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Editorial

Bolstering an accountability system and a just culture for healthcare safety in Ethiopia

Bereket Yakob[1*]

[1]Fenot Project, University of British Columbia, School of Public Health and Population, Addis Ababa, Ethiopia,

Corresponding author*: bereket.yota@ubc.ca

The prevalence of healthcare errors is increasing despite efforts by governments, health agencies, and advocacy organizations. Though avoidable, they are causing deaths, complications, disability, and economic losses. A meta-analysis of evidence shows that one in 20 patients is harmed, and 12% is severely harmed or died from preventable healthcare errors (1). Technological advances have helped record, trace, report, and regulate medical errors and hazards, but significant achievements are only future targets. With the increasing renaissance of patient rights and calls for respectful care and accountability, health systems face more pressure than ever. Developing countries face increased challenges in reducing healthcare safety lapses, addressing medicolegal complaints, and compensating damages caused by errors.

Improvements in the quality of care in Ethiopia have not matched the pace of expansion of health infrastructure, resulting in a considerable prevalence of healthcare errors and medicolegal claims. For instance, a recent study in Ethiopia showed that 57% of patients had medication errors and 25% of surgical patients had surgical site infections (2), and evidence on the magnitude of deaths due to healthcare errors are lacking. A document review of 127 medicolegal complaints between 2011-17 showed that ethical breaches or medical errors were confirmed in 22%, and 39 (31%) practitioners involved in the care of complaints lodged were handed punitive measures, with none of the health facilities implicated in the corrective actions in Ethiopia (3). The lack of clearly defined legal and professional frameworks for healthcare safety has obstacles to establishing an accountability system in Ethiopia. In addition, for most Ethiopian health facilities, technology is not available or used to monitor the care and conditions of critical patients, and care providers are alerted late to initiate interventions for deteriorating patients.

Shortage of skilled care providers, overburdening staff with many patients and prolonged duty hours, inadequate and ineffective supervision practices, and a lack of equipment and medicines for managing emergency health conditions are prevalent and have exacerbated the slipping of healthcare safety in Ethiopia. Clients' low health literacy, poor adherence to prescribed drugs and behavior, and other health conditions that emerge in due course of treatment contribute to adverse health outcomes. Furthermore, the lack of a sound, contextualized, and meticulous probing and litigation system for complaints of healthcare errors reduces incident reporting.

Therefore, creating a culture of accountability is critical to reducing and mitigating unsafe healthcare practices. A just and blame-free culture enhances cooperation between practitioners and health facilities, reinforcing collective accountability (4). Also, errors are reported and analyzed, individuals and the system units involved in the errors are identified, lessons are learned, and support is provided to prevent future errors in patient safety cultures. If blaming and punitive measures are the main strategies for managing errors, they cause the deterrence of reporting and only reduce opportunities for learning and improvements (5). When the health system, i.e., a poorly designed system, facilitates error occurrence, corporate accountability should be instated, liability costs should be tethered to improve the institution's safety practices, and corrective measures be implemented to enhance learning and improvement (4).

In Ethiopia, an accountability system and a just culture for healthcare safety can be bolstered by creating a supportive environment for practitioners and health enterprises. However, it does not come cheap. Meaningful changes in safety culture require shifting from ‘blame and punish’ the practitioner to ‘disclose, learn, and improve’ strategy (4, 5). Practitioners must have the knowledge, skills, motivation, and passion for adhering to professional and ethical standards that can be promoted by training, coaching, supervising, and giving feedback on time. Health systems, being the owners and regulators of health facilities, should have guidelines and accountability frameworks for healthcare safety and drive the availability of suitable and equipped practice environments. Paying for performance and incentivizing good practices can motivate practitioners to seek new scientific knowledge of managing health conditions and improving safety practices. In addition, digitized medical recording should be prioritized to

strengthen pharmacovigilance and report and analyze errors and incidents. Another area to stress is establishing a 'health court' to enhance a fairer and sensible litigation system for safety complaints, promote transparency, instate joint accountability for errors, govern medicolegal issues, and compensate for damages. Last but not least, supporting and conducting healthcare safety research must be emphasized to assess the status of healthcare safety, management practices, and effectiveness of strategies and indicate solutions to pressing challenges.

References

1. Panagioti, M., et al., Prevalence, severity, and nature of preventable patient harm across medical care settings: systematic review and meta-analysis. BMJ, 2019: p. l4185.
2. Birhanu, Y. and A. Endalamaw, Surgical site infection and pathogens in Ethiopia: a systematic review and meta-analysis. Patient Safety in Surgery, 2020. 14(1): p. 7.
3. Wamisho, B.L., M.A. Tiruneh, and L.E. Teklemariam, Surgical and medical error claims in Ethiopia: trends observed from 125 decisions made by the federal ethics committee for health professionals ethics review. Medicolegal and Bioethics, 2019. 9: p. 23.
4. Mayer, C.M. and D. Cronin, Organizational accountability in a just culture. Urol Nurs, 2008. 28(6): p. 427-30.
5. Eng, D.M. and S.J. Schweikart, Why accountability sharing in health care organizational cultures means patients are probably safer. AMA Journal of Ethics, 2020. 22(9): p. 779-783.

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Original Article

Effect of ACE2 expression inhibiting drugs on COVID-19 disease severity, outcome and length of admission in Ethiopian patients: A causal inference using marginal structural model with inverse probability weight

Tigist W. Leulseged[1*], Ishmael S. Hassen[1], Wuletaw C. Zewde[1], Endalkachew H. Maru[1], Lydia K. Naylor [1], Yakob G. Tsegay[1], Mesay G. Edo[1], Naol A. Baruda [1] Fiseha E. Mihretu[1], Zerihun A. Terefe[1], Nardos T. Kidane[1], Henok N. Desalegn [1], Dawit A. Abebe [1]

[1]Millennium COVID-19 Care Center, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

Corresponding author*: tigdolly@gmail.com

Abstract

Background: *There are varying and contradicting reports and in the face of lack of evidence generated on the effect of ACE2 (Angiotensin-converting enzyme inhibitors) expression inhibiting drugs on COVID-19 Disease. The aim of this study was to assess the effect of acute or chronic ACEIs, ARBs (Angiotensin receptor blockers) and/or NSAIDs (Nonsteroidal anti-inflammatory drugs) use on COVID-19 disease severity, outcome and length of admission among patients with COVID-19 admitted to the Millennium COVID-19 Care Center in Ethiopia.*
Methods: *A retrospective cohort study was conducted among 945 patients with COVID-19 who were on follow up from July 2nd to December 25th, 2020. Data was described using frequency tables and cross tabulations. To identify the effect of ACEIs, ARBs and/or NSAIDs use on COVID-19 disease severity, disease outcome and length of admission, Marginal Structural Model (MSM) with inverse probability weighting (IPW) approach was used.*
Results: *Among the 945 patients studied, 115 (12.2%) had a history of ACEIs, ARBs and/or NSAIDs use. At admission, the majority (39.6%) had mild disease and 272 (28.8%) had severe disease. Among the study participants, 900 (95.2%) were discharged improved and the rest 45 (4.8%) died. The median length of admission was 14.0 days (IQR, 13-16). Multinomial Logistic Regression, Log Binomial Regression and Negative Binomial Regression models were fitted to assess the effect of ACEIs, ARBs and/or NSAIDs use on disease severity, outcome and length of admission respectively. In all the three outcome models, ACEIs, ARBs and/or NSAIDs use didn't show a statistically significant association with the outcomes.*
Conclusion: *Acute or chronic use of ACEIs, ARBs and/or NSAIDs showed no effect on COVID-19 disease severity, outcome and length of admission and therefore should not be withdrawn from patients who need these therapies unless new evidences proving clear contraindications emerge.*

Keywords: *COVID-19, ACEIs, ARBs and/or NSAIDs, retrospective cohort, causal inference, Ethiopia*
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Introduction:

The Coronavirus pandemic has affected the entire world causing a tremendous loss to human life and also caused a burden to the existing health care system making it difficult to provide the best care possible for a better outcome especially in the developing countries. As a result, the World Health Organization (WHO) has continuously improved patient admission, treatment, and discharge criteria to accommodate the growing number of cases with more severe disease categories that require advanced care and close monitoring. To that end, risk stratification based on disease presentation, severity, patient characteristics, existing medical conditions and drug intake history has been given great importance. Therefore, providing preventive services and strict observation for high-risk groups should be strictly applied to prevent deterioration and complication at which point the care provided might not bring favorable results. With this aim, different research studies were conducted with results showing geographical disparity and

also inconsistency even in similar setups calling for the need for more research to be conducted especially in the African setup with limited research reports on COVID-19 so far.

Among the proposed important predictors of COVID-19 disease progression and outcome is a history of taking drugs that inhibit the expression of Angiotensin-converting enzyme 2 (ACE2). This is proposed because of the pathological process of the SARS-CoV-2 virus entry into the body using ACE2. Therefore, taking these type of drugs (ACE inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and nonsteroidal anti-inflammatory drugs (NSAIDs)) increase the level of ACE2 and in turn increasing the possibility of the virus to enter the body [1-3]. Therefore, to better understand the effect of these drugs on disease progression and outcome (hospital/ ICU admission, length of hospital stay, complications, need for mechanical ventilation and mortality), different studies in different countries were conducted reporting contradicting results.

Systematic review and meta-analysis reports demonstrated that there is no increased risk of any of the disease related complication or outcome in those with ACEIs and ARBs intake history [2, 4-6]. In addition, NSAIDs were reported to have no effect on disease progression and outcome in another systematic review [7]. Similarly, studies conducted in Italy, China, Korea, Spain and the United States showed that the use of ACEIs, ARBs and NSAIDs did not affect disease progression, complication and outcome [8-13].

On the contrary, studies conducted in Turkey and Saudi Arabia reported that ACEIs and ARBs therapy were associated with higher risk of severe or critical COVID-19 disease, need of ICU care and higher incidence of in-hospital death [14, 15]. As opposed to this, studies conducted in Kuwait, China and Canada showed that use of ACEIs and ARBs is inversely associated with ICU admission and mortality implying that these drugs have a protective effect from adverse disease outcome [3, 16-19].

ACEIs, ARB s and NSAIDs are widely used drugs for the treatment of chronic conditions which are problems in developing countries, as much as it is a developed countries problem, showing an increasing trend in recent years with a larger proportion (77%) of deaths reported from low- and middle-income countries [20]. With such varying and contradicting reports and in the face of lack of evidence generated on the effect of these drugs on the disease in the African population, clinical judgement to continue or discontinue these life-saving medications should solely rely on evidence generated from the local population.

Therefore, the aim of this study was to assess the effect of acute or chronic ACEIs, ARBs and/or NSAIDs use on COVID-19 disease severity, outcome and length of admission among patients with COVID-19 admitted to the Millennium COVID-19 Care Center in Ethiopia from July 2nd to December 25th, 2020.

Methods:

Study setting, design and population

The current study was a cross-sectional study designed to determine the incidence-associated risk factors of bacterial keratitis with their antibiotic susceptibility pattern.

The follow up was made from July 2nd to December 25th, 2020. The source population was all cases of COVID-19 admitted at MCCC with a confirmed diagnosis of COVID-19 using RT-PCR, as reported by a laboratory given mandate to test such patients by the Ethiopian Federal Ministry of Health and who were on follow up from July 2nd to December 25th, 2020 [21].

All consecutively admitted patients with COVID-19 during the follow up period and who consented to participate were included in the study. With these criteria, a total of 945 patients with COVID-19 were included in the final analysis.

Operational Definitions

COVID-19 disease [22]:

Mild Disease: characterized by fever, malaise, cough, upper respiratory symptoms, and/or less common features of COVID-19 (headache, loss of taste or smell etc…)

Moderate Disease: Patients with lower respiratory symptom/s. They may have infiltrates on chest X-ray. These patients are able to maintain oxygenation on room air.

Severe COVID-19 disease: Includes patients who have developed complications. The following features can define severe illness.

- Hypoxia: SPO2 ≤ 93% on atmospheric air or PaO2:FiO2 < 300mmHg (SF ratio < 315
- Tachypnea: in respiratory distress or RR>30 breaths/minutes
- More than 50% involvement seen on chest imaging

Data Collection Procedures and Quality Assurance

Data was extracted from patients' admission, follow up and discharge medical records using a pretested electronic data abstraction tool that is adopted from the WHO CRF (case record form)

by trained data collectors [23]. Appropriate infection prevention and control measures were followed during the data collection process. Data quality was further assured through double data entry, and data cleaning through checking for inconsistencies, numerical errors and missing parameters. Where discrepancies are observed, data entered was verified with the primary data source. Once data cleaning was complete, data was exported to STATA software version 14 (College Station, TX) for analysis

Statistical Analysis

Data was summarized using frequency tables and percentages. To compare the socio-demographic and clinical characteristics between the two groups (ACEIs, ARBs and/or NSAIDs users Vs Non users), Chi-square test, Fischer's exact test and independent t-test were used.

To identify the effect of ACEIs, ARBs and/or NSAIDs use on COVID-19 disease severity (mild vs moderate vs severe), disease outcome (alive vs dead) and length of admission (in days), Marginal Structural Model (MSM) with inverse probability weighting (IPW) approach was used.

Treatment model

The treatment model that uses binary logistic regression was fitted to estimate the probability of exposure given the covariates (propensity score). The estimated probability of exposure was used to compute the inverse probability weights for each individual. The inverse of the probability of exposure was then used to weight each individual in the estimation of the marginal odds ratio. Variables to be included in the final treatment model were selected by univariate analysis at 25% level of significance and also based on the existing literature reviewed.

Outcome models

There are three outcome variables in this study; disease severity (mild vs moderate vs severe), disease outcome (alive vs dead) and length of admission (in days). All the three outcomes were predicted by including the treatment variable alone in the respective models after adjusting for inverse probability weights.

To identify the effect of treatment on COVID-19 disease severity, Multinomial Logistic Regression model was used where adjusted relative risk (ARR), P-value and 95% CI for ARR were used to test the presence of statistically significant relationship.

To identify the effect of treatment on COVID-19 disease outcome, Log Binomial Regression model was used where adjusted relative risk (ARR), P-value and 95% CI . for ARR were used to test the presence of statistically significant relationship.

To identify the effect of treatment on length of admission, Negative Binomial Regression model was used where adjusted relative risk (ARR), P-value and 95% CI for ARR were used to test the presence of statistically significant relationship. Negative binomial Poisson regression model was used instead of Standard Poisson regression model because the assumption of Standard Poisson regression model (mean equals variance) was checked and there was over dispersion depicted by comparison of mean and variance of the outcome variable and confirmed by the significance of dispersion parameter. And finally Model fitness was checked for the Negative binomial Poisson regression model using Pearson chi square and deviance tests and the model fits the data well.

In all the three models, with a p-value of ≤ 0.05, the treatment was considered as a significant predictor of disease severity.

Ethics approval and consent to participate

The study was conducted after obtaining ethical clearance from St. Paul's Hospital Millennium Medical College Institutional Review Board. Written informed consent was obtained from the participants. The study had no risk/negative consequence on those who participated in the study. Medical record numbers were used for data collection and personal identifiers were not used in the research report. Access to the collected information was limited to the principal investigator and confidentiality was maintained throughout the project. And all methods were carried out in accordance with relevant national guidelines and regulations.

Results

Socio-demographic and clinical characteristics

The median age of the participants was 41 (IQR, 29-58) years. More than half of the participants were males (60.6%). Four hundred thirteen (43.7%) had a history of one or more preexisting co-morbid illness. The majority had hypertension (26.9%) followed by Type II diabetes mellitus (TIIDM) (18.5%) and Asthma (5.5%). The most common reported symptoms were cough (52.9%), shortness of breath (SOB) (27.1%), fatigue (24.4%) and fever (21.8%).

One hundred fifteen (12.2%) had a history of ACEIs, ARBs and/ or NSAIDs use. At admission, the majority (39.6%) had mild disease and 272 (28.8%) had severe disease.

Among the study participants, 900 (95.2%) were discharged improved and the rest 45 (4.8%) died. The median length of admission was 14.0 days

Table 1: Socio–demographic and clinical characteristics (n=945)

Variable	Frequency (%)	Variable	Frequency (%)
Age category (in years)		Runny nose	
< 30	250 (26.5)	No	875 (92.6)
30-39	177 (18.7)	Yes	70 (7.4)
40-49	170 (18.0)	Chest pain	
50-59	125 (13.2)	No	802 (84.9)
≥ 60	223 (23.6)	Yes	143 (15.1)
Sex		Myalgia	
Female	372 (39.4)	No	812 (85.9)
Male	573 (60.6)	Yes	133 (14.1)
Preexisting Co-morbid illness		Arthralgia	
No	532 (56.3)	No	812 (85.9)
Yes	413 (43.7)	Yes	133 (14.1)
Cardiac		Fatigue	
No	886 (93.8)	No	714 (75.6)
Yes	59 (6.2)	Yes	231 (24.4)
Hypertension		SOB	
No	691 (73.1)	No	689 (72.9)
Yes	254 (26.9)	Yes	256 (27.1)
Type II Diabetes Mellitus		Headache	
No	770 (81.5)	No	793 (83.9)
Yes	175 (18.5)	Yes	152 (16.1)
Asthma		ACEIs, ARBs and/or NSAIDs use	
No	893 (94.5)	No	830 (87.8)
Yes	52 (5.5)	Yes	115 (12.2)
Fever		COVID-19 Severity	
No	739 (78.2)	Mild	374 (39.6)
Yes	206 (21.8)	Moderate	299 (31.6)
Cough		Severe	272 (28.8)
No	445 (47.1)	Outcome	
Yes	500 (52.9)	Alive	900 (95.2)
Sore throat		Dead	45 (4.8)
No	827 (87.5)		
Yes	118 (12.5)		

Comparison of socio-demographic and clinical characteristics based on drug use history

Based on the chi-square or Fisher's exact test and independent t-test result, a significant difference between those who has a history of ACEIs, ARBs and/or NSAIDs use and those who don't indicated that the two groups showed a significant difference in age category, the presence of shortness of breath, disease severity, outcome and length of admission.

Accordingly, a significantly higher proportion of patients who has a history of ACEIs, ARBs and/or NSAIDs use are in the age range of 50-59 years (27.0 % Vs 11.3%, p-value<0.0001) and 60 years and older (47.0 % Vs 20.4%, p-value<0.0001) compared to those with no drug use history.

In addition, patients with a history of ACEIs, ARBs and/or NSAIDs use were found to present with shortness of breath and severe COVID-19 at a significantly higher proportion as compared with those with no

drug use history (41.7% % Vs 25.1%, p-value<0.0001 for shortness of breath and 47.0% % Vs 26.3%, p-value<0.0001 for severe COVID-19). Moreover, a significantly higher proportion of patients with a history of ACEIs, ARBs and/or NSAIDs use died of COVID-19 compared to those with no drug use history (9.6% % Vs 4.1%, p-value=0.010).

Furthermore, a statistically significant difference was observed in the length of admission, where having a history of ACEIs, ARBs and/or NSAIDs use was associated with a delayed recovery compared to those with no drug use history (14.5 days Vs 14.4 days, p-value=0.002). But this difference might not have a significant clinical implication. **(Table 2**)

Table 2: Comparison of socio-demographic and clinical characteristics based on drug use history (n=945)

Variable	ACEIs, ARBs and/or NSAIDs use		p-value
	No (n=830)	Yes (n=115)	
Age category (in years)			
< 30	246 (29.6 %)	4 (3.5 %)	<0.0001*
30-39	168 (20.2 %)	9 (7.8 %)	
40-49	153 (18.4 %)	17 (14.8 %)	
50-59	94 (11.3 %)	31 (27.0 %)	
≥ 60	169 (20.4 %)	54 (47.0 %)	
Sex			
Female	332 (40.0 %)	40 (34.8 %)	0.283
Male	498 (60.0 %)	75 (65.2 %)	
Fever			
No	642 (77.3 %)	97 (84.3 %)	0.088
Yes	188 (22.7 %)	18 (15.7 %)	
Cough			
No	385 (46.4 %)	60 (52.2 %)	0.244
Yes	445 (53.6 %)	55 (47.8 %)	
Sore throat			
No	726 (87.5 %)	101 (87.8 %)	0.914
Yes	104 (12.5 %)	14 (12.2 %)	
Runny nose			
No	767 (92.4 %)	108 (93.9 %)	0.564
Yes	63 (7.6 %)	7 (6.1 %)	
Chest pain			
No	706 (85.1 %)	96 (83.5 %)	0.657
Yes	124 (14.9 %)	19 (16.5 %)	
Myalgia			
No	712 (85.5 %)	100 (87.0 %)	0.735
Yes	118 (14.2 %)	15 (13.0 %)	
Arthralgia			
No	712 (85.8 %)	100 (87.0 %)	0.735
Yes	118 (14.2 %)	15 (13.0 %)	
Fatigue			
No	626 (75.4 %)	88 (76.5 %)	0.797
Yes	204 (24.6 %)	27 (23.5 %)	
SOB			
No	622 (74.9 %)	67 (58.3 %)	<0.0001*
Yes	208 (25.1 %)	48 (41.7 %)	
Headache			
No	695 (83.7 %)	98 (85.2 %)	0.685
Yes	135 (16.3 %)	17 (14.8 %)	
COVID-19 Severity			
Mild	344 (41.4 %)	30 (26.1 %)	<0.0001*
Moderate	268 (32.3 %)	31 (27.0 %)	
Severe	218 (26.3 %)	54 (47.0 %)	
Outcome			
Alive	796 (95.9 %)	104 (90.4 %)	0.010*
Dead	34 (4.1 %)	11 (9.6 %)	
Length of admission (in days)	14.5 (5.03)	14.4 (5.99)	0.002*

Treatment model: Logistic regression of factors affecting use of ACEIs, ARBs and/or NSAIDs

The treatment model using a binary logistic regression model was run by including variables that were significant on univariate analysis at 25% level of significance and also from variables selected to be useful based on literature review [24-32].

Table 3: Treatment model: Binary Logistic Regression model of factors affecting use of ACEIs, ARBs and/or NSAIDs (n=945)

Variables	AOR	95% CI for AOR	p-value
Age category (in years)			
< 30	1	1	
30-39	2.07	0.58, 7.32	0.261
40-49	1.69	0.49, 5.73	0.398
50-59	3.82	1.14, 12.79	0.030*
≥ 60	1.89	0.57, 6.37	0.300
Male sex (Vs Female)	1.83	1.08, 3.11	0.025*
Cardiac illness (Yes Vs No)	9.95	4.69, 21.09	<0.0001*
Hypertension (Yes Vs No)	14.87	7.89, 28.01	<0.0001*
Type II Diabetes Mellitus (Yes Vs No)	1.52	0.88, 2.64	0.137
Asthma (Yes Vs No)	1.69	0.66, 4.32	0.278
Fever (Yes Vs No)	0.69	0.33, 1.44	0.323
Cough (Yes Vs No)	0.57	0.31, 1.04	0.065
Sorethroat (Yes Vs No)	1.06	0.46, 2.43	0.895
Runny nose (Yes Vs No)	1.40	0.47, 4.18	0.543
Chest pain (Yes Vs No)	1.49	0.69, 3.25	0.313
Myalgia (Yes Vs No)	1.31	0.53, 3.22	0.558
Arthralgia (Yes Vs No)	0.62	0.23, 1.72	0.360
Fatigue (Yes Vs No)	0.53	0.25, 1.12	0.095
Shortness of breath Yes Vs No)	1.67	0.87, 3.19	0.121
Headache (Yes Vs No)	1.55	0.75, 3.24	0.239

Note: AOR, Adjusted Odds ratio; CI, Confidence interval; *statistically significant

Accordingly, age category, sex, cardiac illness, hypertension, TIIDM, asthma, fever, cough, sore throat, runny nose, chest pain, myalgia arthralgia, fatigue, shortness of breath and headache were included in the final treatment model. By fitting the final treatment model, propensity score was estimated and it was used to compute the inverse probability weights for each individual. The inverse of the probability of exposure was then used to weight each individual in the estimation of the marginal odds ratio. (**Table 3**)

Outcome Model: Effect of ACEIs, ARBs and/or NSAIDs use on disease severity, outcome and length of admission

Three outcome models; Multinomial Logistic Regression, Log Binomial Regression and Negative Binomial Regression models were fitted to assess the effect of ACEIs, ARBs and/or NSAIDs use on disease severity, outcome and length of admission respectively. To predict all the three outcomes, the treatment variable was fitted as an explanatory variable after adjusting for inverse probability weights.

The result shows that patients who were taking ACEIs, ARBs and/or NSAIDs had a slightly increased risk of progressing to severe disease and dying from COVID-19. On all the three outcome models, ACEIs, ARBs and/or NSAIDs use didn't show a statistically significant association with all the three outcomes at 5% level of significance. (**Table 4, 5 and 6**)

Table 4: Multinomial logistic regression of Effect of ACEIs, ARBs and/or NSAIDs use on disease severity (n=945)

Variable	Moderate (Vs Mild)		Severe (Vs Mild)	
	ARR (95% CI)	P-value	ARR (95% CI)	P-value
ACEIs, ARBs and/or NSAIDs				
No	1		1	
Yes	0.76 (0.25, 2.31)	0.628	1.21 (0.45, 3.27)	0.708

Note: ARR, Adjusted Relative Risk; CI, Confidence Interval; *statistically significant

Table 5: Log binomial regression of Effect of ACEIs, ARBs and/or NSAIDs use on disease outcome (n=945

Variable	Death(Vs Disharged improved) ARR (95% CI)	P-value
ACEIs, ARBs and/or NSAIDs		
No	1	
Yes	1.14 (0.27, 4.82)	0.861

Note: ARR, Adjusted Relative Risk; CI, Confidence interval; *statistically significant

Table 6: Negative binomial regression of Effect of ACEIs, ARBs and/or NSAIDs use on length of admission (n=945)

Variable	Length of admission ARR (95% CI)	P-value
ACEIs, ARBs and/or NSAIDs		
No	1	
Yes	0.99 (0.88, 1.11)	0.842

Note: ARR, Adjusted Relative Risk; CI, Confidence interval; *statistically significant

Discussion

In this study, we assessed the effect of acute or chronic ACEIs, ARBs and/or NSAIDs use on COVID-19 disease severity, outcome and length of admission among patients with COVID-19 admitted to the Millennium COVID-19 Care Center in Ethiopia from July 2nd to December 25th, 2020. To our knowledge, this is the first study conducted in the African set up. Understanding this helps (provides an input) in modifying the risk stratification, prevention and admission practices so that better patient outcome can be achieved.

One hundred fifteen (12.2%) had a history of ACEIs, ARBs and/or NSAIDs use. At admission, the majority (39.6%) had mild disease and 272 (28.8%) had severe disease. Among the study participants, 900 (95.2%) were discharged improved and the rest 45 (4.8%) died. The median length of hospital admission was 14.0 days (IQR, 13-16).

On comparison of the characteristics of the cohort based on the other exposure variables and the outcomes, a significant difference was observed in some characteristics. Accordingly, a significantly higher proportion of patients with a history of ACEIs, ARBs and/or NSAIDs were 50 years and older, had shortness of breath at admission, severe disease at presentation, had delayed recovery and died from the disease. But on further regression analysis using MSM model with IPW approach, use of ACEIs, ARBs and/or NSAIDs did not show a significant effect on disease severity, outcome and length of admission. Although there are few contradictory reports showing that these drugs have a significant effect on both directions affecting the disease outcome both negatively and positively [14-16], this finding is supported by a number of other institution and community based studies including systematic reviews conducted in non-African setup [4-13]. In addition, a WHO review based on studies conducted outside Africa also showed that there is no well-established evidence that patients on these drugs are at higher risk of poor outcome [32]. It is not known if the finding of the study has consistency across Africa as there is no similar study conducted in the continent so far.

ACEIs, ARBs and/or NSAIDs are drugs which are widely used for the treatment of chronic medical conditions. In the current study, chronic medical conditions were reported in 413 (43.7%) of the participants among which hypertension and cardiac disease, which rely mainly on these drugs for treatment and control, constitutes 313 (75.8%) of the co-morbid illnesses. In addition, at the global and national level, these conditions are found in a considerable proportion of the general population, implying that the issue of continuing or discontinuing these drugs in patients with COVID-19 will continue to be raised. These medical conditions are also found to be significant determinants of disease severity and outcome among patients with COVID -19 [24, 7]. Part of COVID-19 management is stabilizing existing co-morbid conditions so that the body can be at its best immunity for fighting the virus. Therefore, taking these medications is crucial to control the co-morbid conditions which otherwise could exacerbate and lead to progression of the disease leading to complications and death as demonstrated by findings of researches conducted in Ethiopia and other African countries [24-28, 31, 38-40].

Therefore, the use of these drugs is crucial as part of the management of patients with COVID-19

with co-morbid conditions without affecting the COVID -19 disease severity, outcome and length of admission [2, 4-6] or even with the possibility of leading to improved outcome as indicated by recent reports [1-3, 17-19].

The following strengths and limitations should be considered when interpreting the study findings. Its strength is that, it is the only study conducted in the country and one of the few in Africa. In addition, the study is conducted in Ethiopia's largest COVID-19 Center, which also serves as a national referral center, and thus is representative of patients across the country. The other strength is the use of causal inference model to answer the research question which can give us a more accurate inference about the causal relationship between the exposure and outcome. It does, however, have the following limitations: behavioral factors, laboratory and radiologic parameters were not included in the study because information on these variables were not consistently available for every participant.

Conclusion

Based on the finding of this study, acute or chronic use of ACEIs, ARBs and/or NSAIDs showed no effect on COVID-19 disease severity, outcome and length of admission. As a result, unless new evidences proving clear contraindications emerge, we recommend that clinical decision in favor of continuing these drugs for the greater benefit of controlling the co-morbid conditions of patients of any COVID-19 severity would benefit the patient more.

List of Abbreviations

ACE2……Angiotensin-converting enzyme 2
ACEIs……Angiotensin-converting enzyme inhibitors
ARBs……. Angiotensin receptor blockers
ARR…….....Adjusted relative risk
CI…….Confidence Interval
COVID-19…...Coronavirus Disease 2019
IPW……..Inverse probability weighting
IQR……. Interquartile range
NSAIDs……...Nonsteroidal anti-inflammatory drugs
MSM……Marginal Structural Model
OR ……...Odds Ratio
RT-PCR…… Real Time Polymerase Chain Reaction
SARS-COV-2……Severe Acute Respiratory Syndrome Coronavirus 2
TIIDM……Type II Diabetes Mellitus
WHO……. World Health Organization

Consent for publication

Not applicable

Availability of data and materials:

All relevant data are available upon reasonable request from Tigist W. Leulseged, tigdolly@gmail.com.

Competing interests

The authors declare that they have no known competing interests.

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Authors' Contribution:

TWL conceived and designed the study, revised data extraction sheet, performed statistical analysis, and drafted the initial manuscript. ISH, WCZ, EHM, LKN, YGT, MGE, NAB, FEM, ZAT, NTK, HND and DAA contributed to the conception, obtained patient data, reviewed the manuscript and approved the final version.

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Reference

1. Ngcobo GD. Measurement of serum ACE status may potentially improve the diagnosis of SARS-CoV-2 infection. Scientific African. 2021;14:e01039.
2. Ahmad I, Pawara R, Surana S, Patel H. The Repurposed ACE2 Inhibitors: SARS-CoV-2 Entry Blockers of Covid-19. Topics in current chemistry (Cham). 2021;379(6):40.
3. Wu C, Xu Q, Wang H, Tu B, Zeng J, Zhao P, et al. Neutralization of SARS-CoV-2 pseudovirus using ACE2-engineered extracellular vesicles. Acta pharmaceutica Sinica B. 2021.
4. Zhang X, Yu J, Pan L-y, Jiang H-y. ACEI/ARB use and risk of infection or severity or mortality of COVID-19: A systematic review and meta-analysis. Pharmacological Research. 2020;158:104927.

5. van Kimmenade RRJ, Belfroid E, Hoogervorst-Schilp J, Siebelink HJ, Janssen CW, Pinto Y. The effects of ACE2 expression mediating pharmacotherapy in COVID-19 patients. Netherlands Heart Journal. 2021;29 (1):20-34.
6. Mackey K, King VJ, Gurley S, Kiefer M, Liederbauer E, Vela K, et al. Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection in Adults: A Living Systematic Review. Annals of internal medicine. 2020;173(3):195-203.
7. Zhao H, Huang S, Mei K, Shao W, Zhang J, Ma J, et al. Prevalence use of nonsteroidal anti-inflammatory drugs in the general population with COVID-19 and associated COVID-19 risk, hospitalization, severity, death, and safety outcomes: A systematic review and meta-analysis. medRxiv. 2021:2021.05.01.21256428.
8. Felice C, Nardin C, Di Tanna GL, Grossi U, Bernardi E, Scaldaferri L, et al. Use of RAAS Inhibitors and Risk of Clinical Deterioration in COVID-19: Results From an Italian Cohort of 133 Hypertensives. Am J Hypertens. 2020;33(10):944-8.
9. Gao C, Cai Y, Zhang K, Zhou L, Zhang Y, Zhang X, et al. Association of hypertension and antihypertensive treatment with COVID-19 mortality: a retrospective observational study. European heart journal. 2020;41 (22):2058-66.
10. Jung SY, Choi JC, You SH, Kim WY. Association of Renin-angiotensin-aldosterone System Inhibitors With Coronavirus Disease 2019 (COVID-19)- Related Outcomes in Korea: A Nationwide Population-based Cohort Study. Clin Infect Dis. 2020;71(16):2121-8.
11. López-Otero D, López-Pais J, Cacho-Antonio CE, Antúnez-Muiños PJ, González-Ferrero T, Pérez-Poza M, et al. Impact of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on COVID-19 in a western population. CARDIOVID registry. Revista espanola de cardiologia (English ed). 2021;74(2):175-82.
12. Imam Z, Odish F, Gill I, O'Connor D, Armstrong J, Vanood A, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. J Intern Med. 2020;288(4):469-76.
13. Zhou X, Zhu J, Xu T. Clinical characteristics of coronavirus disease 2019 (COVID-19) patients with hypertension on renin-angiotensin system inhibitors. Clin Exp Hypertens. 2020;42(7):656-60.
14. Selçuk M, Çınar T, Keskin M, Çiçek V, Kılıç Ş, Kenan B, et al. Is the use of ACE inb/ARBs associated with higher in-hospital mortality in Covid-19 pneumonia patients? Clin Exp Hypertens. 2020;42(8):738-42.
15. Alrashed AA, Khan TM, Alhusseini NK, Asdaq SMB, Enani M, Alosaimi B, et al. Severity of COVID-19 Infection in ACEI/ARB Users in Specialty Hospitals: A Retrospective Cohort Study. Journal of Infection and Public Health. 2021.
16. ElAbd R, AlTarrah D, AlYouha S, Bastaki H, Almazeedi S, Al-Haddad M, et al. Angiotensin-Converting Enzyme (ACE) Inhibitors and Angiotensin Receptor Blockers (ARB) Are Protective Against ICU Admission and Mortality for Patients With COVID-19 Disease. Front Med (Lausanne). 2021;8:600385.
17. Zhang H, Zhu W, Jin Q, Pan F, Zhu J, Liu Y. Inhalable nanocatchers for SARS-CoV-2 inhibition. 2021;118 (29).
18. Butterworth RF. Potential for the Repurposing of Adamantane Antivirals for COVID-19. Drugs in R&D. 2021;21(3):267-72.
19. Wang X, Lu J, Ge S, Hou Y, Hu T, Lv Y, et al. Astemizole as a drug to inhibit the effect of SARS-COV-2 in vitro. Microbial pathogenesis. 2021;156:104929.
20. World Health Organization. Non-communicable disease report. 13 April 2021.
21. Ethiopian Federal Ministry of Health. Covid19 Management Handbook. 2020.
22. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance. . Geneva: March 2020
23. World Health Organization. COVID-19 Case Record Form Rapid Version. Geneva; March 2020.
24. Leulseged TW, Abebe KG, Hassen IS, Maru EH, Zewde WC, Chamiso NW, et al. COVID-19 disease severity and associated factors among Ethiopian patients: A study of the millennium COVID-19 care center. PloS one. 2022;17(1):e0262896.
25. Leulseged TW, Maru EH, Hassen IS. Predictors of death in severe COVID-19 patients at millennium COVID-19 care center in Ethiopia: a case-control study. PAMJ. 2021;38.

26. Leulseged TW, Alemahu DG, Hassen IS, Maru EH, Zewde WC, Chamiso NW, et al. Factors associated with development of symptomatic disease in Ethiopian COVID-19 patients: a case-control study. BMC infectious diseases. 2021;21(1):759.
27. Leulseged TW, Hassen IS, Ayele BT, Tsegay YG, Abebe DS, Edo MG, et al. Laboratory biomarkers of COVID-19 disease severity and outcome: Findings from a developing country. PloS one. 2021;16 (3):e0246087.
28. Leulseged TW, Hassen IS, Maru EH, Zewsde WC, Chamiso NW, Bayisa AB. Characteristics and outcome profile of hospitalized African patients with COVID-19: The Ethiopian context. PloS one. 2021;16 (11):e0259454.
29. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol. 2020;146(1):110-8.
30. Lechien J, Chiesa-Estomba C, Place S, et al. Clinical and Epidemiological Characteristics of 1,420 European Patients with mild-to-moderate Coronavirus Disease 2019. J I n t e r n M e d. 2020 April 30.
31. Leulseged TW, Hassen IS, Edo MG, Abebe DS, Maru EH, Zewde WC, et al. Duration of Supplemental Oxygen Requirement and Predictors in Severe COVID-19 Patients in Ethiopia: A Survival Analysis. Ethiopian journal of health sciences. 2021;31(4):699-708.
32. Li X, Wang X, Liu Jun, Huang G, Shi X. Epidemiological characteristics of confirmed COVID-19 in Guizhou province, China. Dis a s t e r M e d P u blic H e alt h P r e p. 2020 May 05:1 - 9.
33. World Health Organization. COVID-19 and the use of angiotensin-converting enzyme inhibitors and receptor blockers. May 7, 2021,.
34. Du R-H, Liang L-R, Yang C-Q, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARSCoV-2: a prospective cohort study. Eur Respir J. 2020;2020(55: 2000524).
35. Gupta S, Hayek SS, Wang W, et al. Factors Associated With Death in Critically Ill Patients With Coronavirus Disease 2019 in the US. JAMA Intern Med.2020;e203596.
36. Williamson E.J., Walker A.J., Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature.584:430–6 (2020).
37 Xiaochen Li, Shuyun Xu, Muqing Yu, et al. Risk factors for severity and mortality in dult COVID-19 inpatients in Wuhan. J ALLERGY CLIN IMMUNOL. 2020;146:110-8.
38 Abayomi A, Odukoya O, Osibogun A, Wright O, Adebayo B, Balogun M, et al. Presenting Symptoms and Predictors of Poor Outcomes Among 2,184 Patients with COVID-19 in Lagos State, Nigeria. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2021;102:226-32.
39 Elimian KO, Ochu CL, Ebhodaghe B, Myles P, Crawford EE, Igumbor E, et al. Patient characteristics associated with COVID-19 positivity and fatality in Nigeria: retrospective cohort study. BMJ Open. 2020;10 (12):e044079.
40 Nachega JB, Ishoso DK, Otokoye JO, et al. Clinical Characteristics and Outcomes of Patients Hospitalized for COVID-19 in Africa: Early Insights from the Democratic Republic of the Congo. . Am J Trop Med Hyg. 2020 Oct 2.

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Original Article

Coverage and predictors of pediatric index case testing (ICT) among children of HIV infected parent(s), analysis of population HIV impact assessment (PHIA) surveys

Kesetebirhan Delele Yirdaw[1]*

[1]HIV Service Director, Integrated Services for Health and Development Organization, Addis Ababa, Ethiopia

*Corresponding Author: kesetebirhan@gmail.com

Abstract

Background: *Antiretroviral therapy (ART) coverage in many Sub-Saharan African countries remains low (48%) for children <15 years living with HIV. One possible reason for this low performance is low pediatric HIV case finding. In this study we describe the coverage of HIV testing for children of infected parent(s) (also called index case testing or ICT) and factors affecting it.*

Methods: *Secondary analysis of the Zambia, Malawi, Eswatini, and Tanzania Population HIV Impact Assessment (PHIA) household surveys which were conducted between 2015-2016 were used for this study. Couples , where there is at least one HIV-infected person, were identified and matched to their children <15 years. HIV testing status of children was measured and factors associated with the testing of children were studied using logistic regression. Sampling weights were applied during analysis taking into account the complex sampling design of these surveys.*

Results: *3,435 children <15 years had at least one infected parent. Of those children, 38.9% (32.9%-44.8%) were tested for HIV. Rural areas had more undiagnosed children in all study countries. Maternal HIV testing was associated with the highest odds of testing for children (adjusted Odds ratio: 84.51 (10.72-666)) as was maternal HIV infection (Odds ratio: 5.9 (95% confidence interval (CI): 3.9-8.9)).*

Conclusion: *Pediatric HIV testing for children of HIV infected parent(s) was found to be low. Maternal HIV testing was found to be the single most important factor associated with testing of children of HIV infected parent (s). Rural settings need to be prioritized for ICT in order to address testing gap.*

Key Words: *Pediatric HIV; Index case testing (ICT); PHIA*

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Background

The progress to diagnose 90% of HIV infected adults and put them on treatment has been going well in many PEPFAR-supported sub-Saharan African countries according to UNAIDS with reported treatment coverage of 60%-90% for adults (1). For children, however, the coverage is much lower at an estimated <50% looking at PEPFAR report, and SPECTRUM modeling data (2, 3).

The consequence of undiagnosed and untreated children is detrimental as most end-up having increased morbidity and mortality from opportunistic infections (4). This means around 50% will die before their second birth day (5). A number of factors were identified as contributory for this low treatment coverage. The most important of these factors is low testing and detection of children.

Index case HIV testing (ICT) for children, which is testing of children of HIV infected parent(s), is the most important HIV case finding modality that leads to identification of infected children at high positivity rate (6). It is also associated with early case finding (7).

Even though ICT is the preferred option to identify undiagnosed children, there are several factors leading to the approach not being used optimally. Individual factors included dependence of children on adults for testing (8), caregiver related factors like sense of guilt (9), fear of stigma (10), fear of inadvertent disclosure of HIV status (11), fear of positive result (12), and health system factors like lack of experience with pediatric testing, health care workers considering children low risk, and work load (11, 13). None of these studies have identified individual children and parental socio-demographic factors including HIV testing and infection status as determinants. This study will therefore determine coverage of index case testing (ICT) among children of HIV infected parents and identify determinants at individual level.

Materials and Methods

Study setting and design

Secondary analysis of four Population HIV Impact Assessment (PHIA) studies conducted in Eswatini, Malawi, Tanzania and Zambia are used in this study. These are household surveys with two stage stratified cluster sampling design. Within selected households, a structured questionnaire was used to interview and collect response on variables of interest. Refer to PHIA survey methodologies for the detail. (14) We used a cross-sectional study design to answer the study questions.
Study period: All surveys were conducted from 2015-2016.

Inclusion criteria

all children <15 years who have matching biological parents who consented for home based HIV testing and structured interview were included.

Sample size

taking HIV testing among children <15 for parents where there is at least one HIV infected parent at 50%, acceptable difference of 0.05, assuming design effect of 2, and 901 clusters sampled in the four surveys, a sample size required becomes 768. After inclusion criteria, a sample size of 3,435 was obtained and all were included in the analysis.

Outcome variable

HIV testing status of children <15 years. We also analyzed reason for not getting HIV testing.
Independent variables: child age, child gender, parental gender, parental age, parental education status, wealth status, residence, HIV testing status of parents, HIV infection status of parents, and ART treatment status.

Operational definition

HIV testing: tested for HIV irrespective of being HIV+ or HIV- or being aware of their HIV+ status.

HIV infection: being HIV+ irrespective of HIV testing or awareness of HIV+ status.
Awareness of HIV+ status: knowing HIV+ status. Some people may have tested for HIV in the past while they were HIV negative. Currently they may be HIV infected but may not know they have HIV infection.

ART treatment status: being HIV positive and on antiretroviral therapy.

HIV/ART status: measure of combination of HIV testing, HIV infection, awareness of HIV+ status, and ART treatment status. Here are sub-categories of this variable:

- Not infected, not tested: HIV negative but had never tested for HIV.
- Not infected, tested: HIV negative and had been tested for HIV.
- HIV+ status unknown: HIV positive but status not known whether tested for HIV in the past or not.
- Known+, not on ART: HIV+ and aware of HIV infection status but the person is not on ART.
- Known+, On ART: HIV+ and aware of HIV infection status and on ART.

Data analysis

Stata Version 14.0 statistical software was used for analysis. Sampling weights were applied during calculation of descriptive (frequency, proportion, and mean), and inferential (logistic regression) statistics to measure ICT coverage and identify its determinants taking into account complex sampling design used in PHIA surveys. The role of HIV/ART status in determining ICT coverage of children was analyzed as primary predictor using logistic regression. In addition, each of the following variables was assessed for association with ICT coverage using logistic regression:

- maternal HIV testing, and paternal HIV testing, which were modeled together;
- maternal HIV infection, and paternal HIV infection, which were modeled together;
- awareness of HIV+ status by the mother modeled separately from awareness of HIV+ status by the father as the two subset data don't have identical couples;
- ART treatment status of the mother modeled separately from ART treatment status of the father modeled separately as the two subset data don't have identical couples.

Purposeful selection of variables was used during regression model building. Those with p-value <0.20 during bi-variable analysis were included in the final model. Level of significance was set at 0.05. Pie chart and bar graphs were used to graphically show coverage of testing or gaps. Finally, frequency and percentage were used to describe why children did not receive index case testing.

Ethics statement: This study was done based on secondary analysis of existing data. No human subjects were involved in the study. All databases don't have individual identifiers like names or addresses that can be used to identify people. All PHIA surveys received ethical approval from the institutional review boards of CDC, Columbia University, Westat, the National Institute for Medical Research, and respective country's research and ethics committee before initiation of data collection (14).

Results

Of 13,212 couples included in the surveys, 1,570 had at least one person infected with HIV with a total of 3,435 children (50.9% female, 44.5% under five years, and 34.9% living in urban residence). The average number of children was 2.01 (95% confidence interval (CI): 1.92 -2.09) and 2.36 (95% CI: 2.28-2.44) children per couple with at least one infected parent in urban and rural settings, respectively.

Coverage of ICT

ICT coverage for children <15 years of age born to HIV infected parent(s) varied across different countries with the highest being for Eswatini at 69.8%. The majority undiagnosed children <15 years were located in rural settings, the highest being for Malawi at 83% and the lowest in Zambia at 59.5% (Figure 1)

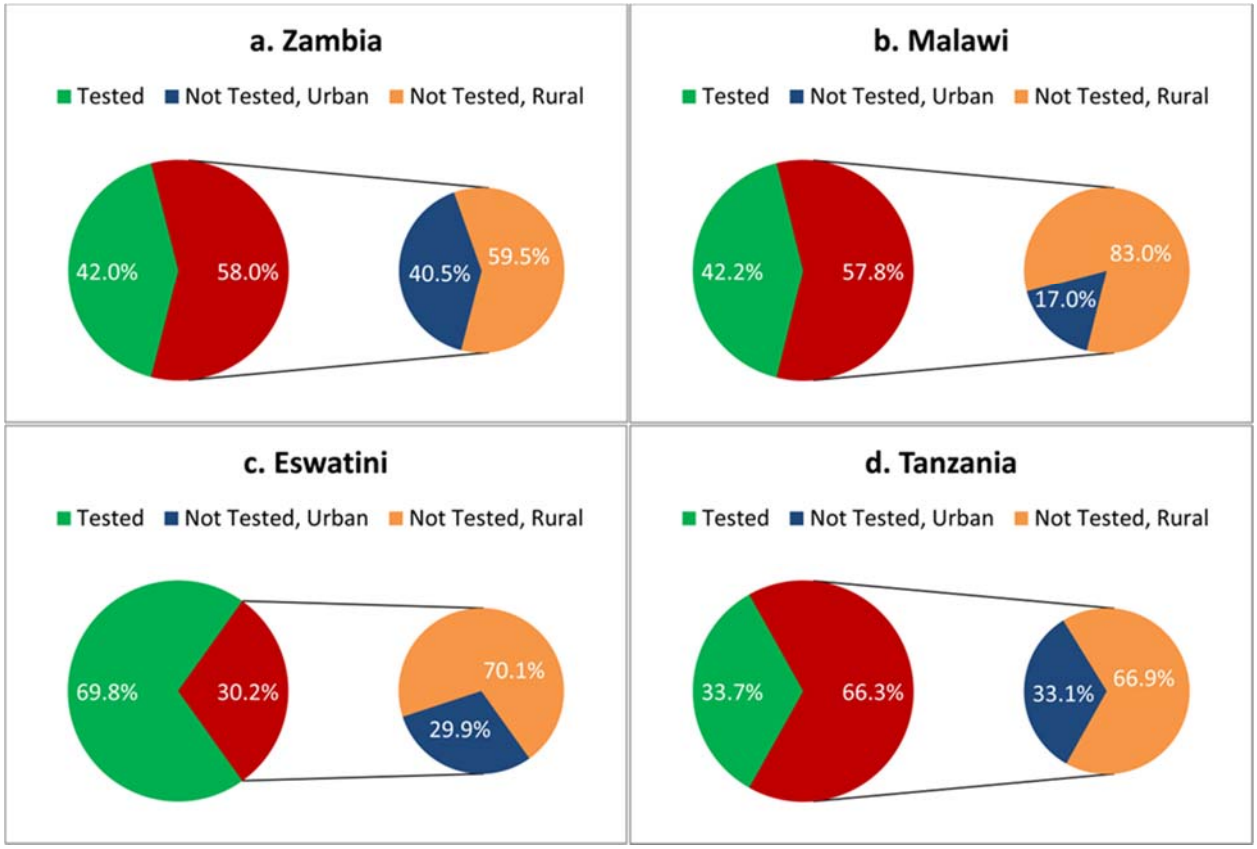

Figure 1. Index Case Testing Coverage by Country and Urban/Rural Settings, by Country:
a. Zambia (tested n=430, not tested n=595, not tested urban n=241, not tested rural=354);
b. Malawi (tested n=417, not tested n=571, not tested urban n=97, not tested rural=474);
c. Eswatini (tested n=397, not tested n=172, not tested urban n=51, not tested rural=121);
d. Tanzania (tested n=192, not tested n=377, not tested urban n=125, not tested rural=252);

Determinants of Coverage of ICT

Looking at determinants of ICT coverage for children <15 years, age of a child and HIV/ART status of the mother (as per operational definition) were found to be independent predictors. Older children (age >5 years old) were found to have lower HIV testing rate, 31.7%, compared to younger children (≤5 years), 47.8% (p value <0.001). Compared to couples where the mother was HIV negative and was never tested (while the father was HIV infected), odds ratio of testing of children was 17.4 (95% CI: 2.4-127.0) when the mother was tested and HIV negative, 15.1 (95% CI: 1.9-120.9) when the mother was infected but status was unknown, 57.5 (95% CI: 7.0-470.5) when the mother was known to be infected but not on ART, and 158.6 (95% CI: 21.4-1178.7) when the mother was infected and on ART. (see Table 1 above)

Table 1. Determinants of HIV Testing among Children <15 years Born to Couples at least one of whom has HIV, data from Four PHIA Surveyed Countries (Zambia, Malawi, Eswatini, and Tanzania), 2015-2016.

Variable	Response	Total n <15 Children	n (%) <15 Children Tested	Odds ratio (95% CI)	P value	Adjusted Odds ratio (95% CI)
Child's Gender	Male	1,688	622 (36.8%)	1	0.305	
	Female	1,747	714 (40.9%)	1.19 (0.85-1.66)		
Child's Age	0-2	733	361 (49.2%)	1	0.002	1
	3-5	795	370 (46.6%)	0.9 (0.59-1.37)		0.97 (0.65-1.45)
	6-10	1,046	294 (28.1%)	0.4 (0.26-0.63)		0.41 (0.25-0.66)
	11-14	861	310 (36.0%)	0.58 (0.34-0.99)		0.59 (0.35-0.99)
Residence	Urban	1,198	555 (46.3%)	1	0.068	
	Rural	2,237	780 (34.9%)	0.62 (0.37-1.04)		
Maternal Age	≤40	1,880	780 (41.5%)	1	0.532	
	41-50	1,194	420 (35.2%)	0.77 (0.48-1.23)		
	>50	361	135 (37.4%)	0.84 (0.36-1.99)		
Paternal Age	≤40	1,575	660 (41.9%)	1	0.422	
	41-50	1,433	502 (35.0%)	0.75 (0.48-1.17)		
	>50	428	173 (40.5%)	0.94 (0.44-2.02)		
Maternal Education	Illiterate	634	257 (40.5%)	1	0.168	
	Primary	2,280	830 (36.4%)	0.84 (0.37-1.92)		
	Secondary	477	223 (46.7%)	1.28 (0.54-3.03)		
	Tertiary	44	25 (58.3%)	2.04 (0.59-7.04)		
Paternal Education	Illiterate	374	93 (25.0%)	1		
	Primary	2,073	783 (37.8%)	1.82 (0.59-5.62)	0.005	
	Secondary	865	378 (43.7%)	2.34 (0.72-7.61)		
	Tertiary	122	80 (65.7%)	5.77 (1.66-20.1)		
Wealth of Household	Lowest	662	207 (31.3%)	1	0.014	
	Lower	698	168 (24.1%)	0.70 (0.29-1.69)		
	Middle	806	374 (46.4%)	1.90 (0.78-4.59)		
	Higher	800	324 (40.5%)	1.49 (0.65-3.42)		
	Highest	469	262 (55.8%)	2.77 (1.19-6.47)		
Maternal HIV Status	Not infected not tested	174	2 (1.1%)	1	<0.001	1
	Not infected tested	1016	179 (17.6%)	18.67 (2.56-136.24)		17.49 (2.41-127.02)
	HIV+ status unknown	545	82 (15.1%)	15.56 (1.97-123.13)		15.13 (1.89-120.89)
	Known+ not on ART	146	59 (40.2%)	58.87 (7.36-471.18)		57.49 (7.02-470.52)
	Known+ on ART	1553	1013 (65.2%)	164 (22.24-1208.64)		159 (21.35-1178.68)
Paternal HIV Status	Not infected not tested	149	66 (44.2%)	1	0.007	
	Not infected tested	703	364 (51.7%)	1.34 (0.53-3.39)		
	HIV+ status unknown	1166	251 (21.5%)	0.34 (0.13-0.92)		
	Known+ not on ART	224	138 (61.7%)	2.01 (0.65-6.24)		
	Known+ on ART	1192	517 (43.4%)	0.96 (0.40-2.34)		

Figure 2 summarizes the relationship between maternal and paternal HIV status on ICT coverage. ICT coverage was high for children of mothers on ART irrespective of HIV infection, testing or treatment status of partner (59%-87%). For HIV+ mothers not on ART, testing of their children was also relatively high when the father was infected irrespective of testing or ART treatment status (45%-66%). When the mother was infected but not tested, ICT for children was generally ≤21%. ICT coverage was ≤18% when the father was infected but mother was HIV negative.

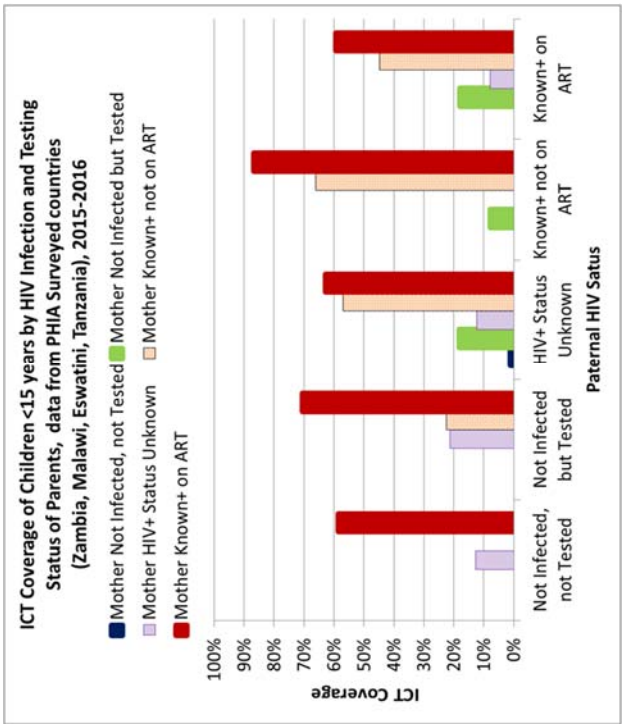

Figure 2. ICT Coverage of Children by HIV Infection, Testing, and Treatment Status of Parents, data from Four PHIA Surveyed Countries (Zambia, Malawi, Eswatini, and Tanzania), 2015-2016.

ICT coverage was high for children of mothers on ART irrespective of HIV infection, testing or treatment status of partner (59%-87%). For HIV+ mothers not on ART, testing of their children was also relatively high when the father was infected irrespective of HIV testing or treatment status. (45%-66%) When the mother was infected but not tested, ICT for children was ≤21%. ICT coverage was ≤18% when the father was infected but mother was HIV negative.

Looking at individual predictors, maternal HIV testing was a significant predictor of testing for children (odds ratio 84.5; 95% CI: 10.7- 666.2) irrespective of HIV infection status of the mother and HIV testing status of the father. Maternal HIV infection was also a predictor of children irrespective of paternal HIV testing of infection status. Both maternal and paternal awareness of HIV+ status were predictors of testing of children: odds ratio 9.42 (5.55-16.0) and 3.2 (2.1-4.8), respectively. Finally, for HIV+ mothers, being on ART was associated with better testing of children (odds ratio 2.8; 95% CI 1.4-5.7). For HIV+ fathers, being on ART was not associated with improved testing of children. (Table 2)

Table 2. Independent Predictors of ICT Coverage among children born to Parent(s) with HIV, data from Four PHIA Surveyed Countries (Zambia, Malawi, Eswatini, and Tanzania), 2015-2016

Variable	Response	Number of <15 Children	Number of <15 Children Tested (%)	Adjusted Odds ratio*	P value
Mother tested for HIV	No	310	2 (0.6%)		
	Yes	3,125	1333 (42.7%)	84.51 (10.72-666)	<0.001
Mother HIV+	No	1,191	181 (15.2%)		
	Yes	2,244	1154 (51.4%)	5.91 (3.91-8.94)	<0.001
Mother aware of HIV+ status	No	588	89 (15.1%)		
	Yes	1,831	1155 (63.1%)	9.42 (5.55-16.0)	<0.001
Father aware of HIV+ status	No	1,158	249 (21.5%)		
	Yes	1,407	650 (46.2%)	3.16 (2.08-4.82)	<0.001
Mother on ART if HIV+	No	168	68 (40.3%)		
	Yes	1,794	1170 (65.2%)	2.78 (1.35-5.73)	0.008

*** Adjusted for socio-demographic factors**

As for the reason why children were not tested for HIV when at least one parent was infected, 58.7% stated that the child didn't need testing followed by 23.4% saying they were very far from testing site (n=652).

ICT Burden for Children of HIV+ mothers

Figure 3 shows ICT burden for children of HIV infected mothers that still needed HIV testing by maternal HIV diagnosis and ART treatment status. Of children who still needed ICT, 50% were children of HIV+ mothers on ART, while 42% were children of undiagnosed HIV+ mothers. A minority 8% children were born to HIV+ mothers who knew their HIV positive status but weren't on ART (n=2120).

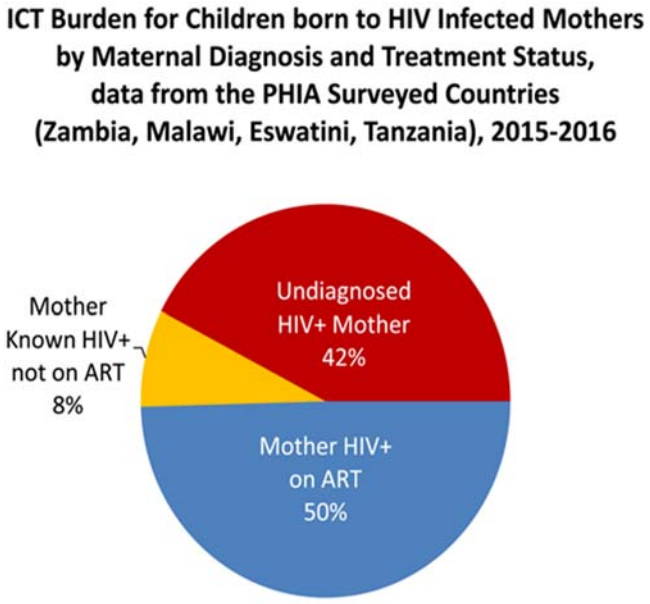

Figure 3. ICT Burden for Children born to HIV Infected Mother by Maternal Diagnosis and Treatment Status, data from the PHIA Surveyed Countries (Zambia, Malawi, Eswatini, Tanzania), 2015-2016.

This figure indicates of children born to HIV+ mothers and were never tested for HIV, 50% had HIV+ mother on ART while 42% had a mother never tested for HIV herself. (n=1090)

Discussion

Pediatric HIV case finding using index case testing was found to be low in all study settings except for Eswatini. Among parents who responded to the question why a child was not tested for HIV, the majority responded as the child didn't need the test. This is a troubling pattern and needs to be addressed through counseling.

Other factors for low ICT performance may include failure of health care workers to provide HIV testing, and low access for early infant diagnosis and each need to be addressed (11, 15-17). Line listing, tracking and testing of eligible children from ART sites, training support for health care workers and support staff, strong monitoring, supervision and coaching focusing on ICT may strengthen health systems (18). At individual level, the use of HIV self-test, home based or community based testing can facilitate testing for children by bringing testing closer to the family (19). This will help to address gaps in testing arising from the need to travel long distance for testing. Offering weekend testing services is another option as eligible children often go to school during normal office hours (15).

All possible entry points at facility and community level need to be explored to minimize missed opportunities for ICT (20, 21). That is why addressing gaps in HIV testing needs to be addressed urgently. However, the low hanging fruit still is ART clinics that serve infected parents on treatment (22). Equally important for pediatric HIV case finding is parental HIV testing as nearly 50% undiagnosed children have undiagnosed parents as indicated in this study. Prioritizing targeted testing of parents in settings providing service for children and adolescents may be needed (23).

ICT seems to be prioritized when there is maternal infection. This is logical as mother to child transmission accounts for the majority of pediatric infection as high as >90%. But, that should not be the only consideration for testing as there is a possibility of transmission from the father through the sharing of sharp objects within a household (24). In addition, the first index identified may be the father, in which case children should be tested without delay irrespective of maternal testing (25).

Maternal testing was found to be the driving force for testing of children irrespective of whether the mother was infected or not. It is therefore important to make use of this in testing of at risk children using family centered approach. Additionally, testing of children was found to be better when mothers knew their HIV+ status. Testing of children was even better when the mother was on ART. Only when fathers knew their HIV+ status did more children got tested compared to those who didn't know their HIV+ status. Even in that case, however, ICT for children was average. That needs to alert health care workers that counseling

including disclosure support needs to be very good when the index is the father (26).
Access for testing may be an issue as most children who were not tested were found to be in rural settings. This needs a strategic approach if the first 95 and second 95 targets are to be met for children. PEPFAR's pivot to high burden settings means mostly urban areas with high HIV burden are targeted (3). Rural settings still need to have targeted interventions like ICT taking into consideration cost of interventions (27, 28).

Looking at age of children, older children were found to be less likely to be tested. This may be due to low perception of the possibility of infection in older children (29). Late progression is a strong possibility especially when the infection occurs late through breast feeding (30). The other possibility is that parents may have false sense of security if PMTCT interventions were received. The determination of final infection status of HIV exposed infants at 12-18 months is an important intervention that should be strengthened. Current trends in Kenya, for instance, show that final status is not determined in 22% of children even after receiving PMTCT interventions (31).

Counseling approaches need to take literacy into account since (15), tertiary education of the father was associated with better ICT coverage. Index parents from highest wealth quintile were associated with low ICT coverage. Wealthy people usually take treatment in private facilities which should be targeted to reach them (32).

The analysis in this study focused on testing of children at least once. As stated earlier, there always is a possibility of infection outside the mother-to-child transmission window and hence, the testing gap reported here shows the minimum. Parents should be educated of this risk and HIV risk assessment conducted on ongoing basis to identify and test eligible children (33).

This study quantified one of the root causes for the low pediatric ART up take in many sub-Saharan African countries which is low pediatric case finding due to low ICT coverage. Important determinants like the role of PMTCT knowledge on ICT coverage, for instance, can be explored in demographic health surveys but these surveys need to measure pediatric HIV testing as a variable (34). Studies are also needed to explore why children eligible for ICT are not tested to design targeted and individualized interventions. The most important limitation of this study was that reason for not getting children tested was not captured for all parents and hence we couldn't present the complete picture.

Conclusion

Pediatric HIV testing for children of HIV infected parent(s) was found to be low. Maternal HIV testing was found to be the single most important factor to get a child tested for HIV. There still are missed opportunities in ICT testing of children even when parents know their HIV+ status and that should be addressed urgently. Rural settings need to be prioritized for ICT in order to address testing gap. Adult case finding is as important for pediatric HIV case finding as nearly half children who need testing are living with undiagnosed mothers.

Conflict of interest: None

Author contribution: KD conceived the idea, designed the methodology, did analysis and write up.

Consent to Publish: Not applicable

Reference

1. UNAIDS: Data (Accessed from https://www.unaids.org/en/resources/documents/2019/2019-UNAIDS-data). 2019.
2. Saito S, Chung H, Mahy M, Radin AK, Jonnalagadda S, Hakim A, Awor AC, Mwila A, Gonese E, Wadonda-Kabondo N: Pediatric HIV treatment gaps in 7 East and Southern African Countries: examination of modeled, survey, and routine program data. JAIDS Journal of Acquired Immune Deficiency Syndromes 2018, 78:S134-S141.
3. PEPFAR: Annual Report to Congress. 2019.
4. Marston M, Becquet R, Zaba B, Moulton LH, Gray G, Coovadia H, Essex M, Ekouevi DK, Jackson D, Coutsoudis A: Net survival of perinatally and postnatally HIV-infected children: a pooled analysis of individual data from sub-Saharan Africa. International journal of epidemiology 2011, 40(2):385-396.
5. Newell M, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F: Ghent International AIDS Society (IAS) Working Group on HIV Infection in Women and Children. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. Lancet 2004, 364(9441):1236-1243.

5. Teklemichael H. Assessment of incidence and treatment outcome of septic shock among patients admitted to adult intensive care unit of Tikur Anbessa specialized hospital in Ethiopia (Addis Ababa): AAU; 2017-06.
6. IbssaA, Solomon G. Common Bacterial Pathogens and Their Antimicrobial Susceptibility PatternsIn Patients with Symptomatic Urinary Tract Infections at Hiwot Fana and Jugal Hospitals in Eastern Ethiopia (Harar). Galore International Journal of Health Sciences and Research. 2018; 3(2):2.
7. Sapkota J, Mishra B, Jha B, Sharma M. Bacteriological profile and their antimicrobial susceptibility pattern in central venous catheter tip culture. Journal of Pathology of Nepal.2017; 7, 1059-1061.
8. Solomon A, Melkamu B, Sisay B, Gebre K, Lule T, Yonas Y, Yesuf A, Netsanet F, Henok A, Mulatu G, Esayas KG. Health care associated infection and its risk factors among patients admitted to a tertiary hospital in Jimma University, Ethiopia. Antimicrobial Resistance and Infection Control. 2018; 7:2-5.
9. H. Hamishehkar H, P. Shadmehr, A. Mahmoodpoor, S. O. Mashayekhi, 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. 2016; 52(3): 3.
10. Mwangi E.G., Karanja, S.M., Wanzala P and Ngumi Z. Bacterial profile and antimicrobial susceptibility patterns of isolates causing urinary tract infections in intensive care unit patients at Kenyatta national hospital. African Journal of Health Sciences. 2020; 33(5): 1-17.
11. Ak O, Batirel A, Ozer S, Çolakoğlu S. Nosocomial infections and risk factors in the intensive care unit of a teaching and research hospital: a prospective cohort study. Med SciMonit.2011; 17: 29-34.
12. Ustun C, Hosoglu S, Geyik MF, Parlak Z, Ayaz C The accuracy and validity of a weekly point-prevalence survey for evaluating the trend of hospital acquired infections in a university hospital in Turkey. Int J Infect Dis. 2011; 15: 684-687.
13. Madani N, Rosenthal VD, Dendane T, Abidi K, Zeggwagh AA. Health-care associated infections rates, length of stay, and bacterial resistance in an intensive care unit of Morocco: findings of the International Nosocomial Infection Control Consortium (INICC). Int Arch Med.2009; 2: 29.
14. Bajpai T, Bhatambare G, Shrivastava G, Deshmukh A, Chitnis V. Microbiological profile of lower respiratory tract infections in neurological intensive care unit of a tertiary care center from Central India. Journal of Basic and Clinical Pharmacy.. 2013; 4(3):51.
15. Pattanayak C, Patanaik SK, Datta PP, Panda P. A study on antibiotic sensitivity pattern of bacterial isolates in the intensive care unit of a tertiary care hospital in Eastern India. International Journal of Basic & Clinical Pharmacology [Internet]. 2017; 2(2):153–9.
16. Deepti C, Avinash L, K. Sadawarte, Tukaram P. Microbiological Profile, and Antimicrobial Sensitivity Pattern of Endotracheal Tube Aspirates of Patients in ICU of a Tertiary Care Hospital in Bhopal, India. Int.J.Curr.Microbiol.App.Sci.2017; 6(3):891-895.
17. Michel K, Amon TD, Julius MN. Bacteriological profile and antimicrobial susceptibility patterns of urine culture isolate from patients in Ndjamena, Chad. Pan African Medical Journal. 2017; 28:258.
18. Kaushal VS, Tejas K Patel, Saklainhaider S Malek, Tripathi. Antibiotic Sensitivity Pattern of Bacterial Isolates from the Intensive Care Unit of a Tertiary Care Hospital in India. Trop J Pharm Res. 2012; 11(6):991.
19. Walelegn WY, Abera K, Feleke MY. Point prevalence of hospital-acquired infections in two teaching hospitals of Amhara region in Ethiopia. Drug Healthc Patient Safty. 2016; 8:71-6.
20. Tsegaye A, Mulubrahan A, Enkosilassie, Et al. The burden of antimicrobial resistance at tertiary care hospital, southern Ethiopia: three years' retrospective study. BMC Infectious Diseases. 2019; 19:585.
21. Lovely B, Kaniz F, J Ashrafu H, Mohammad OF, ASM Areef, Md. Abu HG Morshed, Md. Belayet H. Bacterial profile and their antimicrobial resistance pattern in an intensive care unit of a tertiary care Hospital in Dhaka. Ibrahim Med. Coll. J. 2010; 4(2): 66-69.
22. WHO. Report on the Burden of Endemic Health Care-Associated Infection Worldwide. Geneva, Switzerland: WHO; 2011.Available l4from:http://www.who.int/about/ licensing/copyright form /en/index.html.
23. Radji M, Fauziah S, et al. Antibiotic sensitivity pattern of bacterial pathogens in the intensive care unit of Fatmawati Hospital, Indonesia. Asian Pacific Journal of Tropical Biomedicine. 2011; 1:39-42.
24. Shalini S, Kranthi K, Gopal Krishna BK. The microbiological profile of nosocomial infections in the intensive care unit. J ClinDiagn Res. 2010; 4:3109-12.
25. ZweiZwer F. Definition, Incidence, and Evolution of Sepsis & Septic Shock. Journal of Anesthesia & Critical Care: Open Access. 2016 Jun 1; 5(1).
26. Sharma PR, Barman P. Antimicrobial consumption and impact of "Reserve antibiotic indent form" in an intensive care unit. Indian J Pharmacol. 2010; 42: 301-305.

6. Lewis Kulzer J, Penner JA, Marima R, Oyaro P, Oyanga AO, Shade SB, Blat CC, Nyabiage L, Mwachari CW, Muttai HC: Family model of HIV care and treatment: a retrospective study in Kenya. Journal of the International AIDS Society 2012, 15(1):8-8.
7. Musarandega R, Mutede B, Mahomva A, Nyamayaro W, Mushavi A, Lindan C, Machekano R: Scaling up pediatric HIV testing by incorporating provider-initiated HIV testing into all child health services in Hurungwe District, Zimbabwe. Journal of acquired immune deficiency syndromes (1999) 2018, 77(1):78.
8. Simon KR, Flick RJ, Kim MH, Sabelli RA, Tembo T, Phelps BR, Rosenberg NE, Ahmed S: Family testing: an index case finding strategy to close the gaps in pediatric HIV diagnosis. Journal of acquired immune deficiency syndromes (1999) 2018, 78(Suppl 2):S88.
9. Wagner AD, Mugo C, Njuguna IN, Maleche-Obimbo E, Sherr K, Inwani IW, Hughes JP, Wamalwa DC, John -Stewart GC, Slyker JA: Implementation and operational research: active referral of children of HIV-positive adults reveals high prevalence of undiagnosed HIV. JAIDS Journal of Acquired Immune Deficiency Syndromes 2016, 73(5):e83-e89.
10. Bandason T, Langhaug LF, Makamba M, Laver S, Hatzold K, Mahere S, Munyati S, Mungofa S, Corbett EL, Ferrand RA: Burden of HIV among primary school children and feasibility of primary school-linked HIV testing in Harare, Zimbabwe: a mixed methods study. AIDS care 2013, 25(12):1520-1526.
11. Wagner AD, O'malley G, Firdawsi O, Mugo C, Njuguna IN, Maleche-Obimbo E, Inwani IW, Wamalwa DC, John-Stewart GC, Slyker JA: Disclosure, consent, opportunity costs, and inaccurate risk assessment deter pediatric HIV testing: a mixed-methods study. Journal of acquired immune deficiency syndromes (1999) 2018, 77(4):393.
12. Strauss M, Rhodes B, George G: A qualitative analysis of the barriers and facilitators of HIV counselling and testing perceived by adolescents in South Africa. BMC health services research 2015, 15(1):250.
13. Yeap A, Hamilton R, Charalambous S, Dwadwa T, Churchyard G, Geissler P, Grant A: Factors influencing uptake of HIV care and treatment among children in South Africa–a qualitative study of caregivers and clinic staff. AIDS care 2010, 22(9):1101-1107.
14. Population-based HIV Impact Assessment (PHIA) Data Use Manual 2019. New York; 2019.
15. World Health Organisation: WHO Guidelines on HIV Testing; 2015.
16. Marwa R, Anaeli A: Perceived Barriers Toward Provider-Initiated HIV Testing and Counseling (PITC) in Pediatric Clinics: A Qualitative Study Involving Two Regional Hospitals in Dar-Es-Salaam, Tanzania. HIV/AIDS (Auckland, NZ) 2020, 12:141.
17. Woldesenbet SA, Jackson D, Goga AE, Crowley S, Doherty T, Mogashoa MM, Dinh T-H, Sherman GG: Missed opportunities for early infant HIV diagnosis: results of a national study in South Africa. Journal of acquired immune deficiency syndromes (1999) 2015, 68(3):e26.
18. USAID: Maximizing coverage of index testing for biological children of mothers living with HIV: Standard Operating Procedure (SOP) (from: http://ovcsupport.org/wp-content/uploads/2020/07/OVC-Index-Testing-SOP-07.17.20.pdf). 2020.
19. World Health Organisation: Guideline on HIV self testing and partner notification; 2016.
20. Zambian Ministry of Health: Zambia Population-based HIV Impact Assessment (ZAMPHIA) 2016: Final Report. Lusaka; 2019.
21. Tanzania Commission for AIDS (TACAIDS) ZACZTHIS: Tanzania HIV Impact Survey (THIS) 2016-2017: Final Report. Dar es Salaam, Tanzania. 2018.
22. Cohen D, Lungu M, Van Oosterhout J: HIV testing coverage of family members of adult antiretroviral therapy patients in Malawi. AIDS care 2010, 22(11):1346-1349.
23. Ahmed S, Kim MH, Sugandhi N, Phelps BR, Sabelli R, Diallo MO, Young P, Duncan D, Kellerman SE, Prevention CSWGotITTot et al: Beyond early infant diagnosis: case finding strategies for identification of HIV-infected infants and children. AIDS (London, England) 2013, 27(0 2):S235.
24. Federal Ministry of Health: Reference Manual for PMTCT Option B+ Update Training. 2013.
25. Wall KM, Kilembe W, Nizam A, Vwalika C, Kautzman M, Chomba E, Tichacek A, Sardar G, Casanova D, Henderson F: Promotion of couples' voluntary HIV counselling and testing in Lusaka, Zambia by influence network leaders and agents. BMJ open 2012, 2(5).
26. Kelley AL, Karita E, Sullivan PS, Katangulia F, Chomba E, Carael M, Telfair J, Dunham SM, Vwalika CM, Kautzman MG: Knowledge and perceptions of couples' voluntary counseling and testing in urban Rwanda and Zambia: a cross-sectional household survey. PloS one 2011, 6(5):e19573.
27. Kankasa C, Carter RJ, Briggs N, Bulterys M, Chama E, Cooper ER, Costa C, Spielman E, Katepa-Bwalya M, M'soka T: Routine offering of HIV testing to hospitalized pediatric patients at university teaching hospital, Lusaka, Zambia: acceptability and feasibility. Journal of acquired immune deficiency syndromes (1999) 2009, 51(2):202.
28. McCollum ED, Preidis GA, Kabue MM, Singogo EB, Mwansambo C, Kazembe PN, Kline MW: Task shifting routine inpatient pediatric HIV testing improves program outcomes in urban Malawi: a retrospective observational study. PloS one 2010, 5(3):e9626.

29. UNICEF U, UNFPA, ILO, WHO and World Bank,: Opportunity in crisis: preventing HIV from early adolescence to early adulthood. New York: UNICEF; 2011.
30. Ferrand RA, Luethy R, Bwakura F, Mujuru H, Miller RF, Corbett EL: HIV infection presenting in older children and adolescents: a case series from Harare, Zimbabwe. Clinical infectious diseases 2007, 44(6):874-878.
31. Goggin K, Hurley EA, Staggs VS, Wexler C, Nazir N, Gautney B, Khamadi SA, Maloba M, Lwembe R, Finocchario-Kessler S: Rates and Predictors of HIV-Exposed Infants Lost to Follow-Up During Early Infant Diagnosis Services in Kenya. AIDS patient care and STDs 2019, 33(8):346-353.
32. Gesesew HA, Ward P, Woldemichael K, Lyon P, Mwanri L: Policy and practice suggestions to improve performance on the UNAIDS 90-90-90 targets: Results from a nominal group technique with HIV experts in Southwest Ethiopia. Health Expectations 2020.
33. Ministry of Health: National Comprehensive HIV Prevention, Care and Treatment Training for Health care Providers; 2017.
34. Croft TN, Marshall AM, Allen CK, Arnold F, Assaf S, Balian S: Guide to DHS statistics. Rockville: ICF 2018.

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Original Article

The implementation of global initiative for asthma (GINA) guidelines and Its Impact on asthma control in Ethiopia: A Longitudinal Study

Oumer Fuad[1], Amsalu Bekele[2], Amha Mekasha[3,] Tewodros Haile[2], Eyob Kebede Etissa[2],Yewubdar Gelan[4], Eyasu Makonnen[4], Getnet Yimer[5]

[1]Centre for Innovative Drug Development & Therapeutic Trials for Africa (CDT-Africa), College of Health Sciences, Addis Ababa University, Ethiopia
[2]Departement of Internal Medicine, College of Health Sciences, Addis Ababa University
[3]Department of Pediatrics and Child Health, College of Health Sciences, Addis Ababa University
[4]Departments of Pharmacology, College of Health Sciences, Addis Ababa University
[5]Global One Health initiative, Office of the International Affairs, The Ohio State University, Columbus, Ohio, USA
Corresponding author*:amsalubekele2016@gmail.com

Abstract

Background: *Asthma is one of the common chronic respiratory illnesses that affect approximately 339 million people in the world. This study aimed to assess asthmatic patients' usage of short-acting beta-2 agonist (SABA) medication and Asthma control with GINA recommended asthma management guidelines.*

Methods: *A longitudinal study of data set from the Ethiopian African Severe Asthma Project (ASAP) at Tikur Anbessa Specialized Hospital was used as a data source. The ASAP project was a prospective, multicentered, cohort study designed to investigate the prevalence and clinic characteristics of severe asthma in three African countries. Socio-demographic, comorbid conditions, and medication usage were extracted from the database. Descriptive statistics and binary logistic regression were used in data analyses.*

Results: *A total of 203 asthmatics were included in this analysis; 124 (61.1%) were females and 55 (27.1%) were age group 50-59 years. At baseline, 190 (93.6%) had uncontrolled asthma. Most 110(54.2%) were using only SABA medication. Of those patients using SABA alone, 108 (98.18%) had uncontrolled asthma. After enrollment in ASAP, GINA management guidelines were followed, inhaled corticosteroids (ICS) and long-acting beta-agonist (LABA) medications were the most frequently prescribed medications 182(89.7%), and usage of SABA medication decreased from 54.2% to 29.6%. Asthma control level significantly improved (P<0.0001) at six and twelve months of therapy as compared to baseline. Combination therapies were frequently prescribed at six months 172(84.2%). The frequency of controlled asthma at baseline, six, and twelve months was 6.40%, 65.02%, and 71.92%, respectively.*

Conclusion: *Implementation of GINA guidelines significantly improved asthma control. For a better outcome of asthma treatment, we are highly recommended the adoption of the GINA guideline in the national treatment guideline of Ethiopia.*

Keywords: Short-acting beta agonist, Asthma control, Asthma guidelines

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Introduction:

According to the Global Initiative for Asthma (GINA), asthma is a complex disease defined by chronic airway inflammation and a history of respiratory symptoms such as wheezing, shortness of breath, and chest tightness. Asthma is one of the most common chronic respiratory illnesses that affects 339 million people in the world and causes a significant burden of disease in people of all ages, including early mortality and poor quality of life [1-6].

According to a worldwide cross-sectional survey on asthma, prevalence is expected to rise to 400 million by 2025 [7-10]. According to the most recent WHO statistics, which were published in 2020, there were 4,484 asthma-related deaths in Ethiopia in 2020 or 0.80% of all deaths. Ethiopia was ranked 71st in the world with an age-adjusted death rate of 8.13 per 100,000 people [11].

Asthma's long-term management focuses on symptom control and risk reduction, including lessening the overall health burden as well as exacerbations, airway damage, and medication side effects [6, 12, 13]. Proper implementation of GINA guidelines on the best preventive and management strategies for mild to severe asthma has improved asthma outcomes [12].

In Ethiopia, most asthmatics use short-acting beta agonist (SABAs) medication for asthma treatment due to the lack of availability and high cost of other better controller therapies [14]. Many studies have suggested that asthma control is inadequate with SABA treatment alone [15-18].

One post hoc analysis study showed that the use of only SABA treatment for two weeks led to severe exacerbation of asthma resulting in hospital admission [19]. In 1992, it was reported that the use of SABA was associated with a risk of fatal and nearly fatal asthma, as well as death [20]. The US National Review of Asthma Deaths (NRAD) identified high prescription of SABA treatment as a key factor in over 40% of deaths [21]. Today, the controversy is not only focusing on SABA but also included long-acting beta-agonist (LABA) [15-17, 22].

The Ethiopian Asthma Management Guideline still advocates SABA (salbutamol) for the treatment of acute asthma attacks and severe persistent asthma. However, in high-resource countries, SABA medications have largely been replaced by low-dose inhaled corticosteroid (ICS) and LABA combination therapy for better asthma control [12, 23]. For this reason, we aimed to assess the SABA usage pattern and asthma control of participants in the Ethiopian component of the African Severe Asthma Project (ASAP) using the GINA guideline.

Methods

Study design

This was a longitudinal study of a database from the Ethiopian ASAP project at Tikur Anbessa Specialized Hospital. ASAP Project was a prospective cohort study conducted from August 2016-May 2018 in three African countries; Ethiopia, Uganda, and Kenya [24]. This longitudinal study was done from 2018 to 2019 at Tikur Anbessa Specialized Hospital database archive of the ASAP project.

Source data

The source data was from ASAP Project which was a research project. severe asthma in East Africa. The study sites include of three teaching and national referral hospitals in Kenya (Kenyatta Hospital), Uganda (Mulago Hospital) and Ethiopia (Tikur Anbessa Hospital).

The inclusion criteria for ASAP project were patients with chronic respiratory symptoms (more than 8 weeks) with Physician diagnosed asthma based on symptom, Skin prick test and spirometry and age above or equal to 18 years and below 70 years. For the current analysis the Ethiopian site data was used as the original data for this study, with 419 participant records serving as source data [24].

Based on the data-sharing agreement, the ASAP project data at Tikur Anbessa Hospital, Addis Ababa, Ethiopia was retrieved and reviewed. The extracted information for this study included sociodemographic, comorbid conditions, risk factors, and medications. The severity of asthma, its control, and the medications given and utilized by the patients were the primary factors examined before enrollment, six-month, and during the 12-month treatment period. The study inclusion criteria were $\geq$18 years of age, confirmed asthma diagnosis, and Addis Ababa residents. The exclusion criteria were any missing data on important factors that might impact the primary goal of the study, such as spirometry findings, asthma severity, and control status. (Figure 1).

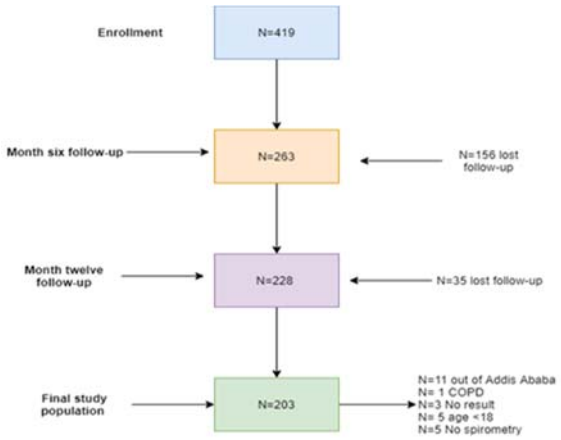

Figure 1: Flow chart for final participant selection from the original dataset for this study.

Operational definitions

The severity of asthma was defined based on the American Thoracic Society (ATS)/European Respiratory Society (ERS) definition [25].

Procedures

At the start of the study, medications use as well as asthma control and severity were evaluated for each subject. The participants were then given standard care asthma medicines based on their asthma severity and control level at baseline following GINA and Expert Panel 3 guidelines [8,12].

Those who received standard asthma medications continued to use it for the next six months. At six months, asthma severity and control were again assessed. Based on these findings, the management of asthma was modified for the next six month. After 12 months from enrollment, asthma control and severity were again reassessed (Figure 2).

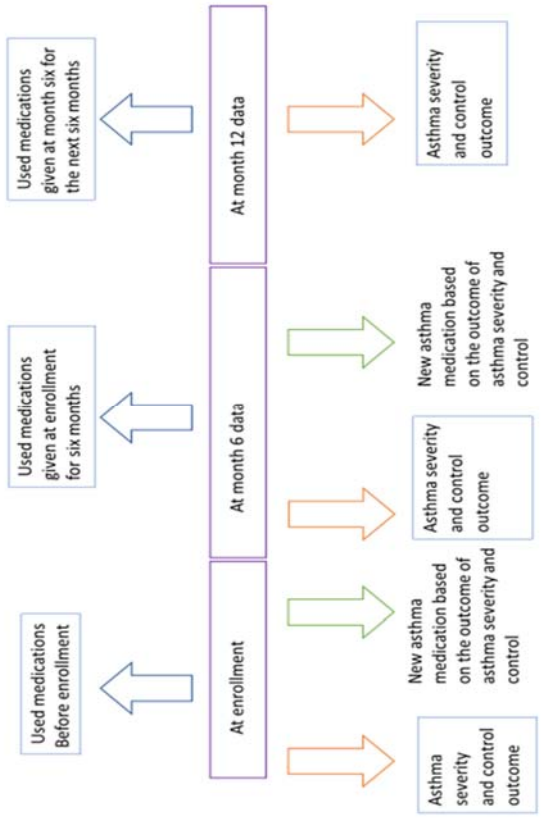

Figure 2: Exposure to asthma medications and the respected outcome related to the exposed medications.

Statistical analysis

Based on the original research case recording forms (CRF) dummy code, data from the baseline, six months' and twelve months' were imported into the STATA software version 15.0 code. In a table, continuous variables were summarized using means (standard deviations). All categorical variables were summarized using percent for the various categories and displayed as bar graphs, pie charts, dot charts, or tables. When comparing two categorical data sets, chi-square test was used while Fisher's exact tests were used when the expected cells were less than 5.

The Cochran Q test was used to compare the result at three distinct periods since our data was matched (Paired), having more than two datasets and it was nominal independent data set. Each pair of independent groups was likewise subjected to the McNamara test.

For numerous comparisons across groups, the p-value is taken as individual comparison alpha = (Overall Alpha)/c = 0.05/3 = 0.01667 for the Cochran Q test. To predict the relationship between different medicines and asthma control status, a binary logistic regression was used. Statistical significance was defined as a p-value of less than 0.05.

Ethical considerations

All participants in the original ASAP research gave their written consent to participate in the study.

The study was authorized by CDT Africa's scientific and ethics committee, as well as the Institutional Review Board at Addis Ababa University College of Health Sciences.

RESULTS

Table 1 summarizes socio-demographic data. There were 203 (48.5%) study participants; 124 (61.1%) were females and 55 (27.1 %) were between the ages of 50 - 59 years. A total of 40 individuals (19.7%) did not have formal education, while 58 (28.6%) started but did not complete elementary school. Most participants (67.2%) were married; 42 (20.7%) were jobless, and 58 (28.6%) were housewives.

At baseline, 114 subjects (56.2%) had severe persistent asthma and 190 (93.6%) had uncontrolled asthma (115, 92.7% women and 75 (94.9%) men). The age of first asthma attack and disease severity differed significantly in proportion (P=0.038).

One hundred and eighty-eight (92.6%) of the participants were nonsmokers. Ten (66.7%) of the 15 smokers had uncontrolled asthma, whereas one (6.67%) had controlled disease. Most of the participants, 148 (72.9%), claimed to have been exposed to biomass smoke, and many of them suffered from uncontrolled asthma. All the smoking-related exposures were not statistically significant (P > 0.05) (Table 2).

The most common co-morbidity was hypertension 28 (13.8%), followed by gastro-esophageal reflux disease 17 (8.4 %). The majority (n=17, 60.7%) of individuals with hypertension had uncontrolled asthma, whereas 2 (7.4%) had well-controlled asthma. Eight (47.1 %) of those with gastro-esophageal reflux had poorly or partially controlled asthma, none of whom had controlled asthma. There were 8 (3.9%) and 10 (4.9%) with rhinosinusitis and eczema/dermatitis, respectively, and both co-morbidities were significantly related to asthma severity (P=0.011 and P=0.018, respectively) (Table 3).

Table 1: Table 1. Shows the descriptive statistics of eligible participants based on their asthma control at Baseline.

Measures	**Overall N=203**	**Asthma severity N (%)**			**Asthma control level N (%)**		
		Severe	Non-severe	P-value	Well controlled	Not controlled	P-value
Sex n (%)							
Male n (%)	79 (38.92)	46 (58.23)	33(41.77)	0.635	4(5.06)	75(94.94)	0.533
Female n (%)	124 (61.08)	68 (54.84)	56(45.16)		9(7.26)	115(92.74)	
Total	203(100)	114(56.16)	89(43.84)		13(6.40)	190(93.60)	
Age n (%)							
18-29	8(3.94)	3(37.50)	5 (62.50)	0.157	0(0.00)	8(100)	0.244
30-39	24 (11.82)	8(33.33)	16(66.67)		4(16.67)	20(83.33)	
40-49	52(25.62)	29(55.77)	23(44.23)		1(1.92)	51(98.08)	
50-59	55(27.09)	34(61.82)	21(38.18)		4(7.27)	51(92.73)	
60-69	43(21.18)	27(62.79)	16(37.21)		3(6.98)	40(93.02)	
>=70	21(10.34)	13(61.90)	8(38.10)		1(4.76)	20(95.24)	
Education level n (%)							
None	40(19.70)	23(57.50)	17(42.50)	0.603	2(5.00)	38(95.00)	0.610
Incomplete Primary	58(28.57)	32(55.17)	26(44.83)		2(3.45)	56(96.55)	
Complete Primary	17(8.37)	7(41.18)	10(58.82)		2(11.76)	15(88.24)	
Incomplete Second-ary	21(10.34)	15(71.43	6(28.57)		1(4.76)	20(95.24	
Complete Second-ary	23(11.33)	13(56.52)	10(43.48)		3(13.04)	20(86.96)	
Tertiary	44(21.67)	24(54.55)	20(45.45)		3(6.82)	41(93.18)	
Marital status n (%)							
Single	19 (9.45)	9(47.37)	10(52.63)	0.299	2(10.53)	17(89.47)	0.661
Married	135(67.16)	77(57.04)	58(42.96)		9(6.67)	126(93.33)	
Separated	14 (6.97)	11(78.57)	3(21.43)		0(0.00)	14(100.00)	
Widowed	32(15.92)	17(53.13)	15(46.88)		1(3.13)	31(96.88)	
Child	1 (0.50	0(0.00)	1(100.00)		0(0.00)	1(0.53)	
Occupation n (%)							
Unemployed	42(20.69)	27(64.29)	15(35.71)	0.542	3(0.932)	40(93.02)	0.299
Housewife	58(28.57)	31(53.45)	27(46.55)		5(8.62)	53(91.38)	
Teacher/ Lecturer	6(2.96)	3(50.00)	3(50.00		1(16.67)	5(83.33)	
Lawyer	2(0.99)	1(50.00)	1(50.00		0(0.00)	2(100.00)	
Armed forces	1(0.49)	1(100.00)	0(0.00)		0(0.00)	1(100.00)	
Student	1(0.49)	0(0.00)	1(100.00)		0(0.00)	6(100.00)	
Factory Worker	7(3.45)	2(28.57)	5(71.43)		1(14.29)	6(85.71)	
Allied Health Worker	2(0.99)	1(50.00)	1(50.00)		0(0.00)	2(100.00)	
Manager	4(1.97)	3(75)	1(25.00)		0(0.00)	3(100.00)	
Clerical Worker	2(1.97)	0(0.00)	1(100.00)		0(0.00)	2(100.00)	
Other	78(37.50)	45(57.69)	33(42.31)		3(3.85)	75(96.15)	
Age asthma Occurs n (%)							
<15	15 (7.39)	7(46.67)	8(53.33)	0.038	1(6.67)	14(93.33)	0.922
15-24	40 (19.70)	29(72.50)	11(27.50)		2(5.00)	38(95.00)	
25-34	82 (40.39)	44(53.66)	38(46.34)		7(8.54)	75(91.46)	
35-44	36 (17.73)	24(66.67)	12(33.33)		1(2.78)	35(97.22)	
45-54	17 (8.37)	5(29.41)	12(70.59		1(5.88)	16(94.12)	
55-64	10 (4.93)	4(40.00)	6(60.00)		1(10.00)	9(90.00)	
>64	3 (1.48)	1(33.33)	2(66.67)		0(0.00)	3(100.00)	

Note: The age of the participants was categorized based on the eligibility criteria but the age that asthma occurred is not necessary to consider any age limit. The age of asthma occur is statistically significant with the severity of asthma $P<0.05$

Table 2: Shows Cigarette smoking, Biomass, and kerosene exposure vs asthma control level

Exposure Measures	Overall N=208	Asthma severity No (%)		P-value	Asthma control level No (%)		P-value
		Severe	Not severe		Well-controlled	Not con-trolled	
Smoking history No (%)							
Current/ Former Smoker	15 (7.39)	10(66.67)	5(33.33)	0.394	1(6.67)	14(93.33)	0.966
Never smoker	188(92.61)	104(55.32)	88(44.68)		12(6.38)	176(93.62)	
Biomass smoking history No(%)							
Yes	148(72.91)	85(57.43)	63(42.57)	0.548	10(6.76)	138(93.24)	0.736
No	55 (27.09)	29(52.73)	26(47.27)		3(5.45)	52(94.55)	
Kerosene Exposure No (%)							
Yes	41(20.20)	24(58.54)	17(41.46)	0.731	4(9.76)	37(90.24)	0.326
No	162(79.80)	90(55.56)	72(44.44)		9(5.56)	153(94.44)	

Note: The smoking habits to cigarette, biomass, and kerosene is not statistically significant P >0.05

Table 3: Co-morbidities associated with asthmatic patients grouped versus severity and control level of asthma

Medication changes from enrollment to month 12 of the study are shown in Table 4.

Comorbidities	Overall N=203	Asthma severity		P-value	Asthma control level No (%)		P-value
		Severe n=114	Not severe n=89		Well-controlled	Not con-trolled	
Rhino sinusitis	8(3.94)	1(12.50)	7(87.50)	0.011	0(0.00)	8(100.00)	0.450
Nasal polyps	3(1.48)	2(66.67)	1(33.33)	0.712	0(0.00)	3(100.00)	0.648
Eczema/dermatitis	10(4.93)	2(20.00)	8(80.00)	0.018	0(0.00)	10(100.00)	0.396
Depression	1(0.49)	1(0.49)	0(0.00)	0.430	0(0.00)	1(100.00)	0.793
Gastroesophageal re-flux disease	17(8.37)	8(47.06)	9(52.94)	0.430	0(0.00)	17(100.00)	0.260
Obstructive sleep apnea	2(0.99)	0(0.00)	2(100.00	0.108	0(0.00)	2(100.00)	0.710
HIV	3(1.48)	3 (100.00)	0(0.00)	0.123	0(0.00)	3(100.00)	0.648
COPD	0(0.00)	0(0.00)	0(0.00)		0(0.00)	0(0.00)	
Heart failure	0(0.00)	0(0.00)	0(0.00)		0(0.00)	0(0.00)	
Hypertension	28 (13.79)	17 (60.71)	11(39.29)	0.601	2(7.14)	26(92.86)	0.863
Other diseases	29 (14.29)	19 (65.52)	10(34.48)	0.273	2(6.90)	27(93.10)	0.907

Table 4: The medication used by participants at different points in the study visits and the level of asthma control that corresponds with asthma.

Before enrollment	N=203 n (%)	Asthma control at base line		P-value	N=203 n (%)	Asthma control at six month		P-value	N=203 n (%)	Asthma control at twelve month		P-value
		Well Controlled	Not controlled			Well Controlled	Not controlled			Well Controlled	Not controlled	
SABA only	110 (54.)	2(1.82)	108 (98.1)	0.004	60 (29.56)	41 (68.33)	19 (31.67)	0.522	2 (0.99)	2 (100.0)	0 (0.00)	0.375
ICS only	7 (3.45)	3 (42.86)	4 (57.14)	0.000	3 (1.48)	1 (33.33)	2 (66.67)	0.246	1 (0.49)	1 (100.0)	0 (0.00)	0.531
SA-BA+ICS	20 (9.85)	3 (15.00)	17 (85.00)	0.098	15 (7.39)	8 (53.33)	7 (46.67)	0.324	24 (11.8)	15 (62.5)	9 (37.50)	0.274
ICS+LABA	28 (13.7)	2(7.14)	26 (92.86)	0.863	182 (89.6)	119 (65.3)	63 (34.62)	0.752	171 (84.2)	124 (72.)	47 (27.4)	0.664

SABA-only medications were taken by 110 (54.2%) individuals before enrollment, but this number dropped to 60 (29.56%) once the severity of asthma was assessed at the beginning of the study and patients started with GINA based treatment regimen. Similarly, over the next six months of the study, the use of SABA medicines by study participants decreased significantly (n=2, 0.99 %). In contrast to the baseline, the usage of ICS+SABA and ICS+LABA medicines use significantly increased.

The proportion of asthma control at each visit was substantially different from baseline to month twelve (P= 0.0001), according to the Cochran Q

During the six-month follow-up visit, 132 (65.0%) had controlled asthma and by the end of twelve month, 146 (71.92%) had controlled asthma while 57 (28.08%) of participants had uncontrolled asthma.

Multiple comparison tests were evaluated with the McNemar test where the absolute smallest difference predicted was 12.9%; alpha = (Overall Alpha)/c = 0.05/3 = 0.01667 for individual comparisons. Baseline and six-month asthma control levels, as well as baseline and twelve-month asthma control levels, were substantially different from each other, with absolute differences of 58.6 % and 65.5 %, respectively. The difference in P-value at baselines and six-month as well as baseline and twelve-month was statistically significant (P<0.0001). There was no statistically significant

Table 5: shows the Cochran Q test between the outcome of asthma control following the medication at three different times and the McNamara test between each group pair.

			Cochran's Q	Multiple Comparisons using Minimum Required Absolute Difference				Multiple Comparisons using the McNamara Test
Group Variables	Asthma Control outcome		P-value	Comparison of each group	Absolute difference (π_i (%)-π_j (%)	Minimum required absolute difference	Reject Ho with the overall α*	P-value
	Controlled	Not controlled						
Test at Baseline	13(6.40%)	190 (93.6%)	0.0000	Test at Baseline Vs Test at Month six	(93.60 - 34.98) 58.62	12.88	Yes	0.00000
Test at 6 month	132 (65.0%)	71 (34.98%)		Test at Baseline Vs Test at month twelve	(93.60 - 28.08) 65.52	12.88	Yes	0.00000
Test at 12 month	146 (71.92%)	57 (28.08%)		Test at Month six Vs Test at month twelve	(34.98-28.08)6.90	12.88	No	0.17967

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The proportion of asthma control at each visit was substantially different from baseline to month twelve (P= 0.0001), according to the Cochran Q paired group test. At the start of the study, 190 (93.6%) of the patients had uncontrolled asthma.

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Table 5: shows the Cochran Q test between the outcome of asthma control following the medication at three different times and the McNamara test between each group pair.

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Group Variables	Asthma Control outcome		P-value	Comparison of each group	Absolute difference (π_i (%)-π_j (%)	Minimum required absolute difference	Reject Ho with the overall α*	P-value
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Test at 12 month	146 (71.92%)	57 (28.08%)		Test at Month six Vs Test at month twelve	(34.98-28.08)6.90	12.88	No	0.17967

A binary logistic regression was employed to examine SABA-only medication users, ICS-only medication users, ICS plus SABA as needed medication users, and ICS plus LABA medication users at baseline to predict the effects on the odds of observing Asthma control. The binary logistic regression analysis showed that ICS-only medication users were 10.07 times more likely to control their asthma than non-users (OR = 10.071, CI = 1.683, 60.275, P = 0.011).

Discussion

Our study clearly demonstrates the role of controller medication (ICS or ICS+LABA) in improving asthma control. At baseline, most of the asthmatic individuals were using SABA alone therapy and had uncontrolled asthma. After enrollment in ASAP and starting on GINA guideline-based management, there was gradual and significant improvement in asthma control with ICS and LABA medications. This gradual improvement in asthma control shown over a year of appropriate treatment was also associated with less use of SABA- alone therapy.

Our findings are consistent with previous study findings. Numerous studies, mostly in high-resource countries, have shown that ICS use lessens asthma exacerbations and increases asthmatic quality of life [24, 26-29]. Long -term use of SABA-only medications has been linked to severe asthma exacerbation and inflammation in other studies [21, 30-32]. Furthermore, a post-hoc analysis study published in 2015 found that long-term usage of SABA before admission to the hospital resulted in severe asthma exacerbation [19].

In 2019, GINA reviewed 231 prospective articles and proposed an evidence-based recommendation that SABA-only treatment for asthma in adults and adolescents should no longer be used [12]. For as-needed controller therapy in mild asthma, evidence-based alternatives are offered, with low dosage controllers being preferred for Step 1 and Step 2. If needed, ICS-formoterol can be given as needed for symptom alleviation and before exercise [8,12].

In 2014, the Ethiopian Asthma Management Guidelines proposed first-line therapy for persistent moderate to severe persistent asthma should be ICS + SABA as required. Other drugs, such as OCS and methylxanthines, could be used as a backup. Alternative treatments such as ICS+LABA medicines were mentioned but not recommended [14]. The 2019 GINA guideline, on the other hand, consider ICS to be a major controller and reliever, while SABA is an option, and does not advocate ICS+SABA as first-line therapy [12].

There were two other important study findings. Environmental exposures to cold weather, dust, vehicle fumes, and strong odors played a key role in triggering asthma [33-35]. Avoidance of these environmental triggers may also improve asthma control in our cohort as shown in other studies [36-38].

In our analysis, similar to other studies, comorbidities were common in our study population. Proper management of comorbidities may also improve asthma control [39].

Conclusion :

In Ethiopia, a low-resource country, use of GINA guidelines significantly improved asthma control. The use of SABA medication to control and alleviate asthma symptoms was shown to be ineffective. Furthermore, it was discovered that ICS was the most effective first-line treatment. Societies and regulatory body should advocate for the availability of reasonably priced asthma medications including ICS and LABA for disease control as recommended by current asthma management guidelines.

Limitation of the study

Because we used secondary data that was originally obtained for other purposes, generalization is questionable. But this study clearly showed that guideline-based asthma management improved asthma control.

Conflict of 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

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Contributors:

OF, GY, EM developed the draft manuscript from ASAP data, GM, AB, TH, YB, AM, involved in primary ASAP data generation and EKE reviewed the paper and included all comments from others. All authors contributed to the draft and finalization of the manuscript

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Consent for publication
Not applicable.

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Reference

1. The Global Asthma Report 2018. Auckland, New Zealand: Global Asthma Network, 2018. www.globalasthmanetwork.org
2. Chimeddamba O, Peeters A, Walls HL, Joyce C. Noncommunicable Disease Prevention and Control in Mongolia : A Policy Analysis. 2015;15.
3. Chan M. Global status report on noncommunicable diseases. World Health Organ. 2010.
4. Alberto Papi , Adel H Mansur , Tetyana Pertseva,el.at. Long-Term Fluticasone Propionate/Formoterol Fumarate Combination Therapy Is Associated with a Low Incidence of Severe Asthma Exacerbations . J Aerosol Med Pulm Drug Deliv
2016 Aug;29(4):346-61. doi: 10.1089/jamp.2015.1255. Epub 2016 Apr 22.
5. World Health Organization. (.(2014Global status report on non-communicable diseases 2014. World Health Organization. https://apps.who.int/iris/handle/10665/148114
6. Reddel HK. The Impact of the Global Initiative for Asthma (GINA): Compass , Concepts , Controversies and Challenges. BRN Rev.2019;5(1):4–18.
7. Forum of International Respiratory Societies. The Global Impact of Respiratory Disease – Second Edition. Sheffield, European Respiratory Society, 2017.5-42.
8. 2018 Clinical Practice Guidelines. National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program, Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf
9. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults : findings from the cross-sectional world health survey. *BMC Public Health* [Internet]. 2012;12 (1):204. Available from: http://www.biomedcentral.com/1471-2458/12/204
10 WHO. Global Asthma Network The Global Asthma Report. Auckland, New Zeal [Internet]. 2018;92. Available from: http://www.globalasthmanetwork.org
11. WORLD HEALTH ORGANIZATION 2020. WORLD LIFE EXPECTANCY COM. Available from: https://www.worldlifeexpectancy.com/ethiopia-asthma
12 GLOBAL INITIATIVE FOR ASTHMA. ASTHMA MANAGEMENT AND PREVENTION for adults and children older than 5 years .A POCKET GUIDE FOR HEALTH PROFESSIONALS Updated 2019.
13. Dotan Y, So JY, Kim V. Chronic bronchitis: where are we now? *Chronic Obstr Pulm Dis.* 2019;6(2):178-192. doi: https://doi.org/10.15326/jcopdf.6.2.2018.0151
14. FEDERAL DERAL DEMOCRATIC REPUBLIC OF ETHIOPIA MINISTRY OF HEALTH. Guidelines on Clinical and Programmatic Management of Major Non Communicable Diseases.2016 .Addis Ababa
15. Smucny J, Ca F, La B, Glazier R. Beta2-agonists for acute bronchitis (Review). 2006;(1). National Center for Biotechnology Information. Cochrane Database Syst Rev . 2006 Oct 18;(4):CD001726. doi: 101002/14651858.CD001726.pub3.

16. Moore RH, Khan A, Dickey BF. Long-acting Inhaled β2-Agonists in Asthma Therapy. Chest [Internet]. 1998;113(4):1095–108. Available from: http://dx.doi.org/10.1378/chest.113.4.1095
17. Bisgaard H. Effect of Long-Acting β2 Agonists on Exacerbation Rates of Asthma in Children. Pediatr Pulmonol. 2003;36(5):391–8.
18. Hull SA, Mckibben S, Homer K, Taylor SJC, Pike K, Grif C. Asthma prescribing , ethnicity and risk of hospital admission : an analysis of 35 , 864 linked primary and secondary care records in East London. NPJ Prim Care Respir Med . 2016 Aug 18;26:16049. doi: 10.1038/npjpcrm.2016.49.
19. Patel M, Pilcher J, Hancox RJ, Sheahan D, Pritchard A, Braithwaite I, et al. The use of β 2 -agonist therapy before hospital attendance for severe asthma exacerbations : a post-hoc analysis. Nat Publ Gr [Internet]. 2015;(August 2014). Available from: http://dx.doi.org/10.1038/npjpcrm.2014.99
20. Walter O. Spitzer,Samy Suissa,Pierre Ernst, et al. The Use of β-Agonists and the Risk of Death and near Death from Asthma. N Engl J Med 1992; 326:501-506. DOI: 10.1056/NEJM199202203260801
21. Mckibben S. " Tossing a coin : " defining the excessive use of short-acting beta 2 -agonists in asthma — the views of general practitioners and asthma experts in primary and secondary care. 2018;(February):2018–20.
22. Suissa S, Blais L, Ernst P. Patterns of increasing β -agonist use and the risk of fatal or near-fatal asthma. 1994;1602–9.
23. Food , Medicine and Healthcare Administration and Control Authority of Ethiopia Standard Treatment Guidelines For General Hospital Diseases Investigations Good Prescribing & Dispensing Practices for Better Health Outcomes. Thrid Edition, Stg. 2014;
24. Kirenga B, Chakaya J, Yimer G, Nyale G, Haile T, Muttamba W, et al. Phenotypic
25. characteristics and asthma severity in an East African cohort of adults and adolescents with asthma: findings from the African severe asthma project. BMJ open Respir Res. 2020 Feb;7(1).
26. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS / ATS guidelines on definition , evaluation and treatment of severe asthma. *Eur Respir J* 2014; 43: 343–373 | DOI: 10.1183/09031936.00202013 .
27. Bf C, Chartrand C, M NC, Sj M, Fm D. Addition of long-acting beta 2 -agonists to inhaled corticosteroids for chronic asthma in children .Intervention Review Review .. Evidence-Based Child Health: A Cochrane Review Journal, 2015;(11).
28. O'Byrne P, Fabbri LM, Pavord ID, Papi A, Petruzzelli S, Lange P. Asthma progression and mortality: the role of inhaled corticosteroids. Eur Respir J. 2019 Jul;54(1).
29. Cj C, Schmidt S, Ferrer M, Sayer B, Waterson S. Inhaled steroids with and without regular salmeterol for asthma : serious adverse events. Cochrane Database Syst Rev . 2018 Dec 3;12(12):CD006922. doi: 10.1002/14651858.CD006922.pub4.
30. Takeuchi M, Kano H, Takahashi K, Iwata T. Comparative effectiveness of inhaled corticosteroids for paediatric asthma: protocol for a systematic review and Bayesian network meta-analysis. BMJ Open. 2015 Oct;5 (10):e008501.
31. Magee JS, Pittman LM, Jette-kelly LA. Paradoxical Bronchoconstriction with Short- Acting Beta Agonist. Am J Case Rep . 2018 Oct 9;19:1204-1207. doi:10.12659/AJCR.910888..
32. Zeiger RS, Schatz M, Li Q, Solari PG, Zazzali JL, Chen W. Real-time asthma outreach reduces excessive short-acting β2-agonist use: a randomized study. J allergy Clin Immunol Pract. 2014;2(4):445–56, 456.e1-5
33. Martin MJ, Harrison TW. Is it time to move away from short-acting beta-agonists in asthma management? Eur Respir J [Internet]. 2019 Apr 1;53(4):1802223. Available from: http://erj.ersjournals.com/content/53/4/1802223.a
34. Takaro TK, Krieger JW, Song L. Effect of environmental interventions to reduce exposure to asthma triggers in homes of low-income children in Seattle. J Expo Anal Environ Epidemiol. 2004;14 Suppl 1:S133-43.
35. Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R 3rd, et al. Results of a home-based environmental intervention among urban children with asthma. N Engl J Med. 2004 Sep;351(11):1068–80.
36. Janssens T, Ritz T. Perceived triggers of asthma: key to symptom perception and management. Clin Exp Allergy [Internet]. 2013 Sep;43(9):1000–8. Available from: https://pubmed.ncbi.nlm.nih.gov/23957335
37. Prabhakaran L, Yap CW, Neo L, Gan C, Tham L, Wong W, et al. Effectiveness of the eCARE Programme: A Short Message Service (SMS) for Asthma Monitoring. Ann Acad Med Singapore. 2018 Jun 1;47:233–6.
38. Cockcroft DW. Environmental Causes of Asthma. Semin Respir Crit Care Med. 2018 Feb;39(1):12–8.
39. Strachan DP. The role of environmental factors in asthma. Br Med Bull. 2000;56(4):865–82.
39. Boulet L-P, Boulay M-È. Asthma-related comorbidities. Expert Rev Respir Med. 2011 Jun;5(3):377–93.

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Original Article

Microbiological Culture Profile and Antimicrobial Susceptibility Pattern of patients admitted to Addis Ababa intensive care units

Yemane Gebremedhin[1*], Menbeu Sultan[2], Dagmawi Tesfaye[2]

[1]Department of Emergency Medicine and Critical Care, Saint Paul`s Hospital Millennium Medical College, Addis Ababa, Ethiopia.
[2]Addis Ababa Burn, Emergency, and Trauma Hospital, Addis Ababa, Ethiopia.

Corresponding author*: yeman31@gmail.com

Abstract

Background: *Intensive care unit infections are health care problems affecting millions globally each year. Intensive care unit mortality of infectious patients is increasing and as high as 14.31% to 45.4%. This study aimed to determine the microbiological culture profile and antimicrobial susceptibility pattern of patients admitted to two intensive care units in Addis Ababa.*

Methods and materials*: An institutional-based retrospective observational study was carried out on all patients with microbiological culture and susceptibility results after admission to the adult intensive care unit at two Addis Ababa hospitals from January 2019 to December 2019. Data were collected by trained data collectors using a standard and pretested questionnaire. Collected data were coded, entered into Epi-Info, and analyzed using SPSS version 25. Correlation and regression analysis was used for assessing associations. A p-value of less than 0.05 was taken as significant.*

Results: *A total of 106 patients with 173 culture results were analyzed. The majority, 68(64.2%), were males. The mean age of the patients was 35.08±1.6 years. The most common documented source of infection was the pulmonary system 84(54.5%), followed by urinary tract infection 26(16.9%). Forty-four (25.43%) of cultures had growth. Gram-negative was identified in 35(68.63%) isolates. Acinetobacter species account for 10(28.57%), followed by Klebsiella pneumoniae and E. coli 7(13.725%) respectively. Higher antimicrobial resistance was shown to cephalosporin and penicillin. The mortality rate among subjects was 32.1%.*

Conclusion and Recommendations: *Pulmonary source being the common infection site, resistant gram negatives were the predominant microorganisms identified. Designs of future multicenter and prospectively designed studies are crucial to improve the outcome of critically ill patients.*

Keywords: *Microbiological culture profile, antimicrobial susceptibility pattern, Intensive Care Unit.*
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Background

Intensive care unit infections are among the most serious infections and leading causes of morbidity and mortality in hospitalized patients, where indiscriminate and prolonged use of antimicrobials is common and leads to the emergence of resistant strains (1). A countrywide survey on the capacity of ICU care in Ethiopia showed that critical care service is flourishing. However, inadequate quality of care and poor infection prevention practices were reported. Studies from Africa indicate that the ICU mortality rate is high. For instance, ICU mortality in Uganda, Tanzania, and Kenya were 40.1 %, 41.1%, and 53.6 % respectively. Similar studies from Ethiopia also showed that ICU mortality raged 28% -50 % (2, 3).

It has been reported that ICU-acquired infections are common in low-resource settings. Resistant microorganisms are commonly reported in ICU-admitted patients. The common ones among these resistant microorganisms are *methicillin-resistant s. aureus* (MRSA), *and vancomycin-resistant enterococcus* (VRE) (3, 4). Tracheal aspirate (29.9%) and exudate were the most frequently received clinical specimens that tested positive for culture (22.7%). The most frequent organisms isolated were *Acinetobacter species* from tracheal aspirate and *Pseudomonas species* from blood samples, whereas *Escherichia coli* was the predominant organism found in urine, exudate, and other bodily fluids (5-7).

Knowledge of antimicrobial susceptibility in ICU is crucial and far more important for giving effective treatment and decreasing the spread of drug-resistant micro-organisms. It is a crucial step for early intervention, decreasing healthcare costs, improving the outcome of patients, and treatment provider satisfaction (8, 9). To the best of our knowledge, there was no study done in the ICU setting, both institutionally and country-wise. So, this study will be a significant input in addressing the gap.

Methods

Study setting and design

An Institutional based retrospective observational study was conducted at two intensive care units located at St. Paul`s hospital millennium medical college and Addis-Ababa burns, emergency, and trauma Hospitals. SPHMMC is a referral teaching hospital in Addis Ababa, Ethiopia. AaBET hospital is a branch of SPHMMC with an emergency complex that gives services to emergency, burns, and trauma cases. SPHMMC is a 14-bedded ICU admitting patients above the age of 14 years, and AaBET hospital is also a 14-bedded ICU that gives service to all patients regardless of age and clinical diagnosis, but mainly to trauma and burns. Both are general ICUs.

Sample size and sampling technique

Non-probability- convenience sampling technique was applied to all ICU patients from January 2019 to December 2019, with microbiological culture sent 48 hours after admission.

Data collection procedures

Data were collected from patient charts using pretested and structured questionnaires after ethical clearance was received from St. Paul's hospital millennium medical college`s institutional review board. The study was conducted in accordance with the procedures and guiding ethical principles of SPHMMC. All microbiological cultures and susceptibility results of patients sent after intensive care unit admission from January 2019 to December 2019 were included in the analysis. Data were collected by trained data collectors using pretested standardized checklists developed by the principal investigator. Socio-demographic data, comorbidities, sites of infection, causative micro-organisms, ICU admission category, associated organ failure, type of culture sent, antimicrobials given before culture sampling and based on susceptibility result, and patient outcome to ICU were retrieved. All data was taken from patient record charts with collected laboratory culture and susceptibility results after selecting their MRN from the ICU registration book.

Data management

Data were entered into Epi-Info and statistical analysis was performed using SPSS version 25. The Chi-square test was used for categorical variables. Mean, median, and standard deviation (SD) were used for continuous variables.

Ethical considerations

The need for informed consent was waived by the institutional review committee of St. Paul's hospital millennium medical college due to the retrospective nature of the study. The proposal was approved by St. Paul`s hospital millennium medical college IRB with Ref. No. of pm 23/384.

Results

Demographic characteristics

A total of 106 patients, having culture results after admission to ICU for over one year, were analyzed. The majority, 68(64.2%), were males, and the median age was 30.5 years, with a range of 3-82 years.

Most of the patients, 75(70.8%), were from the emergency department. The median length of ICU stay was 31 days (interquartile range of 3-128 days). And the hospital length of stay before ICU admission was 6.89±10.52 (mean ±SD). More than 99% of the patients have met the systemic inflammatory response syndrome (SIRS) criteria.

Clinical characteristics of patients

In most patients, 49(46.2%) had comorbidities during admission. The most common comorbidity was hypertension 14(28.6%, and congestive heart failure 10(20.4%). The majority of deaths, 22 (64.70%), were associated with comorbidity. The most common site of infection was the pulmonary system 84(54.5%), followed by urinary tract infection 26(16.9%), skin/soft tissue infection 18 (11.7%), Central nervous system 16(10.4%), and 10(6.5%) intra-abdominal focus. The pulmonary 55(65.47%) and urinary focus 18(69.23%) were in male patients, whereas intra-abdominal source was higher in females 9(90%). Organ failure occurred in the majority of 94(88.7%) patients, with the respiratory system comprising 84(44.7%) of organ failures, followed by the neurologic system 60 (31.9%), as shown in **Table 1.**

Table 1: Outcomes to ICU (discharge and death) among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019

Variables	Total (N*=106)	Discharge (N=65)	Death (N=34)	P value
Comorbidity	49(46.2%)	22(33.8%)	22(64.7%)	.196
RVI	3(6.1%)	1(1.5%)	2(5.9%)	.735
DM	8(16.3%)	5(7.7%)	3(8.8%)	.757
HTN	14(28.6%)	8(12.3%)	5(14.7%)	.047
CAD/CHF	10(20.4%)	4(6.15%)	6(17.6%)	.588
COPD/Asthma	2(4.1%)	1(1.5%)	1(2.9%)	.338
CKD	6(12.2%)	3(4.6%)	3(8.8%)	.146
CLD	1(2.0%)	-	1(2.9%)	.588
Malignancy	2(4.1%)	-	1(2.9%)	.977
Infection site	154	95	59	
Pulmonary	84(54.5%)	51(53.7%)	27(45.8%)	.036
Urinary	26(16.9%)	18(18.9%)	4(6.8%)	.282
CNS	16(10.4%)	9(9.5%)	7(11.9%)	.075
Skin/soft tissue	18(11.7%)	9(9.5%)	9(15.25%)	.395
Gastrointestinal	10(6.5%)	8(8.4%)	2(3.4%)	
Organ failure	188	105	71	
Neurologic	60(31.9%)	33(31.4%)	23(32.4%)	117
Respiratory	84(44.7%)	48(45.7%)	30(42.25%)	.119
Renal	31(16.5%)	17(16.2%)	13(18.3%)	.165
Cardiovascular	13(6.9%)	7(6.7%)	5(7.0%)	..603

*Number of patients

RVI- Retroviral Infection, DM- Diabetes Mellitus, HTN- Hypertension, CAD/CHF- Coronary artery disease/ congestive heart failure, COPD- Chronic Obstructive Pulmonary Disease, CKD- Chronic Kidney Disease, CLD- Chronic Liver Disease, CNS- central nervous system

Microbiological profile and antimicrobial susceptibility

Out of the 173 cultures analyzed, 84(48.55%) were blood cultures, urine 69(39.88%), pus 6(3.47%), CSF and body fluid 5(2.89%) each, and 2(1.16%) of the cultures were tracheal aspirate and stool culture each. Forty-four (25.43%) of the cultures had growth of 51 microorganism isolates. Gram-negative microorganisms were identified in 35(68.63%) isolates **(Table 2).**

Table 2: Type of microorganism isolates on microbiological culture among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019 (N=number of microorganism

Type of culture	Gram-negative (N=35)	Percentage % (68.7)	Gram-positive (N=10)	Percent-age %(19.6)	Fungus (N=6) 11.7%
Blood	5	9.80	7	13.73	-
Urine	23	45.10	1	1.96	6
Pus	3	5.90	2	3.92	-
Body fluid	1	1.96	-	-	-
Tracheal-aspirate	3	5.90	-	-	-

Acinetobacter species was the commonest organism isolated accounting for 10(28.57%), followed by *Klebsiella pneumonia* and *E. coli* 7(13.725%). Ten (19.60%) microorganisms were *gram-positive microorganisms*, of which 5(50%) were *coagulase-negative staphylococci*, 2(20%) *enterococci*, and *staphylococcus aureus* each, and 1(10%) *Streptococcus pneumonia*. Six (11.76%) microorganisms grown were fungal, all from urine culture **(Figure 1).** *Acinetobacter species* had shown sensitivity to meropenem 5(55.6%), ceftazidime 1(50%), amikacin 3(42.9%), and gentamicin 2(40%), but resistant at all test times to another cephalosporin (cefazoline, ceftriaxone, cefepime, and cefotaxime), TTC, nitrofurantoin and piperacillin.

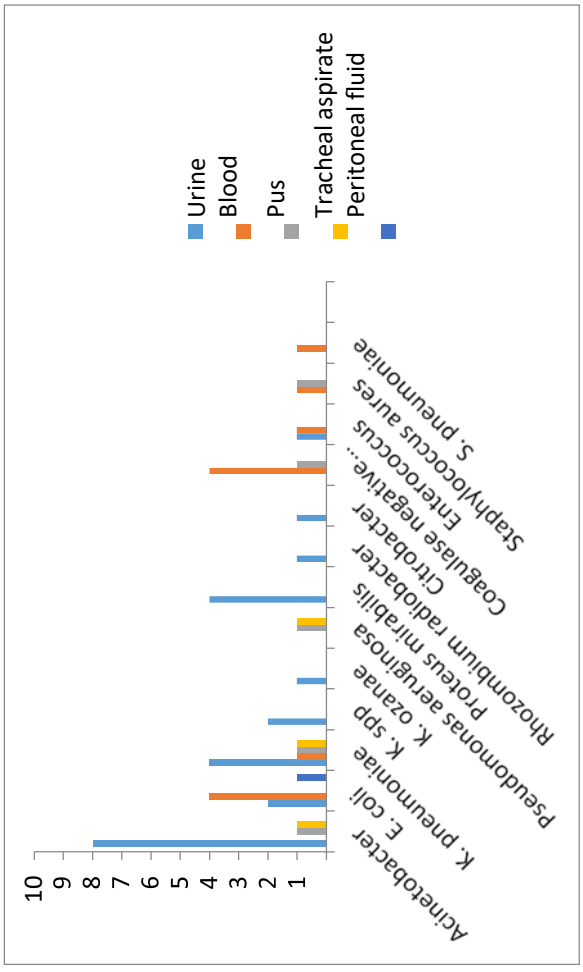

Figure 1: Microorganism isolates from each culture sample among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019 (Y-axis shows the number of microorganism isolates, X-axis shows the name of microorganisms).

Klebsiella pneumonia was sensitive to imipenem 1 (100%), piperacillin/tazobactam 1(50%), chloramphenicol 1(50%), meropenem 3(42.9%), and ciprofloxacin 1 (20%), but resistant to all tested cephalosporin antimicrobials (like cefuroxime, ceftazidime, cefepime, and cefotaxime), nitrofurantoin, ampicillin, and gentamicin.

Escherichia coli had shown sensitivity to meropenem 4(100%), amikacin 1(100%), chloramphenicol and nitrofurantoin 2(100%) each, gentamicin (80%), piperacillin/tazobactam 1(50%), ciprofloxacin 2(33.3%), and TMP/SMX 1(25%). Whereas, resistant to cephalosporin (cefazoline, cefotaxime, and cefuroxime), amoxacillin/clavulanate, piperacillin, and tetracycline at all test times. *Pseudomonas aeruginosa* was sensitive to ciprofloxacin 2 (100%), amoxicillin, cefepime and piperacillin 1 (100%) each, meropenem and tobramycin 1(50%) each. As detailed in (Table 3) (Figure 2) below.

Microorganisms isolated from urine culture which were resistant to all tested antimicrobials were *Klebsiella ozaena* (ceftriaxone, gentamicin, nitrofurantoin, piperacillin, cotrimoxazole, and tobramycin), and *Rhizobium radiobacter* (ampicillin, amoxicillin/clavulanate, ceftriaxone, cefepime, ciprofloxacin, nitrofurantoin, TTC, cotrimoxazole, and tobramycin).

Citrobacter isolated from urine culture was sensitive to amikacin but resistant to a cephalosporin (ceftriaxone and cefuroxime), TMP/SMX, ciprofloxacin, gentamicin, Amox/Clav, TTC, and piperacillin. *Enterococcus* isolated from urine culture had shown sensitivity to ciprofloxacin, daptomycin, and vancomycin, intermediate activity against erythromycin, but resistance to penicillin G.

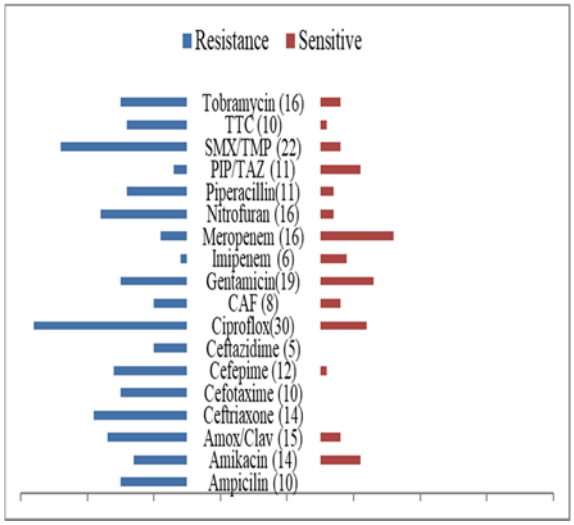

Figure 2: Antimicrobial resistance and sensitivity distribution among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019. (Number in bracket means the frequency of testing with the subsequent antimicrobial, and color is to show the strength of resistance and sensitivity).

TTC- Tetracycline, SMX/TMP- Sulfamethoxazole/ Trimethoprim, PIP/TAZ- Piperacillin/Tazobactam, CAF- Chloramphenicol.

Table 3: Antimicrobial resistance and sensitivity frequency among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019 (N= number of tests).

Antimicrobials	Resistance: N (%)	Sensitive: N (%)
Ampicillin	10(100%)	-
Amikacin	12(80%)	8(57.2%)
Amoxacillin/ Clavulanate	12(80%)	3(20%)
Ceftriaxone	14(100%)	-
Cefotaxime	10(100%)	-
Cefepime	11(91.7%)	1(8.3%)
Cefuroxime	4(100%)	-
Ceftazidime	5(71.4%)	1(14.3%)
Cefazoline	4(100%)	- 7(23.3)
Ciprofloxacin	23(76.7%)	3(37.5%)
CAF	5(62.5%)	1(50%)
Clindamycin	1(50%)	2(100%)
Daptomycin	-	-
Erythromycin	1(33.3%)	8(42.1%)
Gentamycin	10(52.6%)	4(66.7%)
Imipenem	1(16.7%)	2(66.7%)
Intrapenem	1(33.3%)	11(68.7%)
Meropenem	4(25%)	2(13.3%)
Nitrofurantoin	13(86.7%)	1(50%)
Norfloxacin	1(50%)	-
Oxacillin	2(100%)	-
Penicillin	2(100%)	2(18.2%)
Piperacillin	9(81.8%)	6(54.6%)
PIP/TAZ	2(18.2%)	3(13.6%)
SMX/TMP	19(86.4%)	1(10%)
TTC	9(90%)	3(18.7%)
Tobramycn	10(62.5%)	-
Vancomycin	2(66.7%)	-

Antimicrobial use and ICU outcome of patients

Almost all patients, 103(97.3%) took antimicrobials before ICU admission or before culture sampling, and ceftriaxone was used in 67(62.3%) patients, followed by vancomycin in 62(58.5%), and metronidazole in 56 (52.8%) patients. The most common indications were pulmonary infection in 68(37.2%), followed by empiric therapy in 26(14.2%), and urinary-tract infection in 25 (13.7%) patients (see **Table 4).** Almost a third of (32.1%) patients died during their ICU stay. Patients with urinary tract infection and septic shock before admission were significantly associated with a higher risk of death.

Table 4: Comparison among outcomes in ICU and indication for antimicrobial use before admission or before culture sampling among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019 (N= Number of patients).

Indication for antimicrobial use	N (%)	Death	Discharge	P value
Bacterial sepsis	14(13.2%)	3(21.4%)	9(64.3%)	.809
Septic shock	5(4.7%)	1(20%)	4(80%)	.053
CNS infection	11(10.4%)	6(54.5%)	5(45.5%)	.258
Urinary-tract infection	25(23.6%)	5(20%)	16(64%)	.086
Pulmonary infection	68(64.2%)	24(35.3%)	39(57.4%)	.266
Intra- abdominal infection	8(7.5%)	1(12.5%)	7(87.5%)	.255
Soft-tissue/skin ifection	16(15.1%)	7(43.75%)	9(56.3%)	.655
Infective endocarditis	1(0.9%)			-
Empiric therapy	26(24.5%)	6(23.1%)	18(69.2%)	.345
Prophylaxis	9(8.5%)	2(22.2%)	7(26.9%)	.294

Discussion

With this study, we have shown there was a high gram-negative resistant bacterial growth from patients admitted to intensive care units of the hospitals. The patients were also younger with a mean age of 35.8±1.6 years and the median length of stay in the ICU was prolonged to 31 days. The mean age was lower than in studies from other centers (8). The reason for younger age and prolonged stay may be partly the patient population where AaBET hospital is being a trauma center, and trauma victimizes the young.

In patients with culture growth, there was high underlying comorbidity found in 49(46.2%) of patients, hypertension was the most common comorbidity in 14(28.6%), lower than and different from the TASH study revealed 89.5% associated comorbidity and immunosuppression being the most common in 33.9% of patients (9).

It can be from an epidemiologic shift that NCDs are affecting the young. Of the 106 patients studied, 173 cultures were analyzed, and only 44(25.43%) of cultures had growth of microorganisms with 51 isolates, which was similar to a study in eastern Ethiopia hospitals with an isolation rate of 27.9% but higher than in TASH 16.5% and lower than a study done in Nepal 39.6% (10, 12-13).

In the study centers, the most common source of infection was the pulmonary and urinary tract, which is similar to a study of five ICUs of Imam Reza hospital and TASH ICU, but different from Jimma university hospital, from which surgical site infection was the most common source (14, 15).

The pulmonary and urinary focus was higher in male patients 55(65.47%) and 18(69.23%), while the intra-abdominal focus was higher in females 9(90%) in our study (16, 17).

Gram-negative were the most commonly identified microorganisms similar to other studies, but the isolated species were different (13, 18). And patients with CAD/ CHF, urinary tract source of infection, and septic shock before admission had a greater risk of death which was different from other studies which revealed a high risk of death with different factors such as infection with *acinetobacter species*, renal replacement therapy, use of mechanical ventilation, COPD, malignancy, pulmonary cause of infection and antibiotic use before admission (19, 20).

The study found 32.1% mortality with ICU infections was similar to other different studies, 14.31% to 45.4%, lower than that of an African study, 47.2% (19, 21-22). A high antibiotic resistance rate (>60%) was observed with ciprofloxacin, cephalosporin, piperacillin, cotrimoxazole, chloramphenicol, tetracycline, nitrofurantoin, tobramycin, and penicillins similar to a study in Chad-Ndjamena general hospital and other studies (23-25).

Almost all patients 103(97.3%) studied took antimicrobials before ICU admission, which contributes to antimicrobial resistance that was directly proportional to the volume of antimicrobials consumed (25, 26).

Conclusion

This study shows gram-negative bacteria were the predominant microorganisms identified which pose the greatest risk of patient death and prolonged ICU stay complications. It also showed patients with a urinary source of infection, and septic shock pose a greatest risk of death.

This research will help the intensive care unit to consider the targeted provision of antimicrobials and strengthen the quality and availability of microbiology laboratories. It will also use as a reference for future studies.

Abbreviations

AaBET- Addis-Ababa Burn Emergency and Trauma Hospital, CSF- Cerebro Spinal Fluid, ICU- Intensive and Critical care Unit, MRN- Medical Registration Number, SIRS- Systemic Inflammatory Response Syndrome, SPHMMC- Saint Paul`s Hospital Millennium Medical College, TASH- Tikur Anbessa Specialized Hospital.

Conflict of interest

The authors declare no conflict of interest.

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Author Contribution

All authors contributed to the study equally. YG prepared the manuscript. MS edited and commented on the manuscript. DT helped with the study design and literature review. All authors agreed on the final version and publication.

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References

1. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathogens and Global Health [Internet]. 2015 Sep 7; 109(7):309–18.
2. Calfee DP. Methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci, and other Gram -positives in healthcare. Current Opinion in Infectious Diseases. 2012; 25(4):385–94.
3. Moolchandani K, Sastry AS, Deepashree R, Sistla S, Harish BN, Mandal J. Antimicrobial Resistance Surveillance among Intensive Care Units of a Tertiary Care Hospital in Southern India. J Clin Diagn Res. 2017 ; 11 (2): 1-7.
4. Sakr Y, Jaschinski U, Wittebole X, Szakmany T, Lipman J, Ñamendys-Silva SA, et al. Sepsis in Intensive Care Unit Patients: Worldwide Data From the Intensive Care over Nations Audit. Open Forum Infectious Diseases [Internet]. 2018 Nov 19; 5(12).

5. Teklemichael H. Assessment of incidence and treatment outcome of septic shock among patients admitted to adult intensive care unit of Tikur Anbessa specialized hospital in Ethiopia (Addis Ababa): AAU; 2017-06.
6. IbssaA, Solomon G. Common Bacterial Pathogens and Their Antimicrobial Susceptibility PatternsIn Patients with Symptomatic Urinary Tract Infections at Hiwot Fana and Jugal Hospitals in Eastern Ethiopia (Harar). Galore International Journal of Health Sciences and Research. 2018; 3(2):2.
7. Sapkota J, Mishra B, Jha B, Sharma M. Bacteriological profile and their antimicrobial susceptibility pattern in central venous catheter tip culture. Journal of Pathology of Nepal.2017; 7, 1059-1061.
8. Solomon A, Melkamu B, Sisay B, Gebre K, Lule T, Yonas Y, Yesuf A, Netsanet F, Henok A, Mulatu G, Esayas KG. Health care associated infection and its risk factors among patients admitted to a tertiary hospital in Jimma University, Ethiopia. Antimicrobial Resistance and Infection Control. 2018; 7:2-5.
9. H. Hamishehkar H, P. Shadmehr, A. Mahmoodpoor, S. O. Mashayekhi, 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. 2016; 52(3): 3.
10. Mwangi E.G., Karanja, S.M., Wanzala P and Ngumi Z. Bacterial profile and antimicrobial susceptibility patterns of isolates causing urinary tract infections in intensive care unit patients at Kenyatta national hospital. African Journal of Health Sciences. 2020; 33(5): 1-17.
11. Ak O, Batirel A, Ozer S, Çolakoğlu S. Nosocomial infections and risk factors in the intensive care unit of a teaching and research hospital: a prospective cohort study. Med SciMonit.2011; 17: 29-34.
12. Ustun C, Hosoglu S, Geyik MF, Parlak Z, Ayaz C The accuracy and validity of a weekly point-prevalence survey for evaluating the trend of hospital acquired infections in a university hospital in Turkey. Int J Infect Dis. 2011; 15: 684-687.
13. Madani N, Rosenthal VD, Dendane T, Abidi K, Zeggwagh AA. Health-care associated infections rates, length of stay, and bacterial resistance in an intensive care unit of Morocco: findings of the International Nosocomial Infection Control Consortium (INICC). Int Arch Med.2009; 2: 29.
14. Bajpai T, Bhatambare G, Shrivastava G, Deshmukh A, Chitnis V. Microbiological profile of lower respiratory tract infections in neurological intensive care unit of a tertiary care center from Central India. Journal of Basic and Clinical Pharmacy.. 2013; 4(3):51.
15. Pattanayak C, Patanaik SK, Datta PP, Panda P. A study on antibiotic sensitivity pattern of bacterial isolates in the intensive care unit of a tertiary care hospital in Eastern India. International Journal of Basic & Clinical Pharmacology [Internet]. 2017; 2(2):153–9.
16. Deepti C, Avinash L, K. Sadawarte, Tukaram P. Microbiological Profile, and Antimicrobial Sensitivity Pattern of Endotracheal Tube Aspirates of Patients in ICU of a Tertiary Care Hospital in Bhopal, India. Int.J.Curr.Microbiol.App.Sci.2017; 6(3):891-895.
17. Michel K, Amon TD, Julius MN. Bacteriological profile and antimicrobial susceptibility patterns of urine culture isolate from patients in Ndjamena, Chad. Pan African Medical Journal. 2017; 28:258.
18. Kaushal VS, Tejas K Patel, Saklainhaider S Malek, Tripathi. Antibiotic Sensitivity Pattern of Bacterial Isolates from the Intensive Care Unit of a Tertiary Care Hospital in India. Trop J Pharm Res. 2012; 11(6):991.
19. Walelegn WY, Abera K, Feleke MY. Point prevalence of hospital-acquired infections in two teaching hospitals of Amhara region in Ethiopia. Drug Healthc Patient Safty. 2016; 8:71-6.
20. Tsegaye A, Mulubrahan A, Enkosilassie, Et al. The burden of antimicrobial resistance at tertiary care hospital, southern Ethiopia: three years' retrospective study. BMC Infectious Diseases. 2019; 19:585.
21. Lovely B, Kaniz F, J Ashrafu H, Mohammad OF, ASM Areef, Md. Abu HG Morshed, Md. Belayet H. Bacterial profile and their antimicrobial resistance pattern in an intensive care unit of a tertiary care Hospital in Dhaka. Ibrahim Med. Coll. J. 2010; 4(2): 66-69.
22. WHO. Report on the Burden of Endemic Health Care-Associated Infection Worldwide. Geneva, Switzerland: WHO; 2011.Available l4from:http://www.who.int/about/ licensing/copyright form /en/index.html.
23. Radji M, Fauziah S, et al. Antibiotic sensitivity pattern of bacterial pathogens in the intensive care unit of Fatmawati Hospital, Indonesia. Asian Pacific Journal of Tropical Biomedicine. 2011; 1:39-42.
24. Shalini S, Kranthi K, Gopal Krishna BK. The microbiological profile of nosocomial infections in the intensive care unit. J ClinDiagn Res. 2010; 4:3109-12.
25. ZweiZwer F. Definition, Incidence, and Evolution of Sepsis & Septic Shock. Journal of Anesthesia & Critical Care: Open Access. 2016 Jun 1; 5(1).
26. Sharma PR, Barman P. Antimicrobial consumption and impact of "Reserve antibiotic indent form" in an intensive care unit. Indian J Pharmacol. 2010; 42: 301-305.

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9036 Addis Ababa, Ethiopia.

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Original Article

Ultrasound guided drainage of intra-abdominal collections; Results of initial experience from Tikur Anbessa Specialized Hospital

Tesfaye Kebede Legesse*[1], Zeleke Mogne[2]

[1] Radiologist at Addis Ababa university
[2]Radiologist at Dilchora Hospital

Corresponding author*: kebedetesafye@yahoo.com

Abstract

Background: *Image-guided percutaneous aspiration and drainage (PAD) is a safe and cost-effective means of draining an abscess. PAD is noninvasive and has decreased procedure-associated morbidity and mortality, reduced cost of treatment, and reduced length of hospital stay as compared to open surgical drainage. The widely used imaging modalities that can be used for drainage are ultrasound (US) and Computerized Tomography (CT) . This study aims to share our initial experiences in the successful introduction of US-guided percutaneous drainage of intra-abdominal collections in the tertiary center.*

Method : *An institution-based retrospective record review of patients who were diagnosed to have intra-abdominal collections and treated with PAD was done from 2020 back to 2013. Cases were collected from the accessible records of the department of radiology and patient charts were then retrieved. Data was collected using a structured questionnaire and a descriptive analysis of findings was done using SPSS version 25.*

Results: *A total of 53 patients were retrieved from the record. 35 (66%) were males and 18(34%) were females with patients' age ranging from 10 years to 80years with a mean age of 43.1+15.8. 59 patients. Most of the intra-abdominal collections were either idiopathic or surgical complications which accounted for 60.4% & 18.9% respectively and the success rate of PAD with a single attempt was 90.2% with s*uccess increased to 96.2% with a second attempt.

Conclusion: *PAD can be used as an alternative way of managing patients with intra-abdominal collections not only in developed nations but also in developing countries like Ethiopia with a high rate of success.*

Keywords: *ultrasound, CT, aspiration, catheter drainage, abscess, fluid collections, and percutaneous drainage*
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Introduction:

An abscess is a localized collection of infected fluid which has a significant impact on the clinical care and outcome of patients. The presence of an abscess in any body part may result in significant morbidity and mortality mostly associated with sepsis. The mortality of undrained abscesses is also very high which may reach up to 100% (1). Before the introduction of percutaneous aspiration and drainage (PAD), medical treatment of abscesses with antibiotics and surgical drainage of those abscesses which cannot be treated with antibiotics or that failed medical treatment were the usual mode of management. The introduction of PAD challenged the traditional methods of management with antibiotics and surgery and was shown to have less complication rate compared with surgical management. It is also shown to have a low rate of complications compared with surgical drainage of abscesses (2-4).

Because of the increased mortality and morbidity associated with open surgical drainage of abscesses, open surgical drainage should be reserved for abscesses that cannot be percutaneously drained(3, 5-8).

The most widely used imaging modalities for both diagnosis and assessment of extent of collections and also as a guide for insertion of needle and drainage tube are ultrasound (US) and computerized tomography (CT) (9-12). Even if the choice depends on personal experience in addition to the location and depth of an abscess; the wide availability, ease of use, guidance in any plane, and real-time visualization of the needle tip make US the modality of choice in most institutions (13-15).

Until recently in the institution where this research was conducted [Tikur Anbessa Specialized Hospital (TASH)] and in the country as a whole, there was no choice other than the surgical mode of

management for intra-abdominal collections. Although there were attempts in performing US-guided aspiration at some institutions (16), the attempt couldn't change the practice and the surgical management option continued even after that. There were also attempts in a few private institutions in the capital city, Addis Ababa, to use PAD for management of collections and abscesses but couldn't be sustainable because they were performed with visiting foreign professionals mostly coming from developed nations. The percutaneous intervention was introduced in Ethiopia recently and the procedure was performed with Ethiopian professionals with the introduction of radiology fellowship training in 2013. Before the introduction of the procedure, all patients were managed with open surgical intervention by evacuation of the collection and insertion of the drainage tube. Therefore, the objective of this study is to share our experience of the successful introduction of US-guided drainage of abscesses in Tikur Anbessa Specialized Hospital which is the tertiary teaching institution in the country. The study may also serve as the basis for future multicenter studies.

Methods and Materials

Study area

The study was conducted at TASH, which is located in Addis Ababa, the capital city of Ethiopia. It is the largest & one of the oldest public hospitals in the country providing a high level of clinical care for millions of people and training to health science students from different parts of the country and the Horn of Africa. The hospital is selected for this study because it is the first institution to introduce image-guided procedures in the country and is still the leading institution in the volume of image-guided procedures. Close to 50 image-guided procedures are being done per month the majority of them being image-guided diagnostic biopsies and Fine Needle Aspirations Cytology (FNACs).

Study Design and period

An institution-based retrospective record review was conducted from June 2020-August 2020 by retrospectively collecting imaged procedures which were done from 2013 – 2020. This period was chosen because image-guided procedures were introduced as a standard of care in 2013 with the introduction of radiology fellowship training. All patients with an intraabdominal collection for whom US-guided draining was done during the stated period were collected from the department of radiology and patients' chart were retrieved and data were collected using a structured questionnaire.

Source of data

The source population of this study was all patients for whom US-guided intervention was performed for intra-abdominal collections.

Inclusion and exclusion criteria

All patients for whom US-guided aspiration or drainage was done for an indication of intra-abdominal collections were included in the study. Patients who were excluded from the study included those who had incomplete electronic or chart records.

Procedure techniques

Procedures followed standardized techniques which are the trocar and Seldinger techniques. The trocar technique is a single-step procedure where a trocar and catheter are inserted into the abscess cavity with a direct puncture. Seldinger technique is a two-step procedure where an intervention needle and guidewire were inserted, and the tract is dilated using serial dilators and finally the drainage catheter is advanced over the guidewire to the target collection.

Data collection tools and techniques

Data were collected from electronic records of the department procedure log and patients chart using a structured questionnaire. The questionnaire contains sociodemographic characteristics, location, and characteristics of the collection, cause, and site of collection, techniques used, the success of the procedure, and procedure time. The collected data was then entered into SPSS version 23 and analyzed. Descriptive statics was made for sociodemographic characteristics, location and characteristics of the collection, techniques of the procedure, and duration of the drainage. Findings were displayed using graphs and charts.

Ethical considerations

Ethical approval to conduct the research was obtained from the research and ethics committee of the Department of Radiology. All patient identifiers were removed from the data.

Results

Patient demographics

There were 53 patients' information retrieved from the record. Thirty-five were male and 18 were female (Figure 1). Patients' age ranged from 10 years to 80years with a mean age of 43.1+15.8 years. Half of the patients were from the larger cities and the rest were from the rural regions. Nearly a quarter (12/53) of patients have underlying chronic illnesses like HTN, DM, Chronic renal and liver disease, or underlying malignancy. The rest have no documented underlying chronic conditions.

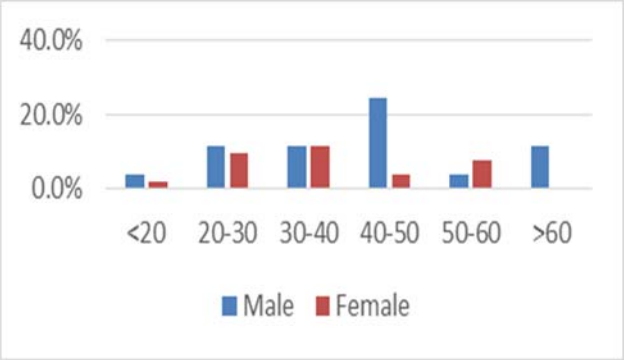


Figure1: Age distribution of patients with an intra-abdominal abscess at TASH

Imaging characteristics of the collection

There were scattered fine internal echoes (debris) in 11 out of 53 collections and there were homogeneous internal echoes (debris) in 42/53 collections.
Collections were unilocular in 12/53 and multilocular in 41/53 of the cases. The size of the collection ranged from 4.2cm to 22.2cm in maximum dimension with a mean size of 10.1cm.

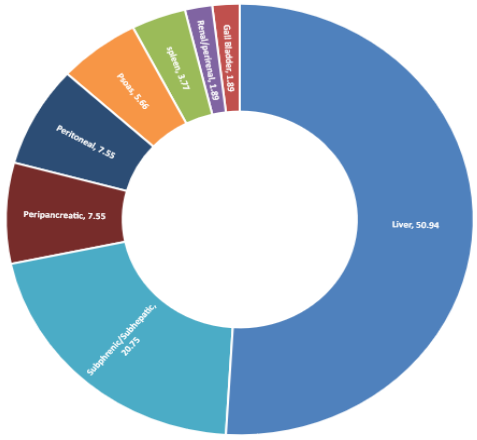
Diagnostic lab investigations were available for 20 of the collections among these two were inconclusive. Two of the collections were transudative. Eleven of the collections were pyogenic in origin, one was amebic, and two were tuberculous abscesses. Two of the collections were peripancreatic fluid collections.

The shortest distance of the abscess collection from the skin ranged from 1cm – 11cm with a mean distance of 2.8cm. Most of the intra-abdominal collections were either idiopathic collections (32/53) or surgical complications (11/53) (figure 2).

Figure 2: Frequency distribution of causes of intra-

abdominal collections for which percutaneous drainage was done

Twenty-seven of the collections out of 53 were in the liver followed by subphrenic/subhepatic collections in 11/53 cases (Figure 3) accounting more than two-thirds of the collections.



Indications and Techniques of the procedure

The procedure was done for diagnostic purpose of characterizing the fluid in 16/53 and for therapeutic drainage for 37/53 cases. There were two types of interventions done; one was just needle aspiration of the collection for 14 cases, and the other was tube drainage which was done for 39 out of 53 cases. Trocar and Seldinger techniques were employed for tube drainage in 18 and 21 out of 39 cases for whom a drainage tube was inserted and left in the collection for progressive drainage over time. The choice of the technique depends on individual preference and availability of the supply at the time of the procedure.
For 34 of the 39 cases for whom a drainage tube was inserted 10/12 French catheters were used and for the rest of the collection 8 French catheters were used. Only a single catheter was used for the majority of the collections except for two collections which were in the liver where two catheters were used at the same time to drain the collection.
Insertion of needle or drainage tube was done with a single attempt in 50/53 of the collections and repeat attempts were made for three of the collections. The mean duration of complete drainage of the collection is 8.7days with duration ranging from 1-22 days (Figure 4)

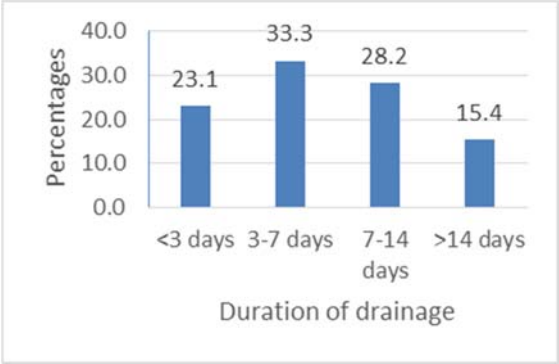


Figure 4: Total duration in days that percutaneous drainage took for complete evacuation of the collection

The success of the procedure

The procedure was successful in 51 out of the 53 cases and failed in two cases. The cases which failed for percutaneous drainage were peripancreatic collections which showed no sign of superinfection and showed no growth on culture. Both collections recurred after 5 and 7 days of the complete evacuation of the collection and underwent surgical drainage.

Discussion

We retrospectively analyzed 53 cases of intra-abdominal collections which were managed with US-guided PAD. Most of the collections have no identified source and are located predominantly in the liver, subphrenic, and subhepatic spaces confirming liver and biliary trees being the most common sources of intra-abdominal abscesses. Post-operative complications account for the majority of abscess collections. More than half of the abscesses in this study were in the liver with more than 2/3rd occurring in males.

Most intra-abdominal abscess collections arise from the colon or appendix, but it is not uncommon that the source may be undetermined (7). For those who have identifiable cause for the collection, most have bowel origin and colon and rectum being the most common source followed by liver and biliary sources (6, 7, 11, 17). Post-operative complication, which also accounted the second most common causes in our study, mostly occur following bowel surgery (7). Among those which diagnostic lab investigation from the fluid were done, most were pyogenic in origin which is also the case in other published literatures. (17). Collections may sometimes grow yeast and significant proportion may not grow organism at all (17). As seen in our case, rarely tuberculosis may be the cause of intra-abdominal abscess.

In all of our cases, PAD was performed under US guidance. Even if each imaging modality offers unique advantages and disadvantages, choice of modality differs with different factors including operator preference, wide availability of US, ease of use and less procedure related complications make US the preferred modality of guidance (7, 18). Use of techniques of inserting drainage tubes may be based on operator experience, size, location and depth of collection as well as presence of a safe access route. Seldinger technique is often used for small deep collections which are difficult to access. The trocar technique is often used for large and superficial collections. This technique has the advantage of the speed and avoids leakage of abscess outside the abscess cavity due to serial access tract dilatations. The limited use of the Seldinger technique in our case may partly be explained by operator preference as well as the limited access of the supply compared with the trocar technique.

Almost all of our cases have collections greater than 4cm in dimension and an abscess size of more than 20cm was also effectively treated with PAD in our series.

Most intra-abdominal abscess collections which are <5cm in dimension can effectively be treated with antibiotics alone. Moreover, due to difficulties in inserting drainage tubes in small abscess collections, most procedures in small collections may result in a failed attempt and are predictors of failure of PAD(1, 6). Abscesses larger than 5cm often fail for conservative management with antibiotics, so percutaneous drainage is the recommended treatment (7).

We found out that more than two-thirds of the cases in our study took a week or less for complete drainage of the collection, however, some collections also took more than three weeks for complete drainage. This has also been the case in multiple published works of literature where drainage took from a couple of days to even more than a month (7, 8, 18) and the recurrence rate following complete PAD is low(7) as is also the case in our study.

In our study, we found out that the success rate of US-guided drainage with a single attempt is 90.6% which has increased to 96.2% with repeated attempts which is encouraging for an institution that attempted to introduce PAD of the intra-abdominal collection as an alternative means of treatment of patients. This was also shown in other literature works where the success of PAD was found to be higher than 70 % (3, 6-8, 11) with up to a 12% increase in the rate with repeated attempts (11).

Two of our failed PADs were peripancreatic collections which recurred after successful drainage and ended up in surgical drainage. The reported success rate for pancreatic-associated abscesses and pseudocysts in other published works is shown to be very low(8).

PAD of intra-abdominal collections can be used as an alternative modality for appropriate candidates. The widely available US in the institution can also be used as guidance. The authors would like also to recommend organized data recording of the image-guided procedures in the department.

Limitations

Due to a lack of central recording of all procedures in the department, we were unable to include all cases.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

First author was the major contributor in conception of the idea, interpreting the data and shaping the research. The second author collected the data, do preliminary analysis, and edited the manuscript

Acknowledgment

Not applicable

References

1. Azzarello G, Lanteri R, Rapisarda C, Santangelo M, Racalbuto A, Vincenzo M, et al. Ultrasound-guided percutaneous treatment of abdominal collections. Chirurgia italiana. 2009;61:337-40.
2. Brown C, Kang L, Kim ST. Percutaneous drainage of abdominal and pelvic abscesses in children. Seminars in interventional radiology. 2012;29(4):286-94.
3. Johnson WC, Gerzof SG, Robbins AH, Nabseth DC. Treatment of abdominal abscesses: comparative evaluation of operative drainage versus percutaneous catheter drainage guided by computed tomography or ultrasound. Annals of surgery. 1981;194(4):510-20.
4. Politano AD, Hranjec T, Rosenberger LH, Sawyer RG, Leon CAT. Differences in Morbidity and Mortality with Percutaneous versus Open Surgical Drainage of Postoperative Intra-abdominal Infections: A Review of 686 Cases. The American surgeon. 2011;77(7):862-7.
5. Brolin RE, Nosher JL, Leiman S, Lee WS, Greco RS. Percutaneous catheter versus open surgical drainage in the treatment of abdominal abscesses. The American surgeon. 1984;50(2):102-8.
6. Benoist S, Panis Y, Pannegeon V, Soyer P, Watrin T, Boudiaf M, et al. Can failure of percutaneous drainage of postoperative abdominal abscesses be predicted? American journal of surgery. 2002;184(2):148-53.
7. Kumar RR, Kim JT, Haukoos JS, Macias LH, Dixon MR, Stamos MJ, et al. Factors affecting the successful management of intra-abdominal abscesses with antibiotics and the need for percutaneous drainage. Diseases of the colon and rectum. 2006;49(2):183-9.
8. Malik S., Gupta K., Wani R., P. P. Image-guided percutaneous management of intra-abdominal collections; A Hospital-based prospective study. Journal of International Research in Medical and Pharmaceutical Sciences. 2015;8(1):13.
9. Gerzof SG, Robbins A, Birkett D, Johnson W, Pugatch R, Vincent MJAJoR. Percutaneous catheter drainage of abdominal abscesses guided by ultrasound and computed tomography. 1979;133(1):1-8.
10. Carvalho ATP, Esberard BC, da Luz Moreira A. Current management of spontaneous intra-abdominal abscess in Crohn's disease. Journal of Coloproctology. 2018;38(2):158-63.
11. Cinat ME, Wilson SE, Din AM. Determinants for Successful Percutaneous Image-Guided Drainage of Intra-abdominal Abscess. Archives of Surgery. 2002;137(7):845-9.
12. Hemming A, Davis NL, Robins REJTAjos. Surgical versus percutaneous drainage of intra-abdominal abscesses. 1991;161(5):593-5.
13. Goletti O, Lippolis PV, Chiarugi M, Ghiselli G, De Negri F, Conte M, et al. Percutaneous ultrasound-guided drainage of intra-abdominal abscesses. The British journal of surgery. 1993;80(3):336-9.
14. Laméris JS, Bruining HA, Jeekel J. Ultrasound-guided percutaneous drainage of intra-abdominal abscesses. The British journal of surgery. 1987;74(7):620-3.
15. Gerzof SG, Robbins AH, Johnson WC, Birkett DH, Nabseth DC. Percutaneous catheter drainage of abdominal abscesses: a five-year experience. The New England journal of medicine. 1981;305(12):653-7.
16. Asefa G, M. T. Ultrasound-guided fine-needle aspiration in Tikur Anbessa Hospital: a report of the preliminary experience. Ethiopian Medical Journal. 2000;38(1):9.
17. Shahnazi M, Khatami A, Jamzad A, Shohitavi S. Safety and Efficacy of Percutaneous CT-Guided Drainage in the Management of Abdominopelvic Abscess. Iran J Radiol. 2014;11(3):e20876-e.
18. Khurrum Baig M, Hua Zhao R, Batista O, Uriburu JP, Singh JJ, Weiss EG, et al. Percutaneous postoperative intra-abdominal abscess drainage after elective colorectal surgery. Techniques in coloproctology. 2002;6 (3):159-64.

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Original Article

Malpositioned chest tubes and their indications; an experience from Addis Ababa, Ethiopia

Tesfaye Kebede Legesse*[1], Azmera Gissial [2] Ayalew Tizatu[2]

[1] Radiologist at Addis Ababa university
[2]Radiologist at Addis Ababa university
[2]Cardiologist at Addis Ababa university

Corresponding author*: kebedetesafye@yahoo.com

Abstract

Background: *Placement of a chest tube drain is the commonest procedure performed, especially in an emergency setting to evacuate fluid, blood, and air from the pleural cavity. Even if it is a simple procedure, it is associated with tube malposition and related complications, which sometimes may lead to death. So, This study analyses malpositioned chest tubes as seen on Computerized tomography (CT) scans.*

Method : *This is a retrospective record review of CT images of patients who have a diagnosis of malpositioned chest tubes.*

Results: *Most of the indications for chest tube placement were done for pleural fluid drain and pneumothorax. The retrospective CT analysis showed most of the chest tubes inserted were for the wrong diagnosis. Most malpositioned chest tubes were located in the normal or diseased lung. Intra-abdominal tube malpositions were seen in the spleen, liver, and retroperitoneum.*

Conclusion: *Chest tube insertion without proper indication may result in a malpositioned drainage tube . Abnormal tube positions may also cause injury to intrathoracic or intra-abdominal organs.*

Keywords: Chest tubes, Ethiopia, Malposition
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Introduction:

Whether the accumulation of air or fluid is rapid as in trauma or gradual as in malignant effusions, placement of a chest tube allows for continuous drainage of the collection until the underlying pathology can be more formally addressed. Most chest tube drain insertions everywhere are done in the emergency setting, particularly in traumatic thoracic emergencies (1).

Knowing and understanding the insertion techniques has paramount importance in reducing tube malposition and associated complications. The level of expertise and years of experience are also shown to affect the rate of complications associated with the insertion of chest tubes (2). So most guidelines recommend that all personnel involved with the insertion of chest drains should be adequately trained and supervised (3, 4). It's also mandatory in some institutions that all doctors who were expected to insert a chest drain should get adequate training using a combination of didactic lectures, simulated practice, and supervised practice until considered competent to reduce the rate of complications associated with the procedure (3).

The rate of complication associated with chest tube insertion is shown to vary among residents in training in different disciplines. Surgical residents were significantly less likely to have complications than nonsurgical residents (risk ratio 0.4, 95% confidence interval [CI] 0.16–0.96) (1).

Even if some previous studies have shown a lower risk of complication and high yield of pleural aspiration when done in the hands of experienced operators without image guidelines (5), most guidelines recommend the use of ultrasound guidance to avoid complications and dry plural tap associated with blind pleural aspirates (3, 6). It is strongly recommended that all chest drains for fluid should be inserted under image guidance even if there is less evidence comparing ultrasound guidance against clinical guidance for chest drain insertion than there is for pleural aspiration. Studies showed that a high level of efficacy and low rate of complication could be achieved when chest tube drain for pleural effusion and pneumothorax was done under ultrasound guidance (7-9).

Proper positioning, aseptic procedures, and proper technique of insertion guidelines should be followed strictly for all levels of expertise. Directly observed procedures and expert supervision during the procedure also improve accuracy and lowers the rate of complications when performed with medical students and residents (1).

The British society of thoracic surgery recommends the percutaneous insertion of chest drains in the safe triangle bordered by the anterior border of latissimus dorsi posteriorly and lateral border of the pectoralis major muscle anteriorly and a horizontal line crossing lateral from the nipple, with the apex below the axilla (4). Drains inserted in this space have a minimal rate of complication. All operators are expected to be appropriately trained and have been initially supervised by an experienced trainer. In addition, the UK national patient safety agency (NPSA) guidance and the new BTS guideline both recommend ultrasound guidance for inserting an intercostal drain for fluid.

It is also a routine practice in most institutions to get a post-procedure radiograph to check the position of the inserted tubes, even if malpositioned tubes may be missed on post-insertion radiographs. Sometimes, malpositioned / misdirected chest tubes may injure not only intrathoracic but also intra-abdominal vital organs resulting in life-threatening hemorrhages (10) and maybe even be fatal(11).

Sensitivity of a chest radiograph to diagnose malpositioned tubes is low and can diagnose only $1/5^{th}$ of the misplaced chest tubes (12). So CT is used for malpositioned chest tubes, and this study reviews malpositioned chest tubes and their complications and the primary indication and appropriateness of chest tube drain insertion.

The rationale behind this study is to evaluate the locations of malpositioned chest tubes and their clinical indication based on the imaging study done after the tube was inserted and to evaluate the value of computed tomography in localizing the exact anatomic location of malpositioned chest tubes.

Methods

This is a retrospective institutional-based study done at Wudassie Diagnostic Center by collecting all CT imaging studies done to asses the inserted chest draining tube and diagnosed to have malpositioned tubes.

Research setting

The study was conducted at Wudassie Diagnostic Center, one of the diagnostic centers located in the capital city, of Addis Ababa. The center has two CT scan machines at the time of data collection. More than ten radiologists are working on a full-time and part-time basis. All imaging was done based on the request made by the referring physician as a routine workup of patients.

In addition to the clinical information documented by the treating/refereeing physician, the full clinical history of the patient were taken by trained nurses before the scanning using a structured electronic record to complete all the necessary information which is needed for imaging, that contains age and sex of the patient, clinical symptoms, vital signs, indication for imaging, previous medical or surgical conditions, history of drug and contrast allergy. All the above procedures are routine practices at the imaging institution for all patients referred for imaging evaluation. The imaging request which is brought by the patient will be scanned and electronically recorded together with the clinical history and consent form.

Data collection.

The electronically archived chest imaging reports were retrieved, and all those reports with the conclusion of mispositioned chest tubes were selected. All imaging studies, with the diagnosis of mispositioned tubes were reviewed to assess the position of the tubes, and other clinical information recorded and stored electronically were also retrieved. A structured questionnaire was used to collect the data, which contains the age and sex of the patient, indication for insertion of chest tube, chest CT findings, assessment of the primary indication based on chest findings, and side and position of the inserted tube.

The primary indication for chest tube insertion was retrieved from the patient's records (from both imaging requests and electronic records of the institution). Findings are displayed using tables and representative images from the chest scan were also selected and displayed too.

Ethical considerations

This is a retrospective review of and imaging study was not done for the research purpose but performed as a routine workup of the patient when requested by the treating physician. All images were anonymized and all individual and institutional identifiers are removed from the data. permission to use the images from the institution server was obtained from the institution.

Results

There were a total of 19 cases over 16 months period from November 2019 up to March 2020 who were diagnosed as having malpositioned chest tubes with chest CT scans. As seen in Table 1 below, Patients' age ranged from 11 years up to 88 years, and a median age of 34 years. Among the cases, 14/19 were males, and 5/19 were females. Most chest tubes 11 (57.9%) were inserted with a clinical indication of pleural effusion, and 5/19 of the chest tubes were inserted for either traumatic or spontaneous pneumothorax. Most of the indica-

Table 1: Patient characteristics, indication, and findings of chest CT scan done for assessment of tube position

Case No.	Age	Sex	Presumed indication	Indications for CT	Chest CT finding	Indicated based on the imaging?	Site of chest tube	Position of the tube
1	11	M	Pleural effusion	No drainage	LLL consolidation	No	L	In consolidated lung
2	11	M	Pleural effusion	No drainage	Anterior mediastinal mass with massive pleural effusion	Yes	L	In mediastinal mass
3	49	M	Pleural effusion	No drainage	Basal atelectasis	No	L	Crossed the mediastinum anterior to the aorta with the tip abutting the right atrium
4	25	M	hemothorax	No drainage	Lung contusion	No		Lung parenchyma
5	25	M	Unknown	No drainage	Bilateral basal atelectasis	No	R	Crossed through the liver and punctured the kidney with perirenal hematoma
6	26	F	Trauma with pneumothorax	Suspected malposition	Diaphragmatic hernia with bowel herniating	No	L	Abutting bowel wall
7	26	F	Trauma with hemothorax	No drainage	Right hydropneumothorax and minimal left hemothorax	Yes	R	In the liver parenchyma
8	27	M	Pleural effusion	No drainage	Pancreatitis with left pleural effusion	Yes	L	Within spleen parenchyma
9	34	F	Pleural effusion	Reduced drainage	Right pleural effusion	Yes	R	Crossed through the lung and abuts the right atrium
10	34	M	Penetrating chest injury with hemothorax	No drainage	Right lung contusion and rib fractures	No	R	Within the contused lung
11	34	M	Pleural effusion	No drainage	Left pleural effusion	Yes	L	Within the oblique fissure
12	42	F	Pleural effusion	Reduced drainage	LLL consolidation and pleural effusion	Yes	L	Crossed through the lung with the tip in the sup mediastinum abutting the left SCA
13	42	M	Pleural effusion	No drainage	Left intrathoracic mass filling the thoracic cavity and right basal atelectasis	No	L	Within the intrathoracic mass
14	43	M	Pneumothorax	Workup for the cause	Lung fibrosis with giant bulla	No	R	Within the bulla
15	48	M	Pleural effusion	No drainage	Complete right lung fibrotic atelectasis with the heart being in the right thoracic cavity and hyperinflated left lung and iatrogenic left pneumothorax	No	R	Crossed from the right anterior to the right ventricle within the left pleural cavity causing left pneumothorax
16	55	F	Pleural effusion	No drainage	Left lung consolidation	No	L	Within the consolidated lung, the tip abuts the thoracic aorta
17	55	M	Pneumothorax	No clinical improvement	Pneumothorax	Yes	R	Within the atelectatic lung
18	65	M	Unknown	Routine workup	Pleural-based RLL mass	No	R	Within the mass
19	88	M	Trauma with pneumothorax	No clinical improvement	Left diaphragmatic hernia with bowel herniating	No	L	Within the lung in the LUL

The absence of clinical improvement was the indication for two cases and CT was done as a routine follow-up in two cases. Only in one case, the indication for tube insertion was for a suspected mispositioned chest tube. Based on the finding of the CT scan done to assess the position of the draining tubes, there was no clear indication for the chest tube insertion in 11/19 of the cases (table 1). Most chest tubes 11/19 were inserted on the left side with one of the tubes inserted on the right side with the tube crossed to the left, causing left iatrogenic pneumothorax (Figure 6).

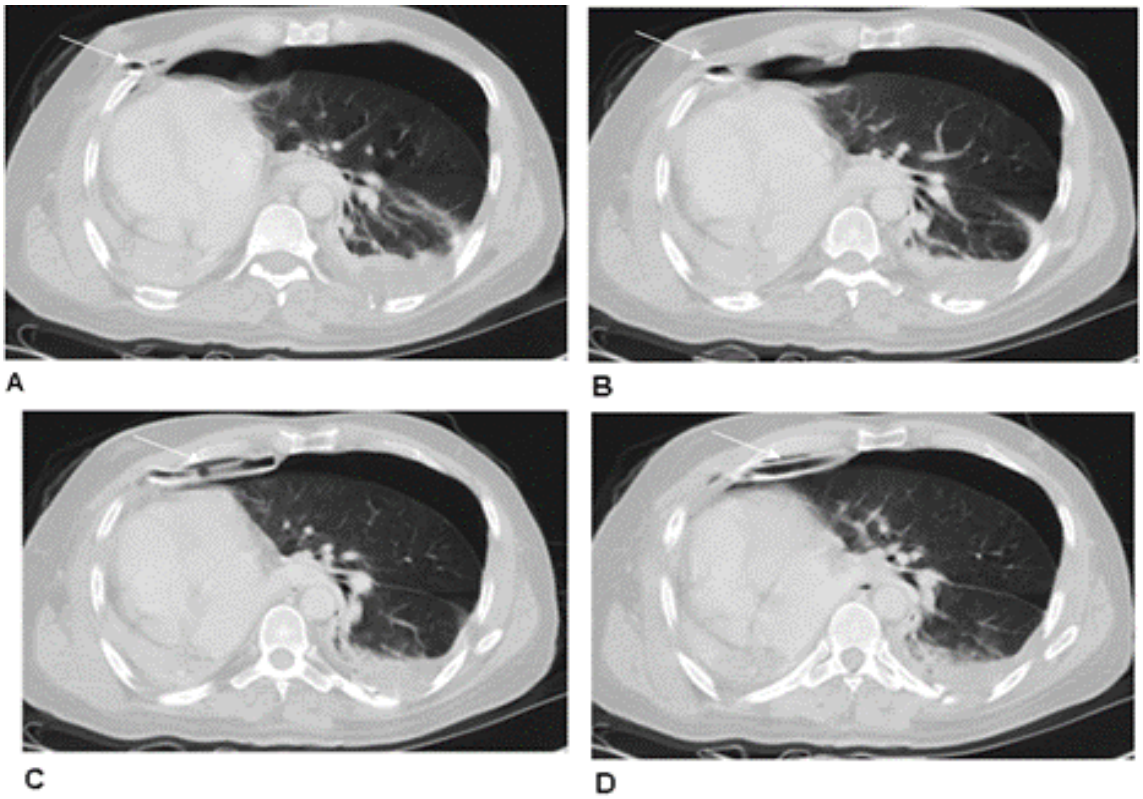

Figure 1 (Case 15): 48 years old male presented with right side chest discomfort and difficulty of breathing. The chest tube was inserted with a clinical diagnosis of right pleural effusion. Chest CT showed a completely collapsed right lung with the heart occupying the right hemothorax. Chest tube inserted from the right side crossed anterior to the heart and punctured the hyperinflated left lung causing left pneumothorax.

One tube was inserted into the destroyed lung with the clinical diagnosis of pneumothorax (figure 4). For two patients, 26 years old female and 88 years old male, the chest tube was inserted with the clinical indication of pneumothorax but later was diagnosed as having a diaphragmatic hernia. The chest tube was extrapleural in the former and crossed to the upper lobe with the tube in the lung parenchyma on the latter (figure 3).

The chest tube in one patient was in the left oblique fissure (figure 5). The chest tube is located within the mass lesion in two cases (figure 1). The chest tube was also located within the abdominal cavity within the spleen (figure 2), liver, and right renal parenchyma.

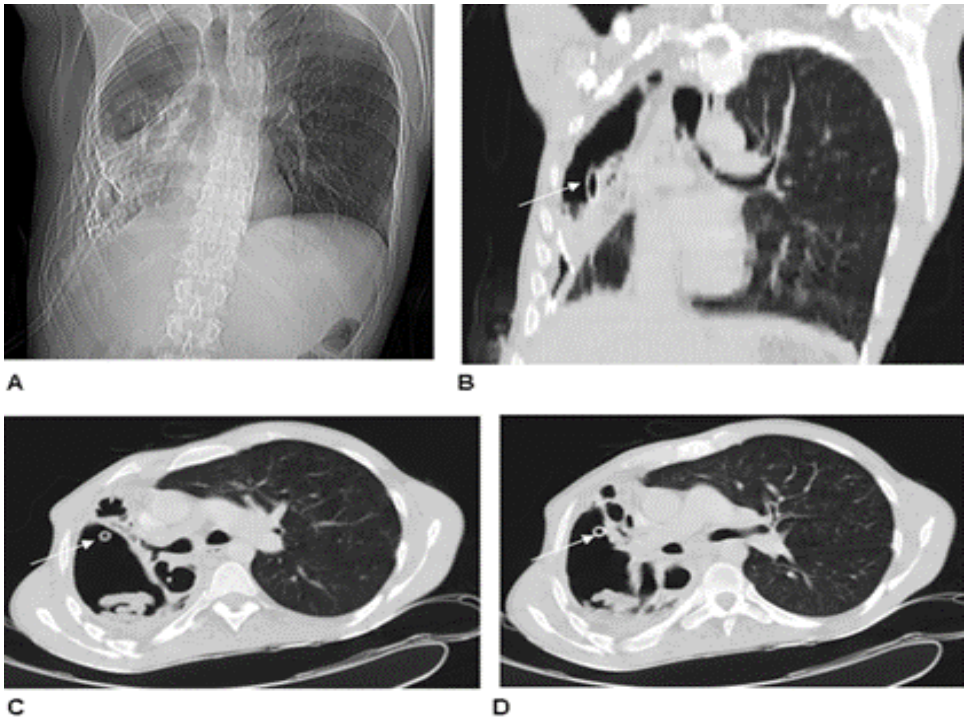

Figure 2 (Case 14): 43 yrs old male presented with chest pain and dyspnea with the CXR and CT scans showing a destroyed right lung with thickened and calcified pleura with a chest tube (arrows) in the destroyed

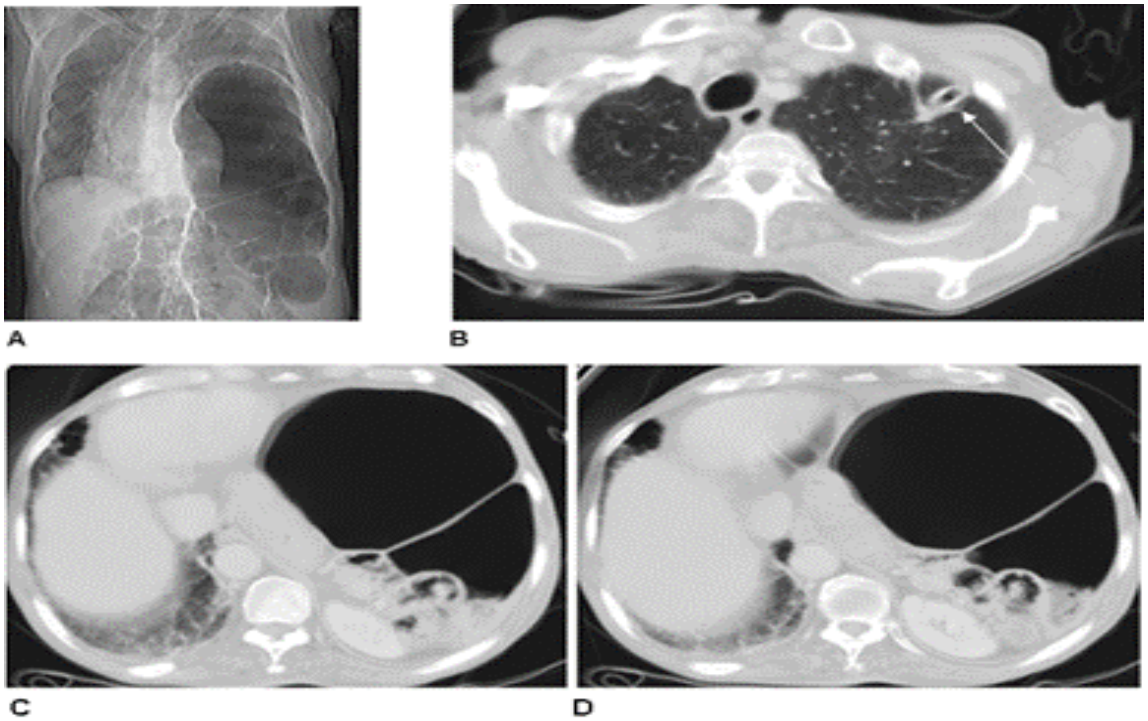

Figure 3 (case 19): An 88yrs old male presented after a fall accident. The scout film and the axial scans showed a diaphragmatic hernia with bowels herniating through the defect. The chest tube (arrow) extends above the herniated bowel into the apical lung.

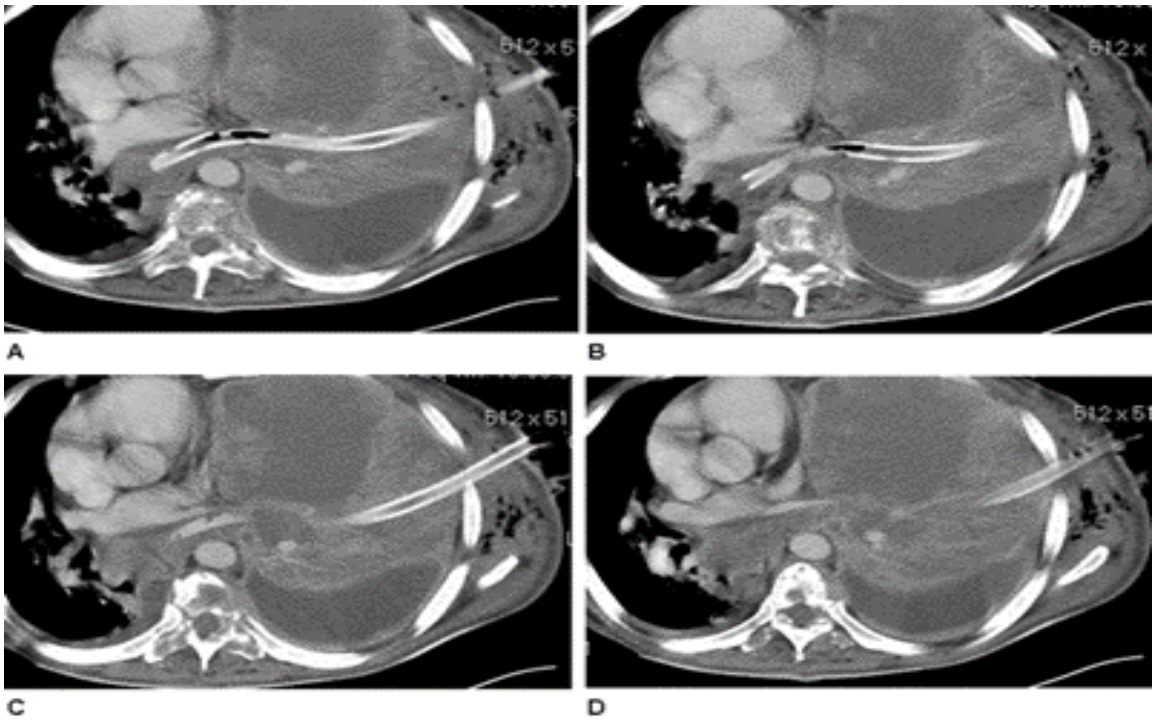

Figure 4 (Case 2): A 49 years old male presented with respiratory distress and a chest scan showed a huge LLL lung mass with massive left pleural effusion and vertebral metastasis. Chest tube inserted on the left passing through the lung mass crossing the mediastinum to the right anterior to the thoracic aorta with its tip adjacent to

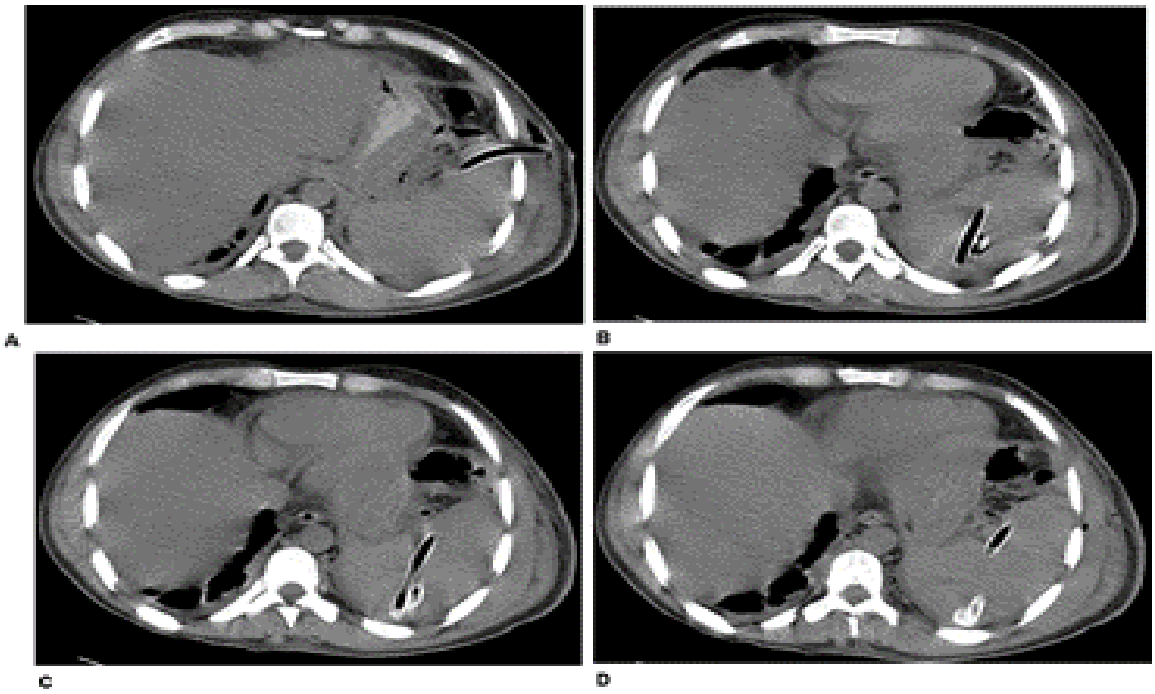

Figure 5 (case 8): A 27 years old male with acute pancreatitis and left pleural effusion. The chest tube was inserted on emergency bases and the tube failed to drain. CT then was done to evaluate the tube position

Discussion

Our study showed that most of the malpositioned chest tubes were inserted for indication of draining a pleural fluid. The next common indication was pneumothoraces, either spontaneous or traumatic. Most of the CT after the procedure was done for an indication of either absent or reduced tube drainage. There were three tubes which were located in the abdominal cavity traumatizing the solid viscera.

Chest tube placement is one of the common procedures performed in the emergency department for both traumatic and nontraumatic pleural air and fluid collections. Proper insertion of chest tubes can treat life-threatening conditions even if there are associated complications, malpositioned chest tubes being the commonest complication which may occur in up to one-third of the procedures. (13). So, subsequent care after insertion of chest drain is of paramount importance for good clinical outcome of patients.

In addition to the wrong position, chest tube insertion may also be complicated by infection or injury to mediastinal structures of the chest. Complications, when they occur, may also be life-threatening (14).

Most of the indications for a chest drain in our study were pleural effusion, hemothorax, or pneumothorax from blunt or penetrating chest trauma. In most institutions, pneumothorax and pleural effusions are the most common indications (13).
Most of the presumed diagnoses or indications for tube placement were unjustified on a retrospective analysis of the control CT which was done for various indications, as seen in table 1.

Even if CT is superior to other modalities in evaluating clinical discissions, proper clinical evaluation and preprocedural imaging will enable treating physicians to make reasonable decisions and avoid unnecessary complications. Chest tubes were positioned outside the pleura in the lung and fissures. Tubes were also located in the mediastinum and crossed the mediastinum to the contralateral lung abutting the major vascular structures. Inserted thoracic draining tubes may be positioned anywhere in the thoracic cavity outside the pleura within the mediastinum (15).

As we can also see in this study tubes may also be positioned outside the thoracic cavity into the abdomen which may result in solid organ trauma like liver, kidney and spleen. Such small, position, tubes within the solid organs particularly in the liver and spleen sometimes cause life-threatening hemorrhage (10, 16). In addition, tubes may also be located anywhere within the hollow organs like the esophagus and stomach (15).

Even if chest tube malposition within the lung and fissures do not have life-threatening complications, it increases hospital stay. As it was seen in one of our cases, bullous emphysema may sometimes mimic a pneumothorax and patients may be subjected to chest tube insertion (17), In four of our cases, tubes were advanced more medial to the mediastinal vascular structures abutting the heart and great vessels and two of the tubes also crossed the mediastinum to the contralateral thoracic cavity with one of the tubes puncturing the contralateral hyperinflated lung causing pneumothorax.

Such location of the tubes may sometimes puncture mediastinal vascular structures resulting in life -threatening hemorrhage. the mediastinal location of the tubes has potential vascular complications and even may result in cardiac injury and life-threatening hemorrhage (11, 18). Huge intrathoracic and mediastinal masses as well as ruptured diaphragm with bowel herniating into the thoracic cavity can sometimes mimic pleural fluid or air collection and may end up in chest tube drain as seen in our cases. This may result in poor drainage and sometimes may result in injury of the herniated bowel (19).

It is well known that preprocedural imaging will play important role in confirming the indication and ruling out other mimickers of fluid and air collection in the pleural cavities but sometimes insertion may be done with clinical evaluation only and it is not uncommon to get tubes in lung bullae (17) as it also occurred in one of our cases. Moreover, giant bullous emphysematous may also obscure the actual finding which needs tube insertion on both clinical examination and preprocedural chest radiography. So, sometimes preprocedural computed tomography may be important in selected patients (20).

Preprocedural imaging should be properly interpreted as the chest tubes inserted in our series showed that most were inserted for a wrong indication. This may arise from using clinical judgments without preprocedural radiographs, wrong interpretation of the radiographs, or blind insertion of the tube. Image guided insertion of chest tubes has been shown to have high efficacy and low rates of complications (7-9). That is why most guidelines strongly recommend the use of ultrasound guidance modality for chest tubes for draining fluid collections (3, 4).

Extra thoracic visceral location of the tube is a rare phenomenon and can inadvertently be inserted into the liver, spleen, and retroperitoneum resulting in renal hemorrhage as seen in our case, and may also result in life-threatening hemorrhage from hepatic injury (10, 16, 21).

(10) and may even be fatal (11).

Sometimes malpositioned / misdirected chest tube may injure not only intrathoracic but also intra-abdominal vital organs resulting in life-threatening hemorrhages .

The rate of malposition and other related complications of chest tube drainage placement depends on the level of training and expertise. Chest tube thoracostomy placement outside the trauma bay residents without surgical training is also a predictor of complications (1).
So, many institutions and international thoracic societies have guidelines (3, 4, 22) on who and how to insert chest drains and reporting mechanisms to track down malposition and associated complications and devise mechanisms to reduce adverse effects. The British Thoracic Society guideline emphasizes that all doctors expected to be able to insert a chest drain should be trained using a combination of didactic lectures, simulated practice, and supervised practice until considered competent (3).

Even if our study would not consider who inserted the chest tube, significant associations between chest tube thoracostomy complications and specialty of resident physician were also observed in the works of literature (1).

Conclusion:
Malpositioned chest tubes may be located within the thoracic or extrathoracic locations. Extra thoracic location of the chest tube within the abdominal cavity may result in injury to the liver, spleen, and even the kidneys.

Limitation:
this is a retrospective analysis of the cases. We took the clinical indication written on the imaging request. The level of training who inserted the tube and the time difference between tube insertion and control CT scan was also not known.

Acknowledgment:
Authors would like to acknowledge the institution for providing permission to use the archive and collect the documentation.

References

1. Ball CG, Lord J, Laupland KB, Gmora S, Mulloy RH, Ng AK, et al. Chest tube complications: how well are we training our residents? Can J Surg. 2007;50(6):450-8.
2. Harris A, O'Driscoll BR, Turkington PM. Survey of major complications of intercostal chest drain insertion in the UK. Postgraduate medical journal. 2010;86(1012):68-72.
3. Havelock T, Teoh R, Laws D, Gleeson F. Pleural procedures and thoracic ultrasound: British Thoracic Society pleural disease guideline 2010. Thorax. 2010;65(Suppl 2):i61.
4. Laws D, Neville E, Duffy J, Pleural Diseases Group SoCCBTS. BTS guidelines for the insertion of a chest drain. Thorax. 2003;58 Suppl 2(Suppl 2):ii53-ii9.
5. Bartter T, Mayo PD, Pratter MR, Santarelli RJ, Leeds WM, Akers SM. Lower risk and higher yield for thoracentesis when performed by experienced operators. Chest. 1993;103(6):1873-6.
6. Raptopoulos V, Davis LM, Lee G, Umali C, Lew R, Irwin RS. Factors affecting the development of pneumothorax associated with thoracentesis. AJR American journal of roentgenology. 1991;156(5):917-20.
7. Akhan O, Ozkan O, Akinci D, Hassan A, Ozmen M. Image-guided catheter drainage of infected pleural effusions. Diagnostic and interventional radiology (Ankara, Turkey). 2007;13(4):204-9.
8. Keeling AN, Leong S, Logan PM, Lee MJ. Empyema and effusion: outcome of image-guided small-bore catheter drainage. Cardiovascular and interventional radiology. 2008;31(1):135-41.
9. Moulton JS, Benkert RE, Weisiger KH, Chambers JA. Treatment of complicated pleural fluid collections with image-guided drainage and intracavitary urokinase. Chest. 1995;108(5):1252-9.
10. Bae J-M. Life-Threatening Hemoperitoneum and Liver Injury as a Result of Chest Tube Thoracostomy. Clinical Medicine Insights: Case Reports. 2015;8:CCRep.S23139.
11. Kim D, Lim S-H, Seo PWJTKjot, surgery c. Iatrogenic perforation of the left ventricle during insertion of a chest drain. 2013;46(3):223.12.
12. Lim K-E, Tai S-C, Chan C-Y, Hsu Y-Y, Hsu W-C, Lin B-C, et al. Diagnosis of malpositioned chest tubes after emergency tube thoracostomy: Is computed tomography more accurate than chest radiograph? Clinical Imaging. 2005;29(6):401-5.
13. Remérand F, Luce V, Badachi Y, Lu Q, Bouhemad B, Rouby J-J. Incidence of Chest Tube Malposition in the Critically Ill: A Prospective Computed Tomography Study. Anesthesiology. 2007;106(6):1112-9.
14. Lamont T, Surkitt-Parr M, Scarpello J, Durand M, Hooper C, Maskell N. Safety Alerts Insertion of chest drains: summary of a safety report from the National Patient Safety Agency. BMJ (Clinical research ed). 2009;339:b4923.

15. Gayer G, Rozenman J, Hoffmann C, Apter S, Simansky DA, Yellin A, et al. CT diagnosis of malpositioned chest tubes. 2000;73(871):786-90.
16. Feola A, La Sala F, De Stefano N, Diurno F, B. DP. A rare case of splenic injury due to a chest drain. Chirurgia 2020;33(68).
17. Ferreira Junior EG, Costa PA, Silveira LMFG, Almeida LEM, Salvioni NCP, Loureiro BM. Giant bullous emphysema mistaken for traumatic pneumothorax. Int J Surg Case Rep. 2019;56:50-4.
18. Anitha N, Kamath SG, Khymdeit E, Prabhu M. Intercostal drainage tube or intracardiac drainage tube? Ann Card Anaesth. 2016;19(3):545-8.
19. Kar SK. Emergency Chest Tube Insertion in A Case of Thoracic Trauma with Hidden Diaphragmatic Rupture Resulted in Injury of Herniated Stomach- A Case Report. EC Anaesthesia. 2015;2(2):5.
20. Tsao Y-T, Lee S-W. Vanishing lung syndrome. Canadian Medical Association Journal. 2012;184(18):E977.
21. Serji B, Mirali H, Chablou M, Kamaoui I, El Harroudi T. Liver injury secondary to chest tube placement: a case report of conservative management and review of the literature. Clin Case Rep. 2017;6(1):45-8.
22. Eisen L. Chest Tube Insertion. In: Oropello JM, Pastores SM, Kvetan V, editors. Critical Care. New York, NY:McGraw-Hill Education.

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Merad et al

Case Report

Gaucher disease discovered incidentally after splenectomy

Zakaria Merad [1*], Houria Belkralladi [1], Yassine Merad [2]

[1*]Department of pathology, Hospital University of Sidi Bel Abbes. Faculty of the médecine, Djilali Liabes University. ALGERIA
[2]Central Laboratory, Hospital Université of Sidi Bel Abbes. Faculty of the médecine, Djilali Liabes University. ALGERIA

Corresponding author*: zmerad79@yahoo.fr

Abstract

*Gaucher disease is a genetically rare overload disease caused by a deficiency in a lysosomal enzyme beta-glucocerebrosidase. However, the discovery of Gaucher disease after splenectomy is rarely described in the literature. We report a clinical, radiological and biological observation of a man with splenomegaly with compression of neighbouring organs at the University- Hospital Center of Sidi Bel Abbes in ALGERIA, splenectomized for diagnosis and whose pathological examination has helped to guide the diagnosis and confirm by the assay of the enzymatic activity of glucocerebrosidase. This unexpected diagnosis of Gaucher disease pos*es a diagnostic problem when the clinical-radiological context is not concordant.

Keywords: *Gaucher disease, splenectomy, Gaucher Cell, Histology*
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Introduction:

Gaucher disease is a rare overload genetic pathology with recessive autosomal transmission, characterized by a deficiency in a lysosomal enzyme beta-glucocerebrosidase (1,2). This disease is characterized by glucosylceramide deposits in the splenic, hepatic and bone marrow cells where it results in hepatosplenomegaly sometimes associated with bone involvement and in some rare forms to neurological involvement (3). Non-neurological forms (type 1) are more frequent than neurological forms (types 2 and 3) (4). We report an observation of Gaucher disease diagnosed after splenectomy at the University- Hospital Center of Sidi Bel Abbes in ALGERIA.

Observation

This was a 40-year-old man from Sidi Bel Abbes city (located 400 km west of the capital Algiers) with normal past medical history, who complained of an easy fatigue lasting 3 months, with pain that had been evolving for two weeks in the left hypochondrium radiating to the left flank and back. On clinical examination, the patient was afebrile with Blood pressure of 110/75mmHg. On abdominal palpation there was a huge splenomegaly occupying almost the entire abdominal cavity. The abdomino-pelvic computed tomography scan showed splenomegaly of 30x15 cm with small nodules of 5mm disseminated throughout the spleen. There was no hepatomegaly and the neighbouring organs was compressed by the huge spleen. The blood count formula was normal (a hemoglobin level of 14.2 g/dL, a hematocrite value of 42%, a white blood cell count of 7000/mm3 and red blood cell count of 4900000/mm3) with a slight thrombocytopenia at 130 000/mm3. In this clinical and radiological context, especially the compression of neighbouring organs, a splenectomy was performed. The surgical specimen weighed 3500 gram and measured 28x15x8 cm, with a reddish-brown colour and rounded contours (figure 1), and showed numerous nodules measuring 05 mm without signs of necrosis on the cut -section (figure 2).

Figure 1: splenectomy piece fixed in 10% buffered formalin, measured 28x15x8 cm

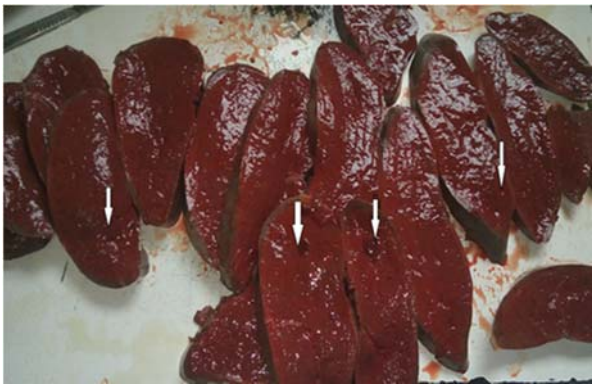

Figure 2: cut-section showed numerous nodules mesuring 5 mm without signs of necrosis

Histologically, the splenic parenchyma was interspersed with numerous macrophagic nodules separated by a few fibrous septa punctuated by a lympho-plasmocytic inflammatory infiltrate, these macrophages are large cells, with fibrillar eosinophilic cytoplasm and with eccentric nucleus of crumpled appearance very characteristic of Gaucher cells. The immunohistochemical study by CD 68 antibody showed diffuse, homogeneous, intense cytoplasmic and membrane labelling of macrophages (Gaucher cells) (figure 3A and 3B).

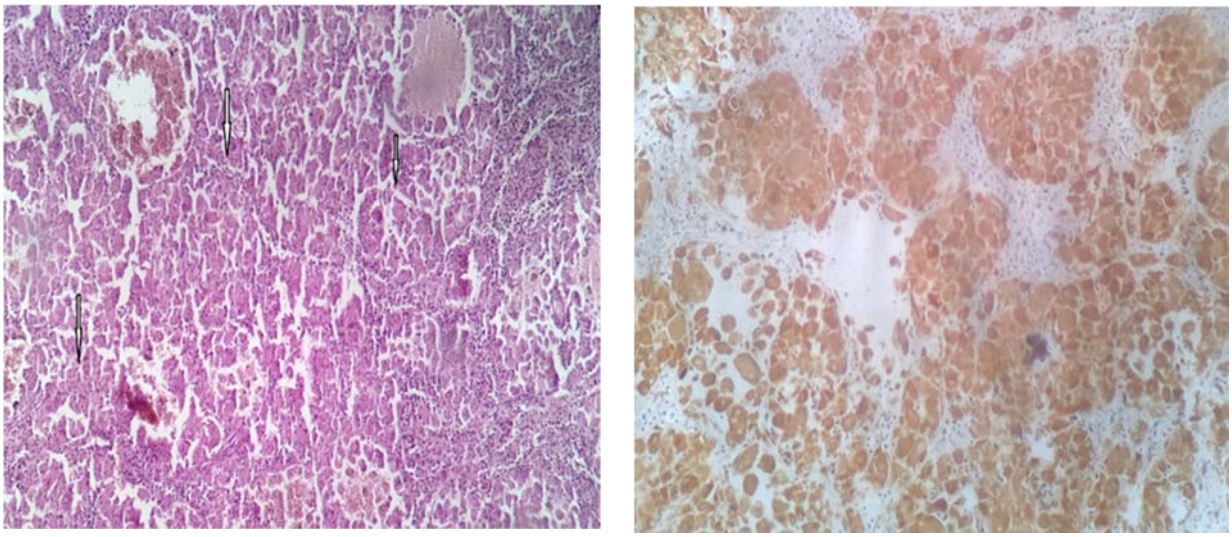

Figure 3:(A) microscopic showing numerous macrophagic nodules separated by a few fibrous septa punctuated by a lympho-plasmocytic inflammatory infiltrate, these macrophages are large cells, with fibrillar eosinophilic cytoplasm and with eccentric nucleus of crumpled appearance very characteristic of Gaucher cells (hematoxylin & eosin, X200), (**B**) microscopic showing diffuse brown, homogeneous, intense cytoplasmic and membrane labeling of macrophages (Gaucher cells) by the antibody CD 68 in the immunohistochemistry study, X200.

In view of this discovery, the diagnosis of Gaucher disease was strongly suspected and the enzymatic analysis found an increase in the enzymatic activity of glucocerebrosidase, which confirmed the diagnosis. A scintigraphy bone scan (99mTc) was performed and found no location and the neurological examination was normal.

Discussion

Gaucher disease was first described by Dr Gaucher in 1882 and its prevalence is around 1/100 000 in the general population (5). However, the diagnosis of Gaucher disease after splenectomy, has been very rarely reported in the literature. Only one observation has been reported in a series of 04 cases by *Adas et al* (6). The age at the time of diagnosis is extremely variable from 0 to 90 years, usually before 10 years, our case is 40 years old. Three types of Gaucher disease are described: type 1, defined by the absence of neurological involvement, representing 94%. Type 2, characterised by early neurological involvement, is the rarest and most severe form 1%. Type 3, characterised by later neurological involvement and a more progressive course, accounts for 5% of the cases. Our patient was classified as type 1 because there was only splenomegaly, no hepatomegaly, no neurological involvement, and no bone involvement. Our observation underlines the importance of anatomopathological examination in the diagnosis by showing nodules of macrophagic cells with a crumpled appearance characteristic of Gaucher cells (8). In this case, the determination of leukocyte beta-glucocerebrosidase enzyme activity confirmed the diagnosis.

Treatment of Gaucher disease is primarily medical therapy with intravenous enzyme replacement therapy, splenectomy is only considered in case of haematological complications: hypersplenism, haemorrhagic syndrome (9). In our patient, splenectomy was performed for diagnostic purposes. The evolution of Gaucher disease is generally favourable with a mortality rate of around 2% (10) and the evolution in our patient was favourable after splenectomy.

Conclusion

Although the diagnosis of Gaucher disease after splenectomy is a difficult one to make when the clinical and radiological features are discordant, it should always be sought, while emphasising the importance of pathological examination in establishing the diagnosis.

Conflict of interest

The authors declare no conflict of interest

Author contribution

All the authors contributed equally to the manuscript. They approved the final and revised version of the manuscript.

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Références

1. Grabowski GA. Treatment of Gaucher's disease. N Engl J Med 1993;328:1565.
2. Stirnemann J, Belmatoug N. La maladie de Gaucher chez l'adulte. Rev Med Interne 2001 ;22(3) :374-383.
3. Belmatoug N, Caubel I, Stirnemann J, Billete De Villemeur T. La maladie de Gaucher. J Soc Biol 2002 ;196 (2) :141-149.
4. Beutler E. Gaucher disease. Blood Rev 1988 ;2 : 59-70.
5. Nguyen Y, Stirnemann J, Belmatoug N. La maladie de Gaucher. La Revue du Praticien 2020 ;70(4) :416-420
6. Adas M, Adas G , Karatepe O, Altiok M, Ozcan D. Gaucher's disease diagnosed by splenectomy. N Am J Med Sci 2009 ; 1(3): 134-136.
7. Ballabio A, Gieselmann V. Lysosomal disorders: From storage to cellular damage. Biochimica et Biophysica Acta 2009;1793:684-696.
8. Stanislas S, Parrens M. Atlas de pathologie splénique. Sauramps Médical 2009. Pp 188-189
9. Hughes DA, Pastores MG. Haematological manifestations and complications of Gaucher disease. Curr Opin Hematol 2013;20:41-47.
10. Kucuk C, Sozuer E, Engin Ok, Altuntas F, Yilmaz Z. Laparoscopic Versus Open Splenectomy in the Management of Benign and Malign Hematologic Diseases: A Ten-Year Single-Center Experience. Journal of Laparoendoscopic & Advanced Surgical Techniques 2005;15:135-139.

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Anbessie et al

Case Series

Serum potassium response to intravenous potassium chloride in severely hypokalemic patients from Ethiopia: A case series

Zablon Mesfin Anbessie[1], Dawit Kebede Huluka[2], Seifemichael Getachew Abebe[3]

[1]Bethzatha General Hospital, Addis Ababa, Ethiopia.
[2]College of Health Sciences Addis Ababa University Addis Ababa, Ethiopia
[3]St. Paul Millennium Medical college, Addis Ababa, Ethiopia
Corresponding author*: Zabalon22@hotmail.com

Abstract

Introduction : *One out of five admitted patients has hypokalemia, among which a similar number has severe hypokalemia, a life-threatening condition. The therapy and response of severe hypokalemia is mainly based on findings from other countries and in Ethiopia patients may have lower than recommended potassium replacement requirements, and as there have been no publications, this series was conducted to guide the clinical management of severely hypokalemic patients.*

Methods: *A nine-month prospective case series in Bethzatha general hospital ICU in Ethiopia were reviewed.*

Case presentation*-Six patients with a median age of 45 years were included. The range of admission serum potassium level was (1 to 1.8) meq/l. An average of 383 meqs of intravenous potassium chloride was infused to raise the serum potassium level by 2.57 meq/l. To raise the serum potassium level by 0.27meq/l an average of 39.4meq of potassium chloride was needed.*

Conclusion: *There was more than a half dose reduction in the potassium chloride infusion required to raise the serum potassium to the same target in the literature.*

Keywords: *Potassium chloride, Potassium response, Severe hypokalemia, Hypokalemia treatment*
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Introduction:

Hypokalemia or low serum potassium level is defined as serum potassium below 3.5meq/l. It is classified as mild (3-3.5meq/l), moderate (2.5-3meq/l), and severe (<2.5 meq/l) based on serum potassium levels(1,2). It is among the most prevalent laboratory abnormality occurring in hospitalized patients, accounting for 12-20% of those patients(1–3). It is estimated that one out of five hypokalemic patients has severe hypokalemia, which can induce muscle paralysis, respiratory failure, and life-threatening cardiac arrhythmias.

In-hospital mortality for hospitalized hypokalemic patients can range from 20-34%, which in large part is attributed to the 31% mortality observed in severely hypokalemic patients.(1,2,4)

Treatment of severe hypokalemia requires intravenous potassium chloride (IV KCL) which itself can lead to serious cardiac arrhythmias and severe infusion site reactions if overdosed or dosed too fast (4,5).

Most publications dealing with the dose, route, and concentration of IV KCL as well as the response to treatment of severe hypokalemia, are empiric guidelines, rather than evidence-based.(1,3–8)

Infusion rates of 10-20meq/l/hr. peripherally and 40 to 60meq/l/hr. centrally are recommended for severe hypokalemia treatment(4,5,8). The rate of response of serum potassium to the different infusion rates recommended above varies, with some studies reporting a rise in serum potassium of 0.4-0.43meq/l for 20meq of IV KCl (7), while others have reported the response to be from 0.27-0.4meq/l for 95-100meq of IV KCL infused (8).

The management of severe hypokalemia is based on retrospective chart reviews and case series with patient populations having significant variability in their demographics and comorbidities. This resulted in varying recommendations on the amount of IV KCL required by different populations(1–5,8). In the Ethiopian context, routine clinical practice suggests lower doses of potassium chloride, and to the author's knowledge, as there has been no publication to guide clinical management and serve as a baseline for further studies, this series was performed to shed some light on the issue.

Methods and Materials

Study Site: Bethzatha general hospital ICU.in Addis Ababa, Ethiopia.

Study Duration- October 2018 to June 2019

Study type-Prospective case series of severly hypokalemic patients managed by standard guidelines

Sample size-A total of six patients met inclusion criteria and were included

Inclusion criteria: All patients with serum potassium below 2.5meq/l, and required ICU care.

Exclusion criteria: Patients who had serum potassium below 2.5meq/l, but did not need ICU admission.

Consent- Informed oral and written consent was taken from patients or next of kin.

Ethical clearance :

was taken from Addis Ababa health bureau as part of a large ICU registry being run in the hospital's ICU (BIRD project) (A/A/H/2464/227)

Data collection: Demographic, clinical, and therapeutic data were collected prospectively using a structured data collection format by the treating physician in the ICU.

Out come

1. The rate of change of serum potassium to IV KCL infusion.
2. The amount of IV KCL required to get to a normal serum potassium level.

Statistical analysis

The collected data was entered into SPSS V25. the mean and median along with the standard deviations were calculated. Initial serum potassium level adjustment was done using a web-based calculator.(9)

Case Summary

Case-1

A 45 years old hypertensive and diabetic female presented with progressively increasing fatigue, vomiting, headache, and fever. On examination, she had pulsus alternans and a regularly irregular pulse. Her investigations showed a sodium of 126meq/l, a potassium of 1.0meq/l, chloride of 67meq/l,magnesium of 2.2mg/dl, phosphate of 1.9mg/dl, creatinine of 1.46mg/dl, and urea of 38mg/dl. Her blood gas analysis showed a PH of 7.59, a PO_2 of 119mmHg, a PCO_2 of 62.8mmHg, an HCO_3 of 60mmol/L, lactate of 0.86mg/dl, and anion Gap of 6.5. Her ECG had a persistent bigeminal rhythm with intermittent bursts of non-sustained ventricular tachycardia. After a central line was secured, 30meq/l/hr. of potassium chloride was infused for four hours after which, the serum potassium became 2.37meq/l, so, the infusion rate was decreased to 20 meq/l/hr. for the next nine hours, and the serum potassium became 3.43meq/l.

Case-2

A 35 years old male patient was admitted to the ICU for hypersplenism and severe diabetic ketoacidosis. On admission he was dehydrated, his random blood sugar was 350mg/dl, and his urine had +3 ketones. Eighteen hours into the management of diabetic ketoacidosis, his blood gas analysis showed a PH of 7.57, HCO_3 of 22.3mmol/L, PO_2 of 67mmHg, PCO_2 of 24.8mmHg, lactate of 0.57mg/dl, anion gap of 7, and the serum potassium dropped to 1.8 meq/l from 2.2 meq/l. The patient had declined to get a central venous line, so, potassium chloride at a rate of 10meq/l/hr. was infused for 12 hours after which the serum potassium became 2.66meq/l. After another 13 hours at the same rate, the serum potassium rose to 2.89meq/l, and after an additional 13 hours, the serum potassium became 3.67meq/l.

Case-3

An 80 years old male patient was readmitted five days post-discharge for possible hospital-acquired pneumonia after he presented with cough and shortness of breath. He was a known diabetic, hypertensive, and adrenal insufficiency patient on follow-up. After admission, the patient developed respiratory failure and septic shock for which ventilatory and vasopressor support was provided. After extubation and discontinuation of vasopressor support, the patient developed polyuria of five liters per day. The arterial blood gas at this time showed a PH of 7.53, HCO_3 of 41.7mmol/L, PO_2 of 62mmHg, PCO_2 of 50.6mmHg, lactate of 2.6mg/dl, and an anion gap of 2. His serum potassium at this time was 1.5meq/l, with serum magnesium of 1.2mg/dl, and serum phosphate of 1.9mg/dl. His ECG showed frequent premature ventricular contractions.

After a central line was inserted intravenous potassium chloride, at a rate of 20meq/hr. was given along with intravenous magnesium sulfate. Twelve hours later, the serum potassium rose to 4.48meq/l and potassium chloride infusion was discontinued.

Case-4

A 56 years old diabetic patient was brought to the hospital after he was found unconscious at a roadside. On evaluation, he had repeated episodes of generalized tonic -clonic seizures with vomiting of coffee ground material. His blood pressure was 140/80mmHg, his pulse rate was 130 beats per minute, and he had a respiratory rate of 42 breaths per minute with an oxygen saturation of 70% on a 15L face mask oxygen. He had diffuse rhonchi and fast deep breaths. His Glasgow coma scale was 8/15. He was admitted to the ICU and was intubated for type I respiratory failure. On the second day of intubation, the patient was producing three to five liters of urine output, his serum sodium rose from 136 meq/l to 155meq/l, his serum creatinine rose from 1.6mg/dl to 2.6mg/dl, and his serum potassium dropped from 4.04meq/l to 1.5meq/l. The arterial blood gas showed a PH of 7.18, a PO_2 of 72mmHg, an $HCO_3$of 11.5mmol/L, a PCO_2 of 31mmHg, a lactate of 1.6mg/dl, and anion gap of 7. A central catheter was inserted and potassium chloride was infused at a rate of 20meq/hr. for six hours. The repeat serum potassium after six hours of infusion was 4meq/L, so intravenous potassium chloride was stopped.

Case-5

A 37 years old known HIV patient for the past five years presented to the hospital complaining of watery diarrhea, intermittent vomiting, and a loss of 13 kilograms of weight over the past month. Two days before his presentation he was unable to move his extremities and became bedridden. On examination, he had cachexia with generalized hypotonia, hyporeflexia, and muscle power of 1/5 in all muscle groups including the neck muscles.His serum sodium was135meq/L, serum potassium was 1.13meq/l, serum magnesium was 4.4mg/dl, and serum phosphate was 1.3mg/dl. His ECG showed ST segment depression and U waves. After ICU admission, a central line was inserted and intravenous potassium chloride was infused at a rate of 20mq/l/hr. for 15 hours, after which the serum potassium became 1.19meq/L. So, the rate of infusion was increased to 30meq/hr. and the serum potassium was checked after six hours. At that time, the level was 1.31meq/l., and another three hours of infusion at the same rate was allowed, after which the potassium became 2.04meq/l. The infusion rate was maintained, as the patient had massive ongoing diarrhea for 14 more hours, and the potassium determined then became 4.26meq/l.

Case-6

An 85 years old hypertensive and diabetic female presented to the hospital complaining of a productive cough for one month with frequent episodes of seizures for 24 hours. On examination, she was agitated and confused with a puffy face, right lung lower lobe crepitation, and an irregularly irregular distant heart sound. She had a serum sodium of 120meq/l, potassium of 1.4meq/l, magnesium of 1.6mg/dl, a chloride of 69meq/l, and phosphate of 3.7mg/dl. Her blood gas showed a PH of 7.53, a PO_2 of 51mmHg, a PCO_2 of 75mmHg, an HCO_3 of 61mmol/l, lactate of 1.18mg/dl, and an anion gap of zero. After a central line was inserted, potassium chloride at a rate of 20meq/l/hr. was infused for six hours after which the serum potassium became 2.2meq/l, and after an additional eight hours at the same rate, the serum potassium became 3.9meq/l.

Results

The median age of the patients was 45 years (35-85), with one-third being females. The commonest comorbidities were diabetes and hypertension. The range mean of baseline serum potassium was from 1 to 1.8meq/l . (Table-1)

The mean IV KCL infusion rate between admission and the first retest time was 20meq/l (10-30meq/l). The median time that elapsed before the first retest was done was 9 hours, 4/6 patients required retesting two times while only 2/6 required retesting three times (Table-2)

A mean of 383.3 meq/l (120-990) IV KCL was infused over 20 hours (6-38) to bring about a change in the serum potassium by 2.57meq/l. The mean change in serum potassium between the first and last retest was 3.96 meq/l (3.43-4.48 meq/l). The mean IV KCl amount needed to raise the serum potassium by 1meq/l, was 146 meq when the baseline serum potassium was not corrected for PH, and 212meq when the baseline serum potassium was corrected for PH. (Table-3, Figure-1)

Table-1 Baseline demographic and clinical characteristics

Patient	**1**	**2**	**3**	**4**	**5**	**6**
Age	45	35	80	56	37	85
Sex	F	M	M	M	M	F
Comorbidity	Diabetes Hyper-tension	Diabetes DKA** Hypersplen-ism	Diabetes Hypertension Malignancy Dementia Heart failure	Diabe-tes	HIV infec-tion††	Hypertension Diabetes
Potassium (meq/l)	1	1.8	1.5	1.5	1.1	1.4
PH	7.59	7.57	7.53	7.18	7.40	7.53
HCO_3 (mmol/l) *	60.00	22.3	41.7	11.5	17.6	61
PCO_2 (mmHg) †	62.8	24.8	50.6	31	28.6	75
Magnesium (mg/ dl)	2.2	2.1	1.2	1.8	4.4	1.6
Phosphate (mg/dl)	1.9	1.1	1.9	2.0	1.3	3.7
Creatinine (mg/ dl)	1.46	0.74	0.8	2.6	0.5	0.8
IV access‡	Central line	Peripheral line	Central line	Central line	Central line	Central line
Hydration status	Dehy-drated	Dehydrated	Dehydrated	Dehy-drated	Dehydrated	Dehydrated
Ongoing loss	Present	Absent	Present	Present	Present	Absent
Loss Site	GI§	No	Renal	Renal	GI	No
Neurologic find-ing	Absent	Absent	Absent	Absent	Generalized hypotonia	Absent
Cardiac finding	Bigeminy NSVT‖	None	PVC¶	None	ST depression U waves	None

*HCO_3- Serum bicarbonate level in the blood, †PCO_2- Partial pressure of carbon dioxide in arterial blood, ‡ IV access-Intravenous access, § GI- gastrointestinal tract, ‖ NSVT- Non-sustained ventricular tachycardia, ¶PVC- Premature ventricular contractions, *DKA- Diabetic Keto acidosis, †† HIV Human immunodeficiency virus

Table-2 IV KCL infusion rates at different serum potassium retest hours

Patient	**Time of potassium retest (hours)**				**Rate of potassium infusion before retest (meq/l/hr.)**			
	1st retest	2nd retest	3rd retest	4th retest	1st rate	2nd rate	3rd rate	4th rate
1	4	9	ND*	ND	30	20	ND	ND
2	12	13	12	ND	10	10	10	ND
3	12	ND	ND	ND	20	ND	ND	ND
4	6	ND	ND	ND	20	ND	ND	ND
5	15	6	3	14	20	30	30	30
6	6	8	ND	ND	20	20	ND	ND

*ND-Not done

Patient	Total IV KCL* required (meq)	Total time of infusion (Hours)	Starting potassium (meq/L)	Last potassium (meq/L)	ΔK† (meq/L)
1	300	13	1	3.43	2.43
2	370	37	1.8	3.67	1.87
3	240	12	1.5	4.48	2.98
4	120	6	1.5	4	2.5
5	990	38	1.13	4.26	3.13
6	280	14	1.4	3.9	2.5

IV KCL- Intravenous potassium chloride, †ΔK- change in potassium

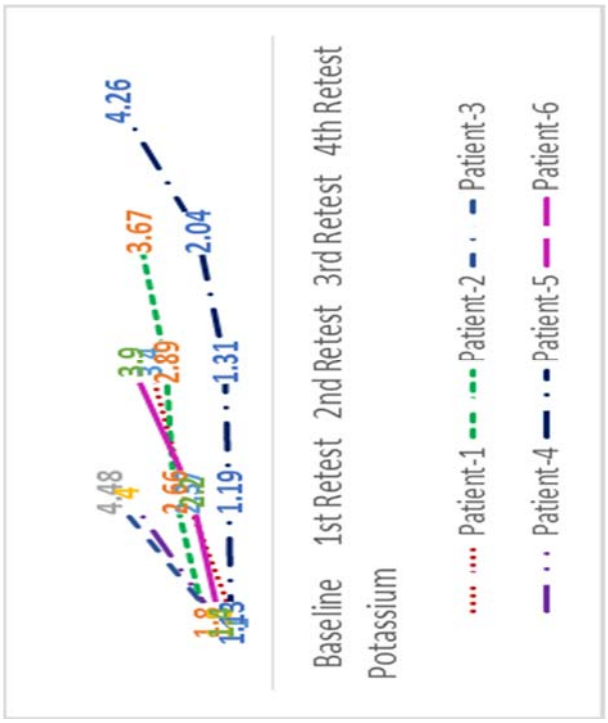

Figure-1 Serum potassium level at different retest hours

We have demonstrated in this case series that the total amount of IV KCl required to treat severe hypokalemia in our institution is at least 50% lower than that recommended in the literature. We have also shown that when the recommended infusion rate of ≥20meq/l/hr., via a central line, was used to replace serum potassium, the patients either reached their target in a short duration or required less amount of IV KCl. This effect was uniformly seen even when the patient's acid-base and hydration status was taken into account.

Discussion:

A computerized administrative and laboratory database review in Israel found that among hypokalemic patients, 54% were males with most of the patients having diabetes, kidney, and cardiovascular disease(1). A case series of patients with hypokalemic periodic paralysis found that the median age of patients was 34 (20-50) years (10), while others had patients aged between 58 to 72 years(5) and a mean age of 54.4± 16.3 years(2). A review of hypokalemic critically ill medical patients showed that 12% had renal dysfunction, and 34% had metabolic alkalosis with the commonest comorbidities being sepsis, respiratory failure, and cardiac arrest(4). These background clinical characteristics are similar to our patients with some variances arising likely due to sampling size and some of the studies including mild and moderate hypokalemia in their study.

In a series of hypokalemic patients with periodic paralysis, the presenting serum potassium was 1.9±0.4mmol/l with all patients achieving normokalemia within 6 hours(10). In a computerized review of hypokalemic patients, the mean and median time from diagnosis of hypokalemia to its correction were 50 and 25 hours respectively(1). A retrospective chart review of trauma patients with mild hypokalemia showed that the infusion of 95meq of KCl induced a 0.4meq/l change in the serum potassium(7), while a hypokalemia update review estimates that

the serum potassium will drop by 0.27meq for a 100meq drop in the total serum potassium level(8). Our patients had more severe hypokalemia but required the same amount of time and a lesser dose of IV KCL. This might have arisen from a potentially low total body water of our patients, early alkalosis correction, and rehydration that might cause transcellular shifts.

A hypokalemia review update shows that a low serum magnesium level worsens hypokalemia response while an impaired renal function decreases the IV KCL requirement of patients(8).

This was shown in our series with patient four having the worst renal dysfunction requiring a shorter duration and a lower dose of IV KCL to reach normokalemia, while it was difficult to see the effect of hypomagnesemia because of concurrent replacement of IV KCL with IV magnesium sulfate during the management of patients three and six.

Based on our results we recommend caution during the infusion of KCL to hypokalemic patients. We also recommend a larger and multicenter study to assess the effect of KCl infusion on serum potassium levels.

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

Ethical clearance

was taken from Addis Ababa health bureau as part of a large ICU registry being run in the hospital's ICU (BIRD project) (A/A/H/2464/227).

Author contribution
ZM did diagnosis, treatment and follow up of the patients, inception of the study, data collection, data analysis, manuscript write up, manuscript revision
DK did diagnosis, treatment and follow up of the patients, manuscript revision and data interpretation.
SG did diagnosis, treatment and follow up of the patients, manuscript revision and data interpretation.

References

1. Ora Paltiel, MD, MSc; Edouard Salakhov, MD, MPH; Ilana Ronen, MPH; David Berg, BSc; Abraham Israeli, MD, MPH Ms. Management of Severe Hypokalemia in Hospitalized Patients. Arches Intern Med. 2001;161.
2. Eliacik E, Yildirim T, Sahin U, Kizilarslanoglu C, Tapan U, Aybal-Kutlugun A, et al. Potassium abnormalities in current clinical practice: Frequency, causes, severity and management. Med Princ Pract. 2015;24 (3):271–5.
3. Kardalas E, Kardalas E, Paschou SA, Anagnostis P, Muscogiuri G, Siasos G. Hypokalemia : a clinical update. 2018;(2):135–46.
4. Kruse JA, Carlson RW. Rapid correction of hypokalemia using concentrated intravenous potassium chloride infusions. Arch Intern Med. 1990;150(3):613–7.
5. Emmett M. Evaluation of the safety and efficacy of the central venous administration of potassium chloride including the measurement of intracardiac potassium concentrations. Baylor Univ Med Cent Proc [Internet]. 2020;33(1):24–7. Available from: https://doi.org/10.1080/08998280.2019.1678339
6. Abramson E, Arky R. Diabetic Acidosis with Initial Hypokalemia: Therapeutic Implications. JAMA J Am Med Assoc. 1966;196(5):401–3.
7. Johnston CT, Maish GO, Minard G, Croce MA, Dickerson RN. Evaluation of an Intravenous Potassium Dosing Algorithm for Hypokalemic Critically Ill Patients. J Parenter Enter Nutr. 2017;41(5):796–804.
8. Lim S. Approach to hypokalemia. Acta Med Indones. 2007;39(1):56–64.
9. Potassium / pH Correction Equation Page :: MediCalculator ::: ScyMed ::: [Internet]. [cited 2021 Oct 22]. Available from: http://www.scymed.com/en/smnxps/pshfp089.htm
10. Alkaabi JM, Mushtaq A, Al-Maskari FN, Moussa NA, Gariballa S. Hypokalemic periodic paralysis: A case series, review of the literature and update of management. Eur J Emerg Med. 2010;17(1):45–7.

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Commentary

An article critique on a publication about Ethiopia's safe abortion law and maternal mortality

Tesfaye H. Tufa[1]*, Mekdes D. Feyissa[1], Demeke Desta[1], Getachew Bekele[1], Yirgu Gebrehiwot [1]

[1] Department of Obstetrics and Gynecology, Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
[2] Ipas Ethiopia
[3] Independent Consultant
[4] Department of Obstetrics and Gynecology, School of Medicine, Addis Ababa University

Corresponding author*: tesfayehurisa50@gmail.com

Abstract

Ethiopia is considered one of the early reproductive health champions in Africa by making huge reproductive health and rights reforms including changing its safe abortion law. A recent publication in Ethiopian Medical Journal by Calum Miller has presented a flawed argument on Ethiopia's safe abortion law and maternal mortality trend over the period following legal reform. Miller claimed that abortion related mortality has already decreased before the legal reform in 2005 and the legal reform has only increased abortion incidence and abortion-related morbidity and mortality. Our review has shown that abortion related mortality was a leading cause of maternal mortality before the legal reform while currently contributing only less than 10%. We have selected outstanding arguments and presented a critique of Miller's article

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Introduction:

A commentary entitled "Legalization of abortion and maternal mortality in Ethiopia" was recently published in the Ethiopian Medical Journal by Calum Miller (1), a medical doctor and researcher with previous similar antiabortion comments evidenced in his publications and interviews (2–4). Unfortunately, his commentary misrepresented the evidence it cited and downplayed the public health successes of abortion law reform in Ethiopia. Ethiopia's safe abortion law was changed in 2005 in an effort to curb the high maternal mortality, a major part of which is contributed by complications from unsafe abortion.

Below, we refute four deeply flawed arguments in Miller's commentary: (1) Miller misrepresents the data on access to safe abortion services and maternal mortality prior to the change in abortion law, (2) Miller inaccurately states that the law reform in Ethiopia has caused an increase in abortion rates, morbidity, and potentially abortion-related mortality, without reducing overall maternal mortality, (3) Miller misrepresented Ethiopia's safe abortion law as "Liberal" and made an inappropriate comparison with other countries, (4) Miller inaccurately associated the increase in abortion rate to the change in safe abortion law. Miller's misrepresentation and distortion of local and regional evidence could result in adverse outcomes on individual and policy levels. Furthermore, it could negatively impact Ethiopia's reproductive health strategic plan and health sector transformation plan that aim to reduce maternal mortality and morbidity through accelerating existing reproductive health service efforts, including improving access to safe abortion services (5,6).

Based on the standards of different local and international journals, this publication has potentially violated the ethical standards of scientific journals (7,8).

Main Body

Flaw 1: Miller misrepresents the data on access to safe abortion and maternal mortality prior to the change in abortion law.

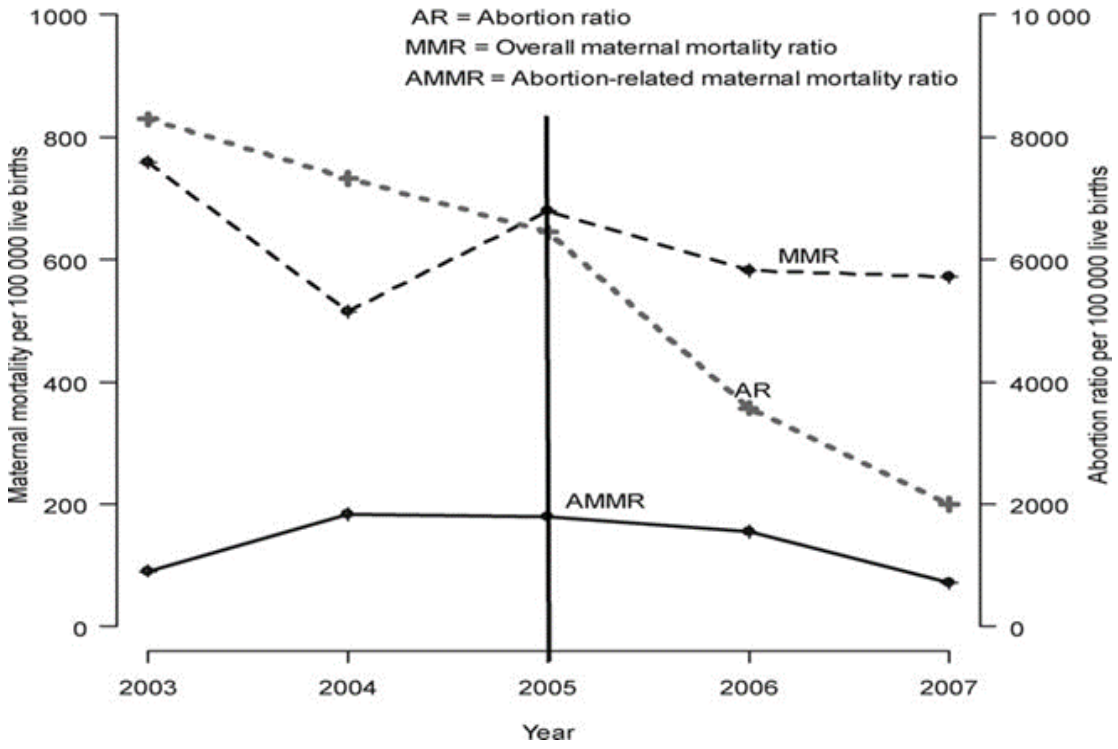

Fig. 1. MMR, AMMR, and AR trends before and after 2005. (Taken from Gebrehiwot et al., 2008).

Miller claims that mortality from abortion (in absolute terms and relative to other causes of death) declined in Ethiopia prior to 2005, when the abortion law was reformed, citing four systematic reviews (9–12). In fact, most of these reviews do not support Miller's claim. For instance, Gaym 2009 concluded that maternal mortality did not change between 1995 and 2005 and showed that during this period, the major contributor to maternal death (according to eleven of twelve included studies) was unsafe abortion (9). Another cited review by Miller, Abdella 2010, has several limitations and mixed findings that need to be critically evaluated before using its results as evidence. Abdella 2010 reported mixed results on maternal mortality patterns before the law reform: the maternal mortality ratio (MMR) from hospital-based studies and national Demographic Health Survey (DHS) data decreased between 1982 and 2005, but community-based studies showed an increase in MMR during the same period. Miller took only the first part of this result and failed to elaborate or explain these differences. So, the generalization that maternal mortality has decreased before the legal reform is questionable. The other major limitation of this review (Abdella 2010) is that the pattern of abortion-related mortality is described without having proper studies that justify it (13–16). Individual studies used in Abdella's review are retrospective chart reviews of the delivery registration book of all laboring mothers admitted to the labor ward in a single hospital from April 1, 1993, to March 30, 2003.

From these data, the author captured the sepsis rate of 12.5% as abortion-related maternal death. Otherwise, abortion-related maternal death is not directly captured in this review. Moreover, the studies in the review have major methodological limitations, including the retrospective nature of the study and the use of medical records as a source of data in a time when abortion was illegal and medical records could be potentially inaccurate. The other two systematic reviews mentioned by Miller are aimed at evaluating the pattern of causes of maternal mortality (case fatality rate) over the period between 1980 to 2016 (11,12). The main conclusion of these two reviews is that causes of maternal mortality have changed over the years from unsafe abortion and obstructed labor/uterine rupture to hemorrhage and hypertensive disorders. Therefore, because these reviews solely address the causes of maternal mortality, they cannot possibly support Miller's claim that abortion-related mortality declined prior to legal reform. According to a systematic review of 18 studies done by Berhan et al. (17), which included nationally representative surveys, small-scale community-based studies, hospital studies, and secondary data analysis, maternal mortality in Ethiopia did not change significantly over three decades between 1980 to 2008.

This finding aligns with the Lancet maternal survival series that suggested no significant change in the maternal mortality ratio in Sub-Saharan countries between 1995 and 2005 (18). So, the argument that maternal mortality is dropping before 2005 is false and none of the cited evidence strongly supports Miller's claim.

Flaw 2: Miller inaccurately states that the law reform in Ethiopia has caused an increase in abortion rates, morbidity, and potentially abortion-related mortality, without reducing overall maternal mortality.

We agree with Miller in that law reform may have preceded increases in documented abortion-related morbidity, though, unlike Miller, we posit that this is due to improved detection of such morbidity. Gebrehiwot 2009 offers compelling evidence for an increase in complications due to unsafe abortion in hospitals following legalization, as does a study by Yifru et al. 2014 (19) (11). This suggests that reported and treated abortion complications did increase after abortion law reform, which we posit is due to massive improvements and increased resources for post-abortion care services, which occurred concurrently with increased access to safe induced abortion services (20). This increased access (including greater geographic proximity to services) and availability likely improved people's trust in services, leading to greater service utilization and ultimately resulting in increased detection of minor and moderate morbidity as more women seek care earlier and fewer women die from unsafe abortion-related mortality. A recent report by the Guttmacher Institute on Sub-Saharan Africa showed that abortions are severely underreported in countries where safe abortion services are restricted (21).

Studies across many countries have noted that without decreasing abortion-related stigma, disseminating reliable information about abortion, and fostering trust among communities to seek services, legalization of abortion cannot reach its full potential in protecting public health (22–24). Despite safe abortion law reform in 2005, illegal and unsafe induced abortions remain common in Ethiopia (25). Legal reform does not guarantee access to or use of safe abortion services, and restrictive abortion laws also do not reduce the prevalence of abortion which is also been demonstrated in other countries (26). Miller cites Gebrehiwot et al. 2009 (19) as a basis for his claim that case fatality from abortion has increased and no change in maternal mortality occurred following the liberalization of abortion law in Ethiopia. But Gebrehiwot excluded community deaths in his analysis. – making it impossible to draw any conclusions about national maternal mortality patterns. Furthermore, the data used to justify this claim is only two years into the new safe abortion law. The data in the figure (Fig.1) were used to justify Miller's claim that MMR did not decrease after abortion was legalized in 2005. But the two years of data are insufficient to support this claim.

In addition to Miller's selectively picked findings of this study, Gebrehiwot and colleagues also noted that within the two years following legal reform, the trend of abortion-related maternal mortality has declined and suggested further longitudinal study for a longer period to have a firm conclusion on the effect of safe abortion legal reform in Ethiopia (19). Twelve years after the legal reform, the MMR in Ethiopia, according to a report by the world bank in 2017, is 401 per 100,000 live births (27). This is significantly lower than the maternal mortality of the country in 2000, which was 1030 per 100,000 live births (27).

Flaw 3: Ethiopian safe abortion laws were never been fully "liberal" and therefore Miller's comparisons are inappropriate

The third outstanding argument by Calum Miller is that the same or higher rates of abortion-related maternal mortality exist in Ethiopia compared to other countries with more restrictive abortion laws. The author presented this statement as if Ethiopia has a more liberal law while other countries have restrictive abortion laws. As a justification for this, he listed countries like Kenya, Rwanda, Uganda, and other countries in North Africa. This assumption is wrong for multiple reasons. One of the fundamental points missed by the author is that abortion is far from liberal in Ethiopia. He misrepresented the country's law as "legalization" in his title and in multiple places in his commentary. Abortion is illegal in Ethiopia unless performed under the circumstances mentioned in the penal code (28). So, in terms of abortion law, there is not much difference between Ethiopia, Kenya, Rwanda, and Uganda (29). Miller cited Say L et al. in his statement about the low abortion rate in prohibitive states in North Africa (30). In this same reference, the challenges of having accurate abortion-related data, particularly in restrictive settings, is mentioned. Abortion-related data could be underreported for political reasons in some of these restrictive countries. But this is not mentioned anywhere in Miller's commentary.

The statement about high abortion-related maternal mortality in Ethiopia compared to these countries is also not supported by strong evidence. A recent report from Ethiopia has shown that abortion-related maternal mortality contributes only less than 3% of total maternal deaths (31). This is much lower compared to abortion-related maternal mortality in Kenya (17%), Uganda (5%), and Rwanda (8%) (32,33).

Flaw 4: Miller inaccurately associated the increase in abortion rate to the change in abortion law.

The fourth argument by the author is an increase in abortion rate in Ethiopia after the legalization of abortion in 2005. As we have outlined in the previous argument (Flaw 2), we agree with Miller on the increase in the rate of abortion and abortion-related morbidity following the legal reform. But this change in the abortion rate and abortion morbidity is mainly related to improved detection and reporting of abortions by health facilities, rather than the legal reform (21). So, this is mainly due to more detection and reporting than an actual increase. Similar findings are reported by other studies A comprehensive report from Sub-Saharan Africa by the Guttmacher institute gives a clear picture of abortion legality and incidence of abortion (21). According to this report, abortion occurs at a similar rate regardless of abortion law in the country. Abortion incidence cannot be reduced by restricting abortion. Instead, restrictive laws make abortion more unsafe. In countries or regions where abortion incidence has decreased, increased use of contraception, rather than a change in abortion law, is the main reason. Another recent global and regional estimate of unintended pregnancy and abortion by the Guttmacher institute also shows similar findings and has demonstrated that abortion incidence is not affected by the legality of abortion (34).

In summary, unlike what was expressed in the commentary, some of the facts in the country are as follows.

- The author's notion of “legalized abortion” is wrong. The revised law still criminalizes abortion. The law states, “The intentional termination of a pregnancy, at whatever stage or however effected, is punishable according to the following provisions, except as otherwise provided under Article 551” (35).
- Unsafe abortion has contributed to 32% of maternal death in Ethiopia before the safe abortion legal reform (28), while currently contributing to less than 10% (12).
- Comparing abortion law and abortion-related morbidity/mortality between Ethiopia and other countries is not a good strategy to evaluate the effects of change in abortion law. Crucial factors such as details of the law, implementation of the law, and other health system issues are not captured in such comparisons and this may result in erroneous conclusions.
- Unlike Miller’s commentary that fatally undermines the country’s effort and measures taken to reduce maternal mortality, the maternal mortality ratio in Ethiopia has dropped from 865 to 401 per 100,000 live births between the year 2005-2017 (27).
- Over the past two decades, the world population has increased in number, and so has the abortion rate. This increase in abortion rate has no linear relationship with the abortion law. Studies have shown that restricting abortion access makes abortion less safe rather than reducing its occurrence (21).

Conclusion

Ethiopia has suffered a huge burden of maternal death from unsafe abortion before the legal reform with 1 out of 3 women dying from the complications of unsafe abortion (10). This unprecedented occurrence unified this highly religious and conservative society to think as one and address the issue. Ten years after the legal reform, abortion-related maternal mortality has decreased to less than 5 % (31). Health financing, task shifting/ sharing, and continuous professional development for mid-level health care providers working in the area of abortion are some of the interventions introduced in the country that contributed to this achievement. Building upon this achievement, the Ethiopian Federal Ministry of Health has developed a health sector transformation plan and reproductive health strategic plan, which incorporate the elimination of unsafe abortion as one strategy to eliminate abortion-related maternal mortality (5). Access to quality sexual and reproductive health in general and safe abortion service, in particular, is still a challenge, especially in the rural regions of the country. The country is working on the missing elements and building upon its strengths to expand access to safe and quality sexual and reproductive health services. Ethiopia is not in a position to look back on those years of clandestine abortion that took the lives of many women and girls.

Miller’s commentary has overlooked the country’s commitment to improving reproductive health and the achievements made through a brave struggle of health care providers, policymakers, partner organizations, researchers, and other relevant stakeholders in the country and beyond. He used superficial information without an in-depth analysis of the studies to justify his flawed narrative. Similar publications in scientific journals should be critically analyzed before publication, and we are optimistic that the journal will retract this paper after examining the evidence presented in this commentary.

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References

1. Miller C. LEGALISATION OF ABORTION AND MATERNAL MORTALITY IN ETHIOPIA. Ethiop Med J [Internet]. 2022 Mar 29 [cited 2022 May 14];60(2). Available from: https://emjema.org/index.php/EMJ/article/view/1855
2. A brief case against abortion | Calum Miller [Internet]. [cited 2022 Jul 8]. Available from: https://calumsblog.com/2014/01/26/a-brief-case-against-abortion/
3. Miller C. Maternal Mortality from Induced Abortion in Malawi: What Does the Latest Evidence Suggest? Int J Environ Res Public Health. 2021 Oct 7;18(19):10506.
4. Abortion Q&A | Calum Miller [Internet]. [cited 2022 Jul 23]. Available from: https://calumsblog.com/abortion-qa/
5. Health M of. Health Sector Transformation Plan II (HSTP II) 2020/21 - 2024/25 (2013 EFY-2017 EFY). 2021 Feb 1 [cited 2022 May 14]; Available from: https://repository.iphce.org/xmlui/handle/123456789/1414
6. Ethiopia: National Reproductive Health Strategy | PPD [Internet]. [cited 2022 May 14]. Available from: https://www.partners-popdev.org/member-resources/ethiopia-national-reproductive-health-strategy/
7. Ethical Standards | Ethiopian Medical Journal [Internet]. [cited 2022 Jun 1]. Available from: https://emjema.org/index.php/EMJ/Ethical-Standards
8. Barbour V, Kleinert S, Wager E, Yentis S. Guidelines for retracting articles [Internet]. Committee on Publication Ethics; 2009 Sep [cited 2022 Jun 1]. Available from: https://publicationethics.org/node/19896
9. Gaym A. Maternal mortality studies in Ethiopia-Magnitude, causes and trends. Ethiop Med J. 2009 Feb 1;47:95–108.
10. Abdella A. Maternal Mortality Trend in Ethiopia. Ethiop J Health Dev [Internet]. 2010 [cited 2021 Apr 17];24(1). Available from: https://www.ajol.info/index.php/ejhd/article/view/62953
11. Berhan Y, Berhan A. Causes of Maternal Mortality in Ethiopia: A Significant Decline in Abortion Related Death. Ethiop J Health Sci. 2014 Sep;24(0 Suppl):15–28.
12. Mekonnen W, Gebremariam A. Causes of maternal death in Ethiopia between 1990 and 2016: systematic review with meta-analysis. Ethiop J Health Dev [Internet]. 2018 [cited 2022 May 29];32(4). Available from: https://www.ajol.info/index.php/ejhd/article/view/182583
13. Survey of unsafe abortion in selected health facilities in Ethiopia [Internet]. [cited 2022 Jun 1]. Available from: https://www.researchgate.net/publication/281232397_Survey_of_unsafe_abortion_in_selected_health_facilities_in_Ethiopia
14. Berhan Y, Abdela A. Emergency obstetric performance with emphasis on operative delivery outcome: Does it reflect the quality of care? Ethiop J Health Dev [Internet]. 2004 [cited 2022 Jun 1];18(2). Available from: https://www.ajol.info/index.php/ejhd/article/view/9944
15. Kwast BE, Kidane-Mariam W, Saed EM, Fowkes FG. Epidemiology of maternal mortality in Addis Ababa: a community-based study. Ethiop Med J. 1985 Jan;23(1):7–16.
16. Gessessew A. Maternal complications--in a zonal hospital. Ethiop Med J. 2007 Jan;45(1):47–54.
17. Berhan Y, Berhan A. Review of Maternal Mortality in Ethiopia: A Story of the Past 30 Years. Ethiop J Health Sci. 2014 Sep;24(0 Suppl):3–14.
18. Ronsmans C, Graham WJ, Lancet Maternal Survival Series steering group. Maternal mortality: who, when, where, and why. Lancet Lond Engl. 2006 Sep 30;368(9542):1189–200.
19. Gebrehiwot Y, Liabsuetrakul T. Trends of abortion complications in a transition of abortion law revisions in Ethiopia. J Public Health Oxf Engl. 2009 Mar;31(1):81–7.
20. HSDP IV.pdf [Internet]. [cited 2022 Jul 9]. Available from: http://tucghe.org/HSDP%20IV.pdf
21. Bankole A, Remez L, Owolabi O, Philbin J, Williams P. From Unsafe to Safe Abortion in Sub-Saharan Africa: Slow but Steady Progress. 2020 Dec 31 [cited 2022 Jul 8]; Available from: https://www.guttmacher.org/report/from-unsafe-to-safe-abortion-in-subsaharan-africa
22. Haddad LB, Nour NM. Unsafe Abortion: Unnecessary Maternal Mortality. Rev Obstet Gynecol. 2009;2(2):122–6.
23. Jewkes RK, Gumede T, Westaway MS, Dickson K, Brown H, Rees H. Why are women still aborting outside designated facilities in metropolitan South Africa? BJOG Int J Obstet Gynaecol. 2005 Sep;112(9):1236–42.
24. Chemlal S, Russo G. Why do they take the risk? A systematic review of the qualitative literature on informal sector abortions in settings where abortion is legal. BMC Womens Health. 2019 Dec;19(1):55.
25. Moore AM, Gebrehiwot Y, Fetters T, Wado YD, Bankole A, Singh S, et al. The Estimated Incidence of Induced Abortion in Ethiopia, 2014: Changes in the Provision of Services Since 2008. Int Perspect Sex Reprod Health. 2016 Sep 1;42(3):111–20.

26. Estimating the incidence of abortion: using the Abortion Incidence Complications Methodology in Ghana, 2017 [Internet]. Guttmacher Institute. 2020 [cited 2022 Jun 18]. Available from: https://www.guttmacher.org/article/2020/04/estimating-incidence-abortion-using-abortion-incidence-complications-methodology
27. Maternal mortality ratio (modeled estimate, per 100,000 live births) - Ethiopia | Data [Internet]. [cited 2022 Jun 18]. Available from: https://data.worldbank.org/indicator/SH.STA.MMRT?locations=ET
28. Health M of. Technical and Procedural Guidelines for Safe Abortion Services in Ethiopia. 2014 Jun [cited 2022 May 21]; Available from: https://repository.iphce.org/xmlui/handle/123456789/1544
29. GAPD - The Global Abortion Policies Database - The Global Abortion Policies Database is designed to strengthen global efforts to eliminate unsafe abortion [Internet]. [cited 2022 Jun 1]. Available from: https://abortion-policies.srhr.org/
30. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014 Jun;2(6):e323-333.
31. FINAL-EmONC-Final-Report-Oct25-2017.pdf [Internet]. [cited 2022 Jun 22]. Available from: https://www.ephi.gov.et/images/pictures/download2010/FINAL-EmONC-Final-Report-Oct25-2017.pdf
32. Mutua MM, Manderson L, Musenge E, Achia TNO. Policy, law and post-abortion care services in Kenya. PLOS ONE. 2018 Sep 21;13(9):e0204240.
33. Nteziyaremye J. Abortion, Maternal Mortality and the Law in Uganda: Mini-Review. :1.
34. Unintended Pregnancy and Abortion Worldwide [Internet]. Guttmacher Institute. 2020 [cited 2022 Jun 18]. Available from: https://www.guttmacher.org/fact-sheet/induced-abortion-worldwide
35. The Criminal Code of the Federal Democratic Republic of Ethiopia 2004 [Internet]. [cited 2021 Apr 17]. Available from: https://sherloc.unodc.org/cld/document/eth/2005/the_criminal_code_of_the_federal_democratic_republic_of_ethiopia_2004.html

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Letter to the Editor

The Elephant in Ethiopian Healthcare: Addressing a Culture of Silence

Mark Stambovsky[1*]

[1]St. Paul Hospital and Millennium Medical College, Addis Ababa, Ethiopia

Corresponding author*: markloveskoki@gmail.com

I've been an ICU nurse for 25 years. For the last nine, I've been working in Ethiopia. Although I will live out the rest of my life here, I accept the fact that I will always be considered a Farengi. As such, some ICU patient-care policies and initiatives I've proposed over the years have been met with the likes of, "This is Ethiopia, not America."

But if change could result in improving the health of our patients, is it not our professional and ethical responsibility to address any barriers that might hinder this progress?

Enter our metaphorical Elephant.

Ethiopians share quick and easy fellowships. This camaraderie reflects visceral trust, strength, and common character. It is beautiful thing and something that endears me to Ethiopia and her people.

But, in healthcare settings, these quick friendships can be a liability when clinicians are disinclined to confront their fellow clinicians in the face of substandard performance. Frustratingly, I have observed this "silence," or failure to comment enumerable times over the years, despite the fact clinicians may be aware of the consequences.

The widespread failure to expose or critique poor-quality practices--in any field of endeavor--not only enables those failures but can even result in the standardization of inadequate performance. Such a scenario has the potential of dooming a system to long-term mediocrity. And in hospitals, reluctance to shed light on errant practices or behaviors can be considered not only an ethical (1) breach but can result in serious consequences.

Frequently, I've encountered floor areas around beds scattered with used gauze pads, discarded IV lines, empty bottles, suction tips, plaster, etc., yet no one asks, "Why the mess"? Surely some families must wonder whether such messiness translates into equally inattentive clinical care.

What about fresh post-op patients whose analgesia orders are inadequate. We all know the various negative effects of persistent pain. Yet, too often, I've witnessed staff remain silent, somehow reluctant to confront the physician, thus allowing the continuation of unnecessary patient suffering.

A study published in 2019 found that pain management of Ethiopian post operative patients was inadequate in well over 50% of patients (2).

Can it be that so many clinicians actually lack empathy?

Some years back I asked a senior consultant to wash his hands before examining one of our patients. He ignored my request saying," You don't understand Habeshas." I was shocked by his cavalier attitude and equally upset that no one else backed me up with this simple, yet fundamental care request. Is there any practicing clinician today who is not aware of the potential consequences of poor hand hygiene practices on vulnerable patients?

A 2019 study conducted in Gondar on practices of hospital infection prevention concluded that even when clinicians possessed good knowledge regarding issues surrounding hospital acquired infections, as well as a "sympathetic attitude" it did not translate into prudent practices (3).

We often talk about treating patients ethically and with compassion. Yet, when we do not (i.e., exposing a patient without the use of a privacy screen or curtain), far too often no one speaks up on the patients' behalf to demand basic dignity.

Finally, there are those who are so unaccustomed to any form of criticism or accountability that they react angrily when confronted. This "invincibility" should not be a total surprise when the system, itself, tacitly approves of this, "go along, to get along" approach.

What's the source of this fear, reluctance, or apathy to honestly address clinical or attitudinal shortcomings? Is being assertive simply contrary to the gentle nature of most Ethiopians?

I realize it takes courage to comment on a co-worker's quality of care. But isn't that a small risk to take for the sake of improved patient care?

Perhaps clinicians see no benefit in challenging behaviors. Or, as a colleague suggested, perhaps the penalties of substandard performance are simply inconsequential.

I do not believe there is a silver-bullet answer to this issue. But, at the very least, I believe medical and nursing schools' curriculums must include dedicated programs emphasizing the critical concept of constructive, congenial criticism. They must also examine the dangers of embracing, however indirectly, "cultures of silence."

Ethiopia is replete with superb clinicians whose brainpower and commitment can, without doubt, move mountains. But we must step out of our comfort zones and begin an honest and vigorous conversation about the status quo of behaviors that can affect the very quality of patient care.

Otherwise, I fear Ethiopian acute care will never advance beyond the bar of mediocrity and the elephant that resides in too many of our units will become a permanent resident.

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References

1. Reporting Incompetent or Unethical Behaviors by Colleagues. https://www.ama-assn.org/delivering-care/ethics/reporting-incompetent-or-unethical-behaviors-colleagues
2. Code of Medical Ethics Opinion 9.4.2. 2022 American Medical Association.
   Eshete MT, Baeumler PI, Siebeck M, Tesfaye M, Haileamlak A, et al. (2019) Quality of postoperative pain management in Ethiopia: A prospective longitudinal study. PLOS ONE 14(5): e0215563. https://doi.org/10.1371/journal.pone.0215563
3. Biruk Bayleyegn,1 Addisu Mehari,2 Debasu Damtie,3 and Markos Negash. Knowledge, Attitude and Practice on Hospital-Acquired Infection Prevention and Associated Factors Among Healthcare Workers at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. Infect Drug Resist. 2021 Jan 27;14:259-266.doi: 10.2147/IDR.S290992. eCollection 2021.

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.

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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.

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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.

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- 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.
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The following examples demonstrate the acceptable reference styles.

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- 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 Ophthalmology. W.B Saunders: Philadelphia, PA 1994 pp257-76.

Website:

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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
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Minimum of three and maximum of 20 cases

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

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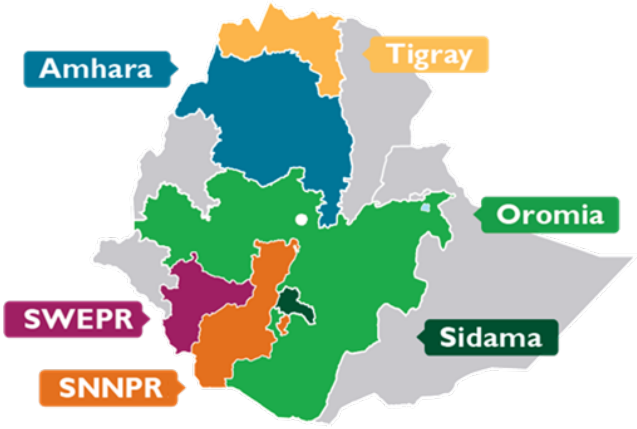
USAID Eliminate Tuberculosis Project

KEY STRATEGIES

USAID Eliminate TB Project (a five year project 2020-25) aims to reduce TB incidence and mortality by increasing the quality, access, utilization, and sustainability of TB services in five regions across Ethiopia. By engaging public and private stakeholders, the project will improve TB services through four key strategies:

- Increase expansion and utilization of TB diagnostics and technology
- Improve quality-assured and patient-centered TB care and management
- Implement high impact case finding strategies and prevention methods
- Build the capacity of health system support, ensuring country ownership and sustainability



IMPLEMENTING PARTNERS

While the project will engage communities, civil society organizations, and other private-sector partners at the local level in TB prevention and control, there are five main implementing partners.

- **Management Sciences for Health** and the **KNCV Tuberculosis Foundation** combined have over 15 years of technical TB expertise and experience in the five target Ethiopian regions.

Amhara Development Association (ADA), Oromia Development Association (ODA), and REACH Et hiopia are local organizations that provide effective community-based TB

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