy Strategy and Research Lead Executive Office (PSR LEO) which reports directly to the Minister. This office, with its specific role of bringing together the different actors in the policy making process, including researchers and policymakers, will have a significant role in further enhancing the culture of evidence use while developing health policies and strategies in the country. There are also various knowledge translation platforms (KTPs) including the Research Advisory Council (RAC) which engages researchers and program implementers to answer policy relevant questions and provide technical advises. The RAC operates by using available evidence and routine data to answer policy questions and provide recommendations. This plays an important role especially in bridging the gap between researchers and policymakers which in most cases appear to be the main hurdle in the EIPM process. Different technical advisory standing committees or technical working groups also ensure that specific issues supported by evidence are included when policies are formulated.

However, as complex as the EIPM process is, one can mention a number of challenges. In most cases, the weak link between researchers and policymakers has remained to be the bigger challenge. As equal as its robustness, trustworthiness of an evidence relies on engagement of the end users from the very onset. Even though it requires a delicate balance on the extent of involvement, co-creating the evidence generation process greatly improves its utilization. The availability and accessibility of high-quality research and data is also one big challenge pushing policymakers to rely on poor quality evidence to inform their decisions. Another challenge is the complexity of the policymaking process. Policymakers must consider a range of factors when developing and implementing policies, including economic, social, and political considerations. At times, policy-makers may under estimate the potential of scientific contributions, inclining to their own perceptions of policy problems. Or, they may want simple answers from research in order to implement quick fixes to pressing policy challenges while ignoring the complexity of conducting research. Policy-makers needing results over relatively short time periods, and sometimes tending to use research only to legitimize political decisions or even rejecting scientific recommendations can also be additional challenges. It is also worth noting the role of special interests and lobbying in the policymaking process. In some cases, special interest groups may exert influence on policymakers by providing them with research or data that supports their agendas.

References

1. Wilson P, Sheldon TA. 4: Using evidence in health and healthcare What Works Now? Bristol, UK: Policy Press; 2019. p. 67-88.
2. Boaz A, Davies H, Fraser A, Nutley S. What Works Now?: Evidence-informed policy and practice. Bristol, UK: Policy Press; 2019 27 Mar. 2019.
3. WHO. Evidence, policy, impact. WHO guide for evidence-informed decision-making. . Geneva; 2021. Report No.: 978-92-4-003987-2
4. Langlois EV, Becerril Montekio V, Young T, Song K, Alcalde-Rabanal J, Tran N. Enhancing evidence informed policymaking in complex health systems: lessons from multi-site collaborative approaches. Health Res Policy Syst. 2016;14:20.
5. Brownson RC, Fielding JE, Maylahn CM. Evidence-based public health: a fundamental concept for public health practice. Annu Rev Public Health. 2009;30:175-201.
6. Chalmers I, Bracken MB, Djulbegovic B, Garattini S, Grant J, Gülmezoglu AM, et al. How to increase value and reduce waste when research priorities are set. Lancet. 2014;383(9912):156-65.
7. Kano H, Hayashi TI. A framework for implementing evidence in policymaking: Perspectives and phases of evidence evaluation in the science-policy interaction. Environmental Science & Policy. 2021;116:86-95.
8. MoH. Health Sector Transformation Plan. Addis Ababa, Ethiopia; 2015.
9. MoH. Health Sector Medium-Term Development and Investment Plan (HSDIP). Addis Ababa, Ethiopia; 2023.

Ethiopian Medical Journal 2024, 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420 Binegdie et al.

Original Article

Risk Factors and Determinants of Pulmonary Function Impairments in Chronic Respiratory Diseases in Ethiopia: A Hospital-based Cross-Sectional Study

Amsalu Bekele Binegdie [1*], Tewodros Haile Gebremariam [1], Aschalew Worku [1], Eyob Kebede Etissa [1], Shifa Hamid [2], Adursemed Awol[2], Addisu Belay,[2] Hellen Meme[3], Asma El Sony[4], Lindsay Zurba[5], Maia Lesosky[6,7] John Balmes[8], Peter Burney[9], Graham Devereux[10], Kevin Mortimer [10,11,12]

[1] Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, College of Health Sciences, Addis Ababa University, Ethiopia
[2] Bishoftu General Hospital, Oromia, Ethiopia
[3] Kenya Medical Research Institute (KEMRI), Kenya
[4] Epidemiological for Public Health, Research and Development.
[5] Spirometry Training Services South Africa
[6] Division of Epidemiology Biostatistics, School of Public Health & Family Medicine, University of Cape Town, South Africa
[7] Department of Biostatistics, Liverpool School of Tropical Medicine, UK
[8] University of California, San Francisco, USA
[9] National Heart and Lung Institute, Imperial College London, UK
[10] Department of Respiratory Medicine, Liverpool School of Tropical Medicine, UK
[11] Department of Respiratory Medicine, Liverpool University Foundation NHS Trust, Liverpool, UK
[12] University of Cambridge, Cambridge, UK

Corresponding authors*: amsalubekele2016@gmail.com

Abstract

Introduction: *Chronic respiratory diseases (CRDs) are diseases of the airways and lung parenchyma. Although they are leading causes of morbidity and mortality globally, chronic respiratory diseases have received relatively little public attention. This study aimed to characterize the common chronic respiratory diseases, along with their lung function and possible determinants in symptomatic patients attending clinics at Bishoftu General Hospital, Ethiopia.*

Methods*: A cross-sectional study was conducted at the outpatient department of Bishoftu Hospital from June 2019 to March 2020. Consecutive adult patients aged 18 and above with chronic respiratory symptoms (lasting more than 8 weeks) and no evidence of active tuberculosis were recruited. Questionnaires were used to collect data on demographics, symptoms, diagnoses, and potential risk factors. Lung function was measured by spirometry. Allergic status was assessed through allergen skin prick testing with standard allergens.*

Results*: A total of 170 participants were recruited, with the majority being female (102, 60.0%). The mean age was 49 years (SD=16). The most common symptoms reported were wheezing in the last twelve months 156 (91.8%), cough 138 (81.2%) and severe exertional breathlessness 137 (80.6%). Thirty-nine (22.9%) participants were either active or passive smokers. Half of the patients (50.3%) were exposed daily to vapors, dust, gases, or fumes and 58 (34.3%) were exposed to biomass smoke. In total, 138 (81.2%) had a positive allergen skin prick test. Chronic bronchitis (49.1%) and asthma (36.1%) were the most common clinical diagnoses. Classification of lung function revealed 23 (15%) normal, 29 (19%) obstructive, 36(23.5%) restrictive and 61(39.9%) mixed obstructive/restrictive patterns. Airflow obstruction (FEV1/FVC ratio) was independently associated with increasing age ($p<0.05$), exertional breathlessness ($p<0.001$), previous history of asthma ($p<0.05$), BMI ($p<0.05$), and doctor-diagnosed chronic obstructive pulmonary disease ($p<0.001$) and asthma ($p<0.05$).*

Conclusion*: This study demonstrated a high burden of abnormal lung function in patients attending clinics due to chronic respiratory symptoms. Increasing age, exertional breathlessness, prior diagnosis of asthma, BMI, and clinically diagnosed COPD and asthma were independently associated with obstructed lung function. These find-*

ings highlight the critical need for spirometry services to identify lung abnormalities in patients with chronic respiratory symptoms.

Epidemiology, and the findings should be factored into clinical decision making and program design for disease prevention, screening, and treatment. It also calls for further prospective research to learn more about the conditions in the context of additional relevant personal and clinical characteristics.

***Keywords**: Chronic respiratory diseases, Determinant, Pulmonary function, Asthma, COPD*
***Citation :** Binegdie AB , Gebremariam TH, Worku A. et al. Risk Factors and Determinants of Pulmonary Function Impairments in Chronic Respiratory Diseases in Ethiopia: A Hospital-based Cross-sectional Study Ethiop Med J 62 (1) 3-14*
***Submission date :** 17 July 2022 Accepted: 22 December 2023 Published: 1 January 2024*

Introduction

Chronic respiratory diseases (CRDs) are diseases of the respiratory airways and lung parenchyma. Asthma, chronic obstructive pulmonary disease (COPD), and occupational lung diseases are usually cited as the most frequent CRDs. Globally, CRDs are important contributors to the increasing burden of non-communicable diseases (NCDs) and are among the leading causes of morbidity and mortality, particularly in low- and middle-income countries. This growing burden is likely to reflect widespread exposure to noxious environmental pollutants, occupational allergens, and inhalation of substances such as tobacco (1-3). Despite their global impact, CRDs did not receive as much public attention or research funding as other non-communicable diseases (4, 5).

The 2017 Global Burden of Diseases study estimated that 545 million people in the world had CRDs, an increase of 39.8% from 1990. In 2017, CRDs were responsible for 3.9 million deaths/year (an 18.0% increase from 1990) and for 1470 disability-adjusted life-years (DALYs) per 100,000 people (a 13.3% increase on 1990). The most prevalent CRDs are COPD (3.9% global prevalence) and asthma (3.6%). Smoking is the leading cause of disability attributable to CRDs in men across all regions. However, the main risk factor for disability in women varies by region, with household air pollution from solid fuel use being the highest in sub-Saharan Africa (6). Surprisingly, when compared to other regions, sub-Saharan Africa had the lowest prevalence of CRDs and lowest mortality attributable to CRDs. This finding does not reflect the experiences of clinicians, suggesting the lower prevalence of CRDs might be due to under diagnosis in settings that lack or underutilize diagnostic capabilities (3, 7).

In Ethiopia, a community-based study reported that the prevalence of COPD was 17.8% and that factors such as age above 50 years, being a smoker, being exposed to biomass smoke, and poorly ventilated kitchens were significantly associated with COPD (8). In recent years, initiatives such as the Burden of Obstructive Lung Disease (BOLD) program have provided detailed information on the prevalence of normal, obstructive, and restrictive spirometry in many high-, medium- and low-income countries. However, there is limited knowledge about how the patterns of lung function deficit translate into clinical disease and impact healthcare services in low- and middle-income country (LMIC) settings such as sub-Saharan Africa (9). Therefore, the objective of this study was to determine the burden of chronic respiratory diseases, lung function, and their determinants among patients with chronic respiratory symptoms attending a clinic in a General Hospital in Ethiopia.

Methods and Materials

Study setting, study period, and study design

This was a cross-sectional study conducted at Bishoftu General Hospital in Oromia, Ethiopia as part of a three-center (Ethiopia, Kenya and Sudan) project on Lung Health Across Life course in Africa (LuLi). A detailed description of the methods used has been published elsewhere (10). Bishoftu General Hospital is located 45km away from the capital Addis Ababa. A total of 169,000 patients were treated at the outpatient unit of the hospital in 2019 (Hospital report) include reference). The study was conducted from June 2019 to March 2020 in the outpatient departments of the hospital. The study population comprised of consecutive adult patients aged 18 years and older with chronic respiratory symptoms (lasting more than 8 weeks), in whom TB had been excluded (negative sputum GeneXpert test), and who were willing to perform spirometry. Patients were excluded if they had acute infections such as pneumonia or active tuberculosis, were unable to perform spirometry, or did not wish to participate (10).

Data collection

Trained nurses administered a respiratory-focused questionnaire (based on the BOLD questionnaire with additional questions from LuLi questionnaires) to collect data on socio-demographics, co-morbidities, past medical history, and symptoms (10). The questionnaire also covered risk factors such as tobacco smoking, exposure to outdoor and indoor pollutants, occupation and known triggers (9, 11).

Spirometry

All participants underwent spirometry performed by trained and Pan African Thoracic Society (PATS) certified nurses for competence in foundational spirometry. Pre- and post-bronchodilator spirometry was performed and forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were recorded. Spirometry was performed in accordance with the standards of the PATS, the American Thoracic Society, and the European Respiratory Society (12). The EasyOne® Spirometer (ndd, Switzerland) with a daily 3L syringe calibration check was used for spirometric measurements. The procedure included at least 3 acceptable and repeatable forced vital capacity manoeuvers. All curves were reviewed by an external assessor and the best value was selected for analysis. The Global Lung Initiative 2012 (GLI2012) reference equations for "black" populations were used (12-16). The patient's lung function was categorized as normal FEV1/FVC, FEV1 and FVC>LLN; obstructed FEV1/FVC<LLN (post-bronchodilator); and restricted FVC<LLN. Bronchodilator responsiveness was defined as an improvement of FEV1 by ≥12% and 200ml after administration of 200ug salbutamol administered by a spacer device. As per GOLD guidelines, post-bronchodilator airflow obstruction (FEV1/FVC<0.7) was categorized into mild (FEV1≥80% predicted), moderate (80%>FEV1≥50% predicted), severe (50% >FEV1≥30% predicted), and very severe (FEV1<30% predicted) (11).

Six-minute walk and allergen skin prick testing

A six-minute walk test and skin prick testing were performed according to ATS and European Standards (12,13). Skin prick testing used the standard allergen solutions including grass, cat, dog, cockroach, dust mite (dermatophagoides pteronyssinus), with positive (10mg/ml histamine), and negative (0.9% saline) controls. The maximum wheal diameter was measured at 15 minutes. A wheal diameter ≥3 mm was considered positive, and a patient was considered atopic if they had one or more positive skin prick tests.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, v26.0 (IBM, Armonk, NY, USA). Descriptive analyses are presented as mean with standard deviation, frequency, and percentages with appropriate measures of variation. Simple comparisons used independent t-tests and ANOVA tests as appropriate. The association between variables and the change in FEV1/FVC ratio was determined using a multiple linear regression model that included variables that were significantly associated ($p < 0.05$) on univariate analysis. Linear regression assumptions (normality, linearity, outliers, homoscedasticity, and multicollinearity) were evaluated and found to be met. All tests were two-sided. P-values less than 0.05 were considered statistically significant.

Ethical considerations

Ethical approvals for the study were acquired from the Institutional Review Board of the College of Health Sciences, Addis Ababa University (062/18/IM) include reference number), and Liverpool School of Tropical Medicine Research Ethics Committee (18-048)include reference number). Informed written consent was obtained from each participant before enrollment.

Results

As outlined in figure 1, a total of 220 patients were approached; of whom, 170 were recruited. Among the 170 participants, the mean age was 49 (SD=16). The majority of the patients were aged 26-35 years (37, 21.8%) and 46-55 years (36, 21.2%) followed by the age group 56-65 years (34, 20.0%). A majority of 102 (60.0%) of the participants were female. The most common occupation was "housewife" (51, 30.0%). Most of the study participants were literate (123, 72.4%). A majority of participants (104, 61.2%) reported comorbidities: 30 (17.6%) reported gastro-esophageal reflux disease, 26 (15.3%) reported allergic rhinitis, 20 (11.8%) were hypertensive, 16 (9.4%) had nasal polyps, 9 (5.3%) were diabetic and 8 (4.7%) had rhinosinusitis. Less frequently reported were obesity, chronic heart failure, eczema, and HIV/AIDS. 33(19.4%) had more than one comorbidity. (Table 1)

A majority of patients reported previous history of lung disease 156 (91.8%); of which asthma and chronic bronchitis being the most common diagnoses reported by patients. The clinician reviewing the patient reported what their leading diagnosis was following the encounter: 83(48.8%) chronic bronchitis, 61(35.9%) asthma, 23(13.5%) COPD, 5(2.9%) post TB chronic lung disease, 4(2.4%) rhinosinusitis, and 3 (1.8%) interstitial lung diseases, OSA and bronchiectasis each. (Table 1). There was poor agreement between physician and patient-reported diagnoses for different CRDs: asthma (kappa for= asthma 0.083), for COPD (kappa = 0.271, and for chronic bronchitis (kappa = 0.009).

Table 1 Baseline characteristics

Variables	n (%)
Age	
18-25	11 (6.5)
26-35	37 (21.8)
36-45	26 (15.3)
46-55	36 (21.2)
56-65	34 (20.0)
>65	26 (15.3)
Female Sex	102 (60.0)
Occupation	
Housewife	51 (30.0)
Employed worker	21 (12.4)
Construction, mining, factory laborer	19 (11.2)
Farmer	5 (2.9)
Merchant	4 (2.4)
Other	70 (41.2)
Educational status	
Literate	123 (72.4)
Comorbidities	104 (61.2)
Gastro-esophageal reflux	30 (17.6)
Allergic rhinitis	26 (15.3)
Hypertension	20 (11.8)
Nasal polyps	16 (9.4)
Diabetes mellitus	9 (5.3)
Rhinosinusitis	8 (4.7)
Obesity	5 (2.9)
Chronic Heart Failure	4 (2.4)
Eczema	2 (1.2)
HIV positive	1 (0.6)
Patient report of known lung disease or treated illness	
Any	156 (91.8)
Asthma	110 (64.7)
Chronic bronchitis	44 (25.9)
Tuberculosis	24 (14.1)
COPD	6 (3.5)
Measles	4 (2.4)
Whooping cough	2 (1.2)
Clinician diagnosis	
Chronic Bronchitis	83(48.8)
Asthma	61(35.9)
COPD	23(13.5)
Post TB chronic lung diseases	5(2.9)
Rhinosinusitis	4(2.4)
ILD	3(1.8)
OSA	3(1.8)
Bronchiectasis	3(1.8)

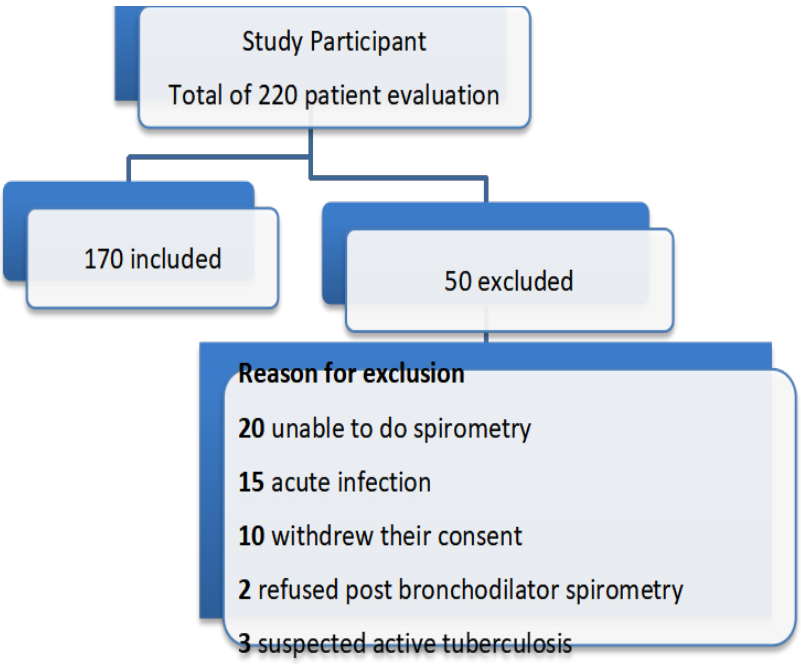


Figure 1: Selection of study participants Study flow diagram illustrating participant selection and consent type

The common presenting symptoms at presentation were wheezing in the last twelve months 156 (91.8), cough 138 (81.2%), severe limiting breathlessness 137 (80.6%), phlegm production 115 (67.6%), weight loss 103 (60.6%), and night sweats 102 (60.0%) (Figure2).

Data on possible risk factors for CRDs were collected: 144 (84.7%) lived in towns or cities, and 39 (22.9%) were either active or passive smokers (Active smokers 13: passive smokers 26 patients). Patients were asked to estimate the distance of their home to a major road, 65 (38.2%) lived less than 100 meters, 59 (34.7%) lived 100 to 500 meters and 46 (27.1%) lived more than 500 meters. More than half of the patients, 50.6% , were exposed daily to vapors, dust, gases, or fumes. Fifty-eight (34.1%) were exposed to smoke from biomass burning. Of the total, only 17 (10.0%) cultivated crops. Most of the participants 96 (56.5%) had contact with animals. BMI was used to categorize weight, 92 (54.1%) were normal weight, 33 (19.4%) overweight, 27 (15.9%) underweight, and 18 (10.6%) obese. (Table 2)

Skin prick testing (SPT) showed that, overall, 138 (81.2%) had one or more positive skin prick tests. Fifty -eight (34.1%) for cat, 75 (44.1%) for dog, 74 (43.5%) for cockroach and 123 (72.4%) were positive for dust-mite skin prick testing. The majority of patients, 158 (92.9%) of study participants, completed 6- minute walk test, whereas, 11(6.5%) paused or stopped. The mean distance walked was 414.5 meters (95% CI (396.7-431.8) and 123 (72.4%) had normal 6MWT (≥400m). (Table 2)

Lung function status of the study population

Classification of spirometry showed that 23 (15%) of patients had normal spirometry, 29 (19%) obstructive, 36(23.5%) restrictive and 61(39.9%) mixed obstructive & restrictive patterns. Mean FEV1 (% predicted) 54% (SD=26), mean FVC (% predicted) 65% (SD=26), and mean FEV1/FVC ratio of 0.64 (SD=0.14).

Table 2: Potential risk factors, Skin prick test (SPT), and 6MWT in study participants.

Variables	No (%)
Active or passive smoker	39 (22.9)
Place of residence	
Town or city	144 (84.7)
Suburban	11 (6.5)
Rural	15 (8.8)
The distance of your home from a major road	
Less than 100 meters	65 (38.2)
100 to 500 meters	59 (34.7)
More than 500	46 (27.1)
Daily breathe in vapor, dust, gases, or fumes	86 (50.6)
Exposure to smoke from burning	58(34.1)
Use of aerosols or spray at home	59 (34.7)
Burn incense at home	39 (22.9)
Fire bricks	7 (4.1)
Cultivate crops	17 (10.0)
Contact with animals	96 (56.5)
BMI	
Underweight	27 (15.9)
Normal weight	92 (54.1)
Overweight	33 (19.4)
Obesity	18 (10.6)
Allergy for SPT	
Positive	138 (81.2)
Negative	32 (18.8)
More than one positive SPT	100 (58.8)
Cat Positive	58(34.1)
Dog Positive	75(44.1)
Cockroach positive	74(43.5)
Dust Mite Positive	123(72.4)
Six –minute walking test	
Normal ≥400m	123(72.4)
Reduced<400m	46(27.1)
Not done	1(0.6)

Educational status, the patient-reported physician-diagnosed asthma and chronic bronchitis, breathlessness, and clinician diagnosed chronic bronchitis, asthma and COPD, showed a significant difference in pulmonary function (FEV1/FVC). No significant difference in pulmonary function testing was seen for environmental and domestic exposures.

In the univariate analysis, a decreasing in the FEV1/FVC ratio (i.e. indicating obstruction) was found to be significantly associated with increasing age, lower educational status (illiteracy), being severely breathlessness during exertion and a diagnosis of asthma or COPD. On the other hand, whereas a diagnosis of chronic bronchitis was associated with an increasing FEV1/FVC ratio (indicating i.e. less obstruction). In the multivariate analysis, decreasing FEV1/FVC ratio (indicating i.e. obstruction) was found to be significantly associated with increasing age, decreasing BMI, being severely breathlessness during exertion and a diagnosis of asthma or COPD. However, it was not associated with rural/urban residence or a diagnosis of chronic bronchitis.

Table 3: Comparison of FEV1/FVC ratio between groups.

Variable	No	Mean FEV1/ FVC	SD	P-value
Age				0.145
18-25	11	0.66	0.13	
26-35	37	0.70	0.14	
36-45	26	0.66	0.17	
46-55	36	0.64	0.12	
56-65	34	0.62	0.15	
>65	26	0.62	0.14	
Educational status				0.034
Literate	123	0.66	0.14	
illiterate	47	0.61	0.14	
Place of residence				0.098
Town or city	144	0.66	0.14	
Suburban	11	0.58	0.15	
Rural	15	0.61	0.14	
BMI				0.063
Underweight	27	0.64	0.16	
Normal weight	92	0.63	0.15	
Overweight	33	0.69	0.12	
Obesity	18	0.71	0.09	
Patient report of known lung disease or treated illness				
Asthma				<0.001
Yes	110	0.61	0.13	
No	60	0.71	0.14	
Chronic bronchitis				0.005
Yes	44	0.70	0.12	
No	126	0.63	0.14	
Common symptoms at presentation				
Breathlessness				<0.001
Yes	137	0.63	0.13	
No	33	0.75	0.13	
Clinician diagnosis				
Chronic bronchitis				0.002
Yes	83	0.68	0.14	
No	87	0.62	0.14	
Asthma				0.020
Yes	61	0.61	0.13	
No	109	0.67	0.14	
COPD				<0.001
Yes	23	0.54	0.10	
No	147	0.66	0.14	

Table 4. A associated factors with the FEV1/FVC ratio using multivariable linear regression analysis

Variable	Multivariable	
	Unstandardized coefficient β (95% CI)	P-value
Age	-0.001 (-0.003, 0.000)	0.017*
Educational status (illiterate Vs literate)	-0.001 (-0.45, 0.44)	0.97
Breathlessness	-0.106 (-0.154, -0.058)	<0.001*
The patient reported doctor-diagnosed		
Asthma	-0.043 (-0.085, 0.000)	0.049*
Chronic bronchitis	0.026 (-0.019, 0.070)	0.256
Place of Residence (Town Vs rural)	0.036 (-0.015, 0.008)	0.163
BMI	0.004 (0.000, 0.008)	0.034*
Clinician diagnosed		
Chronic bronchitis	0.017 (-0.083, 0.050)	0.623
Asthma	-0.074 (-0.142, -0.005)	0.035*
COPD	-0.139 (-0.219, -0.059)	0.001*

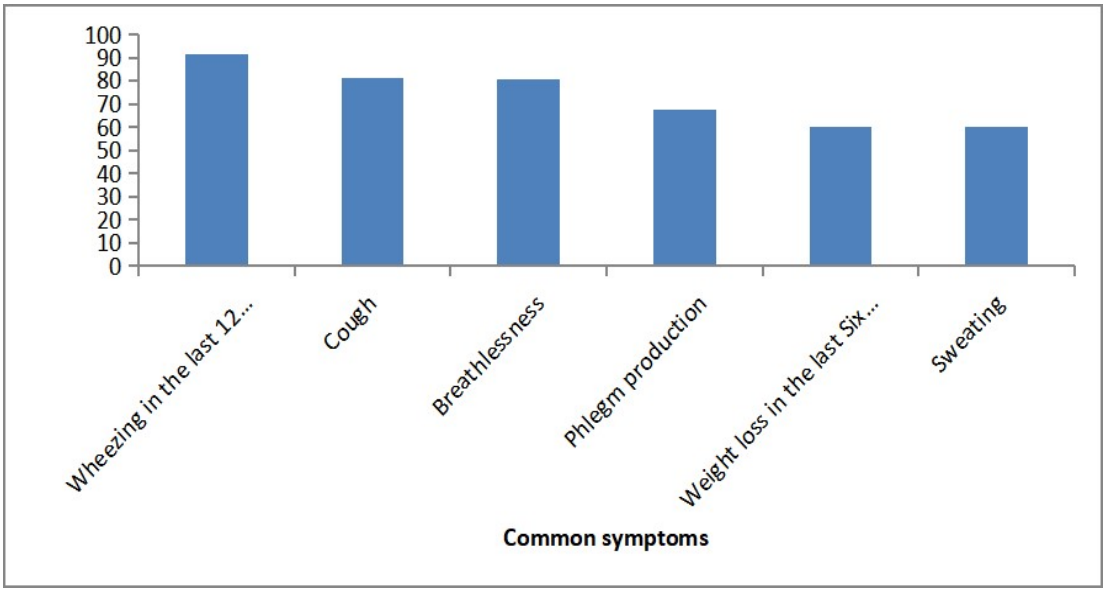


Figure 2: Common symptoms of study participants in Bishoftu general hospital, Ethiopia

Data on possible risk factors for CRDs were collected: 144 (84.7%) lived in towns or cities, and 39 (22.9%) were either active or passive smokers (Active smokers 13: passive smokers 26 patients). Patients were asked to estimate the distance of their home to a major road, 65 (38.2%) lived less than 100 meters, 59 (34.7%) lived 100 to 500 meters and 46 (27.1%) lived more than 500 meters. More than half of the patients, 50.6% , were exposed daily to vapors, dust, gases, or fumes. Fifty-eight (34.1%) were exposed to smoke from biomass burning. Of the total, only 17 (10.0%) cultivated crops. Most of the participants 96 (56.5%) had contact with animals. BMI was used to categorize weight, 92 (54.1%) were normal weight, 33 (19.4%) overweight, 27 (15.9%) underweight, and 18 (10.6%) obese. (Table 2)

Skin prick testing (SPT) showed that, overall, 138 (81.2%) had one or more positive skin prick tests. Fifty-eight (34.1%) for cat, 75 (44.1%) for dog, 74 (43.5%) for cockroach and 123 (72.4%) were positive for dust-mite skin prick testing. The majority of patients, 158 (92.9%) of study participants, completed 6-minute walk test, whereas, 11(6.5%) paused or stopped. The mean distance walked was 414.5 meters (95% CI (396.7-431.8) and 123 (72.4%) had normal 6MWT (≥400m). (Table 2)

Lung function status of the study population
Classification of spirometry showed that 23 (15%) of patients had normal spirometry, 29 (19%) obstructive, 36(23.5%) restrictive and 61(39.9%) mixed obstructive & restrictive patterns. Mean FEV1 (% predicted) 54% (SD=26), mean FVC (% predicted) 65% (SD=26), and mean FEV1/FVC ratio of 0.64 (SD=0.14).

Age, breathlessness, patient-reported doctor-diagnosed asthma, BMI, clinician diagnosed asthma, and COPD remained independently associated factors in multiple linear regression after selecting variables significantly associated with FEV1/FVC in bivariate analysis (simple linear regression).

Our multivariate model explained 35.6 % of the variance in the FEV1/FVC ratio in a multiple regression study ($R2 = 0.356$, $p < 0.001$). Keeping other variables constant, each one-year increase in age decreased the FEV1/FVC ratio by 0.001 ($P = 0.017$). Patients with the presenting symptom of breathlessness had a lower FEV1/FVC ratio by 0.1 ($p < 0.001$) compared to patients without the breathlessness symptom. Patients who reported doctor-diagnosed asthma had a 0.043 ($p = 0.049$) lower FEV1/FVC ratio than those who did not. For each unit, an increase in the BMI index results in an increase of 0.004 ($p = 0.034$) in the FEV1/FVC ratio. Furthermore, the lung function test (FEV1/FVC) of patients diagnosed with asthma and COPD was decreased compared to their counterparts by 0.074 ($p = 0.035$) and 0.139 (p 0.01), respectively. (Table 4)

Discussion

This study characterized the common non-communicable respiratory diseases seen at an outpatient department of general hospital in a low-income countries. This study demonstrated that there was a significant discrepancy between physician and patient reported diagnosis and a high burden of abnormal lung function tests. The patterns with mean FEV1 and FVC were 54% and 65% of the predicted values, respectively, while the mean FVC 65% predicted and mean FEV1/FVC ratio of was 0.64. In this Spirometric evidence of airflow obstruction was associated with increasing age, decreasing BMI, limiting exertional breathlessness on exertion, and previous diagnosis of bronchial ed asthma or COPD, but not with urban/rural residence of or diagnosis of chronic bronchitis.

In the current study of 170 patients presenting with chronic respiratory symptoms to an out-patient clinic in Ethiopia, 19% had purely obstructed spirometry with median FEV1/FVC of 67%. In comparison, a study of patients with treated/cured pulmonary TB with chronic respiratory symptoms in Benin had a median FEV1/FVC ratio of 81%, and a study of textile workers in Kano, Nigeria reported that 10% had obstructive spirometry (14-16). These differences are likely to be the consequence due to the difference in study populations, general respiratory patients, post TB patients, and textile workers.

In our study, we found a low prevalence of smoking and high exposure to biomass and daily exposure to vapors, gases, dusts, and fumes, which contrast with previous studies from developed nations: Sweden, Norway, and Spain reporting high prevalence of smoking and low exposure from biomass or daily exposure to vapors, gases, dusts, and fumes (17-19). Although there was high exposure to vapors, gases, dusts, fumes and biomass. These substances in our study; itthis was not associated with high rates of symptoms and abnormal lung function, most probably reflecting due to the small sample size of 170.

In the current study, The prevalence of allergic sensitization as quantified by skin prick testing was 81.2% in our study. This is higher than the positive SPT rate of 67.3% reported by Africa Severe Asthma projects in Uganda, Kenya, and Ethiopia, despite these studies involved being studies of asthmatic patients investigated with, and an extended panel of twelve allergens. Our rate of positive skin prick tests is higher than the rate of 56.6% reported in Hungary (20, 21). Even though there was high rate of SPT positivity, the associations of SPT positivity with Asthma diagnosis was not significant. The differences in these findings between our study and others are most likely due to reflect differences in study populations, geography, and genetic susceptibility.

A previous study conducted in Ethiopia by Bayisa TTola et. al in Ethiopia reported that 26% of 144 clinically diagnosed patients with obstructive airway disease had a history of prior tuberculosis treatment and almost 17% had ever smoked cigarettes, which was entirely among men. Asthma was the major diagnosis in 86% of patients; the rest being diagnosed with COPD with 55.8% of asthmatic and 63.6 % of COPD patients having obstructed defect. , However, only 56% of their patients had spirometry performed, in contrast to the 100% in our study. Among COPD patients, 40% were females and 40% were ever smokers. When compared with our study, Bayisa T et al this study reported a much higher prevalence of obstructive lung disease, most probably reflecting the focus of the previous study on those patients diagnosed with obstructed lung diseases in a tertiary hospital chest clinic that is a referral center for all patients with a pulmonary problem in the country (22). In contrast, our study included was of all patients with chronic respiratory symptoms, irrespective of their diagnosis attending a general non-tertiary hospital.

In our study, smoking status was not associated with significant difference in lung function, which is consistent with reports from Benin and Taiwan (23, 24). However, it contrasts with studies conducted in Latin America and the USA (25-29). This might reflect our small sample size and the widespread exposure to other inhaled noxious agents in our patients.

Several cross-sectional comparative longitudinal, and cohort studies have reported that as people become age, their FEV1/FVC ratio declines (15,23, 28-31). The current study is in line with these reports. The findings are current study is also consistent with other studies that patient-reported doctor-diagnosed asthma is significantly associated with reduced FEV1/FVC ratio (32).

Our study results suggested a significant association between decreasing BMI and decreasing FEV1/FVC ratio analogous to findings from a study of the Caribbean population.

Finally, our study showed that most of the study patients who were all symptomatic and attending an outpatient clinic had abnormal lung function and that lung function were significantly decreased particularly in those with a diagnosis of COPD. A similar association was observed in studies across different regions (33-35). Although COPD as an obstructive lung disease is defined by a decrease in the FEV1/FVC ratio, its diagnosis in most African countries is often clinical due to limited access for in Africa because spirometry is rarely available, a diagnosis of COPD is usually a clinical one, not based on spirometry. Similarly, the present study reveals that clinically un- diagnosed asthma was independently associated with a decrease in the FEV1/FVC ratio. This suggesting that some patients who are clinically diagnosed with bronchial with a clinical diagnosis of asthma may actually have , not supported by spirometry should in fact be diagnosed with COPD.

Limitations of the study

The study's limitations include its single-center, institution-based design and small sample size, which may limit its generalizability. Despite these limitations, the study provides useful insight into risk factors and lung function status among patients with chronic respiratory symptoms in Ethiopia.

Conclusion

In conclusion, this study indicates a high burden of lung function abnormality patterns with a low mean FEV1/FVC ratio. All patients experienced were symptomatic primarily with such as wheezing, cough, breathlessness, and phlegm production. Chronic bronchitis and asthma were the most common CRDs diagnosed by treating physician-diagnosed respiratory diseases. Older age at presentation, breathlessness, patient-reported doctor-diagnosed asthma, low BMI, clinically un-diagnosed asthma, and COPD are significantly associated with reduced pulmonary function. Given The high prevalence of abnormal lung function tests patterns among patients clinically diagnosed with CRDs, spirometry services should be made readily available for routine evaluation of such patients in Ethiopia. should prompt spirometry services to widely be available to determine the exact patterns of lung abnormality. This study serves will help as a baseline for future large-scale community studies in Ethiopia using more advanced diagnostic tools in order to understand the diseases burden and risk factors more accurately. to design larger sample size and more confirmatory institution and community-based studies to understand the burden of chronic lung disease, and determine what the major risk factors are for CRDs and determinants of pulmonary function in Ethiopia. Additionally, this information can be used toIt also helps in designing preventive measures based on the identified risk factors for CRDs.

Acknowledgments

This work was funded by the MRC GCRF-funded project “Lung Health in Africa across the life course” [grant number MR/P022006/1]. 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. About IMPALA (project reference 16/136/35) specifically: IMPALA was funded by the National Institute for Health Research (NIHR) using UK aid from the UK Government to support global health research. The views expressed in this publication are those of the author (s) and not necessarily those of the NIHR or the UK Department of

Health and Social Care." ML is supported in part by the Academy of Medical Sciences Newton Advanced Fellowship (NAF\R2\180681).

Declaration of competing interest:

The authors declare that they have no known competing financial interests or personal relationships that could potentially influence the work reported in this paper

Contributors: AB, TH, AW, EKE, involved in data collection, monitoring, data analysis, and development of the first draft of the manuscript, SH, AW, AB, involved in data collection. AB, HM, AS, LZ, ML, JB, PB, GD, and KM involved in the conceptualization of the idea, proposal development, and data monitoring. All authors contributed to the draft and finalization of the manuscript.

References

1. James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;392 (10159):1789-858
2. Chronic respiratory diseases (asthma, COPD): WHO; 2021 [Available from: https://www.who.int/ westernpacific/health-topics/chronic-respiratory-diseases.
3. The L. GBD 2017: a fragile world. The Lancet. 2018;392(10159).
4. Boehm A, Pizzini A, Sonnweber T, Loeffler-Ragg J, Lamina C, Weiss G, et al. Assessing global COPD awareness with Google Trends. Eur Respir J. 2019;53(6).
5. Gross CP, Anderson GF, Powe NR. The Relation between Funding by the National Institutes of Health and the Burden of Disease. New England Journal of Medicine. 1999;340(24):1881-7.
6. Soriano JB, Kendrick PJ, Paulson KR, Gupta V, Abrams EM, Adedoyin RA, et al. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet Respiratory Medicine. 2020;8(6):585-96.
7. Vanjare N, Chhowala S, Madas S, Kodgule R, Gogtay J, Salvi S. Use of spirometry among chest physicians and primary care physicians in India. NPJ Prim Care Respir Med . 2016 2016/07//; 26:[16036 p.].
8. Woldeamanuel GG, Mingude AB, Geta TG. Prevalence of chronic obstructive pulmonary disease (COPD) and its associated factors among adults in Abeshge District, Ethiopia: a cross sectional study. BMC Pulmonary Medicine. 2019;19(1):181.
9. Buist AS, Vollmer WM, Sullivan SD, Weiss KB, Lee TA, Menezes AM, et al. The Burden of Obstructive Lung Disease Initiative (BOLD): rationale and design. Copd. 2005;2(2):277-83.
10. Binegdie AB, Meme H, El Sony A, Haile T, Osman R, Miheso B, et al. Chronic respiratory disease in adult outpatients in three African countries: a cross-sectional study. The International Journal of Tuberculosis and Lung Disease. 2022;26(1):18-25.
11. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis Management and Prevention of COPD 2020 Report. 2020 Global Initiative for Chronic Obstructive Lung Disease, Inc.
12. ATS Statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166: 111–117.
13. Heinzerling L, Mari A, Bergmann KC, Bresciani M, Burbach G, Darsow U, et al. The skin prick test – European standards. Clinical and Translational Allergy. 2013;3(1):3.
14. Nagoda M, Okpapi JU, Babashani M. Assessment of respiratory symptoms and lung function among textile workers at Kano Textile Mills, Kano, Nigeria. Nigerian Journal of Clinical Practice. 2012;15 4:373-9.
15. Drummond MB, Huang L, Diaz PT, Kirk GD, Kleerup EC, Morris A, et al. Factors associated with abnormal spirometry among HIV-infected individuals. AIDS. 2015;29(13):1691-700.
16. Johannessen A, Eagan TM, Omenaas ER, Bakke PS, Gulsvik A. Socioeconomic risk factors for lung function decline in a general population. Eur Respir J. 2010;36(3):480-7.
17. López-Campos JL, Fernández-Villar A, Calero-Acuña C, Represas-Represas C, López-Ramírez C, Leiro Fernández V, et al. Occupational and Biomass Exposure in COPD: Results of a Cross-Sectional Analysis of the On-Sint Study. Archivos de Bronconeumología (English Edition). 2017;53(1):7-12.
18. Fell AKM, Svendsen MV, Kim JL, Abrahamsen R, Henneberger PK, Torén K, et al. Exposure to secondhand tobacco smoke and respiratory symptoms in non-smoking adults: cross-sectional data from the general population of Telemark, Norway. BMC Public Health. 2018;18(1):843.

18. Csoma Z, Gál Z, Gézsi A, Herjavecz I, Szalai C. Prevalence and characterization of severe asthma in Hungary. Scientific Reports. 2020;10(1):9274
19. Bayisa T, Parkeh M, Bekele A, Schluger N, Oumer F, Sherman C, et al. Profile and risk factors of patients with obstructive airway diseases at tikur anbessa specialized hospital chest clinic, Addis Ababa, Ethiopia. Ethiopian Medical Journal. 2017;55:97-102.
20. 20.Lee M-R, Yang C-Y, Chang K-P, Keng L-T, Yen DH-T, Wang J-Y, et al. Factors Associated with Lung Function Decline in Patients with Non-Tuberculous Mycobacterial Pulmonary Disease. PLOS ONE. 2013;8(3):e58214.
21. 21.Fiogbe AA, Agodokpessi G, Tessier JF, Affolabi D, Zannou DM, Adé G, et al. Prevalence of lung function impairment in cured pulmonary tuberculosis patients in Cotonou, Benin. The International Journal of Tuberculosis and Lung Disease. 2019;23(2):195-202.
22. Joo MJ, Au DH, Fitzgibbon ML, McKell J, Lee TA. Determinants of spirometry use and accuracy of COPD diagnosis in primary care. J Gen Intern Med. 2011;26(11):1272-7.
23. Guerra S, Carsin A-E, Keidel D, Sunyer J, Leynaert B, Janson C, et al. Health-related quality of life and risk factors associated with spirometric restriction. European Respiratory Journal. 2017;49(5).
24. Sakhamuri S, Lutchmansingh F, Simeon D, Conyette L, Burney P, Seemungal T. Reduced forced vital capacity is independently associated with ethnicity, metabolic factors and respiratory symptoms in a Caribbean population: a cross-sectional study. BMC Pulmonary Medicine. 2019;19(1):62.
25. Pérez-Padilla R, Fernandez-Plata R, Montes de Oca M, Lopez-Varela MV, Jardim JR, Muiño A, et al. Lung function decline in subjects with and without COPD in a population-based cohort in Latin-America. PLOS ONE. 2017;12(5):e0177032.
26. Lindberg A, Larsson LG, Rönmark E, Jonsson AC, Larsson K, Lundbäck B. Decline in FEV1 in relation to incident chronic obstructive pulmonary disease in a cohort with respiratory symptoms. COPD. 2007;4 (1):5-13.
27. Kurth L, Hnizdo E. Change in prevalence of restrictive lung impairment in the U.S. population and associated risk factors: the National Health and Nutrition Examination Survey (NHANES) 1988-1994 and 2007-2010. Multidisciplinary Respiratory Medicine. 2015;10(1):7.
28. Talaminos Barroso A, Márquez Martín E, Roa Romero LM, Ortega Ruiz F. Factors Affecting Lung Function: A Review of the Literature. Archivos de bronconeumologia. 2018;54(6):327-32
29. James AL, Palmer LJ, Kicic E, Maxwell PS, Lagan SE, Ryan GF, et al. Decline in Lung Function in the Busselton Health Study. American Journal of Respiratory and Critical Care Medicine. 2005;171(2):109-14.
30. Sears MR. Lung function decline in asthma. European Respiratory Journal. 2007;30(3):411-3.
31. Mannino DM, Gagnon RC, Petty TL, Lydick E. Obstructive Lung Disease and Low Lung Function in Adults in the United States: Data From the National Health and Nutrition Examination Survey, 1988-1994. Archives of Internal Medicine. 2000;160(11):1683-9.
32. Tantucci C, Modina D. Lung function decline in COPD. International Journal of Chronic Obstructive Pulmonary Disease. 2012;7:95-9

Ethiopian Medical Journal 2024, 62(1)
ISSN 0014-1755 eISSN 2415-2420 Demissie et al.

Original Article

Bacteriologic Profile, Antibiotics Resistance Pattern, and Outcomes of Patients Admitted to Lancet General Hospital from June 2022 to June 2023: A Retrospective Cohort Study

Zekewos Demissie[1], Serkalem Nurlegn[1], Nahom Zemedkun[2], Yidnekachew Demssis[1], Bethel Mekuriya[2], Eyob Beyene[3], Seifemichael Getachew[4], Desalew Mekonnen[3], Yohannes Birhanu[3], Brook Alemayehu[1], Nebiyat Sileshi[1], Gelila Sintayehu[1], Dawit Admasu[5], Kibruyisfaw Zewdie[6]

[1]Department of Internal Medicine Lancet General Hospital, Addis Ababa, Ethiopia
[2]Lancet General Hospital, Addis Ababa, Ethiopia
[3] Department of Internal Medicine, Addis Ababa University, Addis Ababa, Ethiopia
[4] Department of Internal medicine, St. Paul Millennium Medical College, Addis Ababa, Ethiopia
[5] Department of Surgery, Lancet General Hospital, Addis Ababa, Ethiopia
[6] Department of Neurosurgery, Addis Ababa University, Addis Ababa, Ethiopia

Corresponding authors*: zakdem61@gmail.com

Abstract

Background *Prior studies indicated increased antimicrobial resistance in Ethiopia, with related health, economic, and environmental costs. Knowing an institutions and population microbiologic profile allows for proper antibiotic treatment, which substantially impact patients' outcomes such as healthcare related costs, morbidity, and mortality. The current study assessed the bacteriologic profile, resistance pattern, and treatment outcome in Lancet General Hospital.*

Method *A retrospective cohort study on the bacteriologic profile, antibiotics resistance pattern, and outcome of patients was done on 128 eligible patients who were admitted to Lancet General Hospital from June 2022 to June 2023. Data from all hospitalized patients with culture-confirmed infection were analyzed. SPSS version 26.0 was used to analyze the data. Association between independent and dependent variables was analyzed using binary logistic regression model.*

Results *Gram-negative bacteria were recovered in 77% of the cases. Extended-spectrum beta-lactamase producing Enterobacteriaceae was found in 37.5% (54) isolates and carbapenem resistant bacteria were identified in 27.8% of patients. In-hospital mortality from multidrug resistant bacterial infection was 14.8%. Age ≥ 65 years, presence of septic shock, and presence of carbapenem-resistant bacteria were independently associated with increased in-hospital mortality.*

Conclusion *High number of resistant microorganisms was isolated, and increased mortality was documented from infections caused by carbapenem-resistant bacteria. Multi-center studies should be done to determine the extent of resistant organisms in health facilities throughout the country.epidemiology, and the findings should be factored into clinical decision making and program design for disease prevention, screening, and treatment. It also calls for further prospective research to learn more about the conditions in the context of additional relevant personal and clinical characteristics*

Keywords: *Bacteriologic profile, Antimicrobial resistance, carbapenem resistance, extended-spectrum beta-lactamase,methicillin-resistant S. aureus, vancomycin-resistant enterococcus*

Citation : *. Demissie Z , Nurlegn S , Zemedkun N et al. Bacteriologic Profile, Antibiotics Resistance Pattern, and Outcomes of Patients Admitted to Lancet General Hospital from June 2022 to June 2023: A Retrospective Cohort* Study *Ethiop Med J 62 (1) 15-24*

Submission date : *9 November 2023 Accepted: 27 December 2023 Published: 1 January 2024*

Introduction

Treatment with antibiotics is one of the main armaments of modern medicine, with the discovery of antibiotics in the 1930s to 1960s drastically reducing infectious disease mortality. In the absence of discovering new classes of antimicrobials and the increasing emergence and reemergence of resistant pathogens, mortality from infectious disease is increasing [1].
Due to this concerning rise in antimicrobial-resistant pathogens, the WHO has identified twelve species of bacteria as priority pathogens based on their antimicrobial resistance. These priority pathogens are grouped into critical, high, and medium priority groups [2].

Collectively antimicrobial resistance causes at least 700,000 deaths each year according to a report in 2019, making common diseases fatal and lifesaving medical procedures risky. The problem is expected to rise barring extensive interventions resulting in 10 million deaths by 2050. The highest impact is expected to be in Africa, accounting for 4.2 million deaths annually and Asia [3, 4].

A study published in 2023 on situational analysis of antimicrobial resistance in Ethiopia found a rising antimicrobial resistance with associated health, economic, and environmental burdens [5].

A multicenter study evaluated emerging pathogens at four referral hospitals in Ethiopia and found the contribution of gram-negative bacteria for the majority of culture results with Klebsiella species and E. coli being the most frequently identified bacteria and an alarmingly higher frequency of multidrug resistance among the isolated bacteria. [6].

In another study from St. Paul Millennium Medical College and Abet Trauma Center, gram-negative bacteria were the most common isolates in 68% of cases, and drug-resistant pathogens were frequently isolated [7].

Cultures obtained from inanimate objects in the Tikur Anbessa Specialized Hospital intensive care unit showed an even a scarring picture of nosocomial infection risks. The results from this study isolated both gram-positive and gram-negative bacteria with a high drug resistance pattern [8].

Multiple risk factors were linked with acquisition of infection from Multi-drug resistant (MDR) pathogens. These risk factors are variable for different MDR pathogens. The most important risk factors for MDR gram negative bacteria include hospitalization in the past 03 month, antibiotics use in the past 01 month, presence of central venous catheter, and presence of indwelling urinary catheter[9].

Knowing the microbiologic profile of an institution and population tailors the initial empiric antibiotic management of patients, which significantly affects patient's outcome, including health-related costs, morbidity, and mortality. The objective of the current study was, therefore, to assess the bacteriologic profile, resistance pattern, and patient's outcome in Lancet General Hospital.

Methodology

Materials and Method

We conducted a hospital-based, retrospective cohort study on the bacteriologic profile, antibiotics resistance pattern, and outcome of patients admitted to Lancet General Hospital from June2022 to June2023 G.C. Lancet General Hospital is one of the largest private hospitals in Ethiopia. It currently offers complete specialist care through a variety of specialty and subspecialty departments.

Study participants

The study included participants who fulfilled the eligibility criteria. Patients ≥18 years (age 18 and above with known culture-proven microbiologic profiles, and admitted to the medical ward, surgical wards, and adult ICU and received treatment for infection were included in this study. Patients with incomplete medical records and unknown outcome were excluded from the study.

Sampling and Data collection

We included all patients with a known culture-proven microbiologic profile who received inpatient treatment for infection at Lancet General Hospital Medical and Surgical Ward and Adult Intensive Care Unit using a convenient sampling method. Participants were identified using registries for admission logbooks and culture results. Data were collected using pretested and structured questionnaire. Clinical data were collected from electronic medical records, and microbiologic data were collected from culture registries.

Bacterial and antimicrobial resistance identification
The same microbiology lab received all culture specimens, and same method was utilized to examine the results. All cultures were taken after initiation of antibiotics to tailor further management. All culture results were defined by their Gram stain reaction and colony characteristics. Bacterial species were confirmed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI TOF).A disc diffusion test was used to assess the antimicrobial resistance pattern of the isolated species.

Data Analysis

The acquired data were verified, cleaned up, and then given a final analysis. IBM SPSS Statistics software

package version 26.0 was used for analysis. To evaluate the relationship between each independent variable and the treatment outcome, binary logistic regression model was used. Univariable logistic regression analysis was performed to determine the association of each independent variable with patient outcome and variables which showed association at p-value of ≤ 0.2 were analyzed in multivariate analysis. A P-value less than 0.05 was considered to determine the statistical significance of the association, and an odds ratio with a 95% confidence interval will be used to determine the presence, strength, and direction of association between covariates and the outcome variable.

Operational definitions

Bacterial identification and species confirmation: All culture results were defined by their Gram stain reaction and colony characteristics. Bacterial species were confirmed by matrix-assisted laser desorption/ ionization time-of-flight mass spectrometry (MALDI TOF).

Extended-spectrum beta-lactamase-producing Enterobacteriaceae: defined by phenotypic detection of resistance to cefotaxime (oxyimino-beta-lactam substrate) on a disc diffusion test.

Carbapenem resistance:Carbapenem resistance was defined by phenotypic detection of resistance to carbapenem antibiotics on a disc diffusion test and confirmed by the laboratory MIC cutoff value.

Septic shock: It was defined by the need for a vasopressor to maintain a patient's mean arterial pressure (MAP) ≥ 65 mmHg or blood pressure ≥ 90/60 [9].

Patient outcome: Patient outcome was defined as in hospital mortality from any cause in patients with culture-proven bacterial infections.

Ethical Consideration

Ethical clearance was obtained from the institutional review board, and consent was not needed from the patients because wavier was obtained from the IRB of the institution. All the information obtained was confidential and used only for the intended purpose. The obtained data were documented and analyzed anonymously.

Results

A total of 174 patients were identified during the study period, and 46 were excluded for incomplete medical records (24) and unknown outcomes (22). A total of 144 microbiological culture isolates were identified from 128 patients and included in the final analysis.

Sociodemographic characteristics of study participants

The mean [± standard deviation] age of the participants was 54.38 ± (54). The majority of the study participants were male (57%). Two-third of the study participants were from Addis Ababa.

The socio-demographic characteristics of study participants are shown in Table 1.

Characteristics		No	%
Sex	Male	73	57
	Female	55	43
Age Category	< 65	84	65.6
	>/65	44	34.4
Region	Addis Ababa	81	63.3
	Somali	30	23.4
	Oromia	7	5.1
	Amhara	4	3.1
	Tigray	2	1.6
	Sidama	1	0.8
	SWP	1	0.8
	Foreginers	2	1.6

The genitourinary system was the most frequently documented site of infection followed by the pulmonary system, wound site, and soft tissue. Blood stream infection was identified only in 4 patients.

More than two-thirds (88) of the study participants had at least one risk factor for the MDR pathogen, and among those patients, 69.3% (61) had more than one risk factor. The two most often found risk factors were hospitalization within the previous three months and usage of antibiotics during the previous month.

Forty-six (35.9%) research participants had imaging evidence of an abscess and the most frequent locations were the liver, lung, and chest wall, followed by soft tissue and joint spaces.

Clinical characteristics of study participants are shown in Table 2.

Table 2: Clinical Characteristics of Study Participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023.

Characteristics		No	%
Identified focus of infection	Lung	39	30.5
	Gastrointestinal Tract	10	7.8
	Genitourinary system	42	32.8
	Central Nervous System	3	2.3
	Wound and soft tissue infection	28	21.9
	Surgical site	2	1.6
	CRBSI	4	3.1
Identified risk factors for MDR pathogen	Yes	88	68.75
	No	40	31.25
Hospitalization in the past 03 months?		50	39
Antibiotics use in the past 01 month?		53	41.4
Recurrent surgery?		33	25.8
On hemodialysis in the past 01 month?		22	17.2
Presence of central venous catheter?		20	15.6
On immunosuppressive therapy?		12	9.4
Others		10	7.8
Comorbidities	No	37	28.9
	Hypertension	57	44.5
	Diabetes	35	27.3
	Chronic Kidney Disease	35	27.3
	Acute Kidney Injury	24	18.8
	Stroke	10	7.8
	HIV	9	7
	Heart Failure	9	7
	Cancer	20	15.6
	Chemotherapy	12	9.4
Presence of septic shock		16	12.5
Mean WBC Count (± SD)	15,756.98 ± 15,850		
Mean CRP (±SD)	103.92 ± 52.30		
Imaging Evidence of Abscess		46	35.9
Location of Abscess n=46	Soft tissue and Joint	25	54.3
	Liver	7	15.2
	Lung and chest wall	5	10.9
	Renal	3	6.5
	Surgical site	2	4.3
	CNS	2	4.3
	Others	2	4.3

CRBSI: catheter-related blood stream infection

Microbiologic profile of study participants

In this study, a total of 144 specimens from 128 patients generated positive culture results. Among the study participants, 42 (32.8%) had positive blood culture results, and 102 (79.7%) had positive culture results from specimens other than blood. Gram-negative bacteria constituted 77.1% (111) of the isolated microorganism. *E. coli* was the most prevalent bacteria overall and among gram-negative isolates found in 48 (33.3%) cultures followedby *K. pneumoniae.S. aureus* was the most prevalent gram-positive bacteria

isolated in 20 (13.9%) cases. In this study, numerous bacterial isolates with a multidrug resistance pattern were discovered. Gram-negative isolates displayed a higher number of resistance compared to gram-positive isolates. ESBL-PE was found in 37.5% (54) isolates, while carbapenem resistance was found in 27.8% (40). There was no discernible resistance pattern among *S. aureus.*
Microbiologic profile and drug resistance pattern of bacteria isolates from study participants are shown in Table 3 and Figure 1.

Treatment-related characteristics of study participants

Two or more antimicrobial drugs from various classes were administered to all participants in the study. Meropenem was the most commonly used antibiotic followed by cefepime. In accordance with the findings of the culture, a higher class of antimicrobial drugs (polymyxin-B and ceftazidime-avibactam) was prescribed. MRSA coverage was used in 98 (76.6%) cases.
In 55 (43%) patients, source control was indicated.

Table 3: Microbiologic profile and drug resistance pattern of isolates from blood and non-blood culture specimens of the study participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023.

Characteristics		**Number (n)**	**Percentage (%)**
Antibiotics Used	Ceftriaxone	13	10.2
	Ceftazidime	2	1.6
	Cefepime	43	33.6
	Meropenem	68	53.1
	Ceftazidime-Avibactum	12	9.4
	Polmyxin-B	4	3.1
	Ampicillin-sulbactum	2	1.6
Gram positive coverage	No	30	23.4
	Vancomycin	91	71.1
	Linezolide	7	5.5
Intervention for Source control	No	73	57
	Surgical incision and drainage	22	17.2
	Percutaneous ultrasound guided drainage	7	5.5
	Debridement	13	10.2
	Surgery	9	7
	CVC removal	4	3.1
Mean duration of antibiotics use (± SD)	11.14 ± 4.98		
Mean duration of hospital stay (± SD)	20.52 ± 18.49		
Patient outcome	Discharge Improved	109	85.2
	In-hospital Mortality	19	14.8

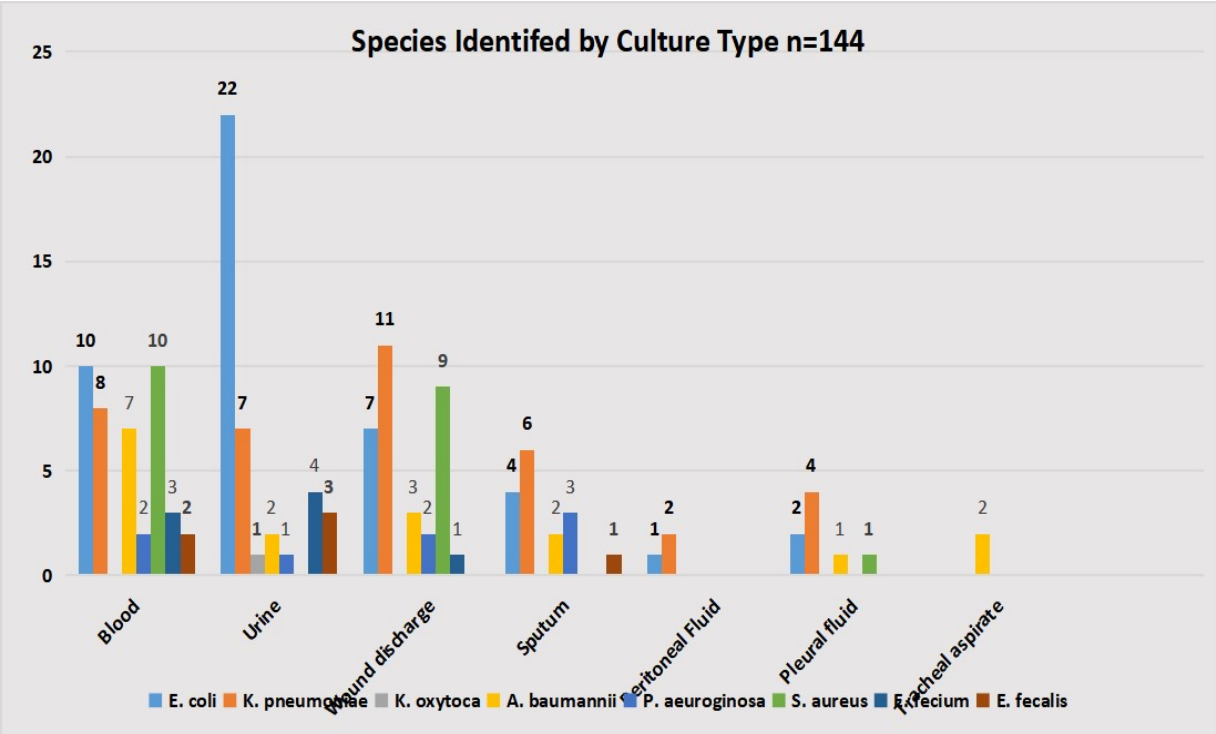


Figure 1: Species identified from blood and non-blood culture specimens of study participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023.

Incision and drainage, debridement, major surgical operations, and percutaneous ultrasound-guided drainage were the most frequently performed procedures.
The mean duration of antibiotic use and the mean duration of hospital stay was 11 and 20.5 days, respectively. Antibiotics were modified based on culture result in 54 (43.7%) patients. In 38 (29.7%) patients' 3rd and 4th generation cephalosporin were changed to Meropenem and In 16 (12.5%) patients Meropenem was changed in to Ceftazidime-Avibactum and Polymyxin-B.

From 128 patients admitted and received inpatient treatment, 109 (85.2%) of the patients completed their course of antibiotics and were discharged. In-hospital mortality was found to be 14.8% (15) in the study.
Treatment-related characteristics of study participants are shown in Table 4

Multivariate analysis of factors associated with in-hospital mortality of patients admitted for treatment of infection at Lancet General Hospital

A logistic regression analysis of the risk factors for in-hospital mortality was performed. Six variables were found to be significantly associated with in-hospital mortality on univariate analysis with a p value of ≤ 0.2. These include age ≥ 65 years, presence of risk factor for MDR pathogen, presence of comorbidities, presence of septic shock, type of bacteria identified, and presence of carbapenem-resistant bacteria.

At a p value ≤ 0.05, the final multivariate regression model revealed that 3 factors had a statistically significant association with in-hospital mortality. These include age ≥ 65 years, the presence of septic shock, and the presence of carbapenem-resistant bacteria. Compared to patients under 65 years old, patients over 65 years old had a 7.5-fold greater chance of mortality in the hospital (adjusted odds ratio (AOR 7.649), 95% confidence interval (CI): 2.018–18.986, p=0.003). In the presence of septic shock, in-hospital mortality was seven times greater than in its absence (AOR 7.051, 95% CI: 1.618-21.732, p=0.009). In-hospital mortality is five times more likely when carbapenem-resistant bacteria are present (AOR 5.062, 95% CI: 1.310-19.566, p=0.019).

Binary logistic regression analysis of factors associated with in-hospital mortality is shown in Table 5.

Table 4: Treatment-related characteristics and outcomes of study participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023

Characteristics		Number (n)	Percentage (%)
Antibiotics Used	Ceftriaxone	13	10.2
	Ceftazidime	2	1.6
	Cefepime	43	33.6
	Meropenem	68	53.1
	Ceftazidime-Avibactum	12	9.4
	Polmyxin-B	4	3.1
	Ampicillin-sulbactum	2	1.6
Gram positive cover-age	No	30	23.4
	Vancomycin	91	71.1
	Linezolide	7	5.5
Intervention for Source control	No	73	57
	Surgical incison and drainage	22	17.2
	Percutaneous ultrasound guided drainage	7	5.5
	Debridemnet	13	10.2
	Surgery	9	7
	CVC removal	4	3.1
Mean duration of antibiotics use (± SD)	11.14 ± 4.98		
Mean duration of hospital stay (± SD)	20.52 ± 18.49		
Patient outcome	Discharge Improved	109	85.2
	In-hospital Mortality	19	14.8

Discussion

Antimicrobials play a crucial role in the treatment of many infectious diseases, saving millions of lives while also easing the burden of the disease and enhancing patients' quality of life [10]. Compared to infections caused by nonresistant pathogens, hospitalization due to infection caused by drug-resistant microbes is associated with a longer hospital stay and increased healthcare expenses, morbidity, and mortality. Previous research conducted in Ethiopia indicated a trend toward an increase in the prevalence of drug-resistant pathogens [5, 11].

The study participants in this study were older on average than those in other studies. The increasing proportion of elderly participants in our study may be attributable to a greater number of older patients receiving follow-up care at the hospital's chronic outpatient services [7, 12].

The genitourinary system was the most common documented focus of infection followed by the pulmonary system. This outcome is different compared with studies conducted at adult intensive care units at Abet Trauma Center, and the Iran ICU. The difference in study populations and study settings might have contributed for the difference in the focus of infection observed in the various studies [7, 13].

Gram-negative bacteria were discovered in 77% of the cases, and E. coli and K. pneumoniae were the most frequent species found and 70% of A.baumannii isolates exhibited carbapenem resistance. This is comparable with other studies [6, 7].

The delivery of adequate empiric antibiotics, the utilization of culture data for individualized antibiotic modification, appropriate imaging surveillance to identify collections, and prompt source control interventions could all contribute to this higher discharge rate in this study.

Three factors were identified in the present study as independent predictors of in-hospital mortality. These include age ≥ 65 years, the presence of septic shock, and the presence of carbapenem-resistant bacteria.

The increased prevalence of comorbidities in this age group may be the cause of the higher mortality. When septic shock was present, fatality rates were greater. The findings from septic shock investigations demonstrated a 30 to 50% greater risk of mortality [14, 15]. The delayed identification of the bacteria from clinical specimens and the lack of higher classes of antimicrobials in our scenario may be the causes of increased mortality brought on by the presence of carbapenem-resistant bacteria.

Discussion

Antimicrobials play a crucial role in the treatment of many infectious diseases, saving millions of lives while also easing the burden of the disease and enhancing patients' quality of life [10]. Compared to infections caused by nonresistant pathogens, hospitalization due to infection caused by drug-resistant mi-

Table 5: Multivariate analysis of factors associated with in-hospital mortality of study participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023.

Variables	In-Hospital Mortality		COR (95% CI)	P value	AOR (95% CI)	P value
	Yes	No				
Age Category						
<65	4	80	1	1		
>/=65	15	29	10.345 (3.173 - 18.731)	0.0001	7.649 (2.018 - 18.986)	0.003
Presence of risk factor for MDR pathogen						
Yes	16	72	2.741 (0.750 - 10.009)	0.127	1.570 (0.232 - 5.049)	0.939
No	3	37	1	1		
Presence of comorbidities						
Yes	18	73	4.315 (0.957 - 19.929)	0.057	1.639 (0.287 - 9.354)	0.578
No	2	35	1	1		
Presence of Septic shock						
Yes	8	8	9.182 (2.876 - 21.315)	0.0001	7.051 (1.618 – 21.732)	0.009
No	11	101	1	1		
Type of Bacteria Identified						
Gram Positive	2	27	1	1		
Gram Negative	17	82	2.799 (0.607 - 12.904)	0.187	1.526 (0.254 – 9.177)	0.644
Presence of Carbapenem Resistance						
Yes	12	22	6.779 (2.389 - 19.236)	0.0003	5.062 (1.310-19.566)	0.019
No	7	87	1	1		

crobes is associated with a longer hospital stay and increased healthcare expenses, morbidity, and mortality. Previous research conducted in Ethiopia indicated a trend toward an increase in the prevalence of drug-resistant pathogens [5, 11].

The study participants in this study were older on average than those in other studies. The increasing proportion of elderly participants in our study may be attributable to a greater number of older patients receiving follow-up care at the hospital's chronic outpatient services [7, 12].

The genitourinary system was the most common documented focus of infection followed by the pulmonary system. This outcome is different compared with studies conducted at adult intensive care units at Abet Trauma Center, and the Iran ICU. The difference in study populations and study settings might have contributed for the difference in the focus of infection observed in the various studies [7, 13].

Gram-negative bacteria were discovered in 77% of the cases, and E. coli and K. pneumoniae were the most frequent species found and 70% of A. baumannii isolates exhibited carbapenem resistance. This is comparable with other studies [6, 7].

The delivery of adequate empiric antibiotics, the utilization of culture data for individualized antibiotic modification, appropriate imaging surveillance to identify collections, and prompt source control interventions could all contribute to this higher discharge rate in this study.

Three factors were identified in the present study as independent predictors of in-hospital mortality. These include age $\geq$ 65 years, the presence of septic shock, and the presence of carbapenem-resistant bacteria. The increased prevalence of comorbidities in this age group may be the cause of the higher mortality. When septic shock was present, fatality rates were greater. The findings from septic shock investigations demonstrated a 30 to 50% greater risk of mortality [14, 15].

The delayed identification of the bacteria from clinical specimens and the lack of higher classes of antimicrobials in our scenario may be the causes of increased mortality brought on by the presence of carbapenem-resistant bacteria.

Conclusion

Gram-negative bacteria were the most frequent isolates, and an increasing number of drug-resistant organisms were identified in clinical specimens from patients in this study. Age greater than or equal to 65 years, the prevalence of septic shock, and the presence of bacteria resistance to carbapenem were all independently associated with greater in-hospital mortality. In regard to selecting antibiotics and directing improved antimicrobial stewardship programs, adequate monitoring and antimicrobial data are crucial. Results from appropriate culture specimens tailors antimicrobial choice. Primary care physicians should use higher classes of cephalosporin and carbapenem with proper indication. Ministry of Health and hospital administrations should ensure a proper infection prevention programs and a controlled mechanism should be established to control appropriateness of antimicrobial prescriptions.

Recommendations

We recommend our institution to advocate antimicrobial stewardship program and prepare antibiogram based on available data. Strengthening infection prevention measures and application of proper use of antibiotics help in mitigating the rising public health concern from MDR pathogens. We also recommend a large multicenter prospective study with pre-specified aims to analyze the microbiologic culture profile, resistance pattern of isolates, outcomes, and factors associated with the outcomes because this is a single-center, retrospective investigation with a small sample size. We also advise institutions to properly prepare for and adhere to infection prevention, as well as to conduct regular surveillance of their antimicrobial data and stewardship programs.

Strengths and Limitations of the Study

To the best of the authors' knowledge, this is the first study on microbiologic profiles and medication resistance patterns from a private facility; therefore, it can serve as a reference and baseline for future research. Because it is a retrospective study, the observer is unable to directly gauge the study variables and timing of infection or new infection that developed after admission.

Acknowledgment

We would like to thank the IT team at Lancet General Hospital for their assistance in extracting data from electrical medical records, as well as Wudasse Advanced Laboratory for providing the culture results.

Conflict of Interest

All authors state that they have no conflicts of interest.

References

1. Aminov RI. A brief history of the antibiotic era: lessons learned and challenges for the future. Front Microbiol. 2010 Dec 8;1:134. doi: 10.3389/fmicb.2010.00134.
2. Asokan GV, Ramadhan T, Ahmed E, Sanad H. WHO Global Priority Pathogens List: A Bibliometric Analysis of Medline-PubMed for Knowledge Mobilization to Infection Prevention and Control Practices in Bahrain. Oman Med J. 2019 May;34(3):184-193. doi: 10.5001/omj.2019.37.
3. Engström, A. (2021). Antimicrobial Resistance as a Creeping Crisis. In: Boin, A., Ekengren, M., Rhinard, M. (eds) Understanding the Creeping Crisis. Palgrave Macmillan, Cham. https://doi.org/10.1007/978-3-030-70692-0_2
4. Oved K. Fighting AMR with Host Immune Response Technology. Drug Discov Today. 2021 Sep;26 (9):2081-2083. doi: 10.1016/j.drudis.2020.11.036.
5.Beyene AM, Andualem T, Dagnaw GG, Getahun M, LeJeune J, Ferreira JP. Situational analysis of antimicrobial resistance, laboratory capacities, surveillance systems and containment activities in Ethiopia: A new and one health approach. One Health. 2023 Mar 17;16:100527. doi: 10.1016/j.onehlt.2023.100527.
6. Legese MH, Asrat D, Swedberg G, Hasan B, Mekasha A, Getahun T, Worku M, Shimber ET, Getahun S, Ayalew T, Gizachew B, Aseffa A, Mihret A. Sepsis: emerging pathogens and antimicrobial resistance in Ethiopian referral hospitals. Antimicrob Resist Infect Control. 2022 Jun 13;11(1):83. doi: 10.1186/s13756-022-01122-x.
7. Gebremedhin Y, Sultan M, Tesfaye D. Microbiological Profile, Antimicrobial Susceptibility, and Outcome Among Patients Admitted to Addis Ababa Intensive Care Units; a Cross-sectional Study.. Research Square; 2021. DOI: 10.21203/rs.3.rs-1178576/v1.
8. Sebre S, Abegaz WE, Seman A, Awoke T, Desalegn Z, Mihret W, Mihret A, Abebe T. Bacterial Profiles and Antimicrobial Susceptibility Pattern of Isolates from Inanimate Hospital Environments at Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia. Infect Drug Resist. 2020 Dec 14;13:4439-4448. doi: 10.2147/IDR.S286293.
9. Guarino M, Perna B, Cesaro AE, Maritati M, Spampinato MD, Contini C, De Giorgio R. 2023 Update on Sepsis and Septic Shock in Adult Patients: Management in the Emergency Department. J Clin Med. 2023 Apr 28;12(9):3188. doi: 10.3390/jcm12093188. PMID: 37176628; PMCID: PMC10179263.
10. Dixon J, Duncan CJ. Importance of antimicrobial stewardship to the English National Health Service. Infect Drug Resist. 2014 May 30;7:145-52. doi: 10.2147/IDR.S39185.
11. Serra-Burriel M, Keys M, Campillo-Artero C, Agodi A, Barchitta M, Gikas A, Palos C, López-Casasnovas G. Impact of multi-drug resistant bacteria on economic and clinical outcomes of healthcare-associated infections in adults: Systematic review and meta-analysis. PLoS One. 2020 Jan 10;15(1):e0227139. doi: 10.1371/journal.pone.0227139.
12. Ali S, Birhane M, Bekele S, Kibru G, Teshager L, Yilma Y, Ahmed Y, Fentahun N, Assefa H, Gashaw M, Gudina EK. Healthcare associated infection and its risk factors among patients admitted to a tertiary hospital in Ethiopia: longitudinal study. Antimicrob Resist Infect Control. 2018 Jan 5;7:2. doi: 10.1186/s13756-017-0298-5.
13. Hamishehkar, H., P. Shadmehr, A. Mahmoodpoor, S. O. Mashayekhi, and T. Entezari-Maleki. " Antimicrobial Susceptibility Patterns Among Bacteria Isolated from Intensive Care Units of the Largest Teaching Hospital at the Northwest of Iran ". Brazilian Journal of Pharmaceutical Sciences, vol. 52, no. 3, Sept. 2016, pp. 403-12, doi:10.1590/s1984-82502016000300006.
14. Annane D, Aegerter P, Jars-Guincestre MC, Guidet B; CUB-Réa Network. Current epidemiology of septic shock: the CUB-Réa Network. Am J RespirCrit Care Med. 2003 Jul 15;168(2):165-72. doi: 10.1164/rccm.2201087.
15. Alberti C, Brun-Buisson C, Burchardi H, Martin C, Goodman S, Artigas A, Sicignano A, Palazzo M, Moreno R, Boulmé R, Lepage E, Le Gall R. Epidemiology of sepsis and infection in ICU patients from an international multicentre cohort study. Intensive Care Med. 2002 Feb;28(2):108-21. doi: 10.1007/s00134-001-1143-z.

https://dx.doi.org/10.4314/emj.v62i1.4

Ethiopian Medical Journal 2024, 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]

ISSN 0014-1755 *eISSN 2415-2420* *Ayele et al.*

Original Article

Factors Associated with Neurocognitive Impairment in Treatment Experienced HIV+ Adults from a Tertiary Care Center in Ethiopia

Biniyam A. Ayele[1]*, Thakur T. Kiran[2], Wondwossen Amogne[3]

[1]Department of Neurology, School of Medicine, College of Health Sciences, Addis Ababa University
[2] Department of Neurology, Columbia University Irving Medical Center, NY, USA
[3] Department of Internal medicine, School of Medicine College of Health Sciences
Addis Ababa University, Addis Ababa, Ethiopia

Corresponding authors*: biniyam.a7@gmail.com

Abstract

Background: Given the improvement in life expectancy of people living with HIV (PLWH) in sub-Saharan Africa, the risk of asymptomatic HIV-associated neurocognitive disorder (HAND) has increased. The study objectives were to investigate the prevalence of HAND and associated factors among treatment experienced adults in Ethiopia.

Methods: A single-center observational cross-sectional study was conducted between December 2019 and June 2020 to investigate HAND. International HIV dementia scale (IHDS) was used to screen for the disorder. Both descriptive and analytical statistics were used to analyze the data.

Results: Total of 324 PLWH (63% females) who were on combination antiretroviral therapy for median of 144 months (IQR: 108-168) were investigated. The mean age was 42.5 years (1SD=12.2). The prevalence of HAND was 75.3% and the difference was significantly more in those above 40 years of age (65.8% vs. 80.7%, p=0.003). Age is the only risk factor identified with multivariable logistic regression analysis. A linear decrement in the total score of cognitive performance was observed as the patient's age increase; age was responsible for 9.4% variation observed in IHDS score (r= -0.31, R^2=0.094, p<0.0001). Although statistically not-significant, the trend for cardiometabolic and behavioral risk factors (hypertension, diabetes mellitus, dyslipidemia, smoking, alcohol and khat use) was higher in the group diagnosed with HAND.

Conclusion: The occurrence of neurocognitive impairment was more pronounced in individuals aged 40 years and above who were HIV positive, compared to those below 40 years. Age was found to be an independent predictor of HAND. Cardiovascular and behavioral risk factors were observed more among patients with HAND compared to no-HAND.

Keywords: *HIV-associated neurocognitive disorder; aging; cardiovascular risk factors; behavioral risk factors; Ethiopia*

Citation : *Ayele BA, Thakur KT, Amogne W et al. Factors associated with neurocognitive impairment in treatment experienced HIV+ adults from a tertiary care center in Ethiopia: A perspective study. Ethiop Med J 62 (1) 25 - 31*

Submission date : *14 March 2023 Accepted: 22 November 2023 Published: 1 January 2024*

Introduction

HIV-associated neurocognitive disorder is an umbrella term, which includes asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND), and HIV-associated dementia (HAD) in individuals suffering from chronic HIV infection (1–3). Post combination antiretroviral therapy (cART) era is characterized by relative decrement in incidence of the severe form of HAND (i.e., HAD) and increment in incidence of ANI and MND (1–3). Likewise, the overall prevalence of HAND has remained similar in the post-cART era with almost affecting half of HIV infected individuals (1–3). Early identification of those at risk, accurate diagnosis, and treatment of HAND is vital especially in low and middle income (LMIC) countries such as Ethiopia, where HAND related health bur- den is highest (3).

Prior studies have identified that decline in cognitive function of HIV + patients were strongly associated with poor cART adherence, engaging in unsafe sex, substance abuse, alcohol addiction, and loss to follow up; ultimately resulting in poor quality of life and increased HIV-associated morbidity and

mortality (1,3–5). Prevalence of HAND in LMICs varies widely ranging from 14% to 64% for adults and 6% for children (3). In Ethiopia, the prevalence of HAND is estimated to be between 33.3% and 67.1% (5–8). In addition, being older age, lack of formal education, low baseline CD4, and un-employment were found to be significantly associated with HAND (5–8).

Unemployment can exacerbate the challenges faced by adults living with HIV, potentially impacting their cognitive health through lack of cognitive stimulation that employment often provides, and higher levels of education are associated with a lifetime of cognitive stimulation and ongoing intellectual challenges, which may contribute to the development and maintenance of cognitive reserve (5–8).

However, little is known about other potential risk factors of HAND such as, peripheral HIV RNA level and presences of cardiovascular risk factors such as hypertension, diabetes mellitus, obesity, and dyslipidemia among HIV + individuals (3,4,9–15). The study objectives of the present study were to investigate association between social determinant of health, behavioral, and cardiovascular risk factors and HIV assocaited cognitive impairments among treatment experienced HIV+ adults at a Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia.

Methods

Study area and duration

The study was conducted at Tikur Anbessa Specialized Hospital (TASH), the largest tertiary referral hospital in Ethiopia with close to 1000 inpatient beds and located at the center of the capital, Addis Ababa. The TASH infectious diseases (ID) clinic cares for more than 2547 HIV + active patients. The study was conducted between December 2019 and June 2020.

Study design and sampling:

A cross-sectional observational study was conducted. We enrolled a consecutive adult who visited the ID clinic during the study period and used a convenience sampling technique. The actual sample size was determined using the single population proportion formula, where the following assumptions were considered: 95% confidence interval, 35.7 % proportion of neurocognitive impairment among HIV-positive patients (7), and 5% margin of error. Finite population correction for the given proportion was done considering the total population of 2547 and then 10% non- responder rate was added, which gave rise to a final sample size of 345. We have included all HIV + patients aged ≥ 18 years, on anti-retroviral treatment at least for six months, not critically ill at the time of the interview, and able to give written or verbal consent. Final data analyses of 324 patients were conducted with a response rate of 97% (Fig. Sup. 1).

Clinical and International HIV Dementia Scale (IHDS) interview

All the included patients were interviewed, and questionnaires were filled by seven trained nurses working in the TASH ID clinics. The training was given by the primary investigator on how to administer the cognitive assessment tool. This tool has been validated in South Africa, Uganda, and Ethiopia and found to have coherent psychometric properties in African populations with sensitivity of 88% and 80% and specificity of 50% and 55% respectively at a cut-off 10 or less (5,7,16–18). Therefore, for our study, we used IHDS cut-off point ≤ 10 to diagnose HAND. Additional clinical data were collected from patient's medical records.

Statistical analysis

We used SPSS version 26. Socio-demographic data, anthropometric data, HIV-related clinical data, CD4 cells counts, HIV RNA level, CV and behavioral risk factors, and IHDS score were first described by their means, frequency, percentile, and standard deviation. Association between HAND and age, CV, and behavioral risk factors were done using chi square or Fisher exact test, logistic regression analysis and results were presented using odds ratio (OR), and p value was set at < 0.05 as statistically significant.

Ethical considerations

The study received ethical approval from Addis Ababa University College of Health Sciences Institutional Review Board (IRB) (Protocol number: 102/19/ Neuro). All questionnaires were coded to maintain maximum confidentiality. All patients gave a written or verbal consent before the interview.

Results

Baseline characteristics of the study participants

The mean (1SD) age of the participants was 42.8 (±12.2) years. Females accounted for 68%. Hundred twenty-four (58.8%) participants were married. Twenty four (7.4%) were illiterate. More than half of the participants were employed (55.6%) and lived on a monthly income <50 USD (54.3%). Hypertension, diabetes mellitus, and dyslipidemia were observed in 9.3%, 4%, and 6.5% of the participants respectively. Likewise, alcohol use, smoking, and khat use was reported by 32.4%, 8.3%, and 13.6%, respectively (Table 1).

HIV associated neurocognitive disorder was observed in 75.3% of the patients. The prevalence of HAND for those above and below 40 years of age was 65.8% and 80.7% p=0.003 respectively. More than half (55.2%) of the study participants received INH preventive therapy. The median duration of HIV treatment was 144 (IQR: 108-168) months. HIV treatment was deferred in 23.8% of our patients. The median baseline CD4 cell count was 165 (IQR: 82-270) cells/uL. Likewise, the median last CD4 cell count of the patients was 477 (IQR: 356-633) cells/uL. The majority (79.6%) of the

Table 1: Characteristics of the study participants (N=324)

Age (mean, 1SD)	**42.8(12.2)**
Comorbidity	
No-comorbidity	259 (79.9%)
1 Comorbidity	44 (13.6%)
2 Comorbidities*	18 (5.6%)
3 comorbidities*	3 (0.9%)
Hypertension	30 (9.3%)
Diabetes mellitus	13 (4%)
Dyslipidemia	21 (6.5%)
Alcohol use, any	105 (32.4%)
Smoking, any	27 (8.3%)
Khat use, any	44 (13.6%)
HIV RNA level not suppressed	22 (6.8%)
HAND diagnosed (n,%)	244 (75.3%)
Age < 40 years	77 (65.8)
Age ≥ 40 years	167 (80.7)

Risk factors of HIV associated neurocognitive disorder (HAND)

Patients with HAND were older compared to those with no-HAND, mean age 44.6 years vs. 37.1 years p=0.001. In the present study, a linear decrement in the total score of cognitive ability (IHDS score) was observed as the patient's age increase; age was responsible for 9.4% variation observed in IHDS score (r= -0.31, R^2=0.094, p<0.0001) (Figure 1).

No difference was observed between HAND and no-HAND based on gender, BMI, and monthly income. Study participants with HAND were more likely married than no-HAND patients, 48.3% vs.10.4%, p<0.001. All illiterate study participants had HAND (p=0.004)(Table 2).No difference was observed between HAND and no-Hand based on the duration of HIV treatment and deferred HIV treatment. Lower median baseline CD4 count was observed among individuals with HAND compared to no-HAND, 157 cells/uL vs. 187 cells/uL, p=0.1 respectively. Similar findings were observed regarding the last CD4 count of our patients, 466 cell/ uL vs. 539 cells/uL, p=0.07, respectively. Detectable HIV RNA level was observed more among patients with HAND compared to no-HAND patients, 4.6% vs. 2.2%, p=0.4 respectively (Table 2).

Cardiovascular risk factors such as hypertension, diabetes mellitus, and dyslipidemia were observed more among patients with HAND compared to no-HAND. Alcohol use was more observed among participants with HAND compared to no-HAND, 27.2% vs. 5.2%, p=0.01. However, no difference was observed between the two groups based on smoking history and khat use. Hundred twenty-seven (39.2%) of the patients with HAND received six months of IPT compared to no-HAND group where only 165 received IPT (p=0.04) (Table 2).

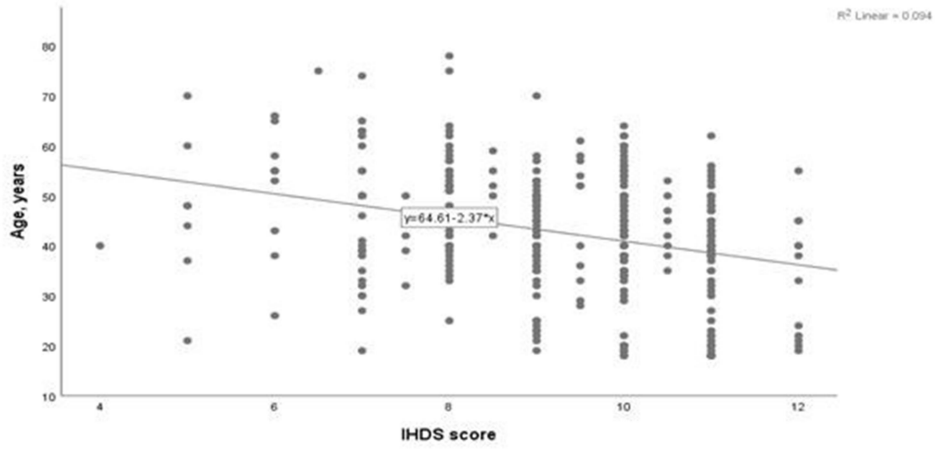


Figure 1: Scatter plot showing a linear decrement in the total score of cognitive ability (IHDS score) was observed as the patient's age increase

Table 2: Risk factors for HIV associated neurocognitive disorder (N=324)

Variable	HAND (n=244)	No-HAND (n=80)	p-value
Mean Age in years (1SD)	44.6 (11.9)	37.1(11.6)	0.001
Female sex (n, %)	156(63.9%)	50(62.5)	0.8
Married (n,%)	102(48.3%)	22(10.4%)	<0.001
Illiterate (n,%)	24(7.4%)	0	0.004
Monthly income < 50 USD (n,%)	126(38.9%)	50(15.4%)	0.09
Months on cART (mean, 1SD)	132(46.8)	126(49.2%)	0.4
cART was deferred (n,%)	55(22.5%)	22(27.5%)	0.4
BMI, Kgs/m2(mean, 1SD)	24.4(4.5)	24.4(4.6)	0.9
Baseline CD4 count, median (IQR)	157(80-265)	187(84-390)	0.1
Last CD4 count, median (IQR)	466(353-618)	539(363-705)	0.07
HIV RNA level not suppressed (n, %)	15(4.6%)	7(2.2%)	0.4
Hypertension (n,%)	24(7.4%)	6(1.9%)	0.53
Diabetes mellitus (n,%)	11(3.4%)	2(0.6%)	0.53
Dyslipidemia (n,%)	15(4.6%)	6(1.9%)	0.67
Alcohol use, any (n,%)	88(27.2%)	17(5.2%)	0.01
Smoking, any (n,%)	21(6.5%)	6(1.9%)	0.76
Khat use, any (n,%)	33(10.2%)	11(3.4%)	0.9
Received IPT for 6 months(n,%)	127(39.2%)	52(16%)	0.04

Multivariable logistic regression modeling to assess the risk of HAND

Age was an independent predictor of HAND in 324 HIV-infected cohort of patients in Ethiopia (AOR 1.04, 95% CI 1.00-1.07, p=0.04). In univariate analysis currently married individuals were associated with HAND (OR 3.12, 95% CI 1.66-5.86, p<0.001) but
not when adjusted for the following variables: demographic, baseline and last CD4 cell counts, alcohol use, and IPT usage. Similarly, in univariate analysis illiterate patents were associated with HAND (AOR 11.1, 95% CI 1.4-87.7, p=0.02) but not when adjusted for covariates. Those patients who were grade 1-12 had near-significant association with HAND (AOR 4.0, 95% CI 1.01-16.5, p=0.05). In univariate analysis, alcohol use and those who did not receive six months of IPT were associated with HAND but not when adjusted for covariates. Monthly income ≤ 50 USD, baseline CD4+ T-cell count, and last CD4+ T- cell count was not associated with HAND (Table 3).

Discussion and conclusion

To our knowledge, this is the first study reported from Ethiopia opted to assess the impact of increasing age, CV, and behavioral risk factors on HIV- associated neurocognitive impairment. In the present study, the overall prevalence of HAND was high, especially among older HIV-infected patients aged 40 years and above. Age was the only independent predictor of HAND in the current cohort of HIV+ patients. These findings were consistent with previously reported studies (3,19,20). Furthermore, the findings indicate the increasing number of HIV-infected aging population in Ethiopia; and the need to develop a proper national policy which can address this issue. Females accounted for most of the participants. This is because, females are more vulnerable to acquiring HIV infection due to factors such as biological, environmental, and cultural (21). Thus, special emphasis needs to be given to vulnerable groups such as females and elderly people living with HIV (PLHIV) in Ethiopia. Cardiovascular and behavioral risk factors were frequently observed among patients with HAND compared to those with no-HAND.

Contrary to the ever-increasing number of aging HIV + population in sub-Saharan Africa (SSA), the num-

Table 3: Multivariable logistic regression modeling to assess the risk of HAND

	Crude Odds Ratio			Adjusted Odds Ratio		
	COR	95% CI	p value	AOR	95% CI	p value
Age	1.06	1.03 – 1.08	<0.001	1.04	1.00-1.07	0.04
Married currently	3.12	1.66-5.86	<0.001	1.6	0.73-3.49	0.2
Educational status						
Illiterate	11.1	1.4-87.7	0.02	4	0.4-36.7	0.2
Grade 1-12	1.06	0.57-1.96	0.09	4	1.01-16.5	0.05
Diploma +	1			1		
Monthly income < 50 USD	1.6	0.9-2.6	0.09	1.5	0.68-3.15	0.3
Baseline CD4+ T-cell count	0.9	0.9-1.0	0.08			
Last CD4 count	0.9	0.9-1.0	0.09			
Alcohol use (any)	2.1	1.2-3.8	0.02	1.69	0.79-3.61	0.18
Received six months of IPT	1.7	1.01-2.9	0.04	1.45	0.74-2.85	0.28

ber of studies from the region addressing HIV and aging were very few (22). According to the 2007 WHO estimation, approximately 3 million people aged ≥ 50 years were living with HIV in SSA; this represents 14.3% of PLHIV aged ≥ 15 years in the region (22). The present study included patient's age between 18 to 78 years; where close to one-third of them are aged ≥ 50 years and age was an independent predictor of HAND. The figure is higher than the previous report from Ethiopia and Uganda (8,23–26) comparable to report from Lesotho where the estimated prevalence of HIV was 27.8% among those aged ≥ 50 years (22). Such discrepancy could be explained by methodological differences. Moreover, our study findings could contribute to the global effort to fill the knowledge gap regarding HIV and aging in SSA.

Higher proportions of cardiovascular risk factors such as, hypertension, diabetes, and dyslipidemia were observed more among patients with HAND. This is indicator of potential contribution of CV risk factors to development of neurocognitive decline among treated HIV-infected patients. This is consistent with study from Kenya by *Achwoka et al* 2019 (26) where the overall NCD incidence rates for men and women were 42.3 and 31.6 per 1000 person years respectively, indicating higher prevalence of NCD among HIV- infected individuals in Kenya. These findings should alert policy makers in sub–Saharan African countries to consider integrating NCD screening and management strategies in the existing routine HIV chronic care.

The present observation showed higher prevalence of substance (alcohol, smoking, and khat) use among patients having HAND. These is likely due to poor cART adherence associated with substance use of, which subsequently predispose the patient to advanced HIV complications such as HAND (3). Our findings were congruent to recent study from Ethiopia (27). These findings should guide both the clinicians and policy makers to address the issue of substance use among PLHIV in Ethiopia. In the present study, no difference was observed regarding HIV RNA level among HAND and no-HAND group. This finding supports the recent agreement regarding the poor predictive ability of peripheral HIV viral load in predicting HAND (12). Thus, it's imperative to look for more reliable biological biomarkers to identify those at risk, diagnosis, and manage HIV associated neurocognitive impairment. Limitations of this study includes lack of control group for com- parison, failure to screen our patients for neuropsychiatric disorders which could overlap with symptoms of HAND, and failure to have brain imaging of our patients, which could further support our diagnosis.

The prevalence of neurocognitive impartment was

higher among HIV+ patients older than 40 years compared with below. Age was found to be an independent predictor of HAND. Cardiovascular and behavioral risk factors were observed more among patients with HAND compared to no-HAND. These findings highlight on the need to have a comprehensive national policy to address the issue of aging, CV, and behavioral risk factors among HIV-infected adults in Ethiopia. Thus, we recommend future con- trolled studies to consolidate these findings.

Acknowledgements: We thank all the patients who participated in this study and all the nurses working at TASH infectious disease clinic. Finally, we are thankful to the Medical Education Partnership Initiative (MEPI) program, Addis Ababa University for the financial support to cover the cost of data collection and stationary costs related to this study.

Declaration:

Ethical considerations

The study received ethical approval from Addis Ababa University College of Health Sciences Institutional Review Board (IRB) (Protocol number: 102/19/ Neuro). All questionnaires were coded to maintain maximum confidentiality. All patients gave a written or verbal consent before the interview.

Consent to publish: Participants consent for publication is not applicable.

Availability of data and materials:

All data sets on which the conclusions of the manuscript rely are available as spread excel sheets documents and available from the corresponding author on reasonable request from the journal.

Supplementary files

Competing interests:

The authors declare they have no actual or potential competing financial interests.

Funding: No funding was received.

Author's contributions:

BA participated in the design of the study concept, analytical data analysis, interpretation, and wrote the manuscript. WA and TK participated in the design of study concept, data interpretation, and critical revision of the manuscript for important intellectual contents.

References

1. Clifford DB, Ances BM. HIV-associated neurocognitive disorder. The Lancet infectious diseases. 2013 Nov 1;13(11):976-86.
2. Coban H, Robertson K, Smurzynski M, Krishnan S, Wu K, Bosch RJ, Collier AC, Ellis RJ. Impact of aging on neurocognitive performance in previously antiretroviral-naïve HIV+ individuals on their first suppressive regimen. AIDS (London, England). 2017 Jul 7;31(11):1565.
3. Thakur KT, Boubour A, Saylor D, Das M, Bearden DR, Birbeck GL. Global HIV neurology: a comprehensive review. AIDS (London, England). 2019 Feb 2;33(2):163.
4. Clifford DB, Mitike MT, Mekonnen Y, Zhang J, Zenebe G, Melaku Z, Zewde A, Gessesse N, Wolday D, Messele T, Teshome M. Neurological evaluation of untreated human immunodeficiency virus infected adults in Ethiopia. Journal of Neurovirology. 2007 Jan;13:67-72.
5. Debalkie M, Id A, Bekele M, Id S, Birhanu YW. High prevalence of neurocognitive disorders observed among adult people living with HIV / AIDS in Southern Ethiopia : A cross-sectional study. 2019;2:1–15.
6. Araya T, Abebaw D, Belete A, Derajew H, Umer H. Prevalence and factors associated with neuro cognitive disorders among HIV-positive patients in Ethiopia: a hospital-based cross-sectional study. Ethiopian Journal of Health Development. 2020 Feb 4;34(1).
7. Yideg Yitbarek G, Mossie Ayana A, Bariso Gare M, Garedew Woldeamanuel G. Prevalence of cognitive impairment and its predictors among HIV/AIDS patients on antiretroviral therapy in Jimma University Medical Center, Southwest Ethiopia. Psychiatry journal. 2019
8. Belete T, Medfu G, Yemiyamrew E. Prevalence of HIV associated neurocognitive deficit among HIV positive people in Ethiopia: a cross sectional study at Ayder Referral Hospital. Ethiopian journal of health sciences. 2017 Feb 6;27(1):67-76.
9. Kabuba N, Menon JA, Franklin Jr DR, Heaton RK, Hestad KA. HIV-and AIDS-associated neurocognitive functioning in Zambia–a perspective based on differences between the genders. Neuropsychiatric disease and treatment. 2016 Aug 11:2021-8.
10. Cohen RA, Seider TR, Navia B. HIV effects on age-associated neurocognitive dysfunction: premature cognitive aging or neurodegenerative disease? Alzheimer's research & therapy. 2015 Dec;7(1):1-0.
11. Awori V, Mativo P, Yonga G, Shah R. The association between asymptomatic and mild neurocognitive impairment and adherence to antiretroviral therapy among people living with human immunodeficiency virus. Southern African journal of HIV medicine. 2018 Jan 1;19(1):1-0.
12. Clifford DB, Ances BM. HIV-associated neurocognitive disorder. Lancet Infect Dis. 2013;13(11):976–86.

13. Salahuddin M, Manzar MD, Hassen HY, Ashuro M, Unissa A, Mohammed MA, Hameed UA, Spence DW, Pandi-Perumal SR. Prevalence and predictors of HIV-associated Neurocognitive Disorder in Ethiopians.
14. Mohamed AA, Oduor C, Kinyanjui D. HIV-associated neurocognitive disorders at Moi teaching and referral hospital , Eldoret , Kenya. 2020;1–11.
15. Zhou L, Saksena NK. HIV associated neurocognitive disorders. Infectious disease reports. 2013 Jun 6;5 (Suppl 1).
16. Nakku J, Kinyanda E, Hoskins S. Prevalence and factors associated with probable HIV dementia in an African population: a cross-sectional study of an HIV/AIDS clinic population. BMC psychiatry. 2013;13:1-7.
17. Sacktor NC, Wong M, Nakasujja N, Skolasky RL, Selnes OA, Musisi S, Robertson K, McArthur JC, Ronald A, Katabira E. The International HIV Dementia Scale: a new rapid screening test for HIV dementia. Aids. 2005 Sep 2;19(13):1367-74.
18. Tsegaw M, Andargie G, Alem G, Tareke M. Screening HIV-associated neurocognitive disorders (HAND) among HIV positive patients attending antiretroviral therapy in South Wollo, Ethiopia. J Psychiatr Res 2016; 10.016
19. Arthur C, Pinheiro T, Dias L, Souza DM, Vieira J, Franco E, *et al*. Original article Aging , neurocognitive impairment and adherence to antiretroviral therapy in human immunodeficiency virus-infected individuals. Brazilian J Infect Dis 2016;20(6):599–604.
20. Levin J, Montano M. What aging with HIV means in the year 2019. AIDS research and human retroviruses. 2019 Nov 1;35(11-12):982-4.
21. Mwangala PN, Newton CR, Abas M, Abubakar A. Screening tools for HIV-associated neurocognitive disorders among adults living with HIV in sub-Saharan Africa: a scoping review. AAS open research. 2018;1.
22. Negin J, Cumming RG. Hiv infection in older adults in sub-Saharan Africa: Extrapolating prevalence from existing data. Bull World Health Organ. 2010;88(11):847–53.
23. Atashili J, Gaynes BN, Pence BW, Tayong G, Kats D, O'donnell JK, Ndumbe PM, Njamnshi AK. Prevalence, characteristics and correlates of a positive-dementia screen in patients on antiretroviral therapy in Bamenda, Cameroon: a cross-sectional study. BMC neurology. 2013 Dec;13:1-7.
24. Saloner R, Cysique LA. HIV-associated neurocognitive disorders: a global perspective. Journal of the International Neuropsychological Society. 2017 Oct;23(9-10):860-9.
25. Bolokadze N, Gabunia P, Ezugbaia M, Gatserelia L, Khechiashvili G. Neurological complications in patients with HIV/AIDS. Georgian medical news. 2008 Dec 1(165):34-8.
26. Achwoka D, Waruru A, Chen TH, Masamaro K, Ngugi E, Kimani M, Mukui I, Oyugi JO, Mutave R, Achia T, Katana A. Noncommunicable disease burden among HIV patients in care: a national retrospective longitudinal analysis of HIV-treatment outcomes in Kenya, 2003-2013. BMC public health. 2019;19(1):1-0.
27. Belete T, Medfu G, Yemiyamrew E. Prevalence of HIV associated neurocognitive deficit among HIV positive people in Ethiopia: a cross sectional study at Ayder Referral Hospital. Ethiopian journal of health sciences. 2017:6;27(1):67-76.

Ethiopian Medical Journal 2024 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420 Yigeremu et al.

Original Article

Sonohysterography Assessment of the Structural Abnormalities of the Uterus in Women with Infertility in Ethiopia

Mahlet Yigeremu[1], Tesfaye Kebede[2], Asefa Getachew[2],Melaku Biruk[2]

[1] Department of Gynecology, Addis Ababa University Collage of Health Science, Addis Ababa, Ethiopia
[2] Department of Radiology , Addis Ababa University collage of Health Science, Addis Ababa Ethiopia

Corresponding authors*: assefagetus@gmail.com

Abstract

Background: *Female factor infertility is associated with a high incidence of the uterine cavity and fallopian tube pathology in developing countries with a high prevalence of STDs, therefore various methods are available for structural evaluation of the female reproductive system, among them is saline infusion sonohysterography (SISHG). The study aimed to assess the role of SISHSG in female infertility evaluation in areas where the gold standard investigating modalities are not readily available.*

Methods: *A hospital-based cross-sectional study was carried out in Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia, between January 2019 to August 2019 G.C. SISHSG consists of instillation of saline into the endometrial cavity with simultaneous pelvic ultrasonography (US). Fifty consecutive female patients referred to the Radiology Department for SISHSG are included in the study. Sensitivity, specificity, positive and negative predictive values were calculated for 26 patients who had both SISHSG and conventional HSG.*

Result: *The majority of the patients were in the age group of 35-40(38%) and 34 (68%) had secondary infertility. The commonest abnormalities detected were uterine myoma 10(20%), Asherman syndrome/cervical stenosis 7 (14%), and tubal blockage 6(10%). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of SISHSG in normal study, Asherman syndrome/cervical stenosis and chronic endometritis was 100%, as compared to the gold standard conventional HSG. For bilateral tubal blockage the SISHSG had 50% sensitivity, 90% specificity, 66.7% PPV and 81.8% NPV, however, for unilateral tubal blockage SISHSG had low sensitivity 33%.*

Conclusion: *SISHSG is readily available, easy-to-do, safe and radiation-free procedure and has high sensitivity and specificity in detecting uterine cavity abnormality. We advocate its use as a first step of investigation modality in the evaluation of female infertility.*

Keywords: Transvaginal sonography (TVS), saline infusion Sonohysterography (SISHG), infertility, Ethiopia
Citation : *Yigeremu Y, Kebede T, Getachew A,Biruk M .Sonohysterography assessment of the structural abnormal ities of the uterus in women with infertility in Ethiopia. Ethiop Med J 62 (1) 33—39*
Submission date : *14 June 2022 Accepted: 28 December 2023 Published: 1 January 2024*

Background

The lifetime prevalence of infertility among reproductive-aged couples ranges between 12.6% and 17.5% worldwide, with relatively higher prevalence rates in some regions such as the Americas, Western Pacific, , and European regions. The lifetime prevalence of infertility for the African region is 13%.(1) . The 12-month prevalence of infertility in the was 24.2% for study in Ethiopian patients of which the majority (90.7%) was secondary infertility (2).

Female infertility in sub-Saharan Africa is associated with a high incidence of uterine cavity and fallopian tube pathology due to prevalent Sexually Transmitted Infections (STI). Diverse methods are available for structural evaluation of the female reproductive system while looking for causes of female infertility which include Pelvic Ultrasound, HSG, SISHSG, MRI, and laparoscopy[3). SISHSG provides superior visuals of the endometrial pathologies compared to some of the routinely performed imaging modalities in gynecology and helps differentiate them from sub-endometrial causes thus providing superior diagnostic results. It has the additional advantage of concurrent assessment of tubal patency with comparable precision (4).

Common indications for SISHG include abnormal uterine bleeding, infertility and repeated abortion, congenital abnormality of the uterine cavity, preoperative or postoperative evaluation of uterine myomas, polyps or cysts, suspected uterine synechiae, further evaluation of suspected endometrial abnormalities detected by transvaginal sonogram (TVS) and inadequate imaging by TVS. [4,5]. SISHSG ideally should be performed early in the follicular phase of the menstrual cycle when the endometrium is thin enough for the installed saline to easily distend the uterine cavity and better accentuate endometrial pathology [6].

Anatomic causes of infertility are more common in developing countries like Ethiopia. In the resource limited settings like ours, the gold standard investigation modalities such as hysterosalpingography, hysteroscopy and laparoscopy with chomopertubation (HLC) as well as other investigation modality like magnetic resonance imaging (MRI) are not readily available. In such setting there has to be an alternative investigation modality like SISHSG, which is readily available, easy to interpret, safer and cheaper which is as accurate as HSG in evaluating the fallopian tubes and uterine cavity in infertile patients [7]. Related to the SISHSG, there is minimal risk of pain and infection for which prophylactic non-steroidal anti-inflammatory drugs and antibiotics may be administered to reduce complications. Reasons for an inability to complete the procedure include the presence of a stenotic cervix and cervical scarring causing backflow of saline. Given that SHG is a relatively safe procedure, mortality has not been described.

To the Authors' knowledge, the study (SISHSG in the evaluation of female infertility) is the first of its kind in Ethiopia and no published or documented research result was found from our region. Therefore, this study aimed to assess the role of SISHG in the evaluation of structural causes of female infertility.

Methods

Study setting: The study was conducted in the department of radiology, School of Medicine, Addis Ababa University, TASH in collaboration with the department of gynecology .The patients were referred from outpatient clinic of the gynecology clinic of TASH for infertility work up.

Study design: A prospective hospital-based cross-sectional study was conducted in the Department of Radiology, School of Medicine, Addis Ababa University, TASH from January 2019 to August 2019 on women who came for infertility and needed structure evaluation of the uterus and fallopian tube as part of the work up in the Department of Obstetrics and Gynecology and Radiology Department.

Study population: All patients with infertility referred to the department of radiology for evaluation of the structural cause of infertility during the study period who fulfilled the inclusion criteria.

Sample size and sampling: We used a non-probability convenient sampling by taking all study subjects that fulfilled the inclusion criteria during the study period (January 2019 to August 2019). Hence, a total of 50 consecutive subjects who fulfilled the inclusion criteria were enrolled in the study which lasted for six months.

Inclusion criteria: All subjects with primary and secondary infertility who are suspected to have structural abnormality.

Exclusion criteria: Active pelvic inflammatory disease, suspected pregnancy, active vaginal bleeding, and those who declined the procedure.

Study Variables include demographic characteristics such as age, parity, and experiences in the earlier pregnancies. The main outcome following SISHSG was the recognition of uterine anomalies and tubal patency. The Data was collected using a structured questionnaire prepared in English. Imaging studies were taken before and after the procedure and stored.

Data collection procedures: All patients were informed about the study, and the procedure was performed with their consent. Each participant was given doxycycline 100mg PO BID, two day before the procedure and 3 days post-procedure with a total of 5 days. On the day of the procedure, every patient was given diclofenac 100mg suppository 30 minutes before the procedure. Initially, all patients were evaluated with pelvic ultrasonography using a transabdominal 3.5MHZ transducer as well as a transvaginal probe with a 7.5 MHz transducer (SSI-8000 SonScape Co.). The dimensions and contours of the uterus, the endometrial lining and thickness, and both adnexal structures and the pouch of Douglas were examined. Then, SISHG was performed with the patient in the dorsal lithotomy position. A standard bivalve speculum was inserted after the cervix was cleaned with povidone–iodine solution. A pediatrics size 8F and 10F Foley catheters were used depending on the parity of the participant. It was threaded through the cervix with a ring forceps, into the cervical canal until it reached the fundus. It was then retracted 1.0–1.5 cm back and the catheter balloon was inflated with 2.0 ml sterile saline. The speculum was then removed carefully, so as not to dislodge the Foley catheter, and the trans-vaginal probe was reinserted in the posterior vaginal fornix. The uterine cavity was distended with a sterile isotonic saline infusion through the

catheter at a rate of 10– 20 ml/min until the Whole uterine cavity was visualized with possible pooling of fluid in the pouch of Douglas. All the SISHSG images and videos were saved on the ultrasound machine and the findings were documented in the data collection sheet.

Data analysis: Data entry, coding and analysis were performed using SPSS version 23 software. Frequency distribution, and percentage were used to describe the findings. The sensitivity, specificity, PPV and NPV value of SISHSG were calculated using Conventional HSG and final clinical diagnosis as Gold standard. Results were presented using tables and figures represented in percentage and measures of central tendency, then summarization and comparison of data was done.

Ethical considerations: The ethical clearance was obtained from Addis Ababa University Department of Radiology Research and Ethics Committee and informed consent was obtained from all the study subjects.

Results

Most of the patients were in the age group of 35-40 (38%) (Table1). A great proportion of them had secondary infertility 34(68%). Half 26(52%) and underwent conventional HSG study.

Table 1: Age of patients who underwent SISHSG

Age(in years)	Number of cases	Percentage (%)
20-24	6	12.0
25-29	11	22.0
30-34	10	20.0
35-40	19	38.0
>40	4	8.0
Total	50	100.0

A large portion of Subjects gave a history of abortion 19(38%). Others had, either pelvic surgery 5(8%); or2(4%) treatment for PID. Thirteen (26%) subjects' spouses had sperm analysis work up and only 1(2%) turned out to be abnormal.

All the patients complained of pain during SISHSG; ranging from mild, 40 (80%) patients; moderate in 9 (9%) patients, and severe in one patient (2%). Out of the 50 patients that were investigated, none had nausea, vomiting, or vaginal bleeding during or after the procedure.

Table 2: Gynecological history of the patients

	Category	Frequency	Percentage
History of abortion	No	31	62.0
	Yes	19	38.0
	Total	50	100
History of ectopic pregnancy	No	49	98.0
	Yes	1	2
	Total	50	100
Previous gynecological surgeries	No procedure	45	90.0
	Cesarean section	1	2.0
	Right salpingectomy	1	2.0
	D&C for abortion	3	6.0
	Total	50	100
Treatment for PID	No	48	96.0
	Yes	2	4.0
	Total	50	100

All study subjects underwent SISHSG study and 18(36%) had normal findings, 10(20%) had uterine myoma, 8(16%) had Asherman syndrome/ cervical stenosis, 6(12%) had a tubal blockage, 3 (6%) had hydrosalpinx, 2(4%) had chronic endometritis, 1(2%) had an endometrial polyp, 1(2%) had large submucous myoma and 1(2%) had complex right adnexal mass (Table 3 and figure 1-5). Those patients diagnosed to have uterine myoma had no conventional HSG study and most of them were to be treated surgically based on our findings on SISHSG.

Twenty-six (52%) patients had conventional hysterosalpingography study and 8 (16%) of them had Asherman syndrome/cervical stenosis, 9 (18%) had normal findings, 9(18%) had tubal blockage, and 2(4%) had chronic endometritis.

In this study, the diagnosis of Asherman syndrome/cervical stenosis both in SISHSG and conventional HSG was mainly based on the failure to infuse saline and contrast into the endometrial cavity after catheterization of the cervix respectively otherwise there is no endometrial cavity traversing bands or adhesion seen.

There were two (4%) patients who were diagnosed to have bilateral tubal blockage by conventional HSG, however, both patients showed an adequate amount of saline within the cul-de-sac

post-saline infusion and the earlier diagnosis was possibly due to tubal spasm during the HSG.

Table 3: Saline infusion sonohysterosalpingography findings

SISHG diagnosis	Number of cases	Percentage (%)
Normal	18	36.0
Uterine Myoma	10	20.0
Asherman syndrome/cervical stenosis	7	14.0
Bilateral tubal blockage	5	10.0
Right hydrosalpinx	2	4.0
Chronic endometritis	2	4.0
Left hydrosalpinx	1	2.0
Right tubal blockage	1	2.0
Endometrial polyp	1	2.0
Large submucous myoma with bilateral tubal blockage	1	2.0
Right adnexal complex mass	1	2.0
PCOS with cervical stenosis and right hemorrhagic ovarian cyst	1	2.0
Total	50	100.0

The sensitivity, specificity, PPV and NPV value of SISHSG in diagnosing normal, Asherman syndrome/cervical stenosis as well as chronic endometritis is 100%,100%,100%, 100% respectively.

For bilateral tubal blockage, the SISHSG had 50% sensitivity, 90% specificity, 66.7% PPV, and 81.8% NPV and for unilateral tubal blockage, SISHSG has sensitivity and specificity of 33% and 100% respectively.

Table 4: Sensitivity, specificity, PPV, and NPV of SISHSG as compared to conventional HSG for 26 infertile patients

SISHSG diagnosis	Test (%)			
	Sensitivity	Specificity	PPV	NPPV
Normal	100	100	100	100
Asherman syndrome/ cervical stenosis	100	100	100	100
Chronic endometritis	100	100	100	100
Bilateral tubal blockage	50	90	66.7	81.8

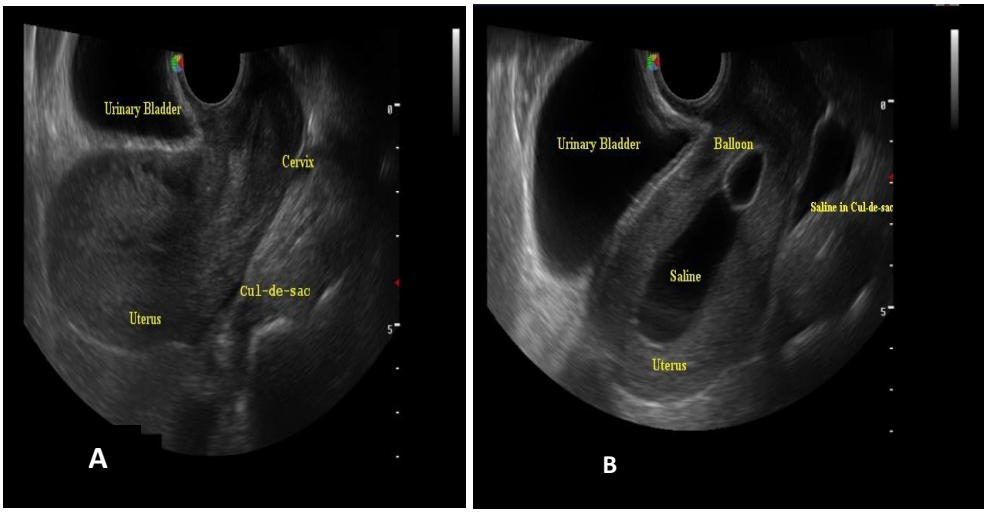


Figure 3: Normal SISHG study: Sagittal transvaginal ultrasound of a 29years old lady with secondary infertility before saline infusion (A) and after saline infusion (B), showing well distended, smoothly outlined endometrial cavity and adequate amount of saline within the cul-de- sac after infusion of saline likely showing patent fallopian tubes

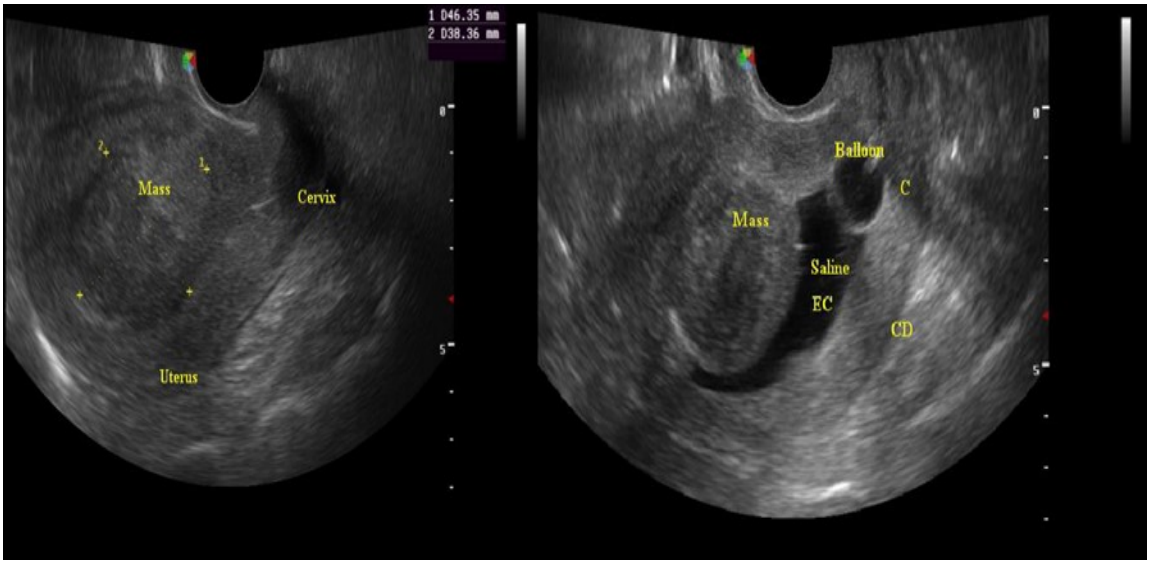


Figure 4: Transvaginal sonogram showing large broad-base submucous myoma with bilateral tubal blockage in a 38-year-old patient with secondary infertility.:

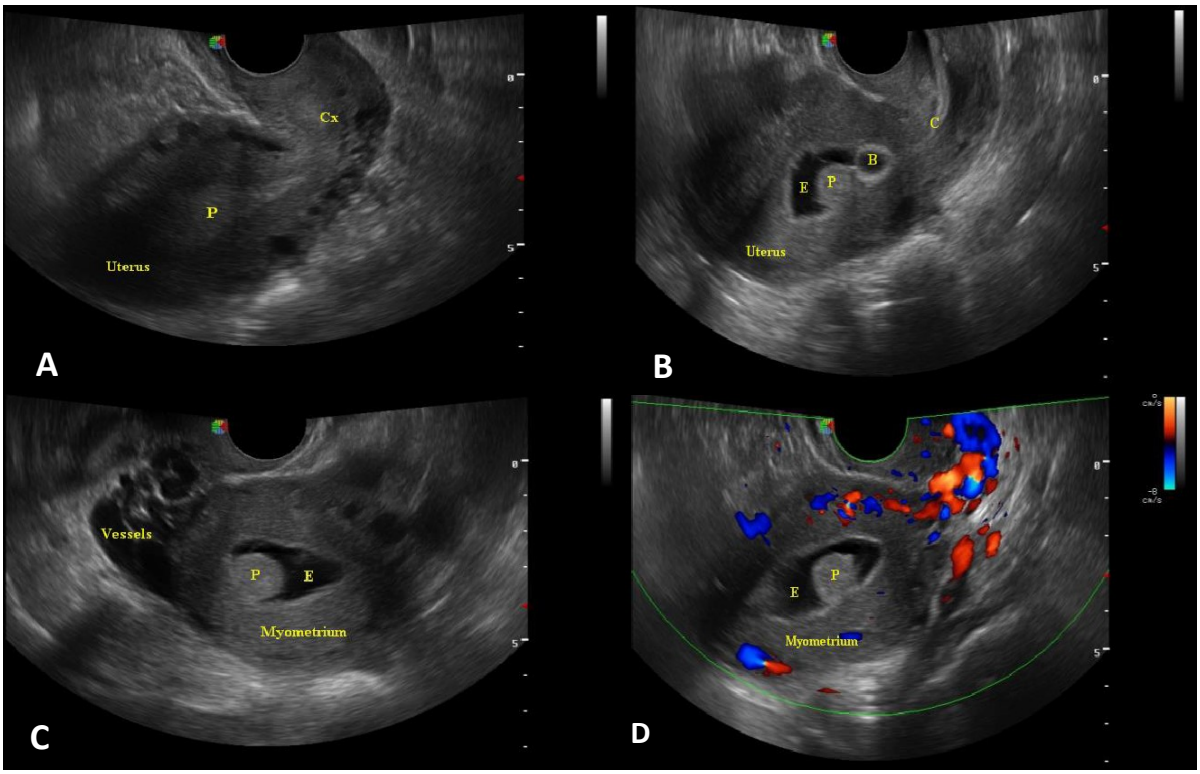


FIGURE 5:- Transvaginal sonogram showing endometrial polyp, making an acute angle with endometrium in a 33 year old woman with primary infertility: The lesion is an ill-defined and difficult to appreciate clearly on pre-saline infusion image **(A)** but well depicted on post-saline infusion images **(B-D)**, [P=polyp, Cx=cervix, E=endometrial cavity filled with saline, B=balloon, C=catheter].

Discussion

Most of the study subjects were in the later part of their reproductive age and two out of three had secondary infertility which is in agreement with a metanalysis done by Abebe et al. which demonstrates secondary infertility of 69.9 % for East African region but a bit higher than the sub-Saharan estimate of about 50% and much higher than estimates for North African (30%) [8]. this could be due to the etiologic factors for various regions.

In our research one-third of the subjects were found to have structural abnormalities of either the tubes or the uterus which is in tandem with research done in Turkey which showed high sensitivity of SISHSG in detecting uterine cavity lesions and intramural lesions as compared to conventional HSG and TVS [9]. Among those patients who underwent SISHSG, the majority of them 18(36%) had normal study which is similar to the study done in Ahvaz, Iran [10].

In this study, the sensitivity, specificity, and predictive value of SISHSG in appreciating diagnosing normal uterine morphology and diagnosing Asherman syndrome/cervical stenosis is comparable to conventional HSG and it is consistent with research done in Nigeria comparing trans abdominal SISHSG with conventional HSG. In bilateral tubal blockage however, SISHSG had 50 % sensitivity, and 90% specificity which was low as compared to the Nigerian research which had 100% sensitivity and specificity [7,11,12].

In our study, the capability of SISHSG to diagnose unilateral tubal blockage was low with a sensitivity of 33% which is similar to the studies done in Nigeria and Turkey [7,9]. Two cases of chronic endometritis diagnosed with SISHSG were consistent with conventional HSG.

All the patients complained of pain during SISHSG; ranging from mild to moderate and severe. This observation is similar to research done in India [11], however, in this study no single patient complained of nausea, vomiting, or vaginal bleeding during or after the procedure which is in contrary to a similar procedure done in the USA in

which few patients had the above complaints [6], suggesting that SISHSG is a tolerable procedure with no significant adverse effect which is in agreement previous studies (12,13).

Conclusion

SISHSG is a cheap, easy to perform, tolerable, and safe procedure with high sensitivity and specificity in detecting uterine cavity abnormality. We therefore advocate its use as a first line investigation modality in the evaluation of female infertility.

Acknowledgment: We are grateful for the nurses working in both Department of Radiology and Obstetrics and gynecology for assisting with the data collection.

Conflict of interest: All authors declare no conflict of interest in the conduct of this study.

Reference

1. Cox CM, Thoma ME, Tchangalova N, Mburu G, Bornstein MJ, Johnson CL, Kiarie J. Infertility prevalence and the methods of estimation from 1990 to 2021: a systematic review and meta-analysis. Human Reproduction Open. 2022 Jan 1;2022(4):hoac051.
2. Legese N, Tura AK, Roba KT, Demeke H. The prevalence of infertility and factors associated with I nfertility in Ethiopia: Analysis of Ethiopian Demographic and Health Survey (EDHS). PLoS One. 2023 Oct 12;18(10):e0291912. doi: 10.1371/journal.pone.0291912. PMID: 37824486; PMCID: PMC10569515.
3. Ibekwe PC, Udensi AM, Imo AO. Hysterosalpingographic findings in patients with infertility in South eastern Nigeria. Niger J Med. 2010 Apr-Jun;19(2):165-7. doi: 10.4314/njm.v19i2.56510. PMID: 20642082.
4. Kumar K, Pajai S, Baidya GR, Majhi K. Utility of Saline Infusion Sonohysterography in Gynecolo gy: A Review Article. Cureus. 2023 Feb 24;15(2):e35424. doi: 10.7759/cureus.35424. PMID: 36987479; PMCID: PMC10040238.
5. Goldstein SR. Modern evaluation of the endometrium. Obstet Gynecol. 2010 Jul;116(1):168-176. doi: 10.1097/AOG.0b013e3181dfd557. PMID: 20567184.
6. O'Neill MJ. Sonohysterography. Radiol Clin North Am. 2003 Jul;41(4):781-97. doi: 10.1016/s0033-8389(03)00038-1. PMID: 12899492.
7. Ademola A. Aremu, Victor A. Adetiloye, Bolanle O. Ibitoye, Daniel A. Adekanle, Tope O.Bello, Transabdominal Saline Contrast Sonohysterography: Can It Replace Hysterosalpingography In Low Resource Countries?, Journal of Clinical and Diagnostic Research 2012, April , Volume : 6 Issue : 2 Page : 239 – 242.
8. Abebe, M.S., Afework, M. & Abaynew, Y. Primary and secondary infertility in Africa: systematic review with meta-analysis. *Fertil Res and Pract* **6**, 20 (2020). https://doi.org/10.1186/s40738-020-00090-3
9. Cengiz Alatas, Esra Aksoy, Cem Akarsu, Kayhan Yakin, Senai Aksoy and Mutlu Hayran. Evaluation of I ntrauterine abnormalities in infertile patients by sonohysterography, Human Reproduction vol.12 no.3 pp.487–490, 1997.
10. . Farideh Moramezi, A Comparative Study Of Saline Infusion Sonohysterogarphy Outcomes Between Infertile And Fertile Patient: A Randomized Clinical Prospective,Res. J. Obstet. Gynecol.,4(2): 44-50,2011.
11. Yeshuta Pujar, A comparative evaluations of SIS and hysterolaparoscopy for diagnosis of uterine cavity abnormalities and tubal patency in infertility, South Asian Federation of obstetrics and gyne cology, May-August 2010;2(2) : 133-135.
12. Malik B, Patil S, Boricha BG, Kurkal N, Choudhry M. A comparative study of the efficacy of sonosalpingography and hysterosalpingogram to test the tubal patency in all women with primary and secondary infertility. Ultrasound Q. 2014 Jun;30(2):139-43. doi: 10.1097/RUQ.0000000000000057. PMID: 24850029.
13. Dessole S, Farina M, Rubattu G, Cosmi E, Ambrosini G, Battista Nardelli G. Side effects and com plications of sonohysterosalpingography. Fertil Steril. 2003 Sep;80(3):620-4. doi: 10.1016/s0015-0282(03)00791-x. PMID: 12969709.

Ethiopian Medical Journal 2024, 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420 Kefeni et al.

Original Article

Magnitude and Factors Associated with Catheter Associated Urinary Tract Infection, and Antimicrobial Susceptibility Profile at Hawassa, Sidama Regional State, Ethiopia: A prospective Cross-sectional Study

Marshet Kefeni[1], Tariku Lambiyo Anticho[2], Israel Tsige Tesema[1], Mulugeta Mengistu [2], Musa Mohammed Ali[2*]

[1]Hawassa University Comprehensive Specialized Hospital, Department of Microbiology, Hawassa, Ethiopia
[2]Hawassa University College of Medicine and Health Sciences, School of Medical Laboratory Science, Hawassa, Ethiopia

Corresponding authors*: musam@hu.edu.et

Abstract
Introduction: *The use of urinary catheter benefit patients who are unable to urinate for various medical reasons. Despite its use, a urinary catheter during its application may introduce bacteria to the urinary tract and result in Urinary tract infection (UTI). Even though the burden of catheter-associated UTI is expected to be high in resource-limited countries, there is limited data. The aim of this study was to determine the magnitude of culture- confirmed catheter-associated urinary tract infection (CAUTI), associated factors, and antimicrobial susceptibility profiles of bacteria.*
Methods: *This prospective cross-sectional study was conducted at Hawassa University Comprehensive Specialized Hospital (HUCSH), Sidama region, from May-August 2022. One hundred forty-nine catheterized patients at HUCSH were included. Socio-demographic, clinical, and laboratory data were collected using structured questionnaire. Urine specimens were cultured on blood and MacConkey agar. Culture-confirmed catheter-associated urinary tract infection was established if $\geq 1 \times 10^5$ colonies of bacteria per milliliters of urine was detected. The disc diffusion method was used for antimicrobial susceptibility testing. For data analysis, SPSS version 26 was used. Factors associated with culture-confirmed CAUTI were assessed using binary logistic regression.*
Results: *The magnitude of culture confirmed CAUTI was 30.2% (n=45; 95% CI=22.8−37.6). The most common bacterial isolates were Escherichia coli (n=12; 26.7%), followed by Klebsiella species (n=10; 22.2%), and Staphylococcus aureus (n=6; 13.3%). Duration of catheterization (AOR=9.6, 95% CI=3.8−24.2) and comorbidities (AOR=4.1, 95% CI=1.7−9.8) were significantly associated with culture-confirmed CAUTI. Most Gram- negative bacteria were resistant to commonly prescribed antimicrobial agents.*
Conclusions: *The magnitude of culture-confirmed CAUTI at HUCSH was high. E. coli was the leading bacteria and most of them were resistant to various types of antimicrobial agents. Duration of catheterization and comorbidities were significantly associated with culture- confirmed CAUTI.*

Keywords*: Catheterized patients, Antimicrobial Susceptibility, Catheter-associated UTI, Hawassa, Ethiopia*
Citation : *Kefeni M, Anticho TL, Tesema IT et al . Magnitude and factors associated with catheter associated urinary tract infection, and antimicrobial susceptibility profile at Hawassa, Sidama Regional State, Ethio pia: A prospective cross-sectional study. Ethiop Med J 62 (1) 41-51*
Submission date : *30 November 2023 Accepted: 28 December 2023 Published: 1 January 2024*

Introduction

The urinary tract is the most common site for nosocomial infections. Most of these infections typically occur after urinary tract catheterization (1). Patients who are unable to urinate for a variety of medical reasons benefit from using a urinary catheter. Urinary catheters, even when used properly, have the potential to cause catheter-associated urinary tract infections (CAUTI) by introducing germs into the urinary system during insertion (2).

In healthy individuals, CAUTI is frequently asymptomatic and usually goes away on its own when the catheter is removed. But if

the infection doesn't go away, it can cause problems including prostatitis, pyelonephritis, cystitis, epididymitis, and Gram-negative bacteremia. High-risk patients frequently experience these side effects (3-5).

After a single catheterization, the prevalence of CAUTI is usually less than 10%; however, it can reach 100% for individuals with long lasting urethral catheters (1-5). Catheterization for long time, drainage bag colonization, diabetes, mistakes made during catheter care, and catheter insertion outside of the operating room are risk factors for bacteruria in catheterized patients (6). Due to anatomical predisposition, a high bacterial load in the urogenital mucosa, and pregnancy, the prevalence is higher in women than in males (7).

The most frequent cause of UTIs in people on catheters is Escherichia coli. Urinary tract pathogens such as Enterobacter, Klebsiella, Enterococcus, and Proteus are prevalent endogenous flora that have the ability to colonize urinary catheters. Healthcare personnel and infected medical equipment may be the source of the pathogen. Healthcare-associated colonic ulcerative therapy (CAUTI) can also be caused by non-intestinal or environmental organisms, such as Pseudomonas aeruginosa, Staphylococcus epidermidis, Staphylococcus aureus, and Acinetobacter (8).

While several patient groups in Ethiopia have been studied for community-acquired UTIs, there are limited studies on the prevalence of UTIs and the bacterial profile of CAUTI (9– 11). There are factors which can predict occurrence of CAUTI such as age, duration of catheterization. According to study conducted in Southern part of Ethiopia Urine output measurement, long duration of catheterization, underlying medical condition, hospitalization form more than or equal to 10 days were significantly associated with CAUTI (11). The aim of this study was to determine the magnitude of culture-confirmed CAUTI, etiology, the antimicrobial profile of the bacteria, and related variables.

Method

Study design and area

A prospective cross-sectional study was carried out From May to August 2022 at Hawassa University Comprehensive Specialized Hospital (HUCSH) among admitted patients who were using urinary catheters for a variety of causes. Sidama Regional State, located in the southern region of Ethiopia, is home to Hawassa City. Hawassa, which is the capital of the region, is situated 273 kilometers to south of Addis Ababa. HUCSH provides services to around 12 million individuals. Clinical services are provided to patients seeking medical attention at various outpatients and inpatient facilities (surgery, gynecology, obstetrics, internal medicine, pediatrics, ophthalmology, psychiatry, radiology, and pathology).The laboratory in the hospital analyzes arrays of tests, including parasitological, microbiological, immunological, haematological, and biochemical analysis

Study population

The study included all patients who were admitted to the Medical, Surgical, Gynecology, ICU, Emergency, and Orthopedics wards at HUCSH and who had been using a urinary catheter for more than 48 hours. Individuals who had a history of urinary tract infection (UTI) within the previous six months, those who had a catheter inserted outside of HUSCH, those who had cystitis and prostatic enlargement, those who were using a suprapubic catheter, nephrostomy tube, or condom catheter, and those who had taken antibiotics within the previous two weeks were all excluded from the study.

Data collection

After reviewing similar studies (9−11), a structured questionnaire was developed for the purpose of gathering socio-demographic and clinical data. The questionnaire was created in English and translated into Amharic; in-person interviews were performed to gather data using the Amharic version. Socio-demographic and clinical information about the patient was gathered, including age, residential location, comorbidities, grounds for admission, admission ward, length of hospital stay, length of catheterization, and purpose of catheterization

Urine collection and isolation of bacteria

Ten milliliters urine specimens from catheterized individuals were aseptically collected after the catheter's outlet was cleaned with 70% alcohol. Urine was aspirated straight from the tubing through a punctured collecting port using a syringe and sterilized needle. Urine was collected, and within an hour it was sent to the HUCSH microbiology laboratory in a sterile, labeled container. Urine samples were stored in a refrigerator at 4oC for less than 24 hours in situations when delays of more than an hour were unavoidable. Two trained professional nurses from each ward collected the data and urine sample. Using a sterile calibrated wire loop, a loop full of urine sample (equivalent to 0.001 ml) was inoculated onto both blood agar and MacConkey agar concurrently. The samples were then incubated aerobically at 37 °C for a duration of 24 hours. After a 24-hour incubation period, bacterial growth was checked on the incubated plates. The colony-forming units (CFU) per milliliter of urine were calculated by counting the number of bacteria colonies. Clinically significant bacteruria, defined as more than or equal to 1×10^5 colonies per

milliliter of urine, were identified (12). According to conventional procedures, colony morphology, hemolytic criteria, staining characteristics, pigment synthesis, and biochemical assays were used to confirm the identity of the bacteri(12–13).

Using the Kirby Bauer disc diffusion method and the Clinical and Laboratory Standard Institute (CLSI) recommendations, antimicrobial susceptibility testing was carried out (14). To prepare turbidity equal to 0.5 McFarland standards, morphologically similar bacterial colonies were suspended in 5 milliliters of normal saline. The suspension was injected onto Mueller Hinton agar (MHA) using a sterilized swab. The antimicrobial discs were equally positioned using sterile forceps. The plates were incubated aerobically at 35oC for 16–20 hours within 30 minutes of applying the discs, with the exception of Acinetobacter, which was incubated for 20–24 hours. Amikacin, ciprofloxacin, piperacillin, trimethoprim-sulfamethoxazole, nitrofurantoin, penicillin, vancomycin, and cefazolin were among the antimicrobials contained in the mixture. Following an overnight incubation period, each zone of inhibition's diameter was measured in millimeters. The zone diameter was considered to be intermediate and resistant.

Operational definition

UTI signs and symptoms: Individuals were classified as having symptomatic CAUTI if they had at least two signs and symptoms of acute UTI, such as fever, suprapubic tenderness, costovertebral angle pain or tenderness, urgency, frequency, and dysuria, and if they had an indwelling urethral catheter that had been in place for longer than two days.

Culture-confirmed CAUTI: Urinary tract infection that occur among patient who are on catheter.
Symptomatic UTI is a type of UTI if there is significant bacteriuria ($\geq 10^5$ CFU/ mL) with at least two signs and symptoms of acute UTI (from the following: fever, suprapubic tenderness, costovertebral angle pain or tenderness, urinary urgency, urinary frequency and dysuria) with an indwelling urethral catheter in place for more than two days.

Quality assurance

The questionnaire was pretested at Adare Hospital to check for its consistency. After pretest, the questionnaire was revised and modified particularly variables that were not clear. All laboratory procedures were conducted according to Standard Operational Procedures (SOP) of HUCSH. Reference strain bacteria: *S. aureus* ATCC 25923, *E. coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853 were used to check the performance of the culture media

Statistical analysis

Epidata was used to enter the data, and SPSS version 26 was used for analysis. Sociodemographic and clinical data were summarized using descriptive statistics including mean, standard deviation (SD), and frequency. In order to evaluate independent variables related to the severity of CAUTI, logistic regression was employed. Multivariable logistic regression was used to examine variables that showed a p-value of less than 0.25 in the bivariable logistic regression study. A 95% confidence level was applied to determine statistical significance for a $p<0.05$.

Ethical consideration

Ethical clearance was obtained from the Institutional Review Board (IRB) Hawassa University College of Medicine and Health Sciences (Reference number: IRB/155/14). Prior to enrolment written informed consent were obtained from all participants. For participant aged less than 18 years, assent and consent from children and parents respectively.

Result

Socio-demographic characteristics

One hundred forty-nine (149) catheterized patients were enrolled in this study. The majority of the study participants were males 91(61.1%). thirty nine (26.2%) of the study participants were in the age group of 21−30 years, with a mean and standard deviation (SD) of 40.8(±16.2) years (Table 1).

Table 1. Socio-demographic characteristics of catheterized patients at HUCSH between May−August 2022 (N=149).

Variable	Category	Frequency (%)
Gender	Male	91 (61.1)
	Female	58 (38.9)
Age (in Years)	<20	14 (9.4)
	21−30	39 (26.2)
	31−40	33 (22.1)
	41−50	22 (14.8)
	51−60	21 (14.1)
	61−70	15 (10.1)
	>71	5 (3.4)
Place of residence	Urban	56 (37.5)
	Rural	93 (62.4)
Marital status	Married	119 (79.9)
	Single	30 (20.1)
Occupation	Employed	10 (6.7)
	Farmer	60 (40.2)
	Merchant	8 (5.4)
	Non employed	71 (47.7)
Educational status	Unable to read and write	67 (45.0)
	Completed primary	56 (37.6)
	Completed secondary	16 (10.7)
	Completed College and above	10 (6.7)
Monthly income in ETB	<2000	125 (83.9)
	2000−3500	17 (11.4)
	3501−5000	5 (3.4)
	>5000	(1.3)

ETB: Ethiopian birr

Clinical characteristics

The emergency ward accounted for the majority of study participants (n = 53, 35.6%), with the surgical ward accounting for another 28.9%. Every study participant had a folly-type catheter, and 33.6% (33/6) of them had catheterizations for drainage before or after surgery. Of them, 16(10.7%) had previously been catheterized, and 41 (27.5%) had been thus for longer than seven days.

Twenty patients (13.5%) out of the thirty (20.1%) with comorbidities had heart or kidney problems. Clinically, 42 (28.2%) of the participants developed symptomatic UTIs related to catheter use (Table 2).

Table 2. Clinical characteristics of catheterized patients at HUCSH between May−August 2022 (N=149).

Variable	Category	Frequency (%)
Ward admitted	Emergency	53 (35.6)
	Surgical	43 (28.9)
	ICU	22 (14.8)
	Others*	31 (20.8)
Reason for admission	Surgery	75 (50.4)
	Follow up	60 (40.3)
	Others**	14 (9.4)
Reason for catheterization	Pre/post-operative drainage	50 (33.6)
	Urine output measurement	45 (30.2)
	Urine retention	33 (22.1)
	Others***	21 (14.1)
Size of the catheter in Fr	<18	142 (95.3)
	>18	7 (4.7)
Duration of catheterization in days	<7	108 (72.5)
	≥7	41 (27.5)
Lubricant application	Yes	148 (99.3)
	No	1 (0.7)
Previous catheterization	Yes	16 (10.7)
	No	133 (89.3)
Previous antimicrobial use	Yes	72 (48.3)
	No	77 (51.7)
Chronic disease	Yes	30 (20.1)
	No	119 (79.9)
Type of chronic disease	Kidney disease	8 (5.4)
	Heart disease	12 (8.1)
	DM	3 (2.0)
	Other****	6 (4.0)
Symptomatic	Yes	42 (28.2)
	No	107 (71.8)

DM: Diabetes mellitus, HIV: Human Immunodeficiency virus, Fr: French size, ICU: Intensive care unit *=Gynecology=11, Orthopedic=4, medical=16 ; **=acute febrile illness (AFI)=1,for treatment=6,medical reason=3,trauma=1,ischemic stroke=1,traumatic brain injury=2;*** keeping patient dry=19,urine incontinence=2;****=breast cancer=2, hypertension=1, HIV=3.

Magnitude of culture-confirmed CAUI and distribution of bacteria

In this study, the magnitude of culture-confirmed CAUI was 30.2% (n=45, 95% CI=22.8−37.6). The majority of bacteria (n=33: 73.3%) were Gram-negative. Of the patients with Gram-negative bacteria, 17 (51.5%) had bacteruria with symptoms. Out of the 12 patients (26.1%) who were infected with Gram-positive bacteria, 7 individuals (58.3%) showed signs of bacteruria. The most frequent bacterial isolates were *E. coli* 12 (26.7%), *Klebsiella* species 10 (22.2%), and *S. aureus* 6 (13.3%) (Figure 2).

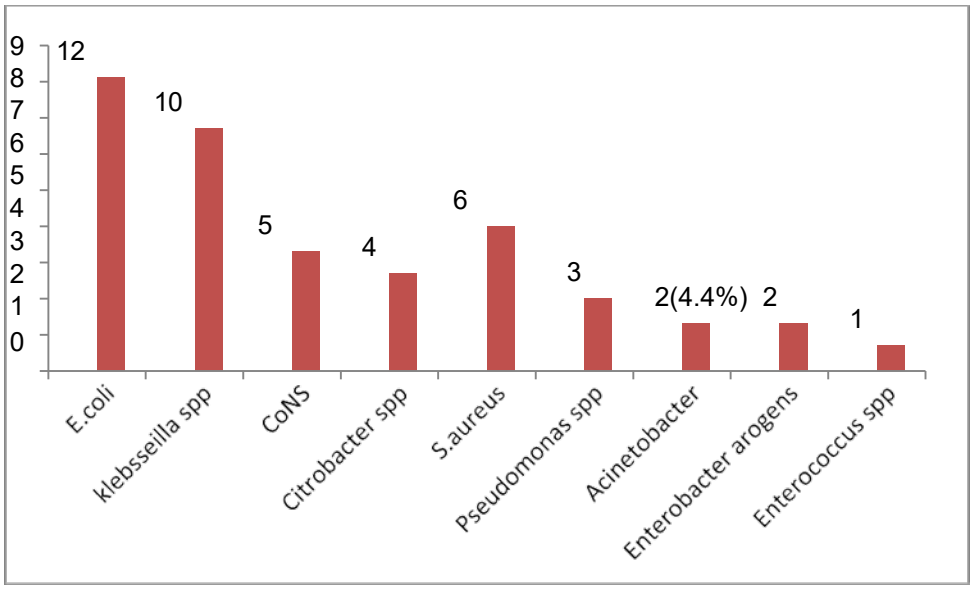


Figure 1. Distribution of bacteria isolated from the urine of catheterized patients at HUCSH between May−August 2022 (N=45). CONS: Coagulase negative staphylococcus

Factors associated with culture-confirmed CAUI

Variables with p<0.25 in bivariate logistic regression such as admission ward, reason for catheterization, length of catheterization, and comorbidities were selected for multivariable binary logistic analysis. Culture-confirmed CAUI was strongly correlated with catheterization duration (AOR=9.6, 95% CI=3.8−24.2) and comorbidities (AOR=4.1, 95% CI=1.7−9.8) (Table 3).

Table 3. Factors associated with culture-confirmed catheter associated urinary tract infection at HUCSH May−August 2022 (N=149).

Variables	Category	Culture result n (%)		COR (95% CI)	p-value	AOR (95% CI)	P-value
		Positive	Negative				
Gender	Female	18(31.0)	40(69.0)	1.1(0.5-2.2)	0.9		
	Male	27(29.7)	64(70.3)	1		1	
Place of residence	Urban	18(32.1)	38(67.9)	1.2(0.6-2.4)	0.7		
	Rural	27(29.1)	66(70.9)	1		1	
Age in years	<20	4(28.6)	10(71.4)	1		1	
	21-30	14(35.9)	25(64.1)	0.6(0.1-5.1)	0.6		
	31-40	7(21.2)	26(78.8)	0.8(0.1-5.6)	0.9		
	41-50	8(36.4)	14(63.6)	0.4(0.1-2.9)	0.4		
	51-60	6(28.6)	15(71.4)	0.9(0.1-6.3)	0.9		
	61-70	4(26.7)	11(73.3)	0.6(0.1-4.5)	0.6		
	>71	2(40.0)	3(60.0)	0.5(0.1-4.5)	0.6		
Educational level completed	Unable to read and write	22(32.8)	45(67.2)	0.7(0.2-2.4)	0.5		
	Primary	16(28.6)	40(71.4)	0.9(0.2-3.7)	0.9		
	Secondary	4(25.0)	12(75.0)	0.8(0.4-1.8)	0.6		
	College and above	3(30.0)	7(70.0)	1		1	
Admission ward	Emergency	12(22.6)	41(77.4)	0.5(0.2-1.4)	0.2	0.4(0.1-1.3)	0.1
	Surgical	15(34.9)	28(65.1)	0.9(0.4-2.6)	0.9		
	ICU	7(31.8)	15(68.1)	0.8(0.3-2.7)	0.8		
	other*	11(35.4)	20(64.5)	1		1	
Reason for Catheterization	Pre/post-operative drainage	14(28.0)	36(72.0)	0.8(0.3-2.3)	0.7		
	Urine output measurement	14(31.1)	31(68.9)	0.9(0.3-2.7)	0.2	1.3(0.3-5.2)	0.7
	Urine retention	10(30.3)	23(69.7)	0.9(0.3-2.8)	0.9		
	Other**	7(33.3)	14(66.7)	1		1	
Duration of catheterization	<7	18(16.7)	90(83.3)	1		1	
	>7	27(65.9)	14(34.1)	0.1(0.0-0.2)	<0.0001	9.6(3.8-24.2)	<0.001
Catheterization history	Yes	4(25.0)	12(75.0)	0.7(0.2-2.5)	0.6		
	No	41(30.8)	92(69.2)	1			
Comorbidity	Yes	26(52.0)	24(48.0)	4.6(2.2-9.6)	<0.0001	4.1(1.7-9.8)	0.001
	No	19(19.2)	80(80.8)	1		1	
Types of comorbidity	Heart diseases	4(30.8)	9(69.2)	1.0(0.3-3.5)	0.9		
	Kidney disease	2(25.0)	6(75.0)	0.8(0.1-3.9)	0.7		
	Others***	0(0.0)	8(100.0)	1		1	

Medical = (16); Gynecology = (18); orthopedic=(4); **=keeping patient dry=(26); urine incontinence=(2); ***= breast cancer=(2); hypertension=(1); Diabetes mellitus=(3); HIV= (3).

Antimicrobial susceptibility profile of bacteria

All strains of *E. coli* were susceptible to amikacin and nitrofurantoin, but over 80% of *Klebsiella* species were resistant to most antimicrobial drugs. Each and every *Citrobacter* species was vulnerable to amikacin and nitrofurantoin. Half of the tested antimicrobials did not work on any *Citrobacter.* Penicillin did not affect any *S. aureus* (Tables 4 and 5).

Table 4. Antimicrobial susceptibility pattern of Gram−negative bacterial isolates recovered from urine of cathetrized patintes at HUCSH, May−August 2022 (n=33).

Tested bacteria		Ampicillin	Gentamicin	Nitrofurantoin	Cefazolin	Cefepime	Ceftriaxone	Amikacin	Piperacillin	Ciprofloxacin	Cotrimoxazole
E. coli (n=12)	S	-	10(83.3)	12(100)	1(8.3)		10(83.3)	12(100)	1(15.4)	10(83.3)	5(41.7)
	R	12 (100)	2(16.7)	-	11(91.7)		2(16.7)	-	11(84.6)	2(16.7)	7(58.3)
Klebsiella species (n=10)	S	1(10)	2(20)	10(100)	-		-	10(100)	1(9.1)	8(80.0)	6(60)
	R	9(90)	8(80)	-	10(100)		10(100)	-	9(90.9)	2(20.0)	4(40)
Citrobacter species (n=4)	S	-	1(25)	4(100)	-		-	4(100)	1(25)	3(75.0)	3(75)
	R	4(100)	3(75)	-	4(100)		4(100)	-	3(75)	1(25.0)	1(25)
Pseudomonas species (n=3)	S	-	3(100)	3(100)	-	3(100)	3(100)	3(100)	2(66.7)	3(100)	2(66.7)
	R	3(100)	-	-	3(100)	-	-	-	1(33.3)	-	1(33.3)
Acinetobacter species (n=2)	S	-	2(100)		1(50)	1(50.0)	1(50)	1(50)	1(50)	2(100)	1(50)
	R	2(100)	-		1(50)	1(50.0)	1(50)	1(50)	1(50)	-	1(50)
Enterobacter species (n=2)	S	-	2(100)	2(100)	1(50)	2(100)	1(50)	2(100)	1(50)	2(100)	-
	R	2(100)	-	-	1(50)	-	1(50)	-	1(50)	-	2(100)

S: Susceptible, R: Resistant

Table 5. Antimicrobial susceptibility pattern of Gram−positive bacteria recovered from catheterized patients at HUCSH, May−August 2022 (n=12).

Tested bacteria		Penicillin	Gentamicin	Nitrofurantoin	Vancomycin
CoNS(n=5)	S	-	3(60)	5(100)	4(80)
	R	5(100)	2(40)	-	1(20)
S. aureus (n=6)	S	-	5(83.3)	6(100)	
	R	6(100)	1(16.7)	-	
Enterococcus Species (n=1)	S	-	1(100)	1(100)	1(100)
	R	1(100)	-	-	-

Discussion

he magnitude of culture-confirmed CAUTI found in the current study (30.2%) is comparable with study conducted in India (15, 16). However, it is higher than studies conducted in Addis Ababa, Ethiopia (21.0%) (17), Chennai, India (21.6%) (18), Vadodara, India (20.2%) (19), Saudi Arabia (21.0%) (20), Arbaminch, Ethiopia (16.8%) (11), China(15.8%) (21), Uganda (15.3%) (22), Sudan 16.4% (23), and Chhattisgarh, India (10.6%) (24). Our finding is lower than studies conducted in India 42.9% (25), and Nigeria 60.9% (26). The variation could be due difference in socio-demographic characteristics, infection prevention policies, duration of catheterization, and immunological status of participants. The proportion of CAUTI in this study was high among male participant which is in line with the study from Saudi Arabia (20).

The most prevalent bacteria was *E. coli* (26.6%) which is lower than report from Arbaminch, Ethiopia (40.5%) (11), Jimma, Ethiopia (42.0%) (27), Yemen (46.3%) (28), and most parts of India (31%-38%) (15, 16, 18, 19, 24). Studies conducted in Yemen (18.5%) (28), Chhattisgarh, India(17%) (24), Maharashtra, India (16.4%) (16), and Chhattisgarh, India (24), reported low proportion of *Klebsiella* species unlike our study (22.2%) which is the second most prevalent bacteria. The proportion of *Klebsiella* species we found were lower than the study from Vadodara, India (24%) (19).

The proportion of *Pseudomonas* species was 6.7% which is lower than report from Yemen (11.9%) (28), Vadodara, India (24%) (19), and Maharashtra, India (8.2%) (16). The proportion of *S. aureus* among the study participants was 13.3% which is higher than the study from Yemen (5.3%) (28).

From the total 45 isolates, the proportion of Gram-positive bacteria was 12 (26.7%), which is lower than report from Addis Ababa (36.7%) (29). S. aureus prevalence (50.0%) was higher than the study done in Nepal 5.9% (30).

E. *coli* was the most frequently isolated bacterium throughout the majority of investigations, despite the fact that the prevalence of specific bacteria varies. Because these bacteria are common in the gut flora and can contaminate the urethra and ascend into the bladder following catheter insertion, they may cause an infection in the urinary tract. These findings were in contrast with studies from Italy (31), Thailand (32), and Sudan (23), where *P. aeruginosa* or *Enterococcus* species were the most frequent bacterial isolates. In studies conducted in Saudi Arabia and Nigeria (18), the predominant bacteria was *Klebsiella* ***pneumoniae*** (20%) (20). The difference in the distribution of bacteria may be due to differences in environmental conditions duration of catheterization, and the organisms' uniqueness to each facility. It may also be explained by the differences in the population studied, such as mean age, pre-morbid state and the reasons for admission.

Catheterized patients with comorbidities were four times more likely to develop culture- confirmed CAUTI. Our result is in line with the studies from Ethiopia (11), India (25), and Korea (23). This may be due to impairment of host defence's, including decreased polymorph nuclear leukocyte mobilization, chemo taxis, and phagocytic activity related to hyperglycemia, which increases the adherence of bacteria to the bladder epithelial cells (34). Patients who were on catheter for more than seven days were about ten times more likely to develop culture-confirmed CAUTI. Our finding is in line with the study done in Arbaminch (11), Addis Ababa (17), and India (19).

Majority of *E. coli, Klebsiella* Species*, pseudomonas* Species, and *Citrobacter* identified in this study were resistant to commonly prescribed antimicrobial agents such as ampicillin, cefazolin, ceftriaxone, and piperacillin. Our finding is in partial agreement with study conducted in Arbaminch general hospital (11) where all bacteria were resistant to ampicillin. In addition, study from Nigeria (1) reported high proportion of Gram-negative bacteria resistant to commonly used antimicrobial agents such as ampicillin (100%), cotrimoxazole (87.3%), and ciprofloxacin (56.4%).

Irrational use and or self-medication of antimicrobials might contribute to the study area's resistance rates. Most Gram-negative bacteria tested were susceptible to nitrofurantoin and amikacin, which is in line with the study conducted in Arbaminch general hospital (11). The lower resistance to this drug could be due to their rare local availability and higher cost than others. In contrast to our study, high proportion of bacteria resistant to nitrofurantoin was reported from Uganda (22) and Nigeria (1). One of the limitation of our study was the small sample size used in the study use of convenient sampling technique.

Conclusions:

This study revealed high magnitude of catheter associated urinary tract infection among patients attending Hawassa University Comprehensive Specialized Hospital.*E. coli* was the leading cause of urinary tract infection, followed by *Klebsiella* species and *S. aureus.* Duration of catheter and comorbidities were significantly associated with culture- confirmed catheter associated urinary tract infection. Majority of Gram-negative bacte-

ria were resistant to commonly prescribed antimicrobial agents while most were susceptible to nitrofurantoin and amikacin.

Acknowledgment
We thank all Nurses and Microbiologists working at HUCSH who contributed during data collection. We would like to acknowledge participants for their willingness to take part in this study.

Authors' contributions
MK: proposal development, data collection, manuscript preparation TLA: Supervision, manuscript review ITT: Participant identification, protocol development, supervision, MM: Checking the quality of data collection tool, provided professional comments MMA Proposal review, supervision during data collection, data analysis, and manuscript preparation. All authors read and approved the final version of the manuscript.

Funding No specific funding was obtained for this study.

Competing interests
The authors declare that they have no competing interests. The final version was approved by all authors.

References

1 Yang X, Chen H, Zheng Y, Qu S, Wang H, Yi F. Disease burden and long-term trends of urinary tract infections: A worldwide report. Frontiers in Public Health. 2022 Jul 27;10:888205.Öztürk R, Murt A. Epidemiology of urological infections: a global burden. World J Urol. 2020 Nov;38(11):2669-2679. doi: 10.1007/s00345-019- 03071-4. Epub 2020 Jan 10. PMID: 31925549..
2 Dellimore KH, Helyer AR, Franklin SE. A scoping review of important urinary catheter induced complications. Journal of Materials Science: Materials in Medicine. 2013;24(8):1825-35.
3 Coleman J. Chronic Catheter Associated Complications and Catheter-Associated Urinary Tract Infection. InPelvic floor dysfunction and pelvic surgery in the elderly 2017 (pp. 91-103). Springer, New York, NY.
4 Hollingsworth JM, Rogers MA, Krein SL, Hickner A, Kuhn L, Cheng A, Chang R, Saint S. Determining the noninfectious complications of indwelling urethral catheters: a systematic review and meta-analysis. Annals of internal medicine. 2013;159(6):401- 10.
5 Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, Saint S, Schaeffer AJ, Tambayh PA, Tenke P, Nicolle LE. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clinical infectious diseases. 2010;50(5):625-63.
6 Sohail M, Khurshid M, Saleem HG, Javed H, Khan AA. Characteristics and antibiotic resistance of urinary tract pathogens isolated from Punjab, Pakistan. Jundishapur journal of microbiology. 2015;8(7).
7 Guide AA. Guide to the Elimination of Catheter-Associated Urinary Tract Infections (CAUTIs). Developing and Applying Facility-Based Prevention Interventions in Acute and Long-Term Care Settings. 2008.
8 Melaku S, Kibret M, Abera B, Gebre-Sellassie S. Antibiogram of nosocomial urinary tract infections in Felege Hiwot referral hospital, Ethiopia. African Health Sciences. 2012;12(2):134-9.
9 Tesfahunegn Z, Asrat D, Woldeamanuel Y, Estifanos K. Bacteriology of surgical site and catheter related urinary tract infections among patients admitted in Mekelle Hospital, Mekelle, Tigray, Ethiopia. Ethiopian Medical Journal. 2009;47(2):117-27.
10 Oumer Y, Regasa Dadi B, Seid M, Biresaw G, Manilal A. Catheter-associated urinary tract infection: Incidence, associated factors and drug resistance patterns of bacterial isolates in southern ethiopia. Infection and drug resistance. 2021:2883-94.
11 CHEESBROUGH, M. 2000. Microbiological tests. District laboratory practice in tropical countries. Part, 2.
12 Dallas J, Skrupky L, Abebe N, Boyle III WA, Kollef MH. Ventilator-associated tracheobronchitis in a mixed surgical and medical ICU population. Chest. 2011;139(3):513-8.
13 CLSI, M. C. A. L. S. I. 2020. Performance Standards for Antimicrobial Susceptibility Testing. 30th Edition.
14 KoshariyAM, Songra MC, Namdeo R, Chaudhary A, Agarwal S, Rai A. Prevalence of pathogens and their antimicrobial susceptibility in catheter associated urinary tract infection. IAIM, 2015;2:96-113.
15 Patil HV and Patil CV. Clinical, Bacteriology Profile, and Antibiotic Sensitivity Pattern of Catheter Associated Urinary Tract Infection at Tertiary Care Hospital. International Journal of Health Sciences & Research, 2018;8:25-35
16 Bizuayehu H, Bitew A, Abdeta A, Ebrahim S. Catheter-associated urinary tract infections in adult intensive care units at a selected tertiary hospital, Addis Ababa, Ethiopia. PLoS ONE, 2020a;17.
17 Nandini M. and Madhusudan K. Bacteriological profile of catheter associated urinary tract infection and its antimicrobial susceptibility pattern in a tertiary care hospital. Journal of Pharmaceutical Sciences and Research, 2016;8, 204.

18. Panjwani DM, Lakhani SJ, Mehta SJ, Kikani KM and Shah KS. A comprehensive study of microbiological profile, risk factors and antibiotic sensitivity pattern of catheter associated urinary tract infection in a teaching hospital of Gujarat. Journal of Applied Biology & Biotechnology, 2021;9, 83-88.
19. Saleem M, Khaja S, Hossain A, Alenazi F, Said KB, Moursi SA, Almalaq HA, Mohamad H, Rakha E, Mishra SK. Catheter-Associated Urinary Tract Infection in Intensive Care Unit Patients at a Tertiary Care Hospital, Hail, Kingdom of Saudi Arabia. Diagnostics 2022;12, 1695.
20 Xie DS, Lai RP, Nie SF. Surveys of catheter-associated urinary tract infection in a university hospital intensive care unit in China. Braz J Infect Dis, 2011;15, 296–297.
21 Musinguzi B, Kabajulizi I, Mpeirwe M, TurugurwA J, Kabanda T. Incidence and etiology of catheter associated urinary tract infection among admitted patients at Kabale Regional Referral Hospital, South Western Uganda. Adv Infect Dis, 2019;09, 183–196.
22. Ahmed M . Pattern of nosocomial urinary tract infections among sudanese patients. Br Microbiol Res J, 2012;2, 53-61.
23. Singh A, Kujur A, Muthulakshmi M, Daharwal A. The study of antibiotic-sensitivity and resistance pattern of bacteria causing catheter associated urinary tract infection. Int J Reprod Contracept Obstet Gynecol, 2020;9.
24. Leelakrishna P and Karthik R. A study of risk factors for catheter associated urinary tract infection. Int J Adv Med, 2018;5.
25. Onipede A, Oyekale T, Olopade B, Olaniran O, Oyelese A, Ogunniyi T. Urinary pathogens and their antimicrobial susceptibility in patients with indwelling urinary catheter. Sierra Leone J Biomed Res, 2020; 2, 47-53.
26. Awoke N, Kassa T, Teshager L. Magnitude of biofilm formation and antimicrobial resistance pattern of bacteria isolated from urinary catheterized inpatients of Jimma University Medical Center, Southwest Ethiopia. Int J Microbiol, 2019;1.
27. Saleh AM, AL-shamahy ha, AL-H, Jaadan BM, AL-magrami RTF, AL-SHARANI AA. Biofilm formation and antibiotic susceptibility of uropathogens in patients with catheter associated urinary tract infections in Ibb city-Yemen. Universal Journal of Pharmaceutical Research 2019;4, 1-7.
28. Bizuayehu H, Bitew A, Abdeta A, Ebrahim S. Catheter-associated urinary tract infections in adult intensive care units at a selected tertiary hospital, Addis Ababa, Ethiopia. Plos one, 2022b; 17, e0265102.
29. Prashamsa K, Devi D, Madhup S, Shrechand J. Catheter associated urinary tract infection: prevalence, microbiological profile and antibiogram at a tertiary care hospital. Ann. Clin. Chem. Lab. Med, 2017;3, 3-10.
30. Barbadoro P, Labricciosa FM, Recanatini C, Gori G, Tirabassi FE, M. Catheter- associated urinary tract infection: role of the setting of catheter insertion. Am J Infect Control, 2015;43, 707–710.
31. Kotikula I and Chaiwarith R. Epidemiology of catheter-associated urinary tract infections at maharaj nakorn chiang mai hospital, northern thailand. . Southeast Asian J Trop Med Public Health., 2018;49, 113–122.
32. Lee jh, Kim SW, Yoon BI, Ha US, Sohn DW, Cho YH. Factors that affect nosocomial catheter-associated urinary tract infection in intensive care units: 2-year experience at a single center. Korean J Urol, 2013;54, 59–65.
33. Hakeem LM, Bhattacharyya DN, Lafong C, Janjua KS, Serhan JT and Campbell IW. Diversity and complexity of urinary tract infection in diabetes mellitus. Br J Diabetes Vasc Dis, 2009;9, 119–125.

Ethiopian Medical Journal 2024, 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420

Original Article

Complete Blood Count, C-reactive Protein, and Erythrocyte Sedimentation Rate Changes in People with Brucellosis

Alireza Mohammadzadeh[1], Mozhgan Khanderoo[1], Abbasali Abbasnezhad[2], Mohammad Ghorbani[3], Sina Nasrollahian[4], Reyhaneh Noorizadeh[5], Jalal Mardaneh[1*]

[1]Department of Microbiology, School of Medicine, Infectious Diseases Research Center, Gonabad University of Medical Sciences, Gonabad, Iran.
[2]Department of Physiology, School of Medicine, Gonabad University of Medical Sciences
[3]Department of Pathology, School of Medicine, Gonabad University of Medical Sciences
[4]Department of Bacteriology and Virology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.
[5]Infectious Diseases Research Center, Gonabad University of Medical Sciences, Gonabad, Iran.

Corresponding authors*: Jalalmardaneh@yahoo.com

Abstract

Background: *Brucellosis is a major health and economic problem in many parts of the world, including the Middle East. Blood disorders such as anemia, leukopenia, and thrombocytopenia can be seen in brucellosis. However, laboratory findings of this disease are different. Therefore, this study aimed to investigate the changes in complete blood count (CBC), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) in people with brucellosis in Gonabad community health centers.*

Methods: *During the 4 years from May 2016 to May 2019, a prospective study was performed on 221 patients with brucellosis. According to the national guidelines for brucellosis, titers greater than 1/80 for Wright and more than 1/40 for 2-ME were considered positive cases of brucellosis. Using the checklist, information related to CBC, CRP, and ESR test parameters was collected.*

Results: *The results showed that out of 221 patients studied, 58.4% were male and 41.6% were female. The mean age was 44.9±19.8 years for men and 49.3±17.3 years for females. High ESR was seen in 43.4% and positive CRP in 59.7% of patients. Leukopenia in 8.6%, leukocytosis in 9%, neutropenia in 6.8%, neutrophilia in 9.5%, lymphopenia in 3.6%, lymphocytosis in 10%, anemia in 17.2% and thrombocytopenia in 9.5% of patients were seen.*

Conclusion: *Brucellosis in endemic areas should be considered in the differential diagnosis of patients presenting with thrombocytopenia. Also in high Wright titers, CRP is a more valuable indicator than ESR.*

Keywords*: Brucellosis, CBC, ESR, CRP*
Citation :*Mohammadzadeh A,Khanderoo M,Abbasnezhad A,et al.Complete blood count, C-reactive protein, and erythrocyte sedimentation rate changes in people with brucellosis. Ethiop Med J 62 (1) 53-59*
Submission date : *13 November 2022 Accepted: 28 December 2023 Published: 1 January 2024*

Introduction

Brucellosis is an irresistible illness caused by a gram-negative coccobacillus of the sort Brucella, with different clinical signs. More than half a million individuals are analyzed with brucellosis each year (1). This disease is observed all over the world, especially in the countries around the Mediterranean (Southern Europe, North, and East Africa), Middle East, India, and Central Asia(2).

Brucella melitensis and *Brucella abortus* are the most common disease-causing species, and most cases of disease in humans are caused by *Brucella melitensis* (3). Early and exact determination of this infection, in this manner, plays a vital part in controlling and eradicating brucellosis for making strides in well-bingeing. Different research facility tests, such as bacteriological, serological, and molecular methods, have been created to analyze brucellosis (4). Although brucellosis has been controlled in many developed countries, it remains an important health problem in developing countries(5).

Brucellosis is a multi-system disease and it has been reported to affect the digestive, cardiovascular, hematopoietic, nervous, skeletal, pulmonary, skin, and eye systems. This disease has many clinical variations and the symptoms can be differentiat-

ed from many infectious and non-infectious diseases (6).

Blood disorders such as leukopenia, anemia, thrombocytopenia, cytopenia,nd pancytopenia are seen in brucellosis, which can be mistakenly diagnosed as a hematological malignancy. The clinical and laboratory findings of brucellosis are non-specific and this should be considered in the differential diagnosis of patients with blood disorders(7).

On the other hand, the laboratory findings of this disease are different in various studies and populations. Therefore, this study is conducted to investigate the changes in complete blood count (CBC), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) in people with brucellosis who refer to health and community health centers in Gonabad city.

Materials and method

Blood sampling and processing

During 4 years from May 2016 to May 2019, a retrospective study of 221 patients with brucellosis was investigated. The sampling method was a census and checklist of information related to age, gender, test date, blood parameters such as CBC test parameters (WBC and their differential count, RBC count, hemoglobin measurement, hematocrit, and platelet count), CRP, ESR and Brucellosis diagnostic serological tests including Wright test and 2-mercaptoethanol (2-ME) were performed for each patient.

Sample size

Using the following formula and with the help of Nasaji et al.'s study (8), also considering the confidence level of 95%, the sample size in this study was calculated to be 174 people, and taking into account 15% possible dropout, the final sample size was determined to be 200 people.

$$n = \frac{z_{1-\frac{\alpha}{2}}^{2} * p * (1-p)}{d^2} = 174$$

where: n = the required sample size; P = estimated prevalence = 0.5; z = level of confidence as 1.96 and d = desired precision level = 0.05.

Diagnosis method

The results of serological diagnostic tests for Brucellosis including Wright and 2-ME were extracted and according to the national guidelines for Brucellosis, titers greater than 1/80 for Wright and greater than 1/40 for 2-ME were considered positive cases of Brucellosis. By using the checklist, relevant information was collected, and based on normal ranges, low, normal and high values were determined for each variable and analyzed.

Statistical analysis

After collecting and entering data into SPSS software version 16, central (mean) and dispersion (standard deviation) indicators were used to describe quantitative variables and frequency and frequency percentage were used to describe qualitative variables. In the analytical analysis, the chi-square test, Kruskal-Wallis's test, and Fisher test were used to investigate the relationship between qualitative variables. A logistic regression test was also used to examine some variables. $P<0.05$ was considered as significance level.

Results

In this study, out of 221 patients with brucellosis, 129 (58.4%) were male and 92 (41.6%) were female, and the average age of the patients was 46.7–18.9 years. There was high ESR in 43.4% and normal ESR in 56.6% of the studied subjects. There was negative CRP in 40.3% and positive CRP in 59.7% of patients with brucellosis. The frequency results of the Wright and 2ME tests of the studied patients are listed in Table 1.

Table 1: Frequency of the Wright and 2ME test.

Test	Titter	Frequency (%)
Wright	1.80	63(28.5)
	1.160	44(19.9)
	1.320	40(18.1)
	1.640	37(16.7)
	1.1280	26(11.8)
	1.2560 and higher	11(5.1)
2ME	1.40	82(37.1)
	1.80	45(20.4)
	1.160	40(18.1)
	1.320	29(13.1)
	1.640	20(9)
	1.1280	3(1.4)
	1.2560 and higher	2(1)

The CBC examination of the subjects showed leukopenia in 8.6%, leukocytosis in 9%, neutropenia in 6.8%, neutrophilia in 9.5%, lymphopenia in 3.6%, lymphocytosis in 10%, anemia in 2.2%, polycythemia in 0.5%, thrombocytopenia in 9.5%, and thrombocyto-

sis in 0.9% of the studied subjects.

In this study, no one had pancytopenia, while 11 patients (5%) had cytopenia, of which 8 patients had leukopenia with thrombocytopenia, 2 patients had leukopenia with anemia, and only one patient had thrombocytopenia with anemia.

In this study, there was no significant relationship between Wright titer and age (P = 0.431) (Table 2), incidence of leukopenia (P = 0.474), neutropenia (P = 0.475), lymphopenia (P = 0.352), anemia (P = 0.705), or thrombocytopenia (p 0.001) (Table 3). There was a significant correlation between the Wright titer and gender (P = 0.004), so the highest frequency was related to the group of females with a Wright titer rate of 1/80 (Table 4).

Table 2: Correlation between the Wright test and age.

Wright titer	**± mean) age (standard deviation**	**p-value**
1.80	48.2 ± 16.7	
1.160	50.2 ±20.2	
1.320	46.3 ± 20.1	0.431
1.640	43.8 ± 20.1	
1.1280	44.6 ± 15.9	
1.2560 and higher	40.8 ± 22.9	
Total	46.7 ±18.9	

Table 3: Frequency distribution of leukopenia, neutropenia, lymphopenia, anemia and thrombocytopenia and investigating the relationship between them and Wright titer

Variable	**Wright titer frequency (%)**							**p-value**
		1.80	1.160	1.320	1.640	1.1280	1.2560 And higher	
Leukopenia	Yes	7 (3.2)	5 (2.3)	2 (0.9)	1 (0.5)	2 (0.9)	2 (0.9)	0.474
	No	) 56 (25.3	39 (17.6)	38 (17.2)	36 (16.3)	24 (10.9)	9 (4.1)	
Neutropenia	Yes	3	3	5	3	0	1	0.475
	No	(1.4) 60 (27.1)	(1.4) 41 (18.6)	(2.3) 35 (15.8)	(1.4) 34 (15.4)	(0) 26 (11.8)	(0.5) 10 (4.5)	
	Yes	2	4	1	1	0	0	
Lymphopenia	No	(0.9) 61 (27.6)	(1.8) 40 (18.1)	(0.5) 39 (17.6)	(0.5) 36 (16.3)	(0) 26 (11.8)	(0) 11 (5)	0.352
	Yes	7	8	9	8	4	2	
Anemia	No	(3.2) 56 (25.3)	(3.6) 36 (16.3)	(4.1) 31 (14)	(3.6) 29 (13.1)	(1.8) 2 (10)	(0.9) 9 (4.1)	0.705
	Yes	3	3	2	3	9	1	
Thrombocytopenia	No	(1.4) 60 (27.1)	(1.4) 41 (18.6)	(0.9) 38 (17.2)	(1.4) 34 (15.4)	(4.1) 17 (7.7)	(0.5) 10 (4.5)	P<0.001

Table 4: Correlation between the Wright test and gender

Wright titer	Gender		p-value
	female (%)	male (%)	
1.80	35(15.8)	28(12.7)	
1.160	22(10)	22(10)	
1.320	12(5.4)	28(12.7)	0.004
1.640	16(7.2)	21(9.5)	
1.1280	6(2.7)	20(9)	
1.2560and higher	1(0.5)	10(4.5)	
Total	92(41.6)	129(58.4)	221(100)

The results of this study showed that there is a significant relationship between high ESR titers ($P < 0.001$) (Table 5) and positive CRP ($P < 0.001$) (Table 6), that the highest frequency is related to the normal ESR group with a Wright titer rate of 1/80, and the highest frequency is related to negative CRP with a Wright titer rate of 1/80, and patients with a Wright titer rate of 1/1280 had the highest frequency of thrombocytopenia.

Table 5: Correlation between high ESR with Wright titer

Wright titer	Coefficient	SE	OR	Confidence interwall For OR	p-value
1.80	Reference level				
1.160	0.79	0.43	2.20	0.94–5.15	0.068
1.320	1.76	0.44	5.83	2.43–13.69	p<0.001
1.640	1.52	0.44	4.59	1.90–11.08	0.001
1.1280	1.25	0.49	3.50	1.32–9.24	0.011
1.2560 And higher	1.43	0.67	4.20	1.11–15.83	0.034

Table 6: Correlation between positive CRP with Wright titer

Wright titer	Coefficient	SE	OR	Confidence interwall For OR	p-value
1.80	Reference level				
1.160	1.25	0.41	3.50	1.56–7.84	0.002
1.320	1.54	0.43	4.16	1.98–10.97	p<0.001
1.640	1.42	0.44	4.66	1.75–9.89	0.001
1.1280	2.12	0.56	8.40	2.77–25.41	P<0.001
1.2560 And higher	2.19	0.82	9	1.78–45.44	0.008

The chance of a positive CRP index in people with a titer of 1/160 is about 3.5 times that of patients with a titer level of 1/80, and this chance ratio for people with a titer level of 1/2560 reaches 9 and its maximum value. The chance of having a high ESR in people with a titer of 1/160 is about 2.20 times that of patients with a titer level of 1/80, and this chance ratio reaches its maximum (5.83) in patients with a titer level of 1/320. And further, with the increase in Wright titer level, the chance ratio of people decreases, so that at the titer level of 1/2560, the chance of having a high ESR in a person is 4.20 times that of a person at the titer level of 1/80.

Discussion

The present study was conducted to determine the changes of CBC, CRP and ESR in patients with brucellosis who were referred to health and community health centers in Gonabad city, and in this regard, the changes of these blood parameters were investigated in 221 patients with brucellosis. In this study, the number of positive cases was higher in men, and the higher prevalence of brucellosis in men can be attributed to work-related infections and stronger humoral and cellular immune systems in female.

The results of the present study showed that high ESR is present in 43.4% of affected patients. This amount has been stated in the studies conducted in Iran (29.5%)(9), India (80%) (10), Iran (38%) (11), Iran (44.5%) (12), Iran (45.3%) (13).

Regarding CRP variable, in our study 59.7% of people with brucellosis had positive CRP. This amount in different studies conducted in Iran were (34%) (9), (63%) (11), (45%) (12), (69.2%) (13).

In our study, comparing the frequency of high ESR and positive CRP in patients with brucellosis showed that positive CRP cases (59.7%) are more than high ESR cases (43.4%). ESR and CRP are two tests to check the presence of inflammation and hidden infections in the body, but CRP has higher sensitivity and specificity than ESR, which has been shown in our study.

The results of ESR test in brucellosis have many challenges because the increase of IgM pentamer, or the excessive increase of IgG titer increases the plasma viscosity and causes no increase in ESR. In brucellosis, depending on the stage of the disease, we may have high or normal ESR, which is affected by plasma viscosity. In such cases, CRP is better because it is not affected by plasma viscosity. Therefore, CRP results are more valuable than ESR. According to our investigation, CRP positive level increased with Wright titer increasing, but high ESR cases did not increase with Wright titer increasing.

Our study showed that leukopenia exists in 8.6% of patients with brucellosis. While in the studies conducted in Iran (31.8%) (9), Iran (8.5%) (14), India (14.7%) (10), Iran (33%) (11), Iran (9%) (12), Turkey (85.5 %) (15), Iran (23.1%) (13), Israel (28%) (16) were seen.

In this study, leukocytosis was seen in 9% of patients with brucellosis, and neutropenia was found in 6.8% and neutrophilia in 9.5% of patients under study. Also, our study showed that there is lymphopenia in 3.6% and lymphocytosis in 10% of the patients under study.

In the present study, anemia is seen in 17.2% of patients with brucellosis. This amount in different studies in Iran (56.8%) (9), Iran (42.6%) (14), India (57.3%) (10), Iran (53%) (11), Iran (19%) (12), Turkey (4.3) (15), Iran (52.1%) (13), India (21.4%)(17) and Israel (13%) (16).

According to our results, thrombocytopenia was present in 9.5% of patients with brucellosis. This amount in different studies in Iran (9.1%) (9), Iran (12.5%) (14), India (33.82%) (10), Iran (12%) (11), Iran (7.4%) (12), Turkey (15.0%) (15), Iran (15.4%) (13), India (18.2%) (17) and Israel (14%) (16).

In our study, none of the patients with brucellosis had pancytopenia, which is similar to the study of Fanni et al.'s (11) as well as the study of Balın et al.'s (3). While in Behnaz et al.'s study (14), pancytopenia was found in 1.5%, in Hoseini et al.'s study in 1.6% (12), in Kaya et al.'s study in 5.7% (17). And in the study of Justman et al., it was present in 2% of affected patients (16).

In our study, bicytopenia is present in 5% of people with brucellosis, which is 4.8% in Hoseini et al.'s study (12) and 4.3% in Balın et al.'s study (3).

In our study, there was a correlation between the titer and sex, so that most female had a titer of 1.80, but in the study of Hoseini et al. (12), there was no correlation. In explaining this case, it can be said that female have a stronger humoral and cellular immune system than men, and as our study shows, female have lower titers of Wright in case of brucellosis.

In the present study, there was no relationship between Wright titer and age, while in the study of Hoseini et al. (12), there was a significant relationship between Wright titer and age over 45 years.

In our study, a statistically significant correlation was observed between Wright titer and ESR, so most people who had normal ESR had a 1/80 Wright titer, but in the study of Hoseini et al. (12), no correlation between two- titer was observed. At low Wright titer levels, the antibody titer is low, the zeta potential of the RBC level is less neutralized and ESR has not increased due to its low sensitivity. As the Wright

titer increases, the ESR also increases, but in cases where the titer is too high, the ESR does not increase due to the increase in plasma viscosity(18, 19).

In the current study, a statistically significant correlation was observed between wright titer and CRP, so most people who had negative CRP had a 1/80 Wright titer, and also in the study of Hoseini et al. (12), the correlation between Wright titer and positive CRP was significant.

The results of this study regarding the relationship between the chance of positive cases of ESR and CRP tests with the antibody titer showed that the graph of ESR changes with the Wright titer is a bell-shaped graph, which is the highest value in the titer of 1/320 and in values higher than this titer, the rate of ESR positivity decreases, but in the case of CRP, with the increase in the Wright titer, the chance of positive cases of this test increases, and this finding shows the effect of the increase in plasma viscosity on the results of the ESR test. In higher titers, due to the increase in the number of antibodies in the plasma, the viscosity increases, and on the other hand, the RBC sedimentation rate decreases, but in the lower titers, due to the absence of plasma hyper-viscosity and the neutralization of the zeta potential. The surface of the RBC forms roulo is more and then the rate of sedimentation of the red blood cells increases (20).

In addition to the diagnostic value of Brucellosis, the two tests ESR and CRP have the value of predicting specific complications and organ involvement. According to various studies (21, 22), two tests, ESR and CRP, especially ESR can be used as an inflammatory biomarker in the prognosis of complications and organ involvement. Therefore, the results of this test are important for doctors in brucellosis and not only cover the issue of diagnosis, but also can be useful for doctors in terms of prognosis. Furthermore, the accuracy of the results of this test should be investigated and paid attention to according to the effectiveness of this test in higher titers. However, it is suggested that the investigation of plasma viscosity should also be taken into consideration in the diagnosis and prognosis program of brucellosis disease.

In this study, a statistically significant relationship was observed between the Wright titer and the incidence of thrombocytopenia, so that the lower the titer, the lower the incidence of thrombocytopenia, and conversely, the higher the Wright titer, the higher the incidence of thrombocytopenia; While in the study of Hoseini et al. (12), there was no connection between the two-titer observed.

In our study, there was no statistically significant relationship between leukopenia, neutropenia, lymphopenia, and anemia with Wright titer, but it was significant for the correlation between Wright titer and thrombocytopenia. Thrombocytopenia, like anemia, is a sign of the existence of another disease, which has many differential diagnoses in its diagnostic approach; Therefore, according to the prevalence of brucellosis in the region, it is possible to consider brucellosis as one of the priorities of differential diagnoses for the diagnostic approach to thrombocytopenia in the case of patients presenting with thrombocytopenia, rather than spending time and money on diagnostic procedures. It should be avoided due to the prevalence of thrombocytopenia in these patients.

Conclusion

The results of this study showed that according to the prevalence of brucellosis in the study area, changes in CBC test, especially thrombocytopenia, can make brucellosis more colorful in the differential diagnosis of thrombocytopenia. Also, the results of two ESR and CRP tests showed that the CRP test has more diagnostic value than ESR due to its higher sensitivity and specificity, and in high Wright titers, the results of the ESR test should be interpreted with caution and the results of the CRP test as well as plasma viscosity should be taken into account.

Data Availability

Data are available on request from the authors.

Ethical Approval

This study was approved by the Research Ethics Committee of Gonabad University of Medical Sciences; Gonabad, Iran, with code number IR.GMU.REC.1398.154.

Conflict of interest

The authors have no conflict of interest to declare.

References

1. Akya A, Bozorgomid A, Ghadiri K, Ahmadi M, Elahi A, Mozafari H, et al. Usefulness of Blood Parameters for Preliminary Diagnosis of Brucellosis. J Blood Med. 2020;11:107-13.
2. Agin M, Kayar Y. Demographic, Laboratory, and Clinical Comparison of Pediatric Brucella Cases With and Without Liver Involvement. Cureus. 2020;12(10):e10862.

3. Balın Ş, Tartar AS, Akbulut A. The predictive role of haematological parameters in the diagnosis of osteoarticular brucellosis. Afr Health Sci. 2018;18(4):988-94.
4. Xu N, Dong X, Yao Y, Guan Y, Chen F, Zheng F, et al. Improved early detection of focal brucellosis complications with anti-Brucella IgG. Journal of clinical microbiology. 2020;58(10):e00903-20.
5. Yagupsky P, Morata P, Colmenero JD. Laboratory diagnosis of human brucellosis. Clinical microbiology reviews. 2019;33(1):e00073-19.
6. Pal M, Kerorsa GB, Desalegn C, Kandi V. Human and animal brucellosis: A comprehensive review of biology, pathogenesis, epidemiology, risk factors, clinical signs, laboratory diagnosis, public health significance, economic importance, prevention and control. American Journal of Infectious Diseases. 2020;8 (4):118-26.
7. Awwad E, Bărăităreanu S, Gurău MR, Faraj M, Essawi T, Adwan K, et al. New trends in the laboratory diagnosis of brucellosis in Palestine: a short review. Revista Română de Medicină Veterinară. 2018;28 (2):5-12.
8. Nassaji M, Govhary A, Ghorbani R, editors. Epidemiological, clinical and laboratory findings in adult patients with acute brucellosis: A case-control study2015.
9. AFSHAR PS, Mamishi S. Brucellosis: review of clinical and laboratory features and therapeutic regimens in 44 children. 2008.
10. Sathyanarayanan V, Razak A, Saravu K, Ananthakrishna SB, Prabhu MM, Vandana K. Clinical profile of brucellosis from a tertiary care center in southern India. Asian Pacific journal of tropical medicine. 2011;4(5):397-400.
11. Fanni F, Shahbaznejad L, Pourakbari B, Mahmoudi S, Mamishi S. Clinical manifestations, laboratory findings, and therapeutic regimen in hospitalized children with brucellosis in an Iranian Referral Children Medical Centre. Journal of health, population, and nutrition. 2013;31(2):218.
12. Hoseini SD, Ghaznavirad E, Farazi AA. Accuracy of Indirect ELISA Prepared from Recombinant Bp26 Gene of Brucella melitensis in Diagnosis of Human Brucellosis. ISMJ. 2020;23(4):292-301.
13. Nassaji M, Govhary A, Ghorbani R. Epidemiological, clinical and laboratory findings in adult patients with acute brucellosis: A case-control study. Acta Medica Mediterranea. 2015:1319-25.
14. BEHNAZ F, Mohammadzadeh M, MOHAMMADI MM. Hematologic manifestations of brucellosis. 2011.
15. Parlak M, Akbayram S, Doğan M, Tuncer O, Bayram Y, Ceylan N, et al. Clinical manifestations and laboratory findings of 496 children with brucellosis in V an, T urkey. Pediatrics International. 2015;57 (4):586-9.
16. Justman N, Fruchtman Y, Greenberg D, Ben-Shimol S. Hematologic Manifestations of Brucellosis in Children. Pediatr Infect Dis J. 2018;37(6):586-91.
17. Kaya S, Elaldi N, Deveci O, Eskazan AE, Bekcibasi M, Hosoglu S. Cytopenia in adult brucellosis patients. The Indian Journal of Medical Research. 2018;147(1):73.
18. Kang YJ. Microfluidic-based biosensor for blood viscosity and erythrocyte sedimentation rate using disposable fluid delivery system. Micromachines. 2020;11(2):215.
19. Cortinovis A, Crippa A, Crippa M, Bosoni T, Moratti R. Relations between plasma-erythrocyte viscosity factors and ESR. Minerva Cardioangiologica. 1992;40(9):323-30.
20. Liu J, Zhao X. Clinical features and serum profile of inflammatory biomarkers in patients with brucellosis. The Journal of Infection in Developing Countries. 2017;11(11):840-6.
21. Sen P, Demirdal T, Nemli SA. Predictive value of inflammation markers in brucellosis. Archives of Iranian Medicine. 2019;22(11):640.
22. Kursun E, Turunc T, Demiroglu Y, Arslan H. Evaluation of four hundred and forty seven brucellosis cases. Internal Medicine. 2013;52(7):745-50.

Ethiopian Medical Journal 2024, 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420 Gebrehiwot et al.

Case Report

A Case Report of Silico-Tuberculosis

Kibrom G. Gebrehiwot[1], Tewodros H. Gebremariam[2]

[1]Mekelle University, College of Health Sciences, Department of Internal Medicine
[2]Addis Ababa University, College of Health Sciences, Department of Internal Medicine

Corresponding authors*: drhaileab@gmail.com

Introduction
The End TB strategy aims to eliminate tuberculosis (TB) by 2035. Silicosis, a serious disease on its own, is also a significant risk factor for TB. It was responsible for 280,000 YLLs (years of life lost) and 376,000YLDs (years lived with disability) in 2019. Here we report a patient with silicosis related to artisan gold mining who developed non-tuberculous mycobacterial infection and discuss on the preventive and diagnostic challenges in a resource-constrained setting.

Citation : *Gebrehiwot KG, Gebremariam TW, A case report of Silico-tuberculosis Ethiop Med J 62 (1) 61-63*
Submission date : *6 March 2023 Accepted: 27 December 2023 Published: 1 January 2024*

Case

On August 2021, a 34-year-old man from North West Tigray, Ethiopia was referred to our hospital (Ayder Comprehensive Specialized Hospital) for cough productive of blood-tinged muco-purulent sputum, shortness of breath, fever, and a weight loss of 10kg over two years. He had previously taken two full courses of anti-tuberculous medications (2RHZE/4RH) with little improvement. The result of the acid-fast stain was not reported by the referring clinic.

He worked in an artisanal gold mining in his village for 5years and he never used any dust protection mechanisms. He reported that a group of young men would dig 2-3meters deep into the rock and then create horizontal tunnels up to20 meters long by hammering the rock. The patient does not know the risk that freshly formed silica poses.

On physical examination: He was wasted with weight of 41kg, RR=28, SaO_2 of 90% and coarse crepitations over the posterior upper chest bilaterally. His chest X-ray and chest CT-scans showed extensive bilateral, predominantly upper lung opacities; cavitations and dilated (bronchiectatic) airways (see Figure1 below). Unfortunately, his initial chest x-ray was lost.

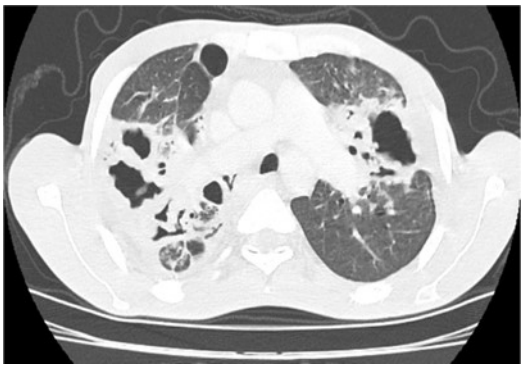


Figure1. Chest CT-scan showing bilateral thick-walled cavitations in the middle-upper lungs

Sputum AFB was positive twice (reported as +4) but the sputum GeneXpert was negative three times. Sputum culture for non-tuberculous mycobacteria (NTM) was not possible due to the war in the region during the time. With the diagnosis of Silico-tuberculosis (Accelerated silicosis complicated by cavitary pulmonary Nontuberculous mycobacteria), the patient was put on daily RHZE+ daily 250mg Azithromycin as an outpatient. Injectable anti-TB medications (streptomycin and amikacin) were unavailable and couldn't be added.

On the second month of treatment, his constitutional symptoms as well as the sputum improved. However, his shortness of breath and weight loss remained the same. On his fifth month of treatment, he showed clinical signs of worsening with additional 2kg weight loss. His chest X-ray showed a new minimal effusion on the right side (Figure2).

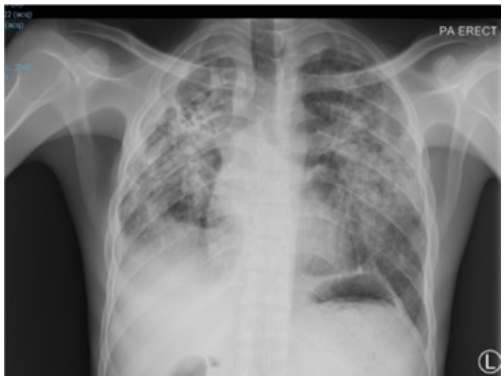


Figure 2: Chest X-ray on the fifth month of treatment. Bilateral patchy opacities and right upper lung cavitation with right costophrenic angle obliteration.

Smear microscopy for AFB at that time was reported as scanty (0-9bacilliperHPF) and GeneXpert was still negative. Due to the clinical worsening; the patient was referred to a hospital with MDR-TB service for addition of Amikacin and inpatient management.

Discussion

Despite the widespread presence of dust-associated occupations, this is the first case of silicosis reported from Ethiopia (3).Silicosis is caused by inhalation of respirable size crystalline silica. It mainly manifests with chronic cough, shortness of breath, fatigue and weight loss. It is diagnosed by a combination of symptoms, exposure history and radiologic findings after excluding other similar lung diseases. The disease is classified into chronic, accelerated and acute (silicoproteinosis) based on the duration of exposure to silica as well as its clinical presentations (4).

Many occupations in developing nations are associated with silica exposure and poor awareness of workers together with limited regulatory mechanisms can lead to silicosis and its complications. Construction related occupations including quarrying of stones, stonecutting, crushing, ground works, demolition of buildings, drilling, and cement production are all sources of silica dust. Construction is especially common in rapidly developing nations like Ethiopia and deserves particular attention in the prevention of the disease (5).

Small scale gold mining is another important risk factor in Ethiopia. In 2015, there were about 271 artisan gold mining areas in Tigray alone, employing only that take on thousands of young men and women (6).This occupation requires the workers to dig deep into the rocks using simple tools under limited ventilation.

Building rock-hewn churches is a long tradition in Ethiopia. The country owns many rock-hewn churches (more than 100 in Tigray alone), some of them as old as17, 000 years (7). This practice continues to this date and is a very important risk factor to address (Figure3).

Figure3. Rock—hewnchurchinthemakingin Adigrat city,Tigray

Tuberculosis very commonly complicates silicosis or silica exposure with an odds ratio reaching about 30 (8).In a patient with silicosis, the presence of constitutional symptoms, hemoptysis and cavitary lesions on radiography should lead to consideration of overlapping tuberculosis (4).The limited availability of culture and sensitivity for mycobacteria in developing nations makes differentiating NTM from MTB difficult. However, currently many developing countries own molecular techniques such as GeneXpert test. A positive sputum AFB together with a negative GeneXpert test for TB suggests an NTM infection (9).

Finally, silicosis is a relentlessly progressive disease with no effective therapy but it can be completely prevented using various techniques. These include elimination (abandoning high- risk occupations), substitution, isolation or containment of high-risk processes, ventilation (natural and artificial means), applying respiratory protective equipment, and training of workers (10). These techniques are effective, but adapting them to the special conditions of non-formal occupations of developing nations is another challenge due to cost implications.

Conflict of interests

None declared

Funding

The authors did not receive any funding for this work

References

1. World Health Organization. Global Tuberculosis Report 2015 World Health Organization; 2015. 204p.
2. Global Health Metrics. Silicosis—Level 4 cause. Lancet [Internet].2019; 4–5.Available from: www.thelancet.com
3. KumieA, AmeraT, BerhaneK,SametJ,HundalN,MichaelFG,etal.Occupational Health and Safety in Ethiopia: A review of Situational Analysis and Needs Assessment.
4. Cecile Rose, MDM. Silicosis.In:uptodate193.2018.
5. International Labor organization. Technical Memorandum Ethiopia Labour Inspection Audit.
6. Meaza H, Ali M, Tesfamariam Z, Abebe N. Impacts of artisanal gold mining systems on soil and woody vegetation in the semi-arid environment of northern Ethiopia. Singap J TropGeogr.2017; 38(3): 386–401.
7. Asrat A.The Rock-Hewn Churches of Tigrai, Northern Ethiopia: A Geological Perspective.Geoarchaeology-AnIntJ.2002;17(7):649–63.
8. Balmes JR. Harrison's principles of internal medicine, 21edition. In 2022.
9. Manual I. Xpert MTB/RIF implementation.2014;
10. The Global Occupational Health Network. gohnet12e. GOHNET Newsl .2007;(12–2007).

Ethiopian Medical Journal 2024, 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420 Demissie et al.

Case Report

Magnesium Toxicity Presented as Quadriparesis in Postpartum Period: Case Report

Zekewos Demissie[1],Seyfemichael Getachew[2],SisayTeklu[3],Abraham Demile[4],Bezawit Endeshaw[5],Amanuel Hintsa[5],

[1]Internist, Lancet General Hospital, Addis Ababa, Ethiopia
[2]Assistant professor of Nephrology, St. Paul Millennium Medical College, Addis Ababa, Ethiopia
[3]Associate professor of Obstetrics and Gynecology, Addis Ababa University, Addis Ababa, Ethiopia
[4]General Practitioner, Lancet General Hospital, Addis Ababa, Ethiopia
[5]General Practitioner, Zewditu Memorial Hospital, Addis Ababa, Ethiopia

Corresponding authors*: zakdem61@gmail.com

Abstract:
Quadriparesis may result from numerous neurologic diseases. Any of the causes could occur in the postpartum period. However, some conditions have increased prevalence during peripartal period, such as cerebral venous thrombosis, eclampsia itself, or its treatment with magnesium sulfate causing neuromuscular dysfunction in case of toxicity. Herein, we report a case of magnesium toxicity in a 34-year-old mother in the early postpartum period. This case signifies the importance of magnesium toxicity in patients with decreased renal clearance.

Keywords: *Hypermagnesemia, Postpartum, Preeclampsia/Eclampsia, Quadriparesis, Lancet General Hospital*
Citation : *Demissie Z, Getachew S, Teklu s et al. Magnesium toxicity presented as quadriparesis in postpartum period: Case report Ethiop Med J 62 (1) 65-67*
Submission date : *11 October 2023 Accepted: 16 December 2023 Published: 1 January 2024*

Introduction

Since the early 1900s magnesium sulfate has been used for the prevention and treatment of eclamptic seizures [1]. Treatment with magnesium sulfate rarely results in hypermagnesemia, which is diagnosed when the serum magnesium level exceeds 2.3mg/dl. Hypermagnesemia is seen in about 15 % of hospitalized patients and renal failure can increase its risk [2, 3].

The normal serum magnesium level is maintained by the renal system. As kidney function declines serum level of magnesium increases. There is no magnesium regulatory mechanism other than urinary excretion. Thus, acute kidney injury (AKI) is an important risk factor for magnesium toxicity [4, 5]. Here, we report a case of quadriparesis after magnesium sulfate administration for atypical preeclampsia in patient with acute kidney injury during early postpartum period.

Case presentation

A 34-year-old para-four mother was referred to our hospital for acute-onset generalized body weakness of three hours duration. At the referring hospital, she had severe globalized headache, blurred vision, two episodes of vomiting, and elevated blood pressure. At the referring institution, she received a magnesium sulphate loading dose of 10 gm intramuscularly and a first maintenance dose of 4 gm for elevated blood pressure.

Three hours after her last dose of magnesium, the patient developed generalized body weakness that affected both her upper and lower extremities, making her unable to move them. Her antenatal course had been uneventful until the third trimester, when she developed a uterine rupture, resulting in a total abdominal hysterectomy. She received a blood transfusion during the surgery. With a stable immediate post-operative period, she was discharged after 48 hours of observation.

Upon examination, the patient was conscious with a blood pressure reading of 140/90, a pulse rate of 102, and normal respiration and temperature. Her neurologic examination revealed quadriparesis, with reduced muscle strength (power 4/5) in both her upper and lower extremities. Additionally, she exhibited hypotonia, reduced reflexes, an equivocal bilateral plantar reflex, and no signs of meningeal inflammation

Initial investigations showed elevated levels of urea and creatinine (urea 165 mg/dl, creatinine 10.6 mg/dl), indicating acute kidney injury. Her electrolyte levels were abnormal (sodium 129 mEq/l, potassium 5.03 mEq/l, and magnesium 8.5 mg/dl). However, complete blood cell counts and liver function tests were normal. Brain magnetic resonance imaging with magnetic resonance venography yielded normal results. Her electrocardiogram was also unremarkable. The diagnosis of quadriparesis secondary to hypermagnesemia due to magnesium toxicity, along with AKI possibly caused by ischemic acute tubular injury, was made.

Immediate treatment involved the administration of calcium gluconate and the initiation of hemodialysis to normalize serum magnesium levels. The patient showed complete neurologic recovery at the time of discharge.

Serial measurements of renal function tests and electrolytes are shown in Table 1 below.

Variable	On Admission	After 1st dialysis session	After 2nd dialysis session	After 3rd dialysis session	On discharge
Creatinine (mg/dl)	10.6	7.4	3.9	2.7	1.16
Urea (mg/dl)	165	116	78	56	44
Magnesium (mg/dl)	8.5	5.6	3.8	2.4	1.9
Calcium (mmol/l)	1.1	1.1	1.0	1.1	1.2
Sodium (mEq/l)	129	131	133	136	140
Potassium (mEq/l)	5.03	4.6	4.0	3.6	3.8

Discussion

Preventing and controlling of preeclamptic/eclamptic seizures are the most common obstetric indications of magnesium sulfate administration [1].

Toxicities from hypermagnesemia correlate with the serum concentration. Non-specific symptoms occur during the early phase. Thus include nausea, dizziness, weakness, and confusion. As the serum level increases, areflexia occurs at 8.5 to 12.0 mg/dl; respiratory paralysis occurs at 12 to 16 mg/dl; cardiac conduction is altered at > 18 mg/dl; and cardiac arrest occurs at > 30 mg/dl [2, 4, 5].

The predominant neurologic manifestations are muscular weakness and paralysis. If untreated, respiratory failure results from respiratory muscle involvement. The muscle weakness is typically flaccid type, and it is caused by blockage of neuromuscular transmission, which resolves only when the magnesium level returns to normal [5, 6].

Treating physicians should maintain a high index of suspicion to consider magnesium toxicity in at-risk patients. The initial evaluation includes the determination of serum magnesium and other electrolyte levels, serum creatinine and blood urea nitrogen determinations, and arterial blood gas analysis [7].

Treatment of magnesium toxicity includes administration of calcium gluconate or chloride, administration of normal saline at a rate of 150 to 200 ml/h if renal function is normal, and hemodialysis in severe toxicities and renal failure [5, 8].

Although it is not a contraindication for the administration of magnesium sulfate, in patients with acute renal insufficiency, the magnesium sulfate dosing should be reduced according to the American College of Obstetricians and Gynecologists' recommendations [9].

Although our patient's serum creatinine level increased serially after magnesium administration, there is no evidence in the literature showing magnesium sulfate causing renal injury. Thus, worsening of the renal condition could be due to the underlying preeclampsia or hemodynamic instability from bleeding [10].

Conclusion

Maintaining a high degree of suspicion is important for the early diagnosis of quadriparesis from magnesium toxicity in at-risk patients during the postpartum period. Initial workup should include serum magnesium and creatinine levels. To prevent toxicity from magnesium sulphate, dose adjustment should be

Reference

1. Hunter LA, Gibbins KJ. Magnesium sulfate: past, present, and future. J Midwifery Womens Health. 2011 Nov-Dec;56(6):566-74. doi: 10.1111/j.1542-2011.2011.00121.x. Epub 2011 Oct 17. PMID: 22060216.
2. Smith JM, Lowe RF, Fullerton J, Currie SM, Harris L, Felker-Kantor E. An integrative review of the side effects related to the use of magnesium sulfate for pre-eclampsia and eclampsia management. BMC Pregnancy Childbirth. 2013 Feb 5;13:34. doi: 10.1186/1471-2393-13-34. PMID: 23383864; PMCID: PMC3570392.
3. Felsenfeld AJ, Levine BS, Rodriguez M. Pathophysiology of Calcium, Phosphorus, and Magnesium Dysregulation in Chronic Kidney Disease. Semin Dial. 2015 Nov-Dec;28(6):564-77. doi: 10.1111/sdi.12411. Epub 2015 Aug 25. PMID: 26303319.
4. Blaine J, Chonchol M, Levi M. Renal control of calcium, phosphate, and magnesium homeostasis. Clin J Am Soc Nephrol. 2015 Jul 7;10(7):1257-72. doi: 10.2215/CJN.09750913. Epub 2014 Oct 6. Erratum in: Clin J Am Soc Nephrol. 2015 Oct 7;10(10):1886-7. PMID: 25287933; PMCID: PMC4491294.
5. Aal-Hamad AH, Al-Alawi AM, Kashoub MS, Falhammar H. Hypermagnesemia in Clinical Practice. Medicina (Kaunas). 2023 Jun 24;59(7):1190. doi: 10.3390/medicina59071190. PMID: 37512002; PMCID: PMC10384947.
6. Cavell GF, Bryant C, Jheeta S. Iatrogenic magnesium toxicity following intravenous infusion of magnesium sulfate: risks and strategies for prevention. BMJ Case Rep. 2015 Jul 31;2015:bcr2015209499. doi: 10.1136/bcr-2015-209499. PMID: 26231187; PMCID: PMC4521523.
7. DynaMed Hypermagnesemia-Approach to the Patient. [(accessed on 1 May 2023)]. Available online: https://www.dynamed.com/approach-to/hypermagnesemia-approach-to-the-patient#GUID-90892592-B90F-48C6-ACF1-D53C3D5648E4
8. Jahnen-Dechent W, Ketteler M. Magnesium basics. Clin Kidney J. 2012 Feb;5(Suppl 1):i3-i14. doi: 10.1093/ndtplus/sfr163. PMID: 26069819; PMCID: PMC4455825.
9. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol. 2020 Jun;135(6):e237-e260. doi: 10.1097/AOG.0000000000003891. PMID: 32443079.
10. Karhu E, Atlas SE, Gao J, et al. Intravenous infusion of magnesium sulfate is not associated with cardiovascular, liver, kidney, and metabolic toxicity in adults. Journal of Clinical and Translational Research. 2018 May;4(1):47-55. PMID: 30873494; PMCID: PMC6410632.

Ethiopian Medical Journal 2024, 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420 Tim et al.

Case Report

Double Intussusceptions in Peutz-Jeghers Syndrome Patient: A Case Report

Lee Mem Tim[1,2*], Wan Zainira Wan Zain [1,2], Muhammad Faeid Othman [1,2]

[1] Department of Surgery, School of Medical Science, Universiti Sains Malaysia, Kelantan, Malaysia
[2] Hospital Universiti Sains Malaysia, Jalan Raja Permaisuri Zainab II, Kelantan, Malaysia

Corresponding authors*: memtim2390@gmail.com

Abstract

Background: *Peutz-Jeghers Syndrome is one of the hereditary gastro-intestinal cancer syndrome with characteristic mucocutaneous pigmentation and histologically distinctive hamartomatous polyps in gastro-intestinal tract. Although it is characteristically benign hamartomatous polyp, majority of affected individuals develop symptoms starting from their second decades. We reported a known Peutz-Jeghers Syndrome case developed recurrent polyps leading to double intussusceptions required bowel resection. Multidisciplinary management and patient compliance to surveillance regime are important in managing PJS patients with potential gastro-intestinal tract complications and relative high risk of developing syndrome specific cancers.*

Citation : *. Tim LM , Zain WZ, Othman MF Double Intussusceptions in Peutz-Jeghers Syndrome Patient: A Case Report Ethiop Med J 62 (1) 69-72*

Submission date : *10 August 2023 Accepted: 28 December 2023 Published: 1 January 2024*

Introduction

Peutz-Jeghers Syndrome (PJS) is one of the familial polyposis syndrome with triad of classical mucocutaneous pigmentations, benign hamartomatous polyps with rare potential of malignant transformation and autosomal dominant inheritance. Jeghers first described the disease with correlation to the autosomal dominance inheritance in 1949. (1)

The prevalence of PJS is reported to be rare with 1 in 100,000 people. (2) Its prevalence is unknown in Malaysia although it was first reported in 1978 by Joishy et al. (3) The patient has typical mucocutaneous pigmentation and intestinal obstruction. Note worthily, the patient came with recurrent intussusception required small bowel resections. A small group of them presented with recurrent intussusceptions signifying the important features of the polyps of which progression by segmental spurts with period of quiescence lasting for months. (4)
We hereby reported an interesting case of double intussusceptions in a known case of PJS patient.

Case Presentation

We reported a 24 years old Malaysian lady with background history of PJS She was diagnosed with PJS when she was 12 years old with small bowel intussusception. Emergency laparotomy, small bowel resection and primary anastomosis was done for the small bowel intussusception.

She presented with symptoms of intestinal obstruction and clinically distended abdomen with tenderness over right iliac fossa. Her blood investigations were non-remarkable and abdominal radiography showed paucity of small bowel gas and absence of rectal gas. (Figure 1) Due to her obstructive symptoms and hostile abdomen, contrasted computed tomography (CT) scan showed 2 intussusceptions: one at right lumbar represented ileo-colic intussusception and one at left lumbar represented jejuno-jejunal intussusception. (Figure 2)

We went to emergency laparotomy due to her obstructive symptom correlated with CT scan findings. Intra-operatively, we noted ileo-colic intussusception from cecum up to proximal transverse colon and jejuno-jejunal intussusception with intramural polyp. (Figure 3) We proceeded to right hemicolectomy, primary ileo-colic anastomosis, wedge resection of jejuno-jejunal intussusception and primary anastomosis. Gross specimen of right hemicolectomy revealed 2 pedunculated polyps both measured 3cm respec-

tively from small bowel while 1 pedunculated polyp was seen at the wedge resection of jejunum. As for microscopic examination, all polyps behaved as Peutz -Jeghers polyps without evidence of dysplasia or malignancy.

Her post-operative period was uncomplicated and she was discharged home on day 8 post operatively.

Discussion

We described a young patient with recurrent intussusceptions 10 years from the first incident. PJS is a rare disease, however, its presentation is simply pathognomonic with its distinctive mucocutaneous pigmentation as presented by the patient. (Figure 4) Often, the diagnosis of the disease occurs when the complications such as intussusception, gastro-intestinal bleeding and intestinal obstruction arise.

Repeated abdominal surgeries are the major concern of the nature progression of the disease. Ninety percent of the PJS patients will have polyps in small intestine in their lifetime. (5) The intestinal polyp is often described as benign. However, PJS is associated with higher risk of gastrointestinal and non-gastrointestinal malignancies. (6) A meta-analysis has shown that an affected individual has 15 times relative risk of neoplasm in any body region as compared to general population. (7,8)

In order to avoid unnecessary repeated abdominal surgeries and risk of short bowel syndrome, an affected individual must comply to surveillance regime according to American College of Gastroenterology clinical guideline. The algorithm of management started with dedicated genetic testing of at-risk individuals and family members. Subsequently, systemic review and throughout physical examinations are important to rule out any syndrome specific cancers includes colon, stomach, small bowel, etc.

Upper GI endoscopy and colonoscopy should be done at the age of 8 years based on guideline and if presence of polyps, there should be repeated procedures every 3 years. If none are found, both examinations should be done at age of 18 and then every 3 years. (9) Our patient has her last upper and lower scope done the year before but did not show any

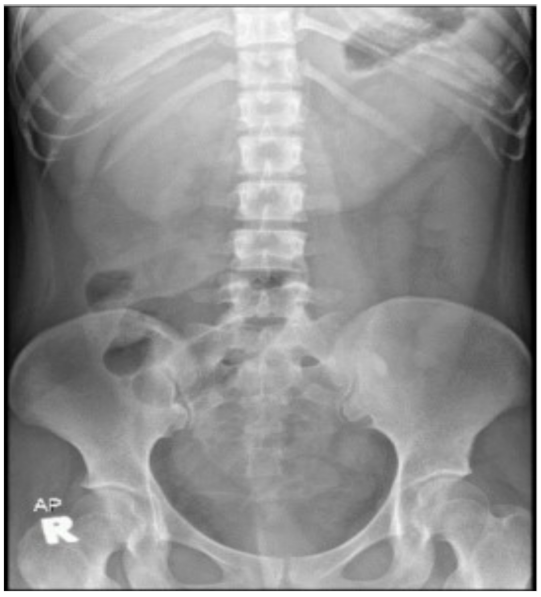


Figure 1. Demonstrated plain abdominal radiography with paucity of small bowel gas and absence of rectal gas.

abnormalities. Small bowels are often involved in 96% of affected individuals. (10) Hence, much efforts should be focus in surveillance of small bowels including video capsule endoscopy and CT enterography. (9)

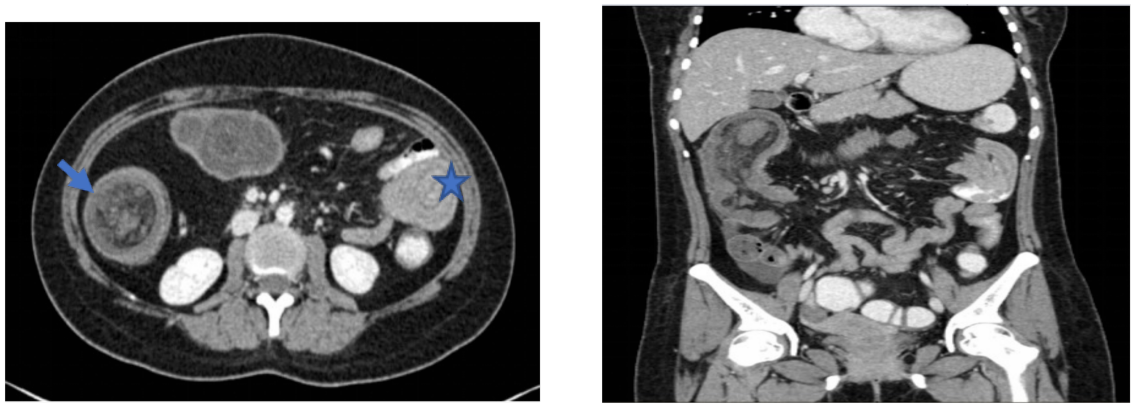
Prevention of short bowel syndrome is ultimately the aim of the management of intestinal polyps. Moving forward, as the patients presented with intestinal obstruction due to intramural polyp, careful examination of entire GI tract and removal of all identifiable polyps through endoscopic polypectomy are essential.

Advancement of technologies has allowed surveillance and non-operative removal of polyps. For examples, video capsule endoscopy, double balloon enteroscopy and CT enterography.

Conclusion

PJS is an unbending disease that will affect an individual lifetime psychologically. Timely diagnosis and family counselling are initial steps in the algorithm. Well-timed surveillance scheme will ensure early discovery of asymptomatic polyps and polypectomy if needed to prevent unnecessary bowel resection.

More modalities should be developed for surveillance of GI tract especially small bowel for early diagnosis and treatment of polyp without putting them into multiple abdominal surgeries. To date, PJS is still tough to be handle due to its rarity and high recurrences.



A) *B)*

Figure 2. (A) CT axial view demonstrated ileocolonic intussusception (arrow) and jejuno-jejunal intussusception (star). (B) CT coronal view demonstrated similar findings particularly showing the ileo-colic intussusception until proximal transverse colon.

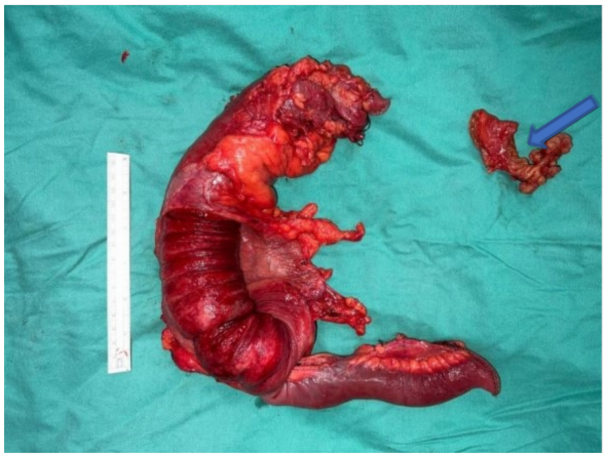


Figure 3. Specimen demonstrated ileocolonic intussusception
on the left and wedge resection of jejunum with intramural polyp on the right. (arrow)

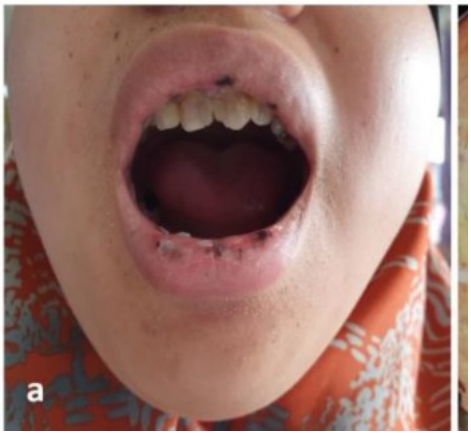


Figure 4. Pigmentation **at lips**

References

1. Jeghers H, McKusick VA, Katz KH. Generalized intestinal polyposis and melanin spots of the oral mucosa, lips and digits; a syndrome of diagnostic significance. N Engl J Med. 1949 Dec 22;241(25):993, illust; passim.
2. Syaiful RA, Supit C, Putranto AS. A Case of Ileocolic Intussusception in an Adult with Peutz-Jeghers Syndrome. Int J Surg Proced. 2018 May;1(2):110
3. Joishy SK, Leela MP, Balasegaram M. Peutz-Jeghers syndrome and its complications. First case report from Malaysia with review of literature. Am J Surg. 1979 Nov;138(5):716-20.
4. Surrinder Kaur, Himmet Singh Sachdeva, Tulsi Dass. The Peutz-Jeghers syndrome: a case report of 2 cases and review of the literature. Aust NZ J Surg 44: 50, 1974.

5.. M. Kopacova, I. Tacheci, S. Rejchrt, J. Bures. Peutz-Jeghers syndrome: diagnostic and therapeutic ap proach. World J. Gastroenterol. 15 (43) (nov 2009) 5397–5408.
6. N. Butt, M. Salih, M. Khan, R. Ahmed, Z. Haider, S.A. Shah. An incidentally discovered asymptomatic para-aortic paraganglioma with Peutz-Jeghers syndrome. Saudi J. Gastroenterol. 18 (2012) 388.
7. J. Loureiro, G.L. Menegazzo, L. Vergamini, R.C. Pestana, F.B. Formiga, M.G.C. deSousa, et al. Diagnostic difficulty in Peutz–Jeghers syndrome. Colorectal Dis. 35 (2015)67–71.
8. 8.F.M. Giardiello. Hereditary colorectal cancer and polyp syndromes. In: Susan Gearhart, Nita Ahuja, Stephen C Yang, editors. Early Diagnosis And Treatment Of Cancer: Colorectal Cancer. Elsevier, 2011, pp. 21–30.
9. Syngal S, Brand RE, Church JM, Giardiello FM, Hampel HL, Burt RW. American College of Gastroenterology. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. Am J Gastroenterol. 2015 Feb;110(2):223-62; quiz 263.
10. Schreibman IR, Baker M, Amos C. The hamartomatous polyposis syndromes: a clinical and molecular review. Am J Gastroenterol. 2005; 100:476–90.

Ethiopian Medical Journal 2024, 62(1)
Open access articles distributed in terms of
Creative Commons Attribution Licence [CC by 4.0]
ISSN 0014-1755 eISSN 2415-2420 Nigussie et al.

Case Series

Pulmonary Tuberculosis Mimicking a Lung Cancer: a Case Series

Mahader Nigussie[1a*], Genet Hagos[1a], Mahlet Alemayhu[1], Meron Yafet[1], Selome Tarekegn[1], Tseganesh Mekonnen[1], Azmera Gissila[1], Melaku Taye[1], Dawit Kebede Huluka[1]

[1]College of Health Sciences Addis Ababa University Addis Ababa, Ethiopia
[a] Co-first authors that contributed equally

Corresponding authors*: macmahader@gmail.com

Abstract
Tuberculosis (TB) is an infectious disease that is caused by Mycobacterium tuberculosis. Despite TB being a preventable and curable disease, it still remains to be one of the leading causes of mortality worldwide and continues to be prevalent. TB can manifest in multiple systems, but its primary target is the lungs. Pulmonary TB can present differently depending on the patient's immune status and comorbidities. One atypical presentation of TB is lung mass, which can mimic lung malignancy and cause diagnostic delays.In this case series, we report on four cases in which TB was initially suspected to be lung malignancy. All four patients had lung masses on diagnostic imaging; microbiological testing was positive in only two of the patients and bronchoscopic abnormalities were seen in two of those. In two of the four cases, caseating granulomas were present on biopsy. All four patients attained clinical and radiologic resolution.In conclusion, despite years of knowledge and the prevalence of TB, atypical presentations can still cause diagnostic delays and unnecessary interventions. This case series provides examples of TB mimicking lung cancer, so considering TB as a differential diagnosis for patients presenting with a lung mass is crucial.

Keywords: *Tuberculosis, lung mass, Ethiopia*
Citation : *Nigussie M, Hagos G, Alemayhu M et al. Pulmonary Tuberculosis Mimicking a Lung Cancer: a Case Series. Ethiop Med J 62 (1) 73 -77*
Submission date : *24 September 2023 Accepted: 923 December 2023 Published: 1 January 2024*

Abbreviations

AFB- Acid- Fast Bacilli
BAL-Bronchoalveolar lavage
COVID- Coronavirus disease
CXR- Chest x-ray
DS- Disseminated
FNA- fine needle aspiration
HIV-Human immunodeficiency virus
LAP- Lymphadenopathy
LUL- Left upper lobe
MDR- Multidrug-resistant tuberculosis **MTB-** Mycobacterium tuberculosis **RUL**- Right upper lobe
SOB- shortness of breath
TB - Tuberculosis
WHO- World Health Organization

Introduction

Tuberculosis (TB) is a preventable and curable infectious disease caused by Mycobacterium tuberculosis. It is the second prevalent cause of death from infectious agents, after COVID-19, and 13th leading cause of death worldwide [1]. The highest prevalence is in Sub-Saharan Africa, India, and Southeast Asia. Ethiopia is one of the 30 high-TB burden countries, with incidence.

>100 per 100,000; which is why early diagnosis and intervention of TB is important [2-3].

TB is known for having multisystem manifestations although its primary target is the lungs. The most common presenting symptoms in TB diagnosed patients are cough greater than 2 weeks, fever, night sweat, fatigue, anorexia and weight loss [4]. Chest radiography findings vary as typical and atypical, with the former having findings of cavitary lesions, pulmonary consolidation, lymphadenopathy, pleural effusions. Atypical radiographic pattern like lung mass

occurs in 3.5 to 4.5% of pulmonary TB cases [5]. It contains caseous material encapsulated by multiple concentric layers of connective tissue without surrounding inflammation or spread.

Although lung masses can have benign etiologies as TB infection, diagnostic dilemma occurs in differentiating it from malignant causes. The overlap of clinical presentations as well as similarities in radiographic findings of lung cancer and tuberculosis necessitates use of histopathology to distinguish between the two [6].

In this case series, we described 4 cases of patients, age 21-41 years and presenting with respiratory and constitutional symptoms. All 4 patients presented with radiographic findings of pulmonary mass. Details of the diagnostic dilemma, clinical presentation, treatment as well as outcome will be presented in the case series.

Case presentation

Case –1

A-28-year-old male office worker and non-smoker presented with a dry cough of 04 months with associated right side chest pain, anorexia and unquantified weight loss. He had no history of TB treatment or contact with chronic cougher. Biochemical investigations were all within normal range. Chest x-ray (CXR) showed right lower lobe opacity and Chest CT showed 3cm x 3cm x 4cm peripheral (subpleural) mass on the posterior segment of right lung, and right hilar lymphadenopathy (LAP), the biggest measuring 2cm x 3cm. With preliminary diagnosis of lung cancer CT guided fine needle aspiration (FNA) cytology from the mass was done and results were inconclusive. Bronchoalveolar lavage (BAL) cytology and Gene Xpert, and trans-bronchial biopsy were non-yielding. For financial reasons, the patient was not investigated further. He was started on anti-TB treatment empirically. After 02 weeks of treatment he showed significant clinical improvement and at the end of the 6th month of anti-TB treatment, he had complete radiologic resolution.

Case –2

A 26 year old female nonsmoker with no contact history presented with dry cough of 03 months duration with associated unquantified weight loss. Biochemical investigations were unrevealing. CXR showed right upper lobe mass like consolidation . and Chest CT revealed right upper lobe (RUL) mass with multiple mediastinal LAP suspicious for lung cancer. Bronchoscopy showed right upper lobe bronchus fungating mass. BAL Gene Xpert showed rifampicin resistant mycobacterium TB (MTB) and endobronchial biopsy showed granuloma of epithelioid cells, giant cells and caseous necrosis. She was then referred to ALERT hospital for initiation of multi- drug- resistant (MDR) TB treatment regimen. On the 4th month of anti-TB, the cough subsided. Repeat Chest CT on the 4th month of treatment showed complete resolution of mass.

Case 3

A 28-year-old male physician presented with a cough productive of whitish sputum of 03 months, shortness of breath (SOB) on exertion, low grade fever, loss of appetite and weight. He smoked a few cigarettes per day for the 3 years before presentation. Biochemical investigations, sputum AFB, Gene X-pert were unremarkable. Chest CT showed 7.7cm x 7.1cm left upper lobe (LUL) mass with spicules and left hilar LAP. Bronchoscopy, done twice, showed narrowed LUL anterior segment bronchus. BAL cytology, BAL Gene X-pert, endobronchial biopsy results were negative. He had a left pneumonectomy and left hilar/para-aortic lymphadenectomy. The intraoperative finding was 10cm x 10cm LUL mass and multiple big hilar and para-aortic LAPs. Biopsy revealed granuloma with caseous necrosis. He was started on anti-TB regimen and symptoms resolved completely.

Case 4

A 41-years old male patient, with 5 pack year smoking history, presented with a dry intermittent cough of one month duration with associated headaches, sweating and a weight loss of 5 kg and loss of appetite. On examination at presentation he was sick looking and tachycardic (PR- 118- 122). Chest x-ray showed lung mass and CT revealed right hilar soft tissue attenuating mass compressing LUL bronchus resulting in narrowing and abutting but no invasion of the adjacent vessels with mediastinal enhancing LAP. There is LUL apicoposterior nodular interstitial septal thickening suspicious for tumor compression of left pulmonary vein resulting in focal pulmonary edema or lymphatic spread of a tumor. BAL showed atypical pleomorphic cells suspicious for malignancy. Endobronchial biopsy showed pseudostratified columnar epithelial lining underneath by granuloma and necrosis with area of mixed inflammatory cells. He was thus started on an anti-TB treatment regimen. Post treatment chest x-ray showed marked resolution of the mass lesion.

Table1. Summary of the clinical characteristics, radiologic presentations, microbiologic findings and treatment outcomes of the cases

S. No.	Age	Sex	Clinical Manifestation	Type of TB	HIV status	CT scan finding	Bronchoscopic finding	Biopsy Finding	Microbiologic	Treatment	Treatment Outcome
1	28	M	Dry cough Right side chest pain Anorexia and Unquantified weight loss	DS	NR	Peripheral (subpleural) mass on the posterior segment of right lung, with right hilar LAP	Non Yielding	None	None	Empirically started on anti-TB regimen	Cured
2	26	F	Dry cough Unquantified weight loss	MDR	NR	Right upper lobe mass with multiple mediastinal LAP	Right upper lobe bronchus fungating mass	Granuloma of epithelioid cells, giant cells and caseous necrosis	BAL Gene Xpert showed rifampicin resistant MTB	Started on MDR TB treatment regimen	Cured
3	28	M	Productive cough SOB on exertion, LGIF, Loss of appetite Unquantified weight loss	DS	NR	LUL mass with spicules and left hilar LAP	Narrowed LUL anterior segment bronchus	Granuloma with caseous necrosis	Non yielding	left pneumonectomy and left hilar/ paraaortic lymphadenectomy Started on anti-TB treatment	Cured
4	41	M	Dry cough Headache - Sweating - Weight loss - Loss of appetite - Smoker - Sick looking - Tachycardiic	DS	NR	RT hilar mass compressing LUL bronchus with mediastinal LAP	Not done	pseudostratified columnar epithelium with necrotic granuloma	Non-yielding	Started on anti-TB treatment	Cured

Discussion

TB is a well-known diagnostic mimicker with a multitude of presentations, one of them being a lung mass imitating malignancy. Pseudotumoral pulmonary TB occurs in 3.5% to 4.5% of immune competent patients even in TB endemic areas [5]. TB and lung cancer have been confused for quite some time as evidenced by a study carried out by Prytz et al. in 1976 on 91 cases of TB who underwent thoracotomy for a presumptive diagnosis of lung cancer [7]. On the other hand, although rare, TB and lung cancer can co-exist, be it through increased susceptibility for new infection or reactivation of a latent one due to the immunocompromised state of malignancy patients [8]. Such dilemmas lead to misdiagnosis, delayed treatment, unnecessary surgeries and further exacerbations of complications of pulmonary TB [9].

The aforementioned challenges partly can be attributed to the great overlap in symptomatology and features of presenting parenchymal infiltrates with lymphadenopathy in both Pulmonary TB and lung cancer [10-11]. Patients with pulmonary TB typically present with cough, chest pain, fever, night sweats and weight loss with infiltrates or cavities on chest imaging which is also seen in lung cancer cases [11]. Such non-specific clinical presentation combined with negative bacteriologic studies and atypical imaging results contribute towards the delay in diagnosis. A study conducted in Chinese PLA general hospital between 2011 and 2015 demonstrated overlapping chest CT findings including spiculation in both pulmonary TB and lung cancer cases [9]. In contrast, bronchoscopy with BAL or guided biopsy was shown to have better yield in reaching definitive diagnosis [12]. Nonetheless, biopsy histopathology studies remain to be the best definitive method of confirming the diagnosis, preferably excisional biopsy [13-14].

In light of the above literatures, accurately diagnosing atypical presentation of TB poses a great hurdle for clinicians, especially in resource limited developing countries. The aim of this case series is to characterize the clinical, radiologic and histologic findings as well as demonstrate diagnostic challenges of tuberculosis patients who were initially diagnosed as lung malignancy or had difficulty ruling out lung malignancy.

In this case series we report 4 cases who had presented with TB mimicking lung malignancy. Age of patients ranges from 21 to 41 years. In our study the cases presented with a constellation of symptoms

Cough and unquantifiable weight loss were the most common symptoms appreciated in all four patients. Other symptoms reported were loss of appetite in three patients; diaphoresis in two patients; headache, pleuritic chest pain and shortness of breath was reported by one patient each.

Although CT scan is an imaging modality commonly used to initially assess masses, evidence indicates chest CT leads to higher rates of misdiagnosis between TB and cancer as compared to head and neck CT and abdominal CT [14]. All of the above cases in this series had undergone chest CT scans which revealed a mass lesion with lymphadenopathies seen on hilar and/or mediastinal lymph nodes, and one of the cases having spicules along the mass. These findings were non-diagnostic and misleading towards the presumption of lung malignancy which warranted further investigation. Therefore, bronchoscopy was done in three of the cases and findings of two cases were revealing. One case revealed a fungating lesion while the other had narrowing of LUL anterior segment bronchus

In concurrence with similar literatures [12-14], definitive diagnosis of pulmonary TB in majority of the cases was reached through biopsy histopathology examination. Of the total cases, three of them had endo-bronchial biopsies performed. One of the cases initially had a non-revealing endo-bronchial biopsy, hence excisional biopsy was performed. All three cases' biopsy demonstrated caseating granulomatous inflammation. BAL from one of the biopsy confirmed case yielded a rifampicin resistant MTB, while the others were non-yielding.

As a result of the above findings, all patients were started on anti-TB medication as per the latest WHO standard. One case was diagnosed retrospectively after response to anti TB medication.

All of the study subjects achieved clinical and radiological resolution.

Conclusion

Despite long years of knowledge about tuberculosis, it still remains a diagnostic challenge due to its chameleon nature. These cases indicate the importance of considering TB in the differential diagnosis of patients presenting with lung masses particularly in the young. The findings also emphasize the need for better diagnostic tools due to its implication on proper management of the disease and reducing its burden. In addition, this calls for deeper

investigations towards understanding the prevalence of similar presentations of tuberculosis mimicking malignancies at both national and global level.

Conflict of interest- The authors have no conflict of interest to declare.

Ethical Clearance- Waiver was obtained from AAU CHS IRB office to publish the case series.

Reference

1. World health organization, Global tuberculosis report 2022. Available at: Global Tuberculosis Report 2022 Factsheet (who.int)
2. World health organization, TB burden estimates. Available at: Global Tuberculosis Programme (who.int)
3. World Health Organization, Global tuberculosis report 2018. Available at: Global Tuberculosis Programme (who.int).
4. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, Keane J, Lewinsohn DA, Loeffler AM, Mazurek GH, O'Brien RJ, Pai M, Richeldi L, Salfinger M, Shinnick TM, Sterling TR, Warshauer DM, Woods GL. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clin Infect Dis. 2017 Jan 15;64(2):e1-e33. doi: 10.1093/cid/ciw694. Epub 2016 Dec 8. PMID: 27932390.
5. Afriyie-Mensah JS, Awindaogo FR, Asomani SK. Pseudotumour presentation of pulmonary tuberculosis. Ghana Med J. 2020 Jun;54(2):126-130. doi: 10.4314/gmj.v54i2.12. PMID: 33536684; PMCID: PMC7829045.
6. Bhatt M, Kant S, Bhaskar R. Pulmonary tuberculosis as differential diagnosis of lung cancer. South Asian J Cancer. 2012 Jul;1(1):36-42. doi: 10.4103/2278-330X.96507. PMID: 24455507; PMCID: PMC3876596.
7. Prytz S, Hansen JL. Surgical treatment of "tuberculoma": A follow-up examination of patients with pulmonary tuberculosis resected on suspicion of tumour. Scand J Thorac Cardiovasc Surg. 1976;10(2):179-82. doi: 10.3109/14017437609167789. PMID: 951591.
8. Saleemi SA, Alothman B, Alamer M, Alsayari S, Almogbel A, Mohammed S. Tuberculosis presenting as metastatic lung cancer. Int J Mycobacteriol. 2021 Jul-Sep;10(3):327-329. doi: 10.4103/ijmy.ijmy_89_21. PMID: 34494575.
9. Lang S, Sun J, Wang X, Xiao Y, Wang J, Zhang M, Ao T, Wang J. Asymptomatic pulmonary tuberculosis mimicking lung cancer on imaging: A retrospective study. Exp Ther Med. 2017 Sep;14(3):2180-2188. doi: 10.3892/etm.2017.4737. Epub 2017 Jul 9. PMID: 28962139; PMCID: PMC5609136.
10. Hammen I. Tuberculosis mimicking lung cancer. Respir Med Case Rep. 2015 Jul 10;16:45-7. doi: 10.1016/j.rmcr.2015.06.007. PMID: 26744652; PMCID: PMC4681891.
11. Nisha Salim Parveen, Bushra Khan. Tuberculosis Mimicking As Lung Cancer. Sch J Med Case Rep, 2023 Apr. 11(4): 444-447.
12. Patel SM, Iyer A, Jayalakshmi TK, Nair G. Endobronchial tuberculosis mimicking malignancy. Lung India. 2015 Sep-Oct;32(5):508-10. doi: 10.4103/0970-2113.164169. PMID: 26628772; PMCID: PMC4587012.
13. Kaur H, Singh D, Pandhi N. Pulmonary Tuberculosis Mimicking Lung Cancer, and Metastasis Radiologically-A Case Report. J Clin Med Res. 2021;3(1):1-4.
14. Xiang Y, Huang C, He Y, Zhang Q. Cancer or Tuberculosis: A Comprehensive Review of the Clinical and Imaging Features in Diagnosis of the Confusing Mass. Front Oncol. 2021 Apr 28;11:644150. doi: 10.3389/fonc.2021.644150. PMID: 33996560; PMCID: PMC8113854.

EDITORIAL POLICY

FOCUS AND SCOPE

The Ethiopian Medical Journal (EMJ) is the official Journal of the Ethiopian Medical Association (EMA) and devoted to the advancement and dissemination of knowledge pertaining to the broad field of medicine in Ethiopia and other developing countries. EMJ is an open access, double blind peer-reviewed medical journal publishing scientifically valued and influential research outputs in the area of clinical medicine, conventional modern medicine, biomedical research, Preventive medicine, traditional medicine, and other related researches in the broad area of Medicine. Prospective contributors to the Journal should take note of the instructions of Manuscript preparation and submission to EMJ which is available on the journal website.

OVERVIEW

Ethiopia's oldest medical journal, The Ethiopian Medical Journal (EMJ) is the official organ of the Ethiopian Medical Association (EMA). The EMJ is devoted to the advancement and dissemination of knowledge pertaining to the broad field of medicine in Ethiopia and other developing countries. The journal first appeared in July 1962 and has been published quarterly (January, April, July, October) without interruption ever since. It has been published in both online (eISSN 2415-2420) (www.emjema.org) and hard copy (ISSN0014-1755) versions. The EMJ continues to play an important role in documenting and disseminating the progress of medical sciences, and in providing evidence for health policy and clinical practice in Ethiopia and Africa at large. Our online journal is open access. Hard copies of the issues of the journal are distributed to institutions and organizations (national and international) based on official subscription.

PEER-REVIEW POLICY

The scientific quality of articles published on EMJ are assessed through a rigorous double-blind peer review system. The integrity of the manuscript with respect to its originality, scientific soundness, methodological relevance and significance to the broad field of medicine is determined by the help of independent researchers in the specific area of the submitted manuscript. The peer-reviewers are recruited from different national and international institutions with relevant professional and research experience.

The Ethiopian Medical Journal uses a double-blind review system for all manuscripts. Each manuscript is reviewed by at least two reviewers. The reviewers are not aware of the list of authors submitting the manuscript sent for their review. The reviewers act independently, and they are not aware of each other's identities. The reviewers are selected solely based on their relevant expertise for evaluating a manuscript. They must not be from the same institution as the author(s) of the manuscript, nor be their co-authors in the recent past. The purpose of peer review is to assist the authors in improving papers and the Editorial Board in making decision on whether to accept or reject a manuscript. Reviewers are requested to decline if they have a conflict of interest or if the work does not fall within their expertise.

MANUSCRIPT MANAGEMENT AND PEER-REVIEW PROCESS

Manuscripts are sent for review only if they pass the initial evaluation (pre-review by the Editorial Board) regarding their style, methodological accuracy, thematic scope, and ethical scientific conduct. Special care is taken to complete the initial (pre-review) evaluation in 3-5 days. The Journal policy is to minimize time from submission to publication without reducing peer review quality. Currently the total period from the submission of a manuscript until its publication takes an average of six months. Peer reviewers are requested to respond within four weeks. During the review process, the Editor-in-Chief may require authors to provide additional information (including raw data) if they are necessary for the evaluation of the manuscript. These materials shall be kept confidential and must not be used for any other purposes. The entire review process takes place under the supervision of the Editor-in-Chief in an online environment, with the assistance of the Journal Secretariat. The online system also allows authors to track the manuscript review progress.

The detailed procedures for manuscript 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" (available online on the journal website and published with all issues starting from February 2016), (ii) relevance of the article to the objectives of the EMJ, (iii) clarity of presentation, and (iv) plagiarism by using appropriate software.style.
- The Editorial Board has three options: accept manuscripts for external review, return it to the author(s) 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 reviewer for brief communica-tion, case reports, and teaching articles or two or more reviewers with appropriate expertise for original articles. 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 to 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 in 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.

RESPONSIBILITIES

Responsibility of authors

Authors are required to submit manuscripts according to the author's guidelines of EMJ. This is provided in the '*Guidelines to Authors' on the journal website and also appears in each issue of the Journal. Authors must guarantee* that their manuscripts are their original work, that they have not been published before, and are not under consideration for publication elsewhere. Parallel submission of the same paper to another journal constitutes misconduct and eliminates the manuscript from further consideration. Work that has already been published elsewhere cannot be reprinted in the Ethiopian Medical Journal. Additionally, if any related work has been submitted or published elsewhere, authors should notify the journal and submit a copy of it with their submission and describe its relation to the submitted work. Authors are exclusively responsible for the contents of their submissions and must make sure that the authors listed in the manuscript include all and only those authors who have significantly contributed to the submitted manuscript. If persons other than authors were involved in important aspects of the research project and the preparation of the manuscript, their contribution should be acknowledged in the Acknowledgments section.

It is the responsibility of the authors to specify the title and code label of the research project within which the work was created, as well as the full title of the funding institution. In case a submitted manuscript has been presented at a conference in the form of an oral presentation (under the same or similar title), detailed information about what was published in proceedings of the conference shall be provided to the Editor-in-Chief upon submission. Authors are required to properly cite sources that have significantly influenced their research and their manuscript. Parts of the manuscript, including text, equations, pictures, tables and graphs that are taken verbatim from other works must be clearly marked, e.g. by quotation marks accompanied by their location in the original document (page number), or, if more extensive, given in a separate paragraph. Full references of each quotation (in-text citation) must be listed in the separate reference section in a uniform manner, according to the citation style used by the journal. References section should list only quoted/cited, and not all sources used for the preparation of a manuscript.

When authors discover a significant error or inaccuracy in their own published work, it is their obligation to promptly notify the Editor-in-Chief and cooperate with him/her to retract or correct the paper. Authors should disclose in their manuscript any financial or other substantive conflict of interest that might have influenced the presented results or their interpretation. By submitting a manuscript, the authors agree to abide by the Editorial Policies of the Ethiopian Medical Journal.

Complaints and appeals

In case that the authors have serious and reasonable objections to the reviews and decision on their manuscripts, they can appeal to the Editor-in-Chief and the Editorial Board will assess whether the review is objective and whether it meets academic standards. If there is a doubt about the objectivity or quality of review and the decision, the Editor-in-Chief will assign additional reviewer(s). Additional reviewers may also be assigned when reviewers' decisions (accept or reject) are contrary to each other or otherwise substantially incompatible. The final decision on the acceptance of the manuscript for publication rests solely with the Editor-in-Chief. The decision on appeal may take extra time due to the regular work of the journal.

Responsibilities of the Editorial Board

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.

Responsibilities of reviewers

Reviewers are required to provide 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 a manuscript for the compliance with the 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 presentation 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 including any duplicate submissions or publications during the review process. 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

Researches Involving Human Participants

Manuscripts of research outputs conducted on human participants should be carried out only by or strictly supervised by, suitably qualified and experienced investigators and in accordance with a protocol that clearly states the aim of the research, the reasons for proposing that it involves human subjects, the nature and degree of any known risks to the subjects, the sources from which it is proposed to recruit subjects, and the means proposed for ensuring that subjects' consent will be adequately informed and voluntary. The protocol should be scientifically and ethically approved by one or more suitably constituted review bodies, independent of the investigators basically operating within the legal framework of each specific country or territory at which the study was conducted and operating with the internationally reputed ethical standards.

Explicitly:

- Any studies involving human participants should be approved by legally registered and accredited institutional review board (IRB) or equivalent research ethics review committee.
- Compliance with the ethical practices and its approval by the responsible IRB should be declared at submission and the review board approval document should be submitted upon request by EMJ
- How the informed consent was sought should be explained clearly with required details.
- Any clinical investigation must be conducted according to the principles expressed in ethical principles for medical research involving human subjects with the internationally reputed ethical standards specifically according to Declaration of Helsinki.
- Clinical trials should provide trial registration details, the study protocol, and trial study report guideline according to the specific study design.

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.

- The 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 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.
    - nforming officially the author's/reviewer's affiliating institution.
    - The formal, announced retraction of publications from the journal in accordance with the Retraction Policy.
    - 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 Responsibilities of authors;

* 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, submitted manuscripts will go through rigorous plagiarism detection process using standard software. The results obtained are verified by the Editorial Board in accordance with the guidelines and recommendations of the Committee on Publication Ethics (COPE).

Confidentiality

EMJ is committed to ensuring the integrity of the peer review process, in accordance with COPE guidelines. Until publication, we strictly keep confidentiality of manuscripts or materials submitted. Reviewers are also required to treat all submitted manuscripts confidentially to make the review process strictly confidential. They should not share information about the manuscript under their review with any third parties. Any breach of confidentiality during the review process will follow COPE guidelines.

Conflict of interest

According to the World Association of Medical Editors (WAME), existence of conflict of interest should be reported if there is a divergence between an individual's private interests (competing interests) and his or her responsibilities to scientific and publishing activities such that a reasonable observer might wonder if the individual's behavior or judgment was motivated by considerations of his or her competing interests. It is the responsibility of authors to disclose any financial/other interest that may have influenced the development of the manuscript. If the reviewers perceive any possible conflict of interest for manuscripts they are assigned to review, they should disclose it and they should decline the review of such manuscripts if needed. The same also applies to the editors.

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 according to Retraction guidelines | COPE: Committee on Publication Ethics. 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 contents are 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 Copyright & 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.

COPYRIGHT & LICENSING

Copyright

Authors retain copyright of the published papers and grant to the publisher the non-exclusive right to publish the article, to be cited as its original publisher in case of reuse, and to distribute it in all forms and media.

Users are required to provide full bibliographic description of the original publication (authors, article title, journal title, volume, issue, pages), as well as its DOI code. In electronic publishing, users are also required to link the content with the original article published in the Ethiopian Medical Journal. Authors can enter into separate, additional contractual arrangements for the non-exclusive distribution of the journal's published version of their work (e.g., post it to an institutional repository or publish it in a book), with an acknowledgement of its initial publication in this journal.

Self-archiving policy

Authors are permitted to deposit publisher's version (PDF) of their work in an institutional repository, subject based repository, author's personal website (including social networking sites, such departmental websites at any time after publication. Full bibliographic information (authors, article title, journal title, volume, issue, pages) about the original publication must be provided and links must be made to the article's DOI and the license.

Disclaimer

The views expressed in the published works do not express the views of the Editors and the Editorial Staff of the Ethiopian Medical Journal. The authors take legal and moral responsibility for the ideas expressed in the articles. The Publisher (The Ethiopian Medical Association) shall have no liability in the event of issuance of any claims for damages. The Publisher will not be held legally responsible should there be any claims for compensation.

.

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 resubmitting 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.

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:

e-mail: emjeditor2018@gmail.com **Tel**. 251-1-158174 or 251-1-533742; **Fax**: 251-1-533742

The Journal contains original articles and research of special relevance to the broad issue of medicine in Ethiopia and in other developing countries. It is listed in the *Index Medicus* and *Current Contents*. Its ISSN number is ISSN 0014–1755.

If you wish to subscribe to the Journal, please complete the section below and return it to the Secretary. The Subscription rates are:

Ethiopia: Eth. Birr 700.00 annually, postage included; **World-wide: US$ 200, airmail postage included**

…….

Request to: The Secretary, *Ethiopian Medical Journal,* P. O. Box 3472, Addis Ababa, Ethiopia. I wish to subscribe to the *Ethiopian Medical Journal* for the Year(s) ……. to …….

Name .....……..

Address .....……

I enclose my subscription fee of .....

Signed .....

Cheques should be made payable to the *Ethiopian Medical Journal*. If payment is made by Bank Transfer (A/C No. 1000000892932, Commercial Bank of Ethiopia, Addis Ababa Branch), please ensure that the Secretary of the Ethiopian Medical Journal is notified of the transfer.

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 .....….