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Clinicians' engagement in clinical research: Existing situation and way forward

Tigist Workneh Leulseged[1*]

[1] Medical Research Lounge Trading PLC, Addis Ababa, Ethiopia

Corresponding author*: tigdolly@gmail.com

The success of any clinical practice is determined by the clinician's competence, which stems not only from the understanding of clinical concepts, but also from the support of clinical decision-making through the generation of appropriate evidence to keep the practice up to date. This contributes to meeting the ever-changing population needs and the challenges of the health care system for better patient outcomes (1,2). As a result, the notion of evidence-based clinical practice (EBP), which combines the best available research evidence with clinical experience and patient values, has moved to the forefront of clinical practice guidelines. EBP is a process that healthcare providers use to make informed decisions about patient care which is targeted to improve patient outcomes, reduce healthcare costs, increase patient satisfaction and enhance provider confidence. EBP plays a vital role in resource-constrained settings to assure the best possible patient-centered care while lowering health-care costs by advocating the deployment of effective and efficient interventions (3-5).

In today's world, EBP is the foundation for every clinical practice, resulting in improved patient outcomes and greater life expectancy, with recent emphasis changing from prognostic to curative research to improving quality of life. However, this is not true for all countries. The developing world has lagged behind in the research field, causing the clinical practice to rely on guidelines developed in affluent nations (7,8). As a result, clinical practice in such countries is mostly based on reading and treating by the book. This is a problem when it comes to a disease that is not a priority condition in the developed world, such as communicable diseases, which have been killing millions of people in the developing world for several years due to a lack of inventions in proper preventive and curative services for such conditions (6,9).

Among the many challenges to implementing EBP in developing countries, inadequate training and limited involvement of clinicians in the evidence generation process is the biggest barrier. Ethiopia, like the rest of the developing world, lags behind in evidence generation to support clinical decision-making. Despite frequent exposure to research programs in undergraduate and postgraduate trainings, our clinicians, who are supposed to be at the forefront of medical innovation and research, are generally unaware of the benefits of clinical research or how to participate in it, have little understanding of the research system including the stakeholders involved, and struggle to properly understand the basic concepts of research and how to conduct it (10). The major gap begins with a misunderstanding of the ultimate objective of research. In the absence of an exemplary research mentor, most clinicians believe that the mere reason for conducting research is to advance their career and they genuinely don't seem to understand the applicability of research in their practice (11). Our academic promotion criteria encourage solo authorship, discouraging multidisciplinary team and junior-senior collaboration, few numbers of papers are required for promotion, the threshold for expedited promotion is relatively low, and lower quality publications are tolerated. Most importantly, the impact of the research publications is not assessed.

In the context of the curriculum, clinicians allege that the program fulfillment courses are delivered in bulk in a short period of time, and that despite the subjects' novelty to medical professionals, there is little practical time allotted for them to better comprehend it. Furthermore, the practical sessions do not provide the necessary guidance to help the trainees make the appropriate decision in properly designing their protocols to fit their research questions. The advisor's dedication to the advisership appears to be unregulated. Due to the lack of proper guidance and support, most students lack motivation to engage in research activities (11,12). The system also appears to tolerate low-quality research at all levels. This, combined with the fact that the program fulfillment research adds little value in the final passing or failing of the clinician from the program, and in some cases, not even taken as a prerequisite, has caused most clinicians not to appreciate its value. This has encouraged most to deprioritize it and depend heavily on very basic descriptive research studies (11). This further has led to inadequate capability for research design and conduct among the clinicians which is reflected by their unfavorable attitude and limited engagement in research endeavors.

Furthermore, there is a scarcity of funds to support clinical research in Ethiopia. The majority of research grants are awarded by government institutions. Apart from being insufficient, these grants typically favor senior professionals and those few who are already experienced in research endeavors, denying a learning opportunity for the growing number of young clinicians who should be shaped in the right direction to balance clinical practice and research. The grants are less stringent in requiring multidisciplinary team research, resulting in a lack of collaboration between clinical and public health professionals, resulting in research outputs that lack an appropriate statistical and clinical balance in the interpretation of results. Additionally, these grants are not consistently and adequately available, forcing most to rely on hunting international grant opportunities, which may steer research into donor interest areas rather than country priority areas, leading to a donor-dependent research system with poor sustainability and relevance to the local context. Furthermore, the regulatory environment for clinical research in Ethiopia is complex and time-consuming, which can deter clinicians from participating in any research (9-12).

For a better health-care system and improved patient outcomes, continuous capacity building is at the heart of the change we are looking forward to. Our clinicians require extensive exposure to clinically oriented, hands-on research trainings in order to understand how to transform their observation into problem-solving research utilizing the appropriate research tools. The Medical school curriculum should ensure adequate and meaningful participation in research activities throughout each year of both undergraduate and postgraduate training, using a multitude of platforms. It is critical to ensure the involvement of local investors and philanthropists in clinical research in order to ensure a sustainable funding source and to focus research on national priority areas. The regulatory environment for clinical research in Ethiopia could be streamlined to make it easier for clinicians to participate. This could include simplifying the application process, reducing the amount of paperwork required, and providing prompt clearance for early initiation of research projects, particularly for time-sensitive themes. In addition, the academic promotion system should be reviewed to ensure that it is based on quality of research publications and the impact of the research work. Furthermore, continuous recognition of researchers, who produce significant research studies contributing to improved clinical decision-making, should be made to foster the culture of clinical research in the country.

In conclusion, as the field of EBP continues to grow, by improving clinicians' engagement in clinical research and by addressing the challenges to EBP implementation, we can create a more favorable environment for clinical research and ensure that all patients, regardless of their location, have access to the best possible care.

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Original Article

Predictors of post operative outcomes and time to full recovery among first time thoracotomy cases at Tikur Anbessa Specialized Hospital in Ethiopia.

Fekadesilassie Henok Moges[1,2*], Adem Ali[1], Dereje Gulilat[1], Seyoum Kassa[1], Abebe Bekele[1,3], Tesfaye Kebede [4], Seifu Hagos[5], Tigist Workneh Leulseged [6]

[1] Department of Surgery, School of Medicine, Addis Ababa University, Addis Ababa, Ethiopia
[2] Department of Internal Medicine, Aurora West Allis Medical Center, WI, USA
[3] University of Global Health Equity, Dean School of Medicine, Kigali, Rwanda
[4] Department of Radiology, Addis Ababa University, Addis Ababa, Ethiopia
[5] School of Public Health, Addis Ababa University, Addis Ababa, Ethiopia
[6] Medical Research Lounge Trading PLC, Addis Ababa, Ethiopia

Corresponding authors*: fshsim@yahoo.com

Abstract

Background*: Thoracotomy is a major surgical procedure requiring a thorough understanding of cardiorespiratory mechanics. Postoperative care requires a high-dependency environment and trained and well-experienced staff. The aim of this study was to determine the post-op outcomes, estimate the time to full post-op recovery, and identify predictors associated with these outcomes among patients who underwent first time thoracotomy at Tikur Anbessa Specialized Hospital (TASH) from April 1, 2011 to March 31, 2012 in Ethiopia.*

Methodology: *A retrospective chart review was conducted among 148 patients. Descriptive analysis using frequencies with percentages and mean survival times were used to characterize the study population. To compare the mean time to post-thoracotomy recovery between groups, Kaplan-Meier survival plot together with Log-rank test was used. To identify significant predictors of post-thoracotomy outcomes and time to post-thoracotomy recovery, a robust Poisson regression model and Cox proportional hazard survival model were run at 5% level of statistical significance.*

Results: *From the 148 patients, 115 (77.7%, 95% CI=71.5%-85.6%) fully recovered, 27 (18.2%, 95% CI=12.0%-23.6%) have recovered with complications and 6 (4.1%, 95% CI=1.4%-6.9%) died. The overall mean time to post-thoracotomy recovery was 13.2 days (95% CI=10.1-16.4). Significant predictors of major complications and death were being male (ARR=1.99, 95% CI=1.02, 3.94, p=0.049), pre-op WHO Performance status score of 3 and 4 (ARR=2.56, 95% CI=1.19, 5.48, p=0.015), developing intraoperative complication (ARR=2.29, 95%CI=1.14, 4.59, p=0.020) and taking systemic analgesia (ARR=4.13, 95% CI=1.05, 16.23, p=0.042). Significant predictors of time to post-op recovery were being male (AHR=0.62, 95% CI=0.42,0.92, p=0.017) and developing intraoperative complication (AHR=0.38, 95% CI=0.18, 0.80, p=0.011).*

Conclusion*: The post-thoracotomy morbidity and mortality in the study population is similar to previous reports, and the mean recovery time is within the expected range for a good outcome. For further improvement in these outcomes, it is crucial to mitigate risks during the preoperative period and closely monitor and manage high-risk patients during the postoperative period.*

Keywords*: Post-thoracotomy outcomes, time to post-thoracotomy recovery, robust Poisson regression, Cox pro portional Hazard survival model, Ethiopia*

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Thoracotomy is a major surgical procedure that is used to diagnose and treat many benign and malignant lesions of the lungs, pleura, esophagus, and other mediastinal structures (1). It is one of the most difficult surgical incisions to deal with in the postoperative period. Postoperative complications result in significant morbidities and mortalities in patients subjected to thoracic surgeries (2). The procedure might cause reduction of lung capacity (forced vital capacity [FVC] and forced expiratory volume in one second [FEV1]). It might also impair gas exchange, cough and mucociliary clearance, eventually developing micro-atelectasis and postoperative hypoxemia (2, 3).

The overall incidence of complications following thoracotomy is variable and ranges between 15% to 37.5% and cardiopulmonary complications may occur in 30-60% of cases in the postoperative period (4-6). Different authors reported life threatening complications in as low as 2% to as high as 27% of their patients (7-9). This is primarily due to the differences in the type of pulmonary complications studied, the clinical criteria used in the definition of the complications and the type of surgery included (10). Various risk factors for complications following thoracic surgery have been identified. The most frequent risk factors include age of the patient, preoperative pulmonary function tests, presence of cardiovascular comorbidity, poor performance status (ASA III and IV) smoking status, and COPD (7,11-23). Furthermore, the incidence of perioperative mortality associated with thoracic surgery ranges from 1 to 12% (24,25). In the presence of these major complications, delayed recovery is expected to occur followed by all potential hospital acquired infections and complications (23,26).

Even though there are recent advances in anesthesia and perioperative care, complications such as myocardial ischemia, thromboembolism, infection, hemorrhage, and death still occur (27). Various authors analyzed outcomes in a specific group of patients with specific diagnoses like lung carcinoma, pulmonary hydatid cyst, pneumonectomy or lobectomy to determine possible risk factors for poor outcome (7-9,28-30). However, our study included all types of thoracic surgeries undertaken for variable diagnoses. Accordingly, the purpose of this study was to determine the post-op outcomes, estimate the time to full post-op recovery, and identify factors associated with these outcomes among patients who underwent first time thoracotomy at Tikur Anbessa Specialized Hospital (TASH) from April 1, 2011 to March 31, 2012 in Ethiopia.

Methods

Study Design and Population

A retrospective chart review study was conducted among patients aged 13 years and older and who had first time thoracotomy for various indications at TASH, the largest referral hospital in Ethiopia, over a period of one year from April 1, 2011 to March 31, 2012. During the one-year observation period, a total of 167 thoracotomies were performed, out of which five were re-thoracotomies for postoperative complications and 14 cases did not have complete information on their chart. Finally, after excluding the 19 ineligible cases,148 patients were included in the study.

Operational Definition

Full Post-thoracotomy Recovery: Is the absence of major non-fatal life-threatening events occurring in the first 30 postoperative days or the absence of death within the first 30 post-thoracotomy days.

Major complication: Non-fatal life-threatening events occurring in the first 30 postoperative days, if pharmacological or technical support was required, if permanent disability ensued or life expectancy was threatened and is classified as respiratory complications or non-respiratory complications.

Operative mortality: Death occurring within 30 days of operation in patients who remained hospitalized since the time of the operation and death occurring later during the same hospitalization.

Event: Full post-thoracotomy recovery

Censoring: Includes patients who were lost to follow -up, transferred out, died or completed the follow-up period before achieving full recovery.

Time to event or censoring: time between thoracotomy to recovery or censoring (in days).

Data Collection and Quality Assurance

A pre-tested data abstraction tool was used to extract data from the charts of the patients. Data on preoperative, operative, and post-operative characteristics of the patients and their post-op outcomes and time to full post-op recovery were collected. To assure data quality, data was collected by two senior surgery residents. Double data entry and data cleaning through checking for inconsistencies, numerical errors, and missing parameters was also performed. After the data cleaning was complete, the data was exported to SPSS version 25.0 software for analysis.

Statistical analysis

To characterize the study population, descriptive statistics using frequencies with percentages and mean survival times were run. To compare the mean time to post-thoracotomy recovery between groups, Kaplan-Meier (KM) survival plot together with Log-rank test was used, where p-value ≤ 0.05 indicated a statistically significant difference.

To identify significant predictors of post-thoracotomy outcomes, a robust Poisson regression model was run. Univariate analysis was run at 25% level of significance to identify significant exposures that are going to be modeled into the final analysis. Then, a multivariable analysis was run at 5% level of significance where adjusted relative risk (ARR), P-value and 95% CI for ARR were used to test significance and interpretation of results. The final multivariable robust Poisson regression model was tested for model adequacy and it showed a good fit to the data based on Omnibus test result of p-value=0.009.

To identify predictors of time to post-thoracotomy recovery, Cox proportional hazard (PH) survival model was used. At 25% level of significance, a univariate analysis was run to screen out significant exposures to be included in the final model. Accordingly, the selected variables were included into the final multivariable Cox PH survival model at 5% level of significance where adjusted hazard ratio (AHR), 95% CI for AHR and p-value were used to interpret the results. The proportional hazards assumption, the basic assumption of the model, was tested using log minus log function and all plots revealed parallel lines between groups showing that the model is a good fit for the data.

Results

Baseline (Pre-operative) characteristics

From the 148 first time post-thoracotomy patients, the majority of the study participants were younger than 40 years old (64.2%). The minimum and maximum ages were 13 and 80 years old, respectively. Seventy-nine patients (53.4%) were male and 15 (10.1%) patients were smokers. Over a quarter of them (27.7%) had one or more comorbid illness at the time of their presentation. Pulmonary tuberculosis and its chronic sequelae were seen in 17/41 patients followed by hypertension in 9/41 patients, bronchial asthma in 5/41 patients, diabetes mellitus in 4/41 patients and toxic goiter in 3/41, HIV in 2/41 and COPD in 1/41. From the 69 females, one was in her second trimester pregnancy. Seventy-two (48.6%) patients had a World Health Organization performance status (WHO-PS) score of 1 while 9 (6.1%) were asymptomatic with a score of 0 and only 2 (1.4%) patients were bed-bound with a score of 4. (**Table1)**

Table 1: Baseline characteristics of the participants who underwent first time thoracotomy (n=148)

Variables	Frequency (%)	Variables	Frequency (%)
Age		Comorbidities	
< 40	95 (64.2)	No	107 (72.3)
≥ 40	53 (35.8)	Yes	41 (27.7)
Sex		Pulmonary tuberculosis	7/41
Male	79 (53.4)	Hypertension	8/41
Female	69 (46.6)	Bronchial asthma	5/41
Smoking		Diabetes mellitus	4/41
No	15 (10.1)	Toxic goiter	3/41
Yes	133 (89.9)	HIV	2/41
WHO-PS		COPD	1/41
0 (Asymptomatic)	9 (6.1)	Others	10/41
1 (Symptomatic but ambulatory)	72 (48.6)		
2 (<50% in bed during the day)	42 (28.4)		
3 (>50% in bed during the day)	23 (15.5)		
4 (bed bound)	2 (1.4)		

Operative and Post-operative characteristics

The commonest indication for thoracotomy was empyema thoracis seen in 38 (25.7%) of the patients followed by esophageal cancer in 20 (13.5%) patients, hydatid cyst of the lung in 19 (12.8%), and mediastinal tumor in 13 (8.8%). The commonest surgical approach was posterolateral thoracotomy performed in 117 (79.1%) patients. Among the posterolateral thoracotomies and the axillary thoracotomies, 73 (49.3%) were performed in the right chest. Decortication was the commonest operative procedure performed on 35 (23.6%) patients followed by hydatid cystectomy in 19 (12.8%) patients. In 118 (79.7%) patients, the operation lasted less than 3 hours; it lasted less than 1 hour in 7, 1 to 2 hours in 66, and 2 to 3 hours in 45 patients. Intraoperative complications occurred in 15 (10.1%) patients. The commonest intraoperative complication was significant bleeding (>1500ml) which occurred in 9 (6.1%) patients. One hundred five (70.9%) patients were transferred to surgical Intensive care unit (ICU) immediately following surgery and 50 (33.8%) of them stayed for 24 hours or less, 34 (23%) of them stayed for 48 hours and 21 (14.2%) of them stayed for more than 48 hours. The most common type of analgesia utilized in the postoperative period was a combination of intravenous (IV) narcotics, parenteral nonsteroidal anti-inflammatory drugs (NSAIDS) and Tramadol used in 95 (64.2%) patients.

Postoperative complications occurred in 31 (20.9%) patients. Respiratory complications occurred in 21/33 of them and non-respiratory complications in 6/33 patients. Both respiratory and non-respiratory complications occurred in 6/33 patients. The commonest respiratory complication was pneumonia which occurred in 12/21 patients followed by broncho pleural fistula which occurred in 6/21 patients. Anastomotic leak and anemia were the most common non-respiratory complications which occurred in 3/6 patients each. Reoperation was required in 5 (3.4%) patients. Post-op control Chest X-ray (CXR) revealed that 112 (75.7%) had a normal finding. (**Table 2).**

Post-thoracotomy outcome, Censoring status and mean recovery time

From the 148 patients, 115 (77.7%, 95% CI=71.5%-85.6%) fully recovered, and the remaining 33 (22.3%, 95% CI=14.7%-28.5%) were censored. Among the censored observations, 27 (18.2%, 95% CI=12.0%-23.6%) have recovered with complications and 6 (4.1%, 95% CI=1.4%-6.9%) died.The overall mean time to post-thoracotomy recovery was 13.2 days (95% CI=10.1-16.4). A comparison of the mean recovery time was made between groups. Accordingly, a significantly delayed post-op recovery was observed for patients who were 40 years and older (10.1 Vs 18.1 days), male (10.8 Vs 14.9 days), WHO-PS score of 2 and above (10.1 Vs 14.4 Vs 13.2 days), developed intraoperative complication (11.5 Vs 18.6 days), and were on IV Narcotics, NSAIDS, and tramadol ± Epidural analgesia in the post-op period (7.2 Vs 14.9 days). **(Table 3)**

Table 2: Operative and post-operative characteristics of the participants who underwent first time thoracotomy (n=148)

Variables	Frequency (%)	Variables	Frequency (%)
Indications		Intraoperative complication	
Empyema Thoracis	38 (25.7)	No	133 (89.9)
Esophageal Ca	20 (13.5)	Yes	15 (10.1)
Hydatid Cyst	19 (12.8)	Patient transferred to SICU post op	
Mediastinal Tumor	13 (8.8)	No	43 (29.1)
Constrictive Pericarditis	12 (8.1)	Yes	105 (70.9)
PDA	12 (8.1)	Post op analgesia used	
Lung Mass	9 (6.1)	Epidural	32 (21.6)
Giant Bullae with Pneumothorax	9 (6.1)	IV Narcotics, NSAIDS, and tramadol	95 (64.2)
Bronchiectasis	5 (3.4)	Epidural + IV medications	21 (14.2)
Aspergilloma	5 (3.4)	Post-op complications	
Others	6 (4.1)	No	115 (77.7)
Type of surgical approach		Yes	33 (22.3)
Posterolateral thoracotomy	117 (79.1)	Respiratory	21/33
Sternotomy	16 (10.8)	Non-respiratory	6/33
Axillary thoracotomy	14 (9.5)	Both	6/33
Hemi Clamshell	1 (0.7)	Re-operation required	
Operative procedure done		No	143 (96.6)
Decortication	35 (23.6)	Yes	5 (3.4)
Cystectomy	19 (12.8)	Finding on control CXR	
Trans Thoracic Esophageal resection	16 (10.8)	Normal	112 (75.7)
Pneumonectomy	14 (9.5)	Pleural fluid collection	12 (8.1)
Pericardiectomy	12 (8.1)	Fluid + Air with air fluid level	9 (6.1)
PDA Ligation	12 (8.1)	Consolidation	6 (4.1)
Mediastinal Tumor Excision	11 97.4)	Collapse	3 (2.0)
Bullectomy	7 (4.7)	Atelectasis	2 (1.4)
Explorative Thoracotomy	5 (3.4)	pneumothorax	2 (1.4)
Others	4 (2.7)	subcutaneous air	2 (1.4)
Total time of surgery			
< 3 hours	118 (79.7)		
≥ 3 hours	30 (20.3)		

Table 3: Censoring status, and comparison of mean time to recovery between groups among patients who underwent first time thoracotomy (n=148)

Variables	Time to recovery		Mean time to recovery (in days)	p-value
	Event	Censored		
Age				
< 40	78	17	10.1	0.013*
≥ 40	37	16	18.1	
Sex				
Female	59	10	10.8	0.011*
Male	56	23	14.9	
Smoking				
No	107	26	12.3	0.056
Yes	8	7	12.6	
Comorbidity				
No	88	19	12.1	0.117
Yes	27	14	11.6	
WHO-PS				
0 and 1	69	12	10.1	0.007*
2	32	10	14.4	
3 and 4	14	11	13.2	
Intraoperative complication				
No	107	26	11.5	0.003*
Yes	8	7	18.6	
Post-op analgesia type				
Epidural	30	2	7.2	0.019*
IV Narcotics, NSAIDS, and tramadol ± Epidural	85	31	14.9	

*Statistically significant

This difference is also demonstrated on the KM survival plot of these groups where a shorter recovery time for the above groups is observed. (**Figure 1**)

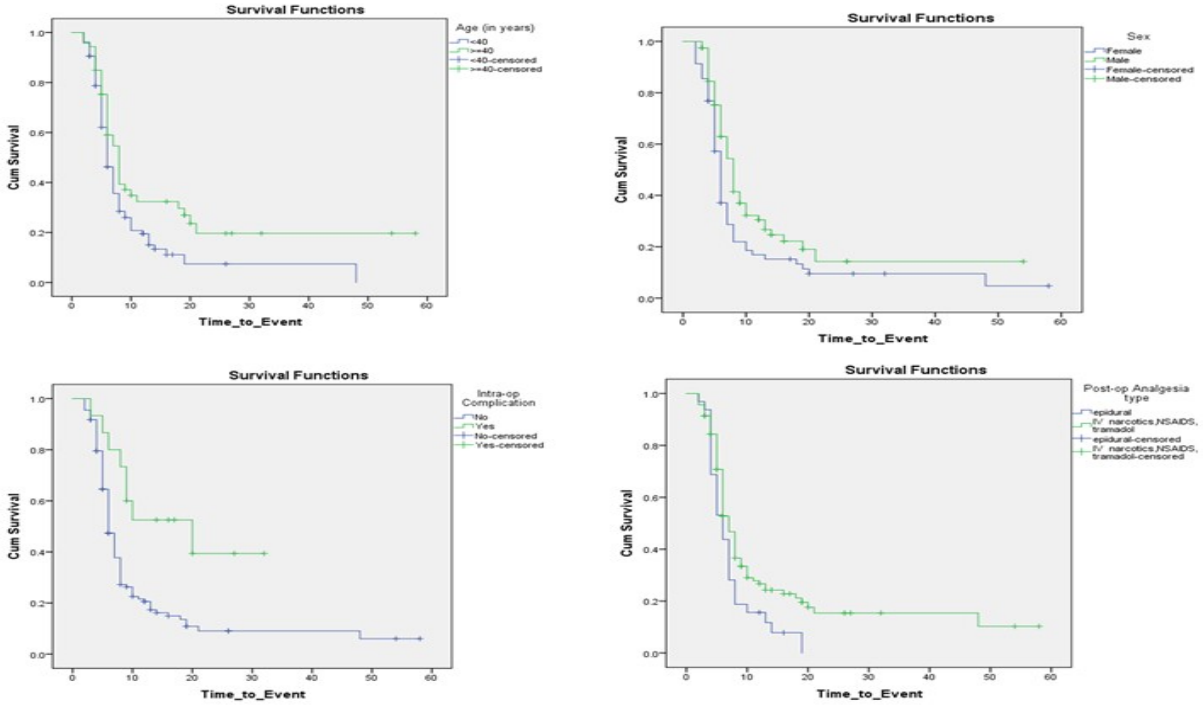

Fig 1: Kaplan-Meier survival graph of time to post-thoracotomy recovery stratified by age, sex, intraoperative complication, and post-op analgesic type.

Predictors of Post-thoracotomy Outcome

To identify the predictors of post-thoracotomy outcomes, a multivariable robust Poisson regression model was run after adjusting for age, sex, smoking, comorbidity, WHO-PS, intraoperative complications, and post-op analgesia type which were found to be significantly associated on the univariate analysis. From these, sex, WHO-PS, intraoperative complications, and post-op analgesia types were found to be significantly associated with the outcome.

Accordingly, after adjusting for other variables, the risk of developing major complications and/or death among males was almost twice that of females **(ARR=1.99, 95% CI=1.02, 3.94, p=0.049)**. Patients with pre-op WHO-PS score of 3 and 4 were found to have a 2.56 times increased risk of developing major complication and/or death as compared with those with a score of 0 or 1 **(ARR=2.56, 95% CI=1.19, 5.48, p=0.015)**. Furthermore, developing intraoperative complication and taking systemic analgesia during the post-op period were associated with an increased risk of developing major complication and/or death by 2.29 times **(ARR=2.29, 95%CI=1.14, 4.59, p=0.020)** and 4.13 times **(ARR=4.13, 95% CI=1.05, 16.23, p=0.042)** as compared with those with no complication and were taking epidural analgesic, respectively. (**Table 4**)

Table 4: Predictors of post-thoracotomy outcomes among patients who underwent first time thoracotomy (n=148)

Variables	Post-thoracotomy outcome		CRR (95% CI)	ARR (95% CI)	p-value
	Full recovery	Complication/ death			
Age					
< 40	78	17	1	1	
> = 40	37	16	1.69 (0.93, 3.06)	1.27 (0.64, 2.51)	0.497
Sex					
Female	59	10	1	1	
Male	56	23	2.01 (1.03, 3.92)	1.99 (1.02, 3.94)	0.049*
Smoking					
No	107	26	1	1	
Yes	8	7	2.39 (1.26, 4.53)	0.85 (0.35, 2.08)	0.725
Comorbidity					
No	88	19	1	1	
Yes	27	14	1.92 (1.07, 3.47)	1.57 (0.82, 2.99)	0.171
WHO PS					
0 and 1	69	12	1	1	
2	32	10	1.61 (0.76, 3.41)	1.28 (0.64, 2.55)	0.487
3 and 4	14	11	2.97 (1.49, 5.89)	2.56 (1.19, 5.48)	0.015*
intraoperative complication					
No	107	26	1	1	
Yes	8	7	2.39 (1.26 (4.53)	2.29 (1.14, 4.59)	0.020*
Post-op analgesia type					
Epidural	30	2	1	1	
IV Narcotics, NSAIDS, and tramadol ± Epidural	85	31	4.23 (1.08, 16.92)	4.13 (1.05, 16.23)	0.042*

CRR, Crude relative risk; AHR, Adjusted relative risk; CI, Confidence interval; *Statistically significant

Predictors of Time to Post-thoracotomy Recovery

To identify predictors of time to full post-thoracotomy recovery, Cox proportional hazard (PH) survival model was run. From univariate analysis, age, sex, smoking, comorbidity, WHO-PS, intraoperative complications, and post-op analgesia type were found to be significant and were fed into the final multivariable regression model.

In the final model, at a 5% level of significance, sex and intraoperative complication were found to be significantly associated with time to post-thoracotomy recovery.

Accordingly, after adjusting for other covariates, the rate of achieving full post-thoracotomy recovery among males was 38.0% lower than females (AHR=0.62, 95% CI=0.42,0.92, p=0.017). In addition, intraoperative complication was associated with a 62.0% lower rate of achieving full post-thoracotomy recovery as compared to those with no complication (AHR=0.38, 95% CI=0.18, 0.80, p=0.011). (Table 5)

Table 5: Predictors of time to full post-thoracotomy recovery among patients who underwent first time thoracotomy (n=148)

Variables	CHR (95% CI)	AHR (95% CI)	p-value
Age			
< 40	1	1	
> = 40	0.63 (0.42, 0.94)	0.73 (0.48, 1.13)	0.156
Sex			
Female	1	1	
Male	0.65 (0.45, 0.93)	0.62 (0.42, 0.92)	0.017*
Smoking			
No	1	1	
Yes	0.53 (0.26, 1.09)	1.05 (0.44, 2.46)	0.920
Comorbidity			
No	1	1	
Yes	0.73 (0.47, 1.12)	0.86 (0.52, 1.41)	0.544
WHO PS			
0 and 1	1	1	0.129
2	0.65 (0.42, 0.99)	0.77 (0.49, 1.20)	0.253
3 and 4	0.49 (0.27, 0.87)	0.56 (0.31, 1.01)	0.055
intraoperative complication			
No	1	1	
Yes	0.38 (0.18, 0.78)	0.38 (0.18, 0.80)	0.011*
Post-op analgesia type			
Epidural	1	1	
IV Narcotics, NSAIDS, and tramadol ± Epidural	0.63 (0.42, 0.96)	0.78 (0.50, 1.21)	0.266

CRR, Crude relative risk; AHR, Adjusted relative risk; CI, Confidence interval; *Statistically significant

Discussion

In this study, we assessed the potential post-thoracotomy outcomes, estimated the mean time to full post-op recovery, and identified predictors associated with these outcomes among 148 eligible patients who underwent first-time thoracotomy at Tikur Anbessa Specialized Hospital in Ethiopia from April 1, 2011 to March 31, 2012. Of the 148 patients, 115 (77.7%) fully recovered, 27 (18.2%) recovered with complications, and 6 (4.1%) died. The rate of major complications was in the lower range of expected rates, based on reports from other studies. Life-threatening complication rates of up to 27%-60% have been reported in many studies, while rates as low as 2-10% have been reported in a few studies (4,7-9). Similarly, the perioperative mortality rate was also in the lower range of reported rates from other studies (24,25).

The overall mean time to post-thoracotomy recovery was 13.2 days. The average mean time to post-thoracotomy recovery is 7-10 days, but this can vary depending on the type of surgery, the patient's overall health, and other factors (32-34). In this study, the mean time to recovery was a bit longer than the average, but this is likely due to the fact that a considerable proportion of the participants had high-risk factors, such as old age, smoking, and comorbidity. Considering these factors, 13.2 days is a reasonable duration of stay.

The study showed that the risk of major complications and death after thoracotomy was significantly higher in men, in those with a preoperative WHO-PS score of 3 or 4, in those who developed intraoperative complications, and amongst those who received systemic analgesia. In addition, a significantly delayed post-thoracotomy recovery was observed amongst males and those with intraoperative complications. The increased risk with male sex could be because men are more likely to have chronic health conditions that increase the risk of intraoperative complications and poor postoperative outcomes. In addition, in this study, a large proportion of men were smokers and had other comorbidities, which are known to be associated with poor outcomes. Male sex has also been reported as a risk factor for adverse outcomes after surgery in another study (8). Poor preoperative WHO -PS measures a patient's overall health and ability to function. Patients with poor PS are more likely to have chronic health conditions, be older, have a lower BMI, be malnourished, and have other risks. These factors can increase the risk of complications during and after surgery. Other studies have also shown this increased risk (7,21-23, 26).

In addition, intraoperative complications can lead to several negative consequences, including increased length of stay in the hospital and increased risk of infection, leading to further complications and death. Such increased risk is also demonstrated in other studies (21-23, 26). Furthermore, systemic analgesics are commonly used to manage pain after surgery. However, they can also increase the risk of complications, such as respiratory depression, nausea, and vomiting. These complications can lead to a more extended hospital stay and even death, especially among those with additional underlying medical conditions. Regional analgesics, on the other hand, are less likely to cause these complications. Studies have shown that patients who receive epidural analgesia have a lower risk of death, complications, and a shorter hospital stay (35,36).

The retrospective nature of the study made it impossible to collect data on some important variables, such as preoperative pulmonary function tests, information on the status of diagnosis of COPD, whether chest physiotherapy has been performed, and details of smoking status. These limitations should be considered when interpreting the results of the study.

Conclusions

The post-thoracotomy morbidity and mortality in the study population are similar to previous reports, and the mean recovery time is within the expected range for a good outcome. Male sex and intraoperative complications were significant predictors of increased risk of major postoperative complications, death, and delayed recovery. Preoperative WHO-PS score of 3 or 4 and systemic analgesia were significant predictors of increased risk of major postoperative complications and death. Therefore, mitigating risks during the preoperative period and closely monitoring and managing high-risk patients during the postoperative period is essential. We recommend conducting a prospective cohort study to investigate additional risk factors in a larger patient population.

Declaration

Ethical Considerations

The study was conducted after obtaining ethical clearance from the Department of Surgery Research Committee. The patients' privacy was protected by only using their medical record numbers to identify them, and their identifiers were not used in the research report. Only the research team could access the collected information, and confidentiality was maintained throughout the project.

Availability of data and materials: All relevant data are available upon reasonable request.

Competing interests: The authors declare that they have no known competing interests

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Author's Contribution: FSH conceived and designed the study, performed the statistical analysis and drafted the initial manuscript. AA, DG, SK, and AB contributed to the conception of the study and reviewed the manuscript. TK, SH, and TWL contributed to the conception and design of the study, statistical analysis, and manuscript drafting. All authors revised the manuscript and approved the final version.

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Original Article

Effect of pregnancy on COVID-19 severity: A retrospective cohort study in Ethiopia

Abebaw Bekele[1], Eyob Kebede Etissa[2], Yonas Gebreegziabher[1], Nuru Mohammed[1], Bethel Dawit[1], Hiruy Araya[1], Bisrat Kassa[1], Tsegaye Gebreyes[1], Tariku Soboka[1], Abdurahman Mohammedamin[1], Tinsaye Zergaw[1], Hanan Yusuf Ahmed[3], Tewodros Haile Gebremariam[3], Dawit Kebede Huluka[3]

1 Eka Kotebe Hospital, Addis Ababa, Ethiopia
2 East African Training Initiative, Addis Ababa, Ethiopia
3Department of Internal Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia

Corresponding authors*: dndrda97@gmail.com

Abstract

Background: *There is a scarcity of data on the clinical features, severity of disease and treatment outcomes of COVID-19 during pregnancy in Sub-Saharan Africa. The main purpose of this study was to evaluate illness severity and pregnancy.*

Methods: *Between May 21, 2020 and May 20, 2021, medical records were reviewed as part of this single-center retrospective cohort study. Descriptive statistics, including chi-square tests, two independent sample t-tests, and the Mann-Whitney U test, were used as needed. A Poisson regression was also done to determine the effect of pregnancy on severity independently.*

Results: *There were no differences in the comorbidities between pregnant and non-pregnant groups, except for hypertension, which was more common among non-pregnant women. Pregnant women had a greater number of headaches, myalgia, and anosmia. In the pregnant group, absolute lymphocyte counts below 1000/mm^3, and platelet counts below 150,000/mm^3 were more common. Regarding the severity of the diseases, there were similarities between the groups. There was no difference between the groups in terms of disease severity, in-patient care unit admission, type of treatment given, and mortality. Non-pregnant women, however, have a shorter length of hospital stay. Two (5.0 %) of the 40 patients who gave birth at the study facility had a neonatal outcome of death. In a multivariable regression analysis, there was no association between pregnancy and disease severity.*

Conclusion: *Although some of the symptoms and laboratory factors were more prevalent in pregnant women, pregnancy was not found to affect severity or mortality from COVID-19.*

Keywords*:* COVID-19, Pregnancy, Ethiopia
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Introduction

Pregnancy was reported to be predictive of unfavorable outcomes in severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) and in 2002 and 2013. Pregnancy-related physiologic and immunologic changes have been linked to a more severe disease course and prognosis in pregnant women. The high risk of maternal death surpasses the possible fetal harm(1, 2). As a result, pregnant women have raised increased concern, as previous experiences have shown that this vulnerable group is prone to serious consequences. Data regarding implications of COVID-19 in pregnancy have been reported mostly in small series of patients from high-income settings (3-5)). Data on the risk of severe illness and in-patient care unit (ICU) admission in pregnant women have been inconsistent, with some studies reporting a higher likelihood for adverse outcomes, and others not. Non-pregnant individuals' test abnormalities were like those reported in pregnant patients(3, 6-11)). COVID-19 is known to induce a variety of effects, including respiratory failure and hypercoagulability, problems that can be exacerbated during pregnancy.

To the best of our knowledge, no research on the outcome and severity of pregnancy with COVID-19 has been conducted in our country, and few data are available from other low-income and middle-income nations. The purpose of this study was to compare the clinical features, treatment, and out-

comes of pregnant and non-pregnant women with COVID-19 and to assess the effect of pregnancy on disease severity among patients treated at Eka Kotebe General Hospital.

Methods

Area and time of study

This study was conducted at Eka Kotebe General Hospital, the first institution in Addis Ababa specifically designed to treat COVID-19. The facility was used as an outpost of the Amanuel General Psychiatric Hospital until April 2020, at which point it was transformed into one of the stand-alone government facilities tasked with caring for COVID-19 patients. Data from May 21, 2020, through May 20, 2021, were used for the study.

Study design

Retrospective cohort analysis of women with COVID -19 disease, both pregnant and not, was done. The clinical course of exposed and non-exposed women who were followed at the Eka Kotebe COVID-19 treatment facility was used to analyze the difference in clinical characteristics and patient outcomes. Two non-exposed patients were selected randomly from consecutive non-pregnant patients for each patient on the exposed arm (pregnant women).

Source/study population

The source population consisted of all pregnant and non-pregnant women admitted to Eka Kotebe Hospital with a laboratory-confirmed diagnosis of COVID-19 infection in the reproductive age group (15–49 years). The source population comprised all women in childbearing age groups admitted to Eka Kotebe Treatment Center with a laboratory-confirmed diagnosis of COVID-19 infection using reverse transcription-polymerase chain reaction at the time of study.

Inclusion and exclusion criteria

Inclusion criteria: Pregnant women between the ages of 15 and 49 who were hospitalized at Eka Kotebe Hospital with a gestational age of at least 20 weeks and a diagnosis of SARS CoV-2 infection that had been confirmed by a laboratory. And non-pregnant women between the ages of 15 and 49 who had a confirmed lab diagnosis of COVID-19 infection and were hospitalized at Eka Kotebe Hospital were included.

Exclusion criteria:

Patients whose primary outcome has not been recorded and patients who have stayed less than 24 hours in the hospital.

Sample size calculation

The sample size was determined for the ratio of two populations using EPI-Info. The study calls for 91 pregnant women and 181 non-pregnant women using the following assumptions: 5% of women will develop a severe form of the disease, a two-sided significance level of 95% confidence level, 80% power, a ratio of non-exposed to exposed of 2, and a three-fold increase in severity among pregnant women (12, 13). The sample size is raised to 100 pregnant women and 200 non-pregnant women by adding 10% for non-response (incomplete data).

Data collection procedures, and quality assurance

A case report format (CRF) that had been modified from the World Health Organization (WHO) was used to collect data about the demographic, obstetric, laboratory, clinical, radiological, and therapeutic characteristics, complications, and clinical outcomes of enrolled patients from their medical records. The data also included the dates of onset, admission, and change in severity, as well as the dates of discharge, death, or transfer. For pregnant patients, obstetric and neonatal outcomes were documented. Phone calls were made using their contact addresses when necessary. Two different researchers carefully examined the data. Disagreements between the reviewers were resolved by discussion or the third researcher. At the Eka Kotebe Hospital, trained physicians gathered data on every factor.

Trained data collectors used the data collection instrument daily to assure consistency and minimize inter- and intra-observation differences in variable measurement. Every day, a supervisor analyzed the gathered data for completeness and consistency. Every day, the designated supervisors and primary investigators supervised and monitored.

Data management and analysis

After data collection, the survey findings were entered into the Epi Info program version 7.2.6 and exported to SPSS version 25.0 for analysis. Frequency and percentages (%) for categorical data were provided, while the median and interquartile range (IQR) for continuous data were reported. The study used the Fisher exact test for predicted frequency less than 5 or the chi-square test for categorical data to compare factors between the pregnant and non-pregnant groups. Depending on the situation, either the Mann-Whitney U test or the two independent sample t-test was used to compare continuous data across the two groups. To determine independent factors associated with the severity of COVID-19, data were analyzed using Poisson regression. In the bivariate analysis, variables with p-value <0.25 were used to identify potential significant factors for the final models. The adjusted relative risk with a 95% confidence interval and a p-value <0.05 was used to determine statistical significance.

Result

The study included 301 COVID-19-positive women of reproductive age, including 103 pregnant and 198 non -pregnant women. There were 193 people (61.4% of the population), whose median age was 30 (interquartile range: 26–37). The overall median age was 30 (IQR: 26-37), and 193 (61.4%) were under the age of 35. Compared to non-pregnant women, pregnant women's median age was lower (30 (26-34) versus 32 (24-40) years, p=0.014), and 22/103 (21.4%) versus 86/198 (43.4%) were ≥35 years (p<0.001). Diabetes mellitus was the most frequent comorbidity, accounting for 18 (6.0 %), followed by hypertension 15 (5.0 %), and cardiovascular disease 12 (4.0 %). Except for hypertension, which was more prevalent in non-pregnant women (0 vs 15, p=0.004), the presence of comorbidities did not vary between the groups. Cough, fever, headache, and dyspnea were the most prevalent clinical symptoms in both groups. Pregnant women had a significantly greater proportion of headache, myalgia, and anosmia than non-pregnant women (P <0.05), with 38.8% vs. 23.2%, 32.0% vs. 19.7%, and 15.5% vs. 6.6%, respectively (Table 1)

Table 1. Comorbidities and symptoms of the study participants, Eka Kotebe General Hospital, 2020-21

Characteristics	All patients	Pregnant (n=103)	Non-pregnant (n=198)	P-value
Age in years (median, IQR)	30(26-37)	30 (26-34)	32 (25-40)	0.014
Age, <35, n(%)	193(61.4)	81 (78.6)	112 (56.6)	0.001
Diabetes, n (%)	18(6.0)	3 (2.9)	15 (7.6)	0.105
Hypertension, n (%)	15 (5.0)	0 (0.0)	15 (7.6)	0.004
Cardiovascular disease, n (%)	12 (4.0)	1 (1.0)	11 (5.6)	0.064
Tuberculosis, n (%)	8 (2.7)	0 (0.0)	8 (4.0)	0.054
Chronic respiratory disease	6 (2.0)	1 (1.0)	5 (2.5)	0.668
Cancer, n (%)	6 (2.0)	0 (0.0)	6 (3.0)	0..098
HIV/AIDS, n (%)	6 (2.0)	1 (1.0)	5 (2.5)	0.668
Cough n (%)	119 (39.5)	46 (44.7)	73 (36.9)	0.19
Fever, n (%)	90 (29.9)	38 (36.9)	52 (26.3)	0.056
Headache, n (%)	86 (28.6)	40 (38.8)	46 (23.2)	0.004
Dyspnea, n (%)	72 (23.9)	24 (23.3)	48 (24.2)	0.856
Myalgia, n (%)	72 (23.9)	33 (32.0)	39 (19.7)	0.017
Anosmia, n (%)	29 (9.6)	16 (15.5)	13 (6.6)	0.012

In comparison to the non-pregnant group, the median length of stay in the hospital was shorter in the pregnant group 12 (8-15) days vs 14 (11-20) days P<0. 001. The percentage of women who required supplemental oxygen, mechanical ventilation, therapeutic anticoagulant, vasopressors, and steroids were similar in both groups. In laboratory findings, absolute lymphocyte count <1000/mm^3 and platelet count <150,000/mm^3 were more frequent in the pregnant vs non-pregnant group (p < 0.05). However, non-pregnant women had a significantly higher proportion of acute kidney injury, with creatinine ≥1.3 (10 (6.6%) vs. 0 (0.0%) p<0.0001) and urea ≥20 (19 (13.4%) Vs 0 (0.0%) P<0.0001) than pregnant women. No significant variations were seen between the groups in terms of ICU admission or illness severity. There was no difference in mortality between the groups; two pregnant women and seven non-pregnant women died. Forty (38.9%) of the 103 pregnant women gave birth in the hospital, and two (5%) of the neonates died (Table 2).

Both neonatal deaths were to mothers who had intrauterine fetal death (IUFD) from the outset. The first mother had a retroviral infection and severe COVID-19. She had a spontaneous vaginal delivery (SVD) but she progressively deteriorated and was admitted to ICU. She passed away from progressive respiratory failure and sepsis. The other lady had IUFD with severe oligohydramnios. She had SVD to a dead neonate and was discharged home alive.

In regression analysis, women's relative risk of developing severe COVID-19 was determined by cough and dyspnea symptoms. Women with cough and dyspnea had a higher relative risk of having severe COVID-19 (RR = 3.18, 95% CI 1.61, 6.27, P-value = 0.001, and RR = 4.14, 95% CI 2.35, 7.30, P-value = 0.000 respectively) (Table 3).

Table 2. Treatment, clinical outcome, and laboratory findings of the participants, Eka Kotebe General Hospital, 2020-21

Characteristics		All patients	Pregnant (n=103)	Non-pregnant (n=198)	P-value
Length of stay (median, IQR)		14(10-18)	12 (8-15)	14 (11-20)	<0.001
Oxygen support, n (%)		75(24.9)	21 (20.4)	54 (27.3)	0.19
Mechanical ventilation, n (%)		5(1.7)	2 (1.9)	3 (1.5)	1
Anticoagulant, n (%)		108 (35.9)	39 (37.9)	69 (34.8)	0.605
Vasopressor use, n (%)		6 (2.0)	4 (3.9)	2 (1.0)	0.186
Steroid, n (%)		87 (28.9)	29 (28.2)	58 (29.3)	0.894
ALC, n (%) (n=264)	<1000	62 (23.5)	33 (33.0)	29 (17.7)	0.004
	≥1000	202 (76.5)	67 (67.0)	135 (82.3)	
AST, n (%) (n=207)	<37	159 (76.8)	57 (80.3)	102 (75.0)	0.393
	≥37	48 (23.2)	14 (29.2)	34 (25.0)	
ALT, n (%) (n=179)	≤63	165 (92.2)	54 (96.4)	111 (90.2)	0.231
	>63	14 (7.8)	2 (3.6)	12 (9.8)	
Platelet, n (%) (n=266)	<150000	227 (85.3)	97 (96.0)	130 (78.9)	<0.001
	≥150000	39 (14.7)	4 (4.0)	35 (21.2)	
Creatinine, n (%) (n=235)	<1.3	225 (95.7)	83 (100.0)	142 (93.4)	0.016
	≥1.3	10 (4.3)	0 (0.0)	10 (6.6)	
Urea, n (%) (n=220)	<20	201 (91.4)	78 (100.0)	123 (86.6)	0.001
	≥20	19 (8.6)	0 (0.0)	19 (13.4)	
Admission, n (%)	ICU	18 (6.0)	6 (5.8)	12 (6.1)	0.935
	Ward	283 (94.0)	97 (94.2)	186 (93.9)	
Severity outcome¸ n (%)	Severe	74 (24.6)	21 (20.4)	53 (26.8)	0.223
	Non-severe	227 (75.4)	82 (79.6)	145 (73.2)	
Outcome, n (%)	Alive	292 (97.0)	101 (98.1)	191 (96.5)	0.723
	Dead	9 (3.0)	2 (1.9)	7 (3.5)	

Discussion

This study showed that the majority of pregnant women with acute COVID-19 experience excellent results in terms of their survival and the survival of their unborn children. A larger proportion of pregnant women had a greater frequency of headache, myalgia, and anosmia compared to non-pregnant women. The prevalence of hypertension was also higher in non-pregnant women. Women of reproductive age who were nonpregnant had longer duration of hospital stay. Pregnant women had lower absolute lymphocyte count, platelets, creatinine, and urea levels. Although there were statistical differences in presenting symptoms and laboratory findings, most of them were not clinically significant. Overall, pregnant women fared similarly to those who were not pregnant. In a multivariable analysis, the presence of cough and dyspnea was found to be significantly associated with severe COVID-19. There was no association between pregnancy and the risk of having severe COVID-19.

Pregnant women were younger than non-pregnant women. This is consistent with the finding in a systematic review and meta-analysis by Khan et al and another study by Ozer et al. (14, 15). Symptoms such as headaches, myalgia, and anosmia were more prevalent in the pregnant group. Similar findings were reported previously as well (14, 16). However, another study revealed that pregnant patients complained more of anosmia and myalgia. This disparity might be explained by the relatively small sample size in our study (408 vs 302) (17, 18).

Hypertension was more common in the non-pregnant group which is supported by Ozer KB et al (15). It could be related to the inclusion of relatively younger pregnant ladies in this study, 78.6% <35 years, which might be translated into less likelihood of pregnancy-related hypertension (16). It might also be due to the existing low threshold to admit pregnant ladies with SARS CoV-2 infection for in-hospital treatment and monitoring. Non-pregnant women are admitted if they have comorbidities that makes them likely to have hypertension compared to their counterpart pregnant ones. The median hospital stay for the pregnant group was significantly shorter

Table 3. Determinants of disease severity among women with COVID-19, Eka Kotebe General Hospital, 2020-21

Characteristics		Unadjusted RR (95% CI)	P-Value	Adjusted RR (95% CI)	P-value
Pregnancy	Pregnant	0.4761 (0.487, 1.189)	0.222	0.692 (0.462, 1.036)	0.074
	Non-pregnant	1		1	
Age	<35	1		1	
	≥35	2.478 (1.666, 3.687)	0.000	1.077 (0.704, 1.648)	0.731
Diabetes	Yes	2.176 (1.308, 3.621)	0.009	0.903 (0.540, 1.510)	0.700
	No	1		1	
Hypertension	Yes	2.64 (1.657, 4.203)	0.001	1.172 (0.665, 2.066)	0.582
	No	1		1	
Cardiovascular disease	Yes	2.919 (1.856, 4.590)	0.000	1.080 (0.653, 1.786)	0.762
	No	1		1	
TB	Yes	1.017 (0.301, 3.435)	0.977		
	No	1			
Chronic respiratory disease	Yes	2.077 (0.910, 4.742)	0.144	0.976 (0.630, 1.512)	0.916
	No	1		1	
Cancer	Yes	1.365 (0.432, 4.310)	0.615		
	No	1			
HIV/AIDS	Yes	0.673 (0.111, 4.075)	0.649		
	No	1			
Cough	Yes	7.901 (4.453, 14.019)	0.000	3.183 (1.614, 6.274)	0.001
	No	1		1	
Fever	Yes	3.251 (2.201, 4.804)	0.000	1.139 (0.818, 1.584)	0.440
	No	1		1	
Headache	Yes	2.125 (1.449, 3.115)	0.000	1.243 (0.887, 1.741)	0.205
	No	1		1	
Dyspnea	Yes	8.587 (5.533, 13.326)	0.000	4.148 (2.357, 7.300)	0.000
	No	1		1	
Myalgia	Yes	3.013 (2.079, 4.366)	0.000	1.204 (0.854, 1.698)	0.288
	No	1		1	
Anosmia	Yes	2.188 (1.412, 3.391)	0.001	1.053 (0.726, 1.527)	0.782
	No	1		1	

than for the non-pregnancy group. Although the days are close (14 vs. 12 days), this has little clinical implication. This result is in line with the related retrospective study done in Wuhan, Hubei, China, USA, and Tehran, Iran (19-21).

There were two pregnant women and seven non-pregnant women who passed away, but there were no appreciable differences in ICU admission, disease severity, or mortality between the two groups. On the other side, a study in the USA, Egypt, and a systematic review discovered that pregnant women had a much higher chance of being admitted to the (ICU), develop severe diseases, and die(12, 14, 18, 22)). This disparity might be attributed to the larger sample size in those studies and the relatively younger age of the pregnant versus non-pregnant women. Lack of difference in mortality of pregnant women versus non-pregnant women was also reported by Bahaa Eldin H et al and Qeadan et al (18, 20).

In our study, pregnant women's lymphocyte counts were lower than those of non-pregnant women. This is inconsistent with previous studies(19, 23) Similarly, lower platelets, creatinine, and urea levels were found among pregnant women which might be due to hemodilution, higher renal flow rate, and pregnancy-related thrombocytopenia, which as reported by Januszewski M et al. (23).

Finally, in multivariable analysis, our study showed that pregnancy has no effect on the severity of COVID-19. This finding is contrary to a retrospective cohort study in Egypt and a systematic review and

meta-analysis by Khan et al., which found that severe illness (ICU admission and need for MV) were significantly higher in pregnant patients (14, 17). Similar to what we found, K. Khoiwal et al. reported that pregnancy has no impact on the severity of COVID-19 (24).

One of the limitations of this study is the retrospective nature of the design associated with difficulty retrieving missed data on some variables like the laboratory parameters. The other is the small sample size in this study which might have affected some outcome variables like ICU admission, disease severity, and mortality. This study included participants who were admitted to the hospital during the first two waves and findings might not be reflected in pregnant ladies who were admitted during the subsequent waves.

Conclusion

Pregnancy did not cause an additional risk of severe disease or mortality. However, pregnant women had frequent headaches, myalgia, and anosmia, a shorter length of hospital stay, and a lower absolute lymphocyte count, platelets, creatinine, and urea levels.
This study was presented on the ATS 2022.

Declaration

Authors have no conflict of interest to declare.

Ethical consideration
The Eka Kotebe Institutional Review Board provided ethical approval (Date August 26, 2021, Ref. No. Eka/150/5/109). Subjects' anonymity was maintained by using their identification numbers throughout the data collection and analysis process.
Conflict of interest
No competing interests to disclose.
Funding source
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Authors Contributions
AB: inception, proposal draft and organization EKE: data analysis and manuscript write up YG: inception and data collection NM: inception BD: inception and data collection HA: inception and data collection BK: data collection TG: inception and supervision of data collection TS: inception AM: data collection TZ: data collection HYA: proposal draft THG: proposal draft DKH: inception, proposal draft, overall organization of the study and write up.

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Original Article

Treatment outcomes and associated factors among infants under 6-Month-Old with severe acute malnutrition in Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia

Mohammed Nasir[1*], Ermias Abebaw[2], Muluken Ahmed [3], Bethlehem Birhanu[1], Muluken Berhanu[3]

[1]Pediatrics Department, Hawassa university, Hawassa, Ethiopia
[2]Pediatrics Department, ALERT comprehensive specialized hospital, Addis Ababa, Ethiopia
[3]Pediatrics Department, Arba Minch University, Arba Minch, Ethiopia

Corresponding author*::mn2572338@gmail.com

Abstract

Background*: Infants under the age of six months are considered to have severe acute malnutrition if their weight for length Z-score is below -3 standard deviations (SD) and/or they exhibit bilateral pitting edema. It is frequently diagnosed in infants under 6 months of age and is frequently associated with higher rates of morbidity and mortality in infants than in older children. The current study aimed to assess the treatment outcome of severe acute malnutrition and associated factors among infants under 6 months of age in Hawassa Comprehensive Specialized Hospital, southern Ethiopia*

Methods*: An institution-based cross-sectional study was carried out from September to November 2021. A total of 261 records were evaluated between September 2007 and October 2021. After the data were collected, they were subject to EPI-data version 31 and then exported to STATA version 16 for analysis. Before exporting anthropometry data to Stata, Z scores of anthropometric measurements were calculated using WHO Anthro V3.2.2 software.*

Results*: Our study included 261 infants with severe acute malnutrition who were admitted. The outcomes were cure, default, transfer out, non-respondent, death, and unknown with the rate of 57.2%,11.5%,9.2%, 4.2%, 14.2%, and 3.8%. respectively. Gestational age, pneumonia, Pre-lacteal feeding, and tuberculosis were significantly associated with mortality.*

Conclusions*: The mortality from malnutrition was high in this study. While administering treatment for severe acute malnutrition to infants younger than 6 months, attention should be paid to infants who have pneumonia and tuberculosis. Counseling on the risk of Pre-lacteal feeding through health education is necessary.*

Keywords: *under six months infant, malnutrition, treatment outcome, anthropometric characteristics*

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Introduction

Malnutrition is described by the World health organization (WHO) as a person's energy intake that is insufficient, excessive, or out of balance with their nutritional needs. Typically, straightforward anthropometry is used to define it(1). Stunting, also known as impeded linear development, wasting, a type of acute malnutrition brought on by recent weight loss or inability to gain weight, and underweight, which is defined as a child's weight is low compared to his/her age, are the classifications made based on anthropometric criteria.

A cutoff point of weight for age Z score less than -2, length for age Z score of -2, and weight for age Z score of -2 is used for the diagnosis of underweight, stunting, and wasting, respectively, according to the WHO 2013 malnutrition Guideline. A cut-off point of -3 Z score is used to diagnose severe underweight, severe stunting, and severe wasting. Although the data are of low quality in this age period, these cutoff points are also applied to children between the ages of 6 months and 5 years, as well as to infants under 6 months(U6M) of age(2).

About two-thirds of the world's wasted children live in Asia and Africa combined(3). Around 52 million children under the age of five are affected globally by wasting, which is responsible for 8% of all child fatalities(4). Severe wasting, which has an incidence of 2.9 percent worldwide, affects 19 million children. A child's risk of dying increases by 3 and 9.4 times for underweight and severely underweight children, respectively compared to children whose weight for height is greater than a Z score of -1 (3).
A significant decrease in the frequency of stunting and underweight was observed in Ethiopia, but the prevalence of wasting was less, which is 8% and 5% in riral and urban regions, respectively (5). In 2020, 1.2 million children in Ethiopia received services for moderate wasting, and 438,763 children with severe wasting were brought to care (6).Worldwide, there are roughly 4.7 million U6M infants who are moderately wasted and 3.8 million who are severely wasted. Evidence suggested that inadequate nutrition during the first 1000 days, a crucial time for a child's growth and brain development, is a substantial cause of morbidity and mortality (3).Anthropometry still has a high value despite absence of a gold standard for the diagnosis of malnutrition in infants, under 6 months of age (7).Severe wasting, bilateral leg pitting edema, or both are indicators of severe malnutrition (8).
The 2007 Ethiopian national malnutrition guideline recommends only inpatient treatment of malnutrition for infants U6M of age or less than 3 kilograms with SAM. According to the 2019 national guideline for the management of acute malnutrition, infants under 6 months with SAM will be admitted if they have recent weight loss or failure to gain weight, ineffective feeding, the presence of medical complications, or other medical or social issues needing more detailed assessment or intensive support. The priority of treatment is re-establishing effective exclusive breastfeeding (9,10).Even though guidelines recommend weight for length Z Score to identify wasting in infants, under 6 months of age, many are questioning its diagnostic ability and predicting mortality(11,12).

For the care of severe acute malnutrition in infants under 6 months of age, the national and WHO guidelines advocate use of diluted F-100, F-75, and infant formula and encouraging breastfeeding along with standard drugs and appropriate follow-up. In babies who struggle to suckle, supplemental sucking techniques should be used(2,13).

Identification of the cause of malnutrition is crucial in the management of severe malnutrition; for instance, primary malnutrition is caused by lack of adequate food, for which parents should receive advice on feeding, whereas secondary malnutrition has a secondary cause that needs to be addressed (4).Treatment outcomes are measured by SPHERE key indicators. These Indicators are based on the percentage of discharges from targeted supplementary feeding programs that have died, recovered, or defaulted(14).

To the best of our knowledge, there is no research that has been done in our country regarding treatment outcomes and the factors associated with it in infants under the age of six months. Therefore, this study aimed to assess the treatment outcome of severe acute malnutrition and associated factors among U6M Infants in Hawassa University Comprehensive Specialized Hospital.

Methods

Study Design, Period, and population

A hospital-based cross-sectional study was conducted from September 1 to November 30, 2021. The study was carried out in the pediatric ward of the therapeutic feeding unit (TFU) of the comprehensive specialized hospital of Hawassa University (HUCSH). Hawassa is the seat of the Sidama region and is situated 275 kilometers south of Addis Ababa, the Ethiopian capital. HUCSH has been providing medical and surgical care to both adult and pediatric patients. The pediatric unit is divided into 4 sections: the surgical unit, critical ward, neonatal ICU, and TFU unit. There are 12 beds in 2 rooms at the TFU. The care of malnourished children is handled by 6 nurses, 6 physicians, and 6 pediatric residents and interns. Infants younger than six months are taken care for in the same wards as older children. F-75 is used to treat edematous infants under 6 months old while diluted F100 is used to treat non-edematous infants. Infants' weights were recorded by suspending scales, and their lengths by sliding measuring boards.

The source population was all records of Infants aged <6 months with SAM admitted to the therapeutic Feeding unit (TFU) at the Hawassa university comprehensive specialized hospital. The study population included infants aged <6 months with SAM admitted to the therapeutic Feeding Unit (TFU) who fulfilled the inclusion criteria at Hawassa university comprehensive specialized hospital from September 2007 to October 2021.

Eligibility criteria

Inclusion criteria

All infants <6 months of age with SAM that have been admitted and treated at the inpatient TFU of the hospital from September 2007 to October 2021were included in the study.

Exclusion criteria

Infants with incomplete medical records concerning variables of interest such as baseline sociodemographic characteristics were excluded. Patients with improperly labeled as having severe acute malnutrition and whose anthropometry was out of range were excluded.

Sample size determination and procedure
The therapeutic feeding center admission logbook was used to retrieve the medical record number (MRN) of infants under the age of six who had severe acute malnutrition. These admissions occurred between September 2007 and October 2021.The records of 261 under-six-month-old infants who met our eligibility criteria and had severe acute malnutrition were then extracted, and were reviewed.

Data collection procedure
Data were gathered using a checklist, which made it feasible to extract all relevant information from the patient's record. The format was divided into four sections: the patient's demographic characteristics wew covered in the first section, anthropometric measurements taken at admission were covered in the second section, child nutrition and treatment-related variables were covered in the third section, and co-morbidity and complication-related variables were covered in the fourth section. The checklist and data-collecting format were created in English. Four nurses who had received training in SAM management procedure and who would be overseen by two general practitioners who were working in the hospital collected the data. The principal investigator made constant monitoring and supervision during the data collection period.

Data processing and analysis
Data were subjected to EPI-data version 3.1 for cleaning after data collection and were afterward exported to STATA version 16 for analysis. Shapiro Wilk test was used to check normality for continuous variables. Tables and figures were used to summarize the results using descriptive statistics. The odds ratio was used in bivariate analysis to analyze the statistical relationship between the outcome variable and independent factors, and variables with values less than 0.25 were incorporated into a multivariate logistic regression to test the significance of the statistical association. To determine if the patient meets the anthropometric requirements for severe malnutrition, the anthropometry of the patient was calculated and checked using WHO anthro V3.2.2.

Operational Definition

The treatment outcome of SAM will be cure, death, defaulter, and medical transfer based on the criteria of SAM treatment protocol Ethiopian minster of health, 2014 (8).

Cured: - Patient that has reached the discharge criteria which are breastfeeding effectively or feeding well with replacement feeds, and have adequate weight gain, and having a weight-for-length ≥–2 Z-score
Death: - infant that has died while he/she was in the in-patient treatment program in a facility
Defaulter: - Patient that is absent for 2 consecutive weighing/2 days in an in-patient or who the caregiver sign to go against medical advice
Medical transfer: - Patient that is referred to a health facility/ hospital for medical reasons and this health facility will not continue the nutritional treatment or transfer the patient back to the program.
Non-responder: -patient who is in inpatient treatment and doesn't fulfill the discharge criteria even after 40 months of treatment.
Unknown: -a patient whose treatment outcome is not documented.

Results

Socio-demographic and anthropometric characteristics of infants

After excluding 39 U6M children due to incomplete and inaccurately documented charts, a total of 261 infants with SAM ages less than six months who were admitted to Hawassa referral hospital over the period from September 2007 to October 2021 were included in our study. This study showed that the age range of infants was 1-5 months, with a median age of 3 months and an IQR (2-5months) range. More than half of the infants were less than 3 months old; 146 (55.9%), were born at term, and 65.9 % came from rural regions. Females accounted for 154 (59%). The median length of hospital stay was 15 days, with an IQR (12-70 days) and a range of 3-140 days. Most infants were severely underweight and had normal lengths for their age (Table 1).

Nutritional status, treatment, complication, and comorbidity-related variables

This study showed that only 29.1% of infants were on exclusive breastfeeding, 48 (20.3%) had used supplemental suckling technique, and oral antibiotic was the common routine drug to be administered (37.5%). Diluted F-100 was used as therapeutic feeding in 87.7% of infants. The most common complication encountered was pneumonia 83 (31.8%) followed by sepsis 65 (24.9%). Only 16.1% of infants were edematous (table 2) .

Treatment outcomes and associated factors

Only slightly higher than half of the participants were cured (57.1 %). Others were dead, defaulted, transferred out, non-respondent, or had an unknown outcome in 14.2 %, 11.5 %, 9.5 %, 4.2 %, and 3.8 %, respectively (Figure 1).

Table 1: Sociodemographic and anthropometric characteristics of infants under 6 months old with severe acute malnutrition in Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia, 2021.

Characteristics	Category	Frequency	Percentage
Sex	Female	154	59.0
	Male	107	41.0
Age group of infants	Less than 3 months	146	55.9
	Greater than 3 months	115	44.1
Gestational age of the infants at birth	Preterm	66	25.3
	Term	175	67.0
	post term	20	7.7
Residence	Urban	89	34.1
	Rural	172	65.9
Marital status of parents	Married	102	39.1
	Single	43	16.5
	Widowed	45	17.2
	Divorced	35	13.4
	Unknown	35	13.8
Infant's caretaker	Mother	205	78.5
	Father	28	10.7
	Grandparents	28	10.7
Birth order of the infant	First	97	37.2
	Second	54	20.7
	Third and above	110	42.2
Weight for age Z score	Less than -3	143	54.8
	Between -2 and -3	57	21.8
	Above -2	61	23.4
Length for age Z score	Less than-3	30	11.5
	Between -2 and -3	55	21.1
	Above -2	176	67.4
Combination anthropometry	Severely underweight and severely stunted	30	11.5
	Severely underweight and stunted	55	21.1
	Severely underweight and normal length for age	58	22.2
	Underweight and normal length for age	57	21.8
	Normal weight for age and normal length for age	61	23.4

Infants with severely underweight had a higher proportion of deaths, and infants with stunting had a higher proportion of deaths in terms of length for age group. From the combined anthropometry group, the category of infants with severe wasting and severe stunting had the highest death rate (Figure 2). Bivariate and multivariate logistic regression analysis was done to identify factors associated with bad treatment outcomes of severely malnourished hospitalized U6M infant patients.

On the bivariate analysis, residence, infant caretaker, gestational age, birth order, supplementary suckling, feeding at admission, Prelacteal feeding, pneumonia, dehydration, and tuberculosis showed a p-value of <0.2 and became a candidate for multivariate analysis.

Table 2: Nutritional status, treatment, and complication/comorbidity variables of infants under 6 months old with severe acute malnutrition in Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia, 2021

Characteristics	Category	Frequency	Percentage
Feeding at admission	Exclusive breast feeding	76	29.1
	Cow's milk	40	15.3
	Infant formula	59	22.6
	Mixed feeding	86	32.9
Supplementary suckling technique	Yes	53	20.8
	No	208	79.7
Prelacteal feeding	Yes	124	47.5
	No	137	52.5
Therapeutic feeding started at admission	Diluted F-100	229	87.7
	F-75	32	12.3
Iron supplementation	Yes	45	17.2
	No	216	82.8
Folic acid supplementation	Yes	47	18
	No	214	82
Vitamin A supplementation	Yes	64	24.5
	No	197	75.5
Po Antibiotics given	Yes	98	37.5
	No	163	62.5
IV Antibiotics given	Yes	75	28.5
	No	186	71.5
Pneumonia	Yes	83	31.8
	No	178	68.2
Sepsis	Yes	65	24.9
	No	196	75.1
Dehydration	Yes	47	18
	No	214	82
Shock	Yes	29	11.1
	No	232	88.9
Anemia	Yes	64	24.5
	No	197	75.5
Tuberculosis	Yes	17	6.5
	No	244	93.5
HIV exposed	Yes	24	9.2
	No	237	90.8
Congenital heart disease	Yes	12	4.6
	No	249	95.4
Infantile pyloric stenosis	Yes	32	12.3
	No	229	87.7
Edema	Yes	42	16.1
	No	219	83.9

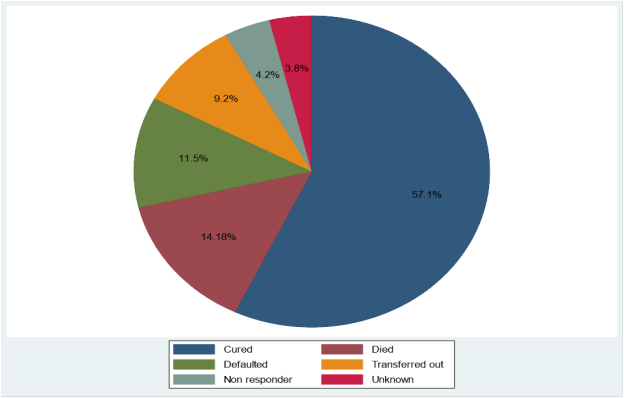

Figure 1: proportion of treatment outcomes in infants under 6 months old with severe acute malnutrition in Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia, 2021

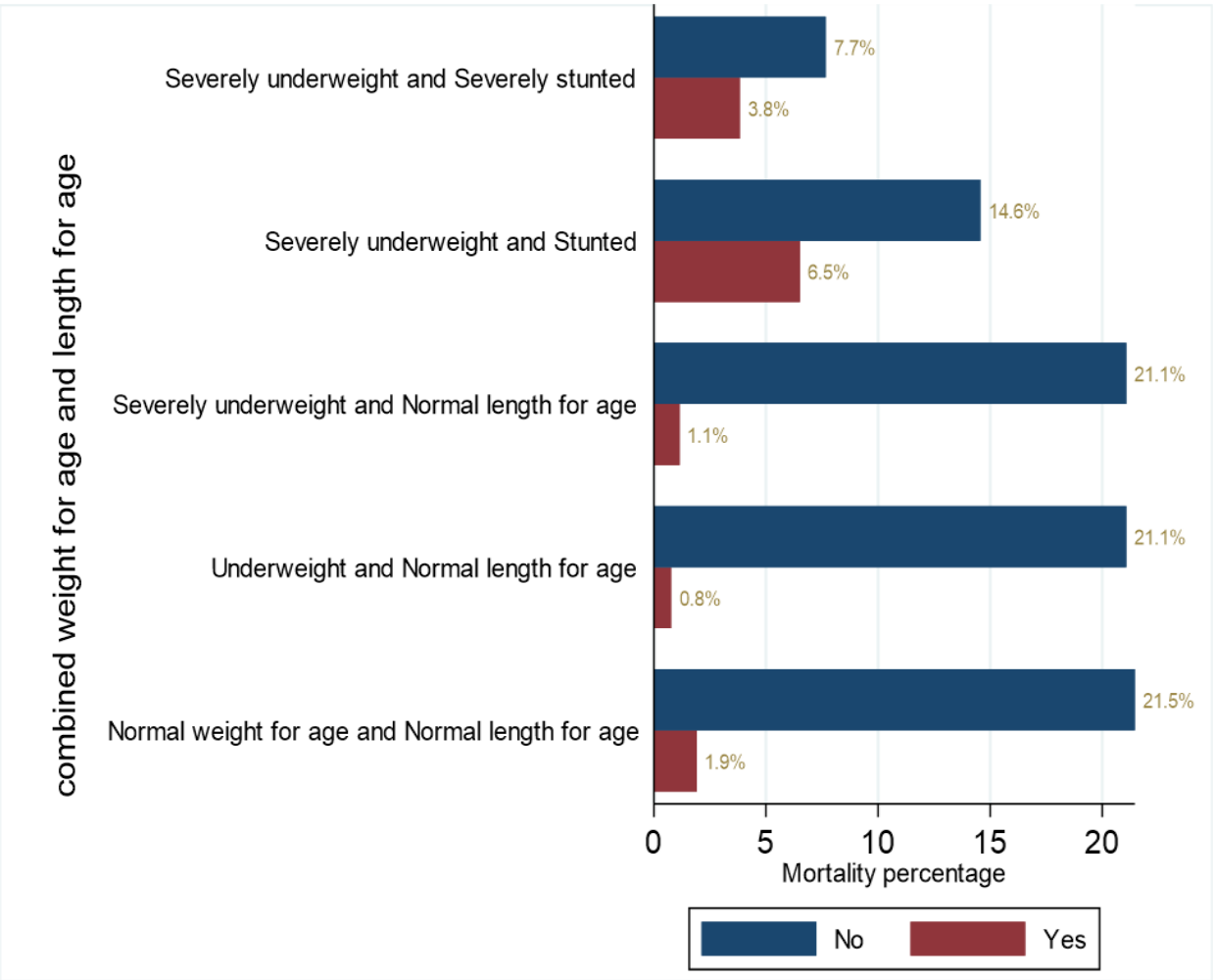

Figure 2: Proportion of mortality in the combined weight and length for infants under 6-Month-Old with SAM in Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia, 2021

On multivariate analysis, preterm infants, and infants with pneumonia, tuberculosis and Pre-lacteal feeding were significantly associated with bad outcomes (death) of malnourished infants. By taking other variables constant, preterm infants were 3 times more likely to die than the term ones [AOR=2.984; 95%CI (1.270, 7.010)]. Infants with a history of Pre-lacteal feeding were 2.6 times more likely to die than infants without a history of Pre-lacteal feeding [AOR=2.659; 95 % CI (1.145, 6.173)], infants with tuberculosis were 4 times more likely to die than infants without tuberculosis [AOR=4.096;95 % CI (1.072,15.659)], and infants with pneumonia were 2.5 times more likely to die than infants without pneumonia [AOR=2.543;95 % CI (1.072,6.022)] (Table 3).

Discussion

Compared to other anthropometric subcategories, U6M infants who were severely wasted had a larger proportion of severely underweight. In contrast to studies conducted in Bangladesh and Kenya as well as collected demographic survey data reports from 20 countries, the majority of patients in the present study were females, as was the case in studies conducted in Nigeria and Malawi(7,15–18).

In many studies, it was explored how breastfeeding could reduce malnutrition and lower its mortality(19,20,21). One of the parameters for assessing proper breast feeding is the rate of exclusive breastfeeding rate. In our study, the exclusive breastfeeding rate was 29.1%.

Table 3: Multivariate analysis showing factors associated with mortality of infants under 6 months old with severe acute malnutrition in Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia, 2021**.**

Characteristics	Category	Crude OR	Adjusted OR	p-value	[95% Confidence Interval]
Place of residence	Urban	1	0.491	0.126	0.197-1.221
	Rural	1.73(0.78-3.84	1	0.1	1
Classification based on gestational age	Preterm	2.85(1.37-5.9)	2.984	0.012	1.270-7.010
	Term	1	1	0.665	1
	Post term	0.43(0.05-3.41)	0.617	.	.069-5.482.
Birth order of infants	First	1	1	0.1	1
	Second	1.3(0.46-3.63)	1.165	0.797	.363-3.740
	Third and	1.93(0.86-4.4)	1.372	0.52	.524-3.590
Infant's caregiver	Mother	1	1	0.1	1
	Father	1.1(0.35-3.41)	0.87	0.848	.209-3.618
	Grandparents	1.8(0.67-4.83)	1.112	0.863	.333-3.712
Maternal marital status	Married	1	1	1	
	Single	2(0.7-5.8)	1.481	0.55	.409-5.359
	Widowed	1.9(0.66-5.5)	1.417	0.579	.413-4.855
	Divorced	3.1(1.1-8.7)	1.824	0.359	.505-6.583
	Unknown	2.1(0.68-0.19)	0.982	0.978	.262-3.681
Infants feeding at admission	Breast feeding	1	1	0.1	1
	Cow's milk	1.5(0.48-4.7)	1.272	0.72	.341-4.744
	Infant formula	1.33(0.47-3.8)	0.918	0.89	.274-3.080
	Mixed	1.8(0.72-4.51)	1.771	0.314	.583-5.378
Prelacteal feeding	No	1	1	1	1
	Yes	2.63(1.26-5.5)	2.659	0.023	1.145-6.173
Supplemental suckling technique	No	1	1	1	1
	Yes	0.43(0.15-1.28)	0.359	0.099	.106-1.214
Pneumonia	No	1	1	1	1
	Yes	2.7(1.4-5.6)	2.543	0.034	1.074-6.022
Dehydration	No	1	1	.	1
	Yes	1.87(0.84-4.2)	1.436	0.456	.554-3.724
Tuberculosis	No	1	1	0.1	1
	Yes	4.1(1.51-11.3)	4.096	0.039	1.072-15.659

Compared to findings from the Gondar research, which showed only 72 percent of the infants had evidence of breastfeeding practices, and only 39.1% were the exclusively breastfed, the exclusive breastfeeding rate was lower in our study(22)**.**However, the proportion of exclusive breastfeeding was higher than that found in the Nigerian studies(18)**.**The mothers' employment in recent years and traditional beliefs may be the factors in the nonexclusive breastfeeding pattern, which contributes to poor breastfeeding behaviors.

Even though the use of supplementary sucking technique has improved the outcome of underweight infants with lactation failure, the practice was only 21.5% in this study(23)**.** Compared to a study done in Niger, its use was lower(24)**.**

Based on cure, default, transfer out, non-respondent, and death rates, the treatment outcome was 57.1%, 11.5%, 9.2%, 4.2%, and 14.18%, respectively.

This study demonstrated a death rate higher than that in Bangladesh (3.9 %), Niger (6%) and Kenya (9%) without considering deaths that might have occurred in cases with defaulted and transferred out (15,16,24)**.**The death rate was also greater than what is recommended by the national guidelines and SPHERE standards, which consider values of < 10% and <3 %, respectively to be good indicators of care **(**13**,**14**).** The recovery rate in our study was significantly lower(17,25) compared to those of the Malawian studies (17, 25) on uncomplicated SAM in U6M (75.4%) and on inpatient in rural setting (83.3%)**,.**The significant increase in SAM treatment-related deaths and decline in cure rates in our study might be attributed to the fact that the majority of the infants were transferred from other treatment facilities due to being critically ill, resistant to conventional management, or experienced complications. The default rate was below the cut-off point of both the national guideline and SPHERE recommendations**(**13**,**14**).**
Infection is one of the causes that contribute to the death of malnourished infants. Similar to the Niger study, pneumonia was identified as one of the factors associated with the death of malnourished infants (24)**.** Pneumonia may associate with dehydration and also predispose the patient to hypoxemia(26)**.**The presence of severity features is predictor for mortality as reported by the Bangladesh study(27)**.** Malnutrition's immune-suppressing effects caused infections to become more severe. This might also explain the association of tuberculosis with death in u6m infants with SAM. Despite WHO and national guidelines recommending oral antibiotics for uncomplicated cases and iv antibiotics for complicated ones, only 35% of patients, i.e.,27.5% with oral antibiotics and 28.7% with iv antibiotics—were put on antibiotics treatment **(**2**).** This might also contribute to the high mortality of infants due to infection by not addressing it properly. Prematurity was also associated with mortality in our study, also supported by a Kenyan study which reported being small at birth was associated with mortality in u6m infants with SAM(15)**.** Because prematurity is linked to numerous medical issues, preterm infant mortality is high. Therefore, it might be challenging to determine if a preterm infant's death was brought on by an underlying medical condition or a nutritional shortage.

The association of Pre-lacteal feeding with mortality observed in this study was supported by other studies. Pre-lacteal feeding is one of the factors that predispose to wasting, according to a study from Bangladesh and northern India (16,28)**.** It was also associated with neonatal mortality (29)**.** This study explored 47.5% of mothers practiced Pre-lacteal feeding which is much higher than that of a study done in Gondar which showed that 23.5% of mothers in their study practiced pre-lacteal feeding with butter being a prevalent diet provided.

Exclusive Breastfeeding is recommended for the first 4-6 months with no pre-lacteal feeding to avoid the risk of infection(25)**.**

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Consent and ethical clearance

The study complied with the Declaration of Helsinki. A letter of ethical clearance was obtained from Hawassa University, College of Health Sciences, Institutional Review Board (protocol number =IRB/1007/2021). Written informed consent was obtained from each patient to participate in the interview and to extract data from their medical charts. Privacy and confidentiality were ensured during patient interview and medical chart review.

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Conflict of interest
The authors declare that there is no conflict of interest regarding the publication of this article
Data sharing statement
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
Author contributions
All authors made substantial contributions to conception, design, analysis and interpretation of data, reviewed the manuscript critically for important intellectual content, gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

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Original Article

Knowledge and perception of surgical informed consent among adult surgical patients in Arba Minch and Jinka General Hospitals, Southern Ethiopia

Tigabu Daniel[1*], Yonas Abera[1] , Menaye Yihune[2]

[1]Department of Surgery, Arba Minch University college of Medicine and Health Science

[2]School of public health, Arba Minch University college of Medicine and Health Science

Corresponding authors*: danieltigabu96gmail.com

Abstract

Background: *The surgical informed consent process and format are not uniform nationally and internationally. The objective of this study was to assess the knowledge and perception of adult patients towards the legal nature of surgical informed consent in Arbaminch and Jinka General Hospitals, South Ethiopia.*

Methods: *Responses from 423 post-operative adult surgical patients were taken using pretested structured interviewer-administered questionnaires for five months. A hospital-based cross-sectional study of all adult surgical patients who were operated were involved before discharged from December 1 2021-April 30, 2022 in Arbaminch and Jinka general hospitals, Southern Ethiopia. Stratified sampling technique was used. The collected data entered into EPI-data version 3.1 and exported to SPSS (version 25) software for statistical analyses. A significant level was determined at a P-value <0.05 with 95% confidence interval.*

Results: *A total of 423 adults with a response rate of 100% were included in the study. Of the respondent's consent, only 210 (49.6%) was taken by an operating surgeon, and the majority was taken by a general practitioner, nurse, and midwife. Surprisingly consent taken by the porter was 5(1.2%). Of the respondents, only 188(44.4%) had good knowledge and only 58 (13.7%) had a good perception regarding surgical informed consent. Patients exposed for consent signing previously, had 4.06 times higher knowledge than those unexposed (AOR=4.06, 95% CI :-(1.80, 4.492)). Those patients living in an urban area were well aware of surgical informed consent (AOR=0.246, 95% CI :- (0.212, 1.660)). Level of understanding of surgical informed consent, significantly increased for those informed by an operating surgeon (AOR=4.45, 95% CI :- (1.95, 5.09)).*

Conclusion: *Majority of our patients had poor knowledge and poor perception regarding the legal nature of surgical informed consent. Living in urban, signing informed consent previously and consent taken by operating surgeon affected level of knowledge positively. The consent had to be taken at least by the operating surgeon.*

Keywords: *Knowledge, Perception, Surgical informed consent*

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Background

Surgical informed consent is an agreement between patient and surgeon. It secures 100% autonomy of patient on decision of the procedure either to proceed or cancel (1–3). The consent process started since early 1970s(2,4). Surgical informed consent is a process involving information exchange, understanding, decision and giving a written consent(1,3–5). In India, only 13.48% were informed about complication of the surgery and only 33.15% informed about alternatives of treatment(1). There is limited literature on surgical informed consent globally(1). Study done in china, showed significantly poor knowledge on medical information because of limited information delivery to patients(5). Another study done in Iran showed either inadequate or absent information delivery about core points of informed consent for surgical patients(6). Informed consent is a tool that increases mutual trust between patients and health personnel(6). Globally there is no a well-structured uniform surgical informed consent, and it is different from country to country(1,6–8). Giving of the patient(7,9).

adequate time for the patient while delivering relevant information about specific disease increases satisfaction. Delivering clear understandable information to patient by operating health personnel increases satisfaction and decreases unnecessary expectations(4,9). According to different studies, majority of patients do not know complications of surgery and risks of anesthesia adequately(3). Factors associated with poor performance of surgical informed consent process are patient living status, health system functionality status of the nation and attitude of the health worker based on salary and job satisfaction(2). The surgical informed consent should be taken either by the surgeon himself/herself or by specially trained expert in consent taking(8). According to the United nation goal decision on surgical informed consent, every country should have equivalent practice regarding the informed consent process(7).

In Egypt, data for surgical informed consent process is incomplete(2). In Ghana, Only few patients know what the diagnosis is and procedure done(8). There is limited awareness regarding surgical management risk and the right to reject treatment in South Africa (7). Study done in Sudan showed 54% of patients have poor knowledge on informed consent(5).

Knowledge of patients regarding surgical informed consent is only 10.5%(1). Another study done in Ethiopia showed incomplete surgical informed consent form and process(10). A study from Jimma University showed 77.2% of patients have poor knowledge regarding surgical informed consent(11). One study in Ethiopia showed less than 50% level of understanding in Ethiopia(12). Northern Ethiopia report showed, more than 50% of patients are giving their autonomy to their doctors(4). The objective of this study was to know the level of knowledge and perception of the surgical patients and associated factors regarding surgical informed consent in the study period and place.

Material and Methods

Study settings and period:

Hospital based cross-sectional study was done on Knowledge and perception towards surgical informed consent and associated factors among adult surgical patients in Arba Minch and Jinka General Hospitals, Southern Ethiopia, from December 1st 2021 to April 30th 2022. Arbaminch General Hospital is found in Arba Minch town which is the administrative center of Gamo zone. Arba Minch town is located 505 km southwest from Addis Ababa, the capital city of Ethiopia and 275 km Southwest of Hawassa, capital city of Southern nation nationalities and peoples region. There were ten general surgeons, three Obstetrics and gynecological surgeons, one ophthalmologic surgeon, two plastic surgeons, two orthopedic surgeons and one neurosurgeon in this hospital when the study was conducted. At least 300 to 400 operations per month is done including all departments and units of surgery in Arbaminch General Hospital and also is teaching hospital for Arbaminch university medical students. On the other hand, Jinka General Hospital is located in Jinka town South Omo zone that is located in Southwest of Hawassa and Addis Ababa, Ethiopia. In Jinka General Hospital, there were two General Surgeons, two Obstetrics and gynecological Surgeons, one orthopedic Surgeon and one ophthalmologic Surgeon performing at least 100 to 200 operations per month in the study period. Study participants were included from surgical ward, orthopedics ward, ophthalmology unit, plastic and reconstructive unit, and Obstetrics and gynecological wards of the two hospitals. The study was conducted from December 2021 to April 2022 among adult surgical patients in mentioned hospitals.

Source population:
All adult surgical patients in Arbaminch and Jinka General Hospitals, December 2021-April 2022.

Study population
All adult post-surgical patients admitted in both Hospitals during the data collection period.

Study unit:
Each selected post-operative adult surgical patients in both Hospitals during the study period.

Eligibility criteria:
Age below 18years and critical patients were excluded from the study.

Sample size and sampling procedure:
The largest sample size for the study was estimated from p-value for perception (0.5) because the p-value for knowledge and associated factors makes the sample size lower. The p-value for perception was not known and the final sample size was estimated to be 384. By considering 10% non- response rate, over all sample size was 423. Of all operated patients from both hospitals, 423 patients were selected based on the eligibility criteria set. A questionnaire comprising socio-demography, knowledge and perception was developed from different literatures(11,13). A pretested and structured questionnaire was prepared in English and then translated to Amharic and local languages and back translated to English to maintain its consistency. A stratified sampling technique for both hospitals and each department was used, and a systematic sampling technique was used for each patient in the ward based on his/her bed number. Trained BSc nurses were assigned to each ward in both hospitals, and all the process was supervised. By interviewer administered questionnaires, 423 patient's data were collected from patients operated but

before discharge prospectively.

Data collection technique and quality control:
Knowledge and perception level was assessed using sixteen knowledge questions and five perception questions. For both knowledge and perception level, each question was given "1" for those said yes and "0" for those said no. Then the sum of the scores and mean were calculated. Those scored below mean were categorized under poor knowledge and above were categorized under good knowledge. Similarly those below mean were categorized under poor perception and above mean were categorized under good perception.
Data were checked for completeness, accuracy and consistency using Epi-data version 3.1 software. Data were analyzed at multiple levels using SPSS version 25 for socio-demographic data, knowledge and perception regarding surgical informed consent. The results were expresses as text and tables. Bivariate and multivariate logistic regression was done for multivariate after checking chi square test showing p-value ≤0.05.

Operational definitions:
Good knowledge- those scored above the mean among sixteen knowledge questions included (11, 13).
Poor knowledge-those scored below the mean among sixteen knowledge questions included (11, 13).
Good perceptions-those scored above the mean among five perception questions included (11, 13)
Poor perception-those scored below the mean among five perception questions included (11, 13)

Results

Socio-demographic characteristics

All the 423 respondents agreed and responded. Mean age of the respondents was 37.7±15.19years. Minimum and maximum ages of respondents were 18 and 85 years, respectively. Of the respondents, 42.8% were males and 57.2% were females (table 1).

Table 1. -Socio-demographic characteristics for Arbaminch and Jinka General Hospital respondents, Ethiopia 2022

Variables	Category	Frequency (%)
Hospital	Arbaminch general hospital	383 (90.1)
	Jinka general hospital	100(23.6)
Department	General surgery	225(53.2)
	OBGY	102(24.1)
	Orthopedic surgery	53(12.5)
	Plastic and reconstructive	12(2.8)
	Ophthalmologic surgery	31(7.3)
Gender	Male	181(42.8)
	Female	242(57.2)
Age category	18-30	184(43.5)
	31-40	98(23.2)
	41-50	58(13.7)
	51-60	50(11.8)
	>60	33(7.8)
Residency	Urban	227(54)
	Rural	196(46)

Knowledge

More than three fourth of the participants do not know the operation time and similarly more than three fourth do not know the anesthesia risks. Also 71.4% of the patients did not tell complication of surgery. Over all knowledge level of patients regarding surgical informed consent was only 44.4% (table 2).

Table 2. -Knowledge level result for Arbaminch and Jinka General Hospital respondents, Ethiopia 2022.

Perception

Variable	Category	Frequency (%)
Knowledge level	Poor	235(55.6)
	Good	188(44.4)

More than 70% of patients considered signing consent was only for the protection of hospital and surgeons. Also more than half of the participants believed that they had no right to change their decision after signing consent (table 3). Perception results showed only 13.7% of the participants had good perception (table 4).

Table 3. -Perception frequency for Arbaminch and Jinka General Hospital respondents, Ethiopia 2022

Variable	Category	Frequency (%)
Did you think signing consent remove compensation	No	201(47.5)
	Yes	222 (52.5)
Did you think signing consent is protection of surgeon and hospital only	No	298(70.4)
	Yes	125(29.6)
Did you think you can change your mind after signing consent	No	241(57)
	Yes	182(43)
Will you allow your relatives to sign if needed	No	98(23.2)
	Yes	325(76.8)
Did you decide alone confidently	No	235(55.6)
	Yes	188(44.4)

Table 4. -Perception level result for Arbaminch and Jinka General Hospital respondents, Ethiopia 2022

Variable	Category	Frequency (%)
Perception level	Poor	365(86.3)
	Good	58(13.7)

Associated factors for knowledge and perception

Patients exposed for consent signing previously, had 4.06 times higher knowledge than those unexposed (AOR=4.06, 95% CI :-(1.80, 4.492), P=0.001). Those patients living in an urban area were well aware of surgical informed consent (AOR=0.246, 95% CI :- (0.212, 1.660), P=0.001). Level of understanding of surgical informed consent, significantly increased for those informed by an operating surgeon (AOR=4.45, 95% CI :- (1.95, 5.09), P=0.002). Educational status had no significant effect on level of knowledge of patients (table 5). No significantly associated factor identified regarding level of perception.

Discussion

Most of our study participants were females. Of respondents, 70% attended at least above grade 1. Irrespective of the patient attitude and perception, literatures secure 100% patient autonomy(1,2,11–16,3–10). Age of the participants from SPMMCH was nearly similar to our patient age range of 18-85years(14). Majority of our patients had lower educational status which is in agreement with the results a study in Iran(78.7%)(6). Consent taken by operating surgeon in our study was only 49.6% which was different from that of the study in Iran (85%)(6). In our study, even there was consent taken by a porter. It may be because of poor system control and process of the surgical informed consent in Ethiopia, particularly in the study hospitals. Nearly 100% of the patients signed consent which is more than in the study reported from Nigeria, 68.3%. On the contrary, our patients level of understanding was poorer probably because of operating surgeon was not fully involved in the consent process(9). About 66.2% of the patients knew legal ground of surgical informed consent in our study which is less than that from study conducted in SPMMCH, Ethiopia(13). It may be because of low educational level of the respondents. Although only 53.2% knew alternatives of treatment, it was better than those from other studies conducted at different setups majority being less than 50%(1,12,14). Nearly 50% of the respondents had knowledge on ability to change decision even after signing consent which is better than those from the study conducted in SPMMCH(13). About 59.1% of patients knew their operating surgeon which is better than 33.5% reported by Befekadu, et al(13).

Patients from our study knew their operating surgeon for the surgeons might have explained and discussed during OPD visit. Although majority of our respondents knew the reason for surgery, 78.6%, 77.1% and 86.3% of the respondents did

Table 5. -Bivariate and Multivariate analysis result for knowledge of Arbaminch and Jinka General Hospital respondents, Ethiopia 2022.

Variables	Category	Level of knowledge		COR (95%CI)	P value	AOR (95%CI)	P value
		Good	Poor				
Have you signed before	Yes	175	169	4.81(1.309, 5.263)	0.007	4.06(1.80, 4.492)	0.001*
	No	14	65	1			
Educational status	No formal education	90	47	1			
	Formal education	99	187	3.62(2.83, 4.281)	0.223	3.26(2.72, 4.388)	0.381
Residency	Urban	68	159	0.265 (0.204,1.463)	0.004	0.246(0.212, 1.660)	0.001*
	Rural	121	75	1			
Who took consent	Operating surgeon	135	75	5.3(2.329, 7.739)	0.000	4.45(1.95, 5.09)	0.002*
	Others	54	159	1			

not know starting time of the procedure, when to resume work post-operatively and anesthesia risks respectively. This shows lower level of knowledge similar to those from the study reported by Befekedau et al(13).

About 70.4% of respondents perceived that consent was only for protection of Surgeon and Hospital, and 57% of respondents thought that they could not change their mind after signing consent which was worse than study reported from Gondar University, Ethiopia(11). Our study showed 55.6% of respondents had poor knowledge which is in agreement with the ones reported by Nurhusein et al(11). The present finding, however, is not in agreement from those of the studies conducted in Nigeria and South Africa(2,9). Probably it's because of higher educational profile of patients in Nigeria and South Africa. Another study from SPMMCH, Ethiopia showed only 10.5% of patients had good knowledge(13). Study reported from Sudan showed 54% of patients did not understand informed consent at all(16).

Over all except those from Nigeria and South Africa, the level of knowledge on surgical informed consent is low. So over all our study reflected lower level of knowledge and perception regarding legal nature of surgical informed consent.

Conclusion

Majority of our patients had poor knowledge and poor perception regarding the legal nature of surgical informed consent. Living in urban, signing informed consent previously and consent taken by operating surgeon affected level of knowledge positively. The consent has to be taken at least by the operating surgeon.

Declarations

Ethical clearance- ethical clearance was obtained from IRB office of Arbaminch University, college of medicine and health sciences before doing the research. The reference number is IRB/1160/2021.

Consent for publication-written informed consent for each patient was taken while collecting data, identification number was not included. No videos or images specific to patients was included in collected data.

Availability of data and materials: The data in this manuscript will be accessed by the contact address of the corresponding and Co-Authors.

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Authors contributions:

Yonas Abera[1]-have made substantial contributions to conception and design, data collection, analysis and interpretation, drafted and critically revised the article, and finally approved the article for publishment.

Menaye Yihune[2] – have made substantial contributions to conception and design, data collection, analysis and interpretation, drafted and critically revised the article, and finally approved the article for publishment.

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Review Article

A systematic literature review on determinants of COVID-19 vaccine acceptance globally

Habtamu Alganeh Guaide[1*], Tadele Fentabil Anagaw[2], Eneyew Talie Fenta[3], Desta Debalkie Atnafu[1]

[1]School of Public Health, College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia
[2]Department of Health Promotion and Behavioral Sciences, School of Public Health, College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia
[3]Department of Public Health, School of Public Health, College of Medicine and Health Sciences, Injibara University, Injibara, Ethiopia

Corresponding authors*: habtamu.alganeh@yahoo.com

Abstract

Background*: More than dozens of vaccines have been approved by World Health Organization (WHO) against the coronavirus disease 2019 (COVID-19). Determinants of vaccine acceptance are significant for the success of mass vaccination and to minimize the spread of the disease. However, there is no comprehensive evidence on the determinants of vaccine acceptance globally. The aim of this review was to provide an up-to-date evidence on determinants of COVID-19 vaccine acceptance globally.*

Methods*: This systematic review was performed based on the preferred reporting items for systematic reviews and meta-analysis (PRISMA) standards. All published and unpublished search was performed in PubMed, EMBASE, Scopus, Google Scholar and Google on October 30, 2021. Studies that were published in peer-reviewed journals, explicitly describing the determinants of COVID-19 vaccine uptake in various global settings, and studies published in English language were included. Three reviewers independently assessed search results, extracted data, assessed the quality of articles included. Narrative review was undertaken to summarize and report the evidences.*

Results*: A total of Sixty-five studies from 24 countries met the inclusion criteria. According to the findings of this systematic study, a number of variables influenced how well the COVID-19 immunization was received by different communities around the world. This systematic review showed that vaccine acceptance varies among countries. The percentage of vaccine acceptance ranges from 21% in Egypt to 97% in Ecuador. The main factors influencing vaccination acceptability were divided into three categories. The first theme is knowledge, attitude, and perception as behavioral determinants. The second theme is socio-demographic factors: residency, educational attainment, and population age. The third theme is communication related factors: media exposure and information source.*

Conclusion: *Strategies for improving vaccine uptake and mass vaccination should focuses on improving COVID-19 vaccine health education that will improve the knowledge and awareness of the population towards the vaccine. Comprehensive health education, vaccine promotion, training and awareness creation packages have to be done using various mass media outlets to reach large segment of the population.*

Keywords: *COVID-19, Determinants, Vaccine*
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Introduction

The global pandemic, coronavirus disease 2019, has resulted in an economic, social and societal crisis globally, and has become a major public health threat for the world (1). Emerging of coronavirus disease 2019 which is a severe and disastrous communicable disease caused by severe acute respiratory syndrome coronavirus-2 (SARS COV-2), which is mainly transmitted from human to human through respiratory droplet (2). Coronavirus disease 2019 is increasing throughout the world at alarming rate, declared formally as pandemic and public health emergency of international concern (PHEIC) by the WHO (3). As on 12th October 2021, Global prevalence of COVID-19 data available on WHO dashboard revealed that 237,655,302 confirmed cases and 4,846,981 deaths (4).

Different approaches were used to tackle the transmission of COVID-19 pandemic applied at individual, environmental and community level, such as hand sanitation, face mask, social distancing, washing objects and surfaces, limiting access to schools, universities, community meeting places, public transport and other places where people meet together (5).

Immunization is the best cost-effective mechanism in the public health domain than other preventive and protective mechanisms. The global community has recognized the value of immunization to prevent, reduce and control large numbers of infectious diseases and several chronic diseases caused by infectious agents. Immunization is a vital tool for controlling the pandemic when combined with effective testing, treatment and existing prevention measures. COVID-19 vaccinations are the most operational means to minimize and reduce the burden of the pandemic (6). Vaccine development began in numerous research hubs, governments and pharmaceutical companies as shortly epidemics emerged (7). High immunization coverage may be required to stop, reduce and control the COVID-19 pandemic. Globally a total of 6,364,021,792 vaccine doses have been dispensed since the emerging pandemic to stop this public health crisis (4).

Evidence suggested that the majority of participants agreed to take the vaccine with concern of the safety and effectiveness. Vaccine acceptance ranges from 55% to 90% Russia to China respectively, and it was associated with trust in the health information provided from the government concerning the vaccine. In Africa, the acceptance for the COVID-19 vaccine ranges from 65.2 % to 81.6%, Nigeria to South Africa, respectively (8).

In the mindset of the Pandemic crisis, the implementation of COVID-19 vaccines was a spark of hope. Though, having access to the vaccine program, and successfully implementing a mass vaccination campaign is another (9,10).

Furthermore, there are some uncertainties concerning some features of the COVID-19 vaccine, such as: Uncertainty on the long-term security and the need for regular reformulation amid evidence of SARS-CoV-2 evolution and the appearance of hereditary variants (10,11). Beside their importance and efficiency in tackling the pandemic and other infectious disease, individuals raise fears and misunderstandings regarding vaccination programs for different diseases (12,13).

Vaccination program policies play an unconditional role for vaccinating the target population in a given country. Some vaccination policies focus on health promotion, others give emphasis for enrollment of the vaccine (14,15). To reduce the burden of the coronavirus disease 2019 disease and to lessen the socio-economic impact on the population, governments applied various preventive methods and enrolled COVID-19 vaccine for high-risk population at the first stage, currently vaccinating the entire population at large.

To ascertain the scope of this problem, the current systematic literature review aimed to assess the determinants of COVID-19 vaccine acceptance throughout the world in different population groups, which can provide an initial insight on comprehensive determinants COVID-19 vaccine acceptance for further investigation and implementations of strategies.

Methods

This systematic review was performed based on the preferred reporting items for systematic reviews and meta-analysis (PRISMA) standard(1). A method of systematic review was selected to permit a vigorous and reproducible method to makeup an analytical synthesis of the accessible and present evidence.

Research question

> What are the determinants of COVID-19 vaccine acceptance globally?

Search strategy and data sources

Databases such as PubMed/MEDLINE, EMBASE, Google Scholar, the WHO library, African journals, and Ethiopian online health journals were also searched for all published studies. Using the Google search engine, we also try to search gray literature. Those papers that pointed at the determinants of vaccine acceptance were eligible for inclusion in this review. HAG and DDA searched studies in databases. **Key terms:** The search terms that were used were: determinants, COVID-19, and vaccine. Boolean operators “AND” and “OR” were applied to integrate search terms.

In this systematic review we have used the following search terms:
((“determinants” [MeSH Terms] OR “determinants” [All Fields] OR “barriers” OR “barrie*” OR “challen*” OR “factors” OR “factors affecting”) AND (“COVID 19 Vaccines” *OR* “Vaccines, COVID-19” *OR* “COVID-19 Virus Vaccines” *OR* “COVID 19 Virus Vaccines” *OR* “Vaccines, COVID-19 Virus” *OR* “Virus Vaccines *OR* COVID-19” *OR* “COVID-19 Virus Vaccine” *OR* “COVID 19 Virus Vaccine” *OR* “Vaccine, COVID-19 Virus” *OR* “Virus Vaccine, COVID-19” *OR* “COVID19 Virus Vaccines” *OR* “Vaccines, COVID19 Virus” *OR* “Virus Vaccines, COVID19” *OR* “COVID19 Virus Vaccine” *OR* “Vaccine, COVID19 Virus” *OR* “Virus Vaccine, COVID19” *OR* “COVID19 Vaccines” *OR* “Vaccines, COVID19”, “COVID19 Vaccine”, “Vaccine, COVID19”, “SARS-CoV-2 Vaccines”, “SARS CoV 2 Vaccines” *OR* “Vaccines, SARS-CoV-2” *OR* “SARS-CoV-2 Vaccine” *OR* “SARS CoV 2 Vac-

cine" *OR* "Vaccine, SARS-CoV-2" *OR* "SARS2 Vaccines" *OR* "Vaccines, SARS2" *OR* "SARS2 Vaccine" *OR* "Vaccine, SARS2" *OR* "Coronavirus Disease 2019 Vaccines" *OR* "Coronavirus Disease 2019 Vaccine" *OR* "Coronavirus Disease 2019 Virus Vaccine" *OR* "Coronavirus Disease 2019 Virus Vaccines" *OR* "Coronavirus Disease-19 Vaccines" *OR* "Coronavirus Disease 19 Vaccines" *OR* "Vaccines, Coronavirus Disease-19" *OR* "Coronavirus Disease-19 Vaccine" *OR* "Coronavirus Disease 19 Vaccine" *OR* "Vaccine, Coronavirus Disease-19" *OR* "COVID 19 Vaccine" *OR* "Vaccine, COVID 19" *OR* "2019-nCoV Vaccine" *OR* "2019 nCoV Vaccine" *OR* "Vaccine, 2019-nCoV" *OR* "2019 Novel Coronavirus Vaccines" *OR* "2019 Novel Coronavirus Vaccine" *OR* "2019-nCoV Vaccines" *OR* "2019 nCoV Vaccines" *OR* "Vaccines, 2019-nCoV" *OR* "COVID-19 Vaccine" *OR* "Vaccine, COVID-19" *OR* "SARS Coronavirus 2 Vaccines") AND ("Vaccine*" OR "vaccination*" OR "immunization*")).

Eligibility criteria

Inclusion criteria for this literature review were: Articles published in English language; peer reviewed articles indexed in PubMed; articles on general population, healthcare workers, students, patients; publications that assess determinants of COVID-19 vaccine acceptance, and the exclusion criteria for this review were publications with no abstracts, letters to editors, unpublished manuscripts, and non-English publications.

Study selection and data extraction

Data was analyzed using descriptive methods, and qualitative analysis was performed. Items included in this review were; study setting, data collection method, sample size, and prevalence.

In this review, the major outcome was the determinants of vaccine acceptance, which were reported within the original studies. Articles retrieved from online databases were exported to Endnote version 8. Duplicates were managed and findings were exported to Excel. By using search terms titles and abstracts were retrieved and screened for inclusion criteria. Then, those who satisfied the criteria undergo for full text review and extraction. Preferred Reporting Item for Systematic Review and Meta-Analysis (PRISMA) flowchart was used.

Quality assessment

Quality evaluation was done by following the Newcastle -Ottawa Scale (NOS) measures to include in this review. This tool has ten points in the three domains of modified NOS parts for observational studies. The studies which have scored _> 5 points were included

Results
Search results

320 articles were identified and retrieved from different online databases: PubMed/MEDLINE, EMBASE, Google scholar, African Journals, and World health organization libraries. From 320 articles assessed, 188 articles excluded because of not directly related to the topic of interest. Thirty-four studies were excluded after reviewing of the full text because the articles were not related to topic of interest and 33 articles were duplicated. Finally, 65 studies meet the eligibility criteria and included in this review (Figure 1).

Characteristics of articles included in this review

Findings incorporated in this systematic review on the determinants of COVID-19 vaccine acceptance were published up to October 30, 2021, in various peer reviewed international journals. Sixty-five (65) studies were included in this systematic review. Based on the design of the study, 63 articles were cross-sectional and two were mixed (quantitative and qualitative). Thirty eight percent of the articles included in this systematic review were conducted in Ethiopia.

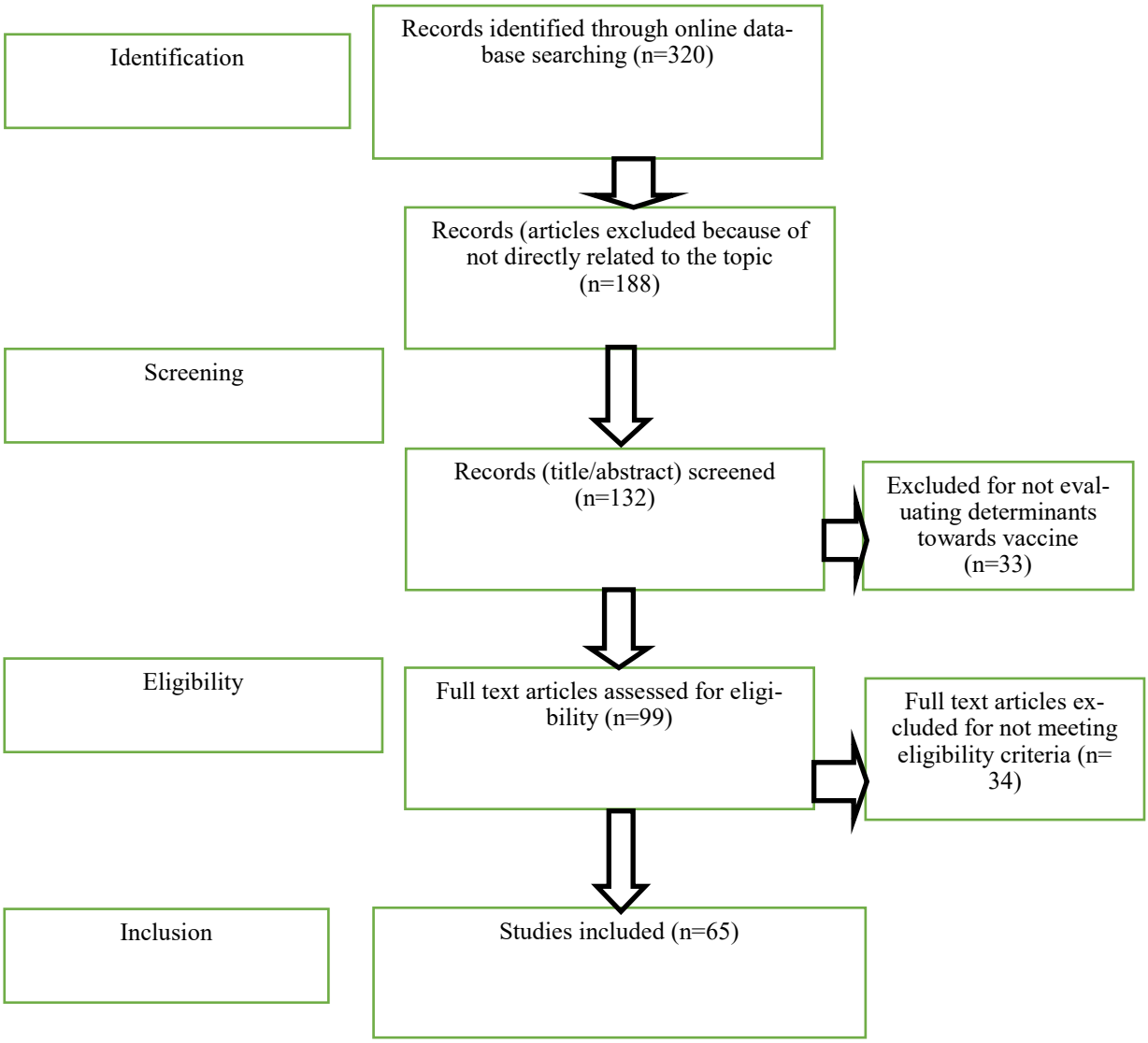

Figure 1: PRISMA flow chart of the study selection process on the determinants of COVID-19 vaccine acceptance

Table 1: Characteristics of articles included in this systematic review on the determinants of COVID-19 vaccine acceptance.

Author	Year of publication	Sample size	Sampling technique	Study design	Country	Vaccine Acceptance	Key findings
Mesele M (2)	2021	415	Simple random sampling	cross-sectional study	Ethiopia	45.5%	Sex, educational, mass media, received any vaccination during child hood, family members diagnosed with COVID-19, friends diagnosed with COVID-19, respondents tested for COVID-19
Mesele M (3)	2021	425	e-Survey	cross-sectional	Ethiopia	24.2%	knowledge, educational level, access to mass media, Residency and awareness towards vaccination
Simegnew et.al (4)	2021	301	Simple random sampling	cross-sectional study	Ethiopia	54.8%	educational, perceived benefit, barrier and cues to action
Birhan et.al(5)	2021	423	simple random sampling	cross-sectional study	Ethiopia		Knowledge, family practicing COVID-19 prevention, being a health science student.
Ahmed et.al(6)	2021	423	Survey/ NA	Cross-sectional study	Ethiopia		Attitude, knowledge, Perception, and age.
Angelo et.al(7)	2021	405	Simple random sampling	Cross sectional study	Ethiopia	48.4%	attitude, professionals with a history of chronic ill-ness, good preventive practices
Seboka et.al(8)	2021	1160	Survey	Cross sectional	Ethiopia	64.66%	perceived susceptibility and perceived benefits
Oyekale A.S(9)	2021	2178	Survey	Cross sectional	Ethiopia	92.33	Having work, age, engagement with non-farm businesses and residence
Belsti et al(10)	2021	1184	Online survey	Cross sectional	Ethiopia	31.4%	female, age, marriage, residence, occupations, job, religion, educational

Mose A, Yeshaneh A(11)	**2021**	**396**	**systematic random sampling**	**Cross sectional study**	**Ethiopia**	**70.9%**	**age, educational, knowledge, and practice towards COVID-19 and its preventive measures**
Berihun et al (12)	2021	416	consecutive sampling	cross-sectional study	Ethiopia	59.4%	diagnosed with COVID-19, knowledge, and attitude
Ahmed et.al (13)	2021	423	simple random sampling	cross-sectional study	Ethiopia	95.6%	Education, age, working experience, marriage, risk level, and gender
Zewude B, Belachew A(14)	2021	384	probability proportionate to size sampling	cross-sectional survey	Ethiopia	61.6%	having children, previous interaction with infected, perception of severe illness, and experience of receiving the first round of vaccine
Shitu et al(15)	2021	302	stratified simple random sampling	cross-sectional study	Ethiopia	40.8%	male, being a private school teacher, perceived susceptibility, seriousness and benefit of the vaccine
Abebe et al (16)	2021	501	multistage sampling	cross-sectional	Ethiopia	62.6%	Age, educational status, having a chronic disease and knowledge
Alle YF, Oumer KE(17)	2021	327	Survey	cross-sectional	Ethiopia	42.3%	Age and profession
Hailemariam et al (18)	2021	423	simple random sampling	cross-sectional	Ethiopia	31.3%	Educational status, residency, compliant with coronavirus disease 2019 guidelines, and perception towards vaccine
Nguyen LH ,et al.(19)	2021	651	Online survey	cross-sectional	Vietnam	60.4%	Income, having children, perceived risk
Banik. R .et al. (20)	2021	894	Survey	cross-sectional	Bangladesh	65.5%	age, male, education, residency, health status, positivity towards COVID-19 vaccination
Stuckelberger, S.et al (21)	2021	1551	Survey	Cross sectional	Switzerland	29.7 % pregnant and 38.6% breastfeeding women	age, education, history of influenza vaccination, being in their third trimester of pregnancy
DiGennaro.F, et al (22)	2021	1723	Survey	Cross sectional	Italy	67%	age, close contact with high-risk groups and received flu vaccination previously

Rabi.R ,etal. (23)	**2021**	**639**	**Survey**	**Cross-section**	**Palestine**	**40%**	**age, knowledge about the vaccine, worry about side effects, worry about injection, natural immunity preference, media misrepresentation and getting COVID-19 from the vaccine**
Wang. K ,et al (24)	2020	806	Online survey	Cross section	China	40%	those in private sector, with chronic disease, meeting with suspected or confirmed patients, accepted influenza vaccination
Luk .TT,et al. (25)	2020	1501	simple random sampling	cross-sectional	China	45.3%	Vaccine efficacy, knowledge, perceived risk, Alcohol drink
Rezende RP, et al (26)	2021	1000	Survey	cross-sectional	Brazil	81.9%	concurrent chronic disease, hydroxychloroquine use, and recent corticosteroid
Wang C,et al.(27)	2021	8742	Survey	cross-sectional	China	67.1	Males, aged , educated, rural residence and in the vaccine-priority groups
Salmon DA ,et al (28)	2020	2525	Panel Survey	cross-sectional	US	50%	men, Age, Bachelor's degree or higher and Democrats
Kuter .BJ ,et al(29)	2020	12034	Survey	cross-sectional	Philadelphia	63.7%	ager, male, educated, up-to-date on vaccinations
Wong MCS ,et al(30)	2020	1200	Simple Random Telephone interview	Survey	China	37.2%	perceived severity and benefits of the vaccine, cues to action, health outcomes, and trust in vaccine manufacturer
Sarasty.O ,et al(31)	2020	1050	Online	Survey	Ecuador	97%	Income, employment, probability of needing hospitalization, residence
Bell.S , et al(32)	2020	1252	Online survey	Mixed	England	55.8% for themselves & 48.2% for children	Income, vaccine safety and efficacy
Detoc.M, et al(33)	2020	3656	Online survey	Cross sectional	France	77.6%	age, gender, fear about COVID-19, and perceived risk
Reiter.PL, et al(34)	2020	2006	Online survey	Cross sectional	US	69%	Health care recommend vaccination, political leaning, perceived infection, perceived effectiveness of vaccine

Berg MB, Lin L (35)	**2020**	**350**	**Quota sampling**	**cross sectional**	**US**	**70.6%**	**attitudes, norms, and trust in the vaccine approval**
Zürcher. K, et al (36)	2020	3793	Web based survey	cross sectional	Switzerland	39.8%	age and vaccinated for influenza
Kaur A, et al(37)	2021	520	Online survey	cross sectional	India	63%	working in COVID duties
Yurttas B,et al(38)	2021	732	Web based survey	cross-sectional	Turkey	29.6%	male, age, working in a hospital, not having COVID-19 infection
Mondal P, et al(39)	2020	2978	Survey	cross-sectional	US	81.1%	education, ethnicity and age
Maraqa. B, et al(40)	2021	1159	Online survey	cross-sectional	Palestine	37.8%	males, younger ages, physicians, HCWs at non-governmental settings, those who previously received the influenza vaccine, good COVID-19 related knowledge
Malik A, et al(41)	2021	5,237	Online survey	cross-sectional	Pakistan	70.2%	age, sex, education, taking direct care of patients, and previous COVID-19 infection
Mahmud S, et al(42)	2021	605	Online survey	cross-sectional	Bangladesh	61.16%	age, gender, residency, level of education, income, perceived risk, previous vaccination experience, knowledge
Paul A, et al(43)	2021	4175	Online survey and in-depth interview	Mixed study	Bangladesh	60.5%	Education, believe on effectiveness of vaccine, knowledge
Mohamed NA, et al (44)	2020	1406	Online survey	Cross sectional	Malaysia	64.5%	age, education levels and female.
Nikolovski J, et al(45)	2020	9106	Online survey	Cross sectional	US	91.3%	gender, race, education, and income
Qin W, et al(46)	2020	1188	Simple random	Cross sectional	China	79.41%	Age, perceived high risk
El-Elimat T, et al(47)	2020	3100	convenience sampling	Cross sectional	Jordan	37.4%	Males, those who took the seasonal influenza vaccine participants

Edwards B, et al(48)	**2020**	**3000**	**Online survey**	**Cross section**	**Aus-tralia**	**59%**	**household income, level of social distancing, used the COVID-Safe App, confi-dence in their government**
Attwell K, et al(49)	2020	1316	Online sur-vey	Cross sectional	Aus-tralia	65%	Perceived severity, trust on information, previous vac-cine for influenza
Lin Y, et al (50)	2020	3541	Web based online	Cross sectional	China	83.5%	Perceived benefit, perceived efficacy and side effects as perceived barrier
Kefi HE, et al (51)	2020	398	Simple ran-dom	Cross sectional	Tuni-sia	58%	worries on side effects
Abuown A, et al(52)	2021	514	Email	Survey	Lon-don	59%	Age, ethnicity, management staff of hospital
Jiang N, et al (53)	2021	1512	conven-ience sam-pling	cross-sectional	China	84.38 %	gender, education, family members' vaccination status and side effects experienced after receiving other vaccines
Ehde DM, et al(54)	2020	486	Online sur-vey	cross-sectional	US	66%	education, perceived risk, and trust in information source
Scherer AM, et al(55)	2021	1022	nonproba-bility-based Internet panel sur-vey	cross-sectional	US	27.6%	Having information on COVID-19 vaccine safety
Tsai FJ,et al (56)	2020	1020		cross-sectional	Tai-wan	52.7%	Age, education , perceived risk perception, previous vaccination history
Fotiadis K ,et al (57)	2021	1456			Greece	77.7%	Fears of safety, lack of infor-mation on vaccination, edu-cation and experience
Mohammed K, et al(58)	2020	521	Online sur-vey	cross-sectional	Saudi Arabia	52%	received influenza vaccina-tion in the past, high levels of concern about contracting COVID-19, believed in man-datory vaccination, male, education
Fares S ,et al (59)	2021	385	Online sur-vey	Cross sectional	Egypt	21%	safety and effectiveness of vaccine.
Choi SH ,et al (60)	2021	226	Online sur-vey	Cross sectional	South Korea	76.5%	confidence in the safety of COVID-19 vaccines

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Choi SH ,et al (60)	2021	226	Online sur-vey	Cross sectional	South Korea	76.5%	confidence in the safety of COVID-19 vaccines

Mascarenhas AK ,et al(61)	**2020**	**248**	**Online survey**	**Cross sectional**	**USA**	**56%**	**believing health experts, worries about side effects, and assenting vaccine mandates**
Pataka A, et al (62)	2020	656	Online survey	Cross sectional	Greece	71.1 %	Being parenthood, being a physician and treating confirmed/suspected COVID-19 patients
Stern MF,et al(63)	2020	5110		Survey	US	44.9 %	Vaccine efficacy, trust of health care information
Caban-Martinez AJ, et al (64)	2021	3169	Online survey	Cross sectional	US	48.2 %	age, ethnicity, education, married, of current rank firefighter/EMS
Alqudeimat Y, et al(65)	2021	2368	Web based survey	Cross sectional	Kuwait	53.1 %	Male, history of influenza vaccine, perceived risk of infection
La Vecchia C, et al(66)	2020	1055	Survey	Cross sectional	Italy	53.7 %	Age, professional, managers and teacher
Baack BN, et al(67)	2021	2726	Online survey	Panel survey	US	51.8 %	Age, vaccine efficacy, income, Health insurance, educational status

Number of study reports based on country

In this systematic review, the number of articles conducted in Ethiopia, USA and China were sixteen, eleven and six, respectively (Figure 2).

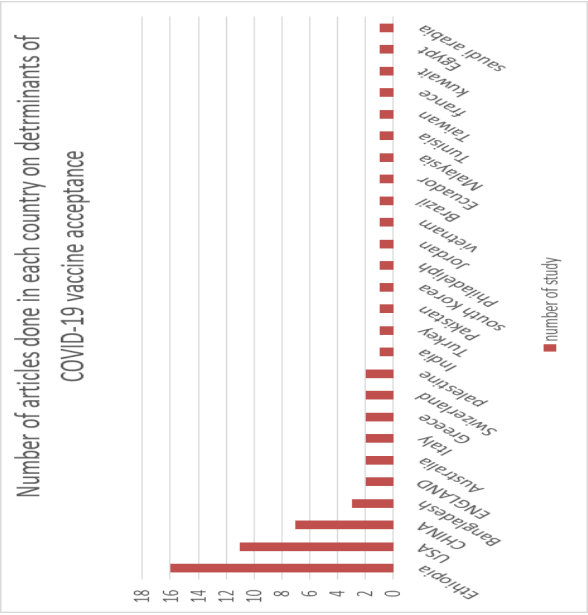

Figure 2: Number of articles done in each country on determinants of COVID-19 vaccine acceptance worldwide *(n=65)*

Determinants of COVID-19 vaccine acceptance

As shown in (Table 1), 65 studies which were done among different populations were incorporated in to the current analysis. This review identified the following determinants for the acceptance of the vaccine; knowledge, attitude, mass media exposure, residency, educational status, perceived benefit, perceived efficacy, perceived barrier, perceived risk, perceived safety, perceived severity, cues to action, age, income, having children, income, previously received an influenza vaccine, marital status, sex. Family members have been diagnosed with COVID-19, respondents tested, being a health worker and individual perceived risk, worry concerning side effects, fear of injection, immunity preference, encountering with suspected or confirmed COVID-19 patients, concurrent malignancy, recent corticosteroid use, health outcomes, and reliance in health system or vaccine company, employment status, occupations, good preventive practices, level of social distancing, used COVID-Safe App, confident in their state government, working experience, earlier contact with someone infected one, perception toward COVID-19 vaccine, perceived risk of COVID-19 infection, being a health science student, subjective norms, and confidence in the vaccine authorization.

Key themes of determinants of COVID-19 vaccine acceptance

In this comprehensive systematic literature review we found that 65 articles reported a number of determinants towards COVID-19 vaccine acceptance in different population of the globe. Majority of determinants were behavioral: knowledge, attitude, perceived benefit, perceived efficacy and Previous vaccination of influenza and sociodemographic determinants: age, sex, residency, educational status and Communication related determinants mainly access to mass media and trusted source of information (Table 2).

Table 2: Key determinants of COVID-19 vaccine acceptance according to reported studies worldwide (n=65)

Key determinants	No. of Studies
Behavioral determinants	22
Knowledge	
Attitude	
Perception	
Perceived ease of use, Perceived barrier, Perceived benefit, Perceived efficacy, Perceived risk, Perceived safety, Cues to action, Subjective norm, Previous vaccination of influenza, Having chronic disease, Good preventive practice Self -confidence on vaccine	
Sociodemographic determinants	34
Sex	
Age	
Educational status	
Residency, Income, Having children, Marital status, occupation, Work experience, Ethnicity	
Communication related determinants	9
Mass media access	
Trust on source of information	
Media misrepresentation	
Getting enough information on vaccine	

Discussion

Currently, there are dozens of vaccines that are under implementation and development to tackle the social, economic and health impact of individuals towards the pandemic globally. To do this, determinants to accept the vaccine had to be explored from different population category perspective in different parts of the globe.

This systematic review showed the determinants of COVID-19 vaccine acceptance globally, as there is no comprehensive evidence that represent the global on the context of determinants of vaccine acceptance.

This systematic review included all articles conducted on the vaccine acceptance and its determinants. This is because understanding various determinants helps to design effective mechanism to create awareness on the vaccine and significant determinants towards the vaccine acceptance in the world. During this, 65 articles from different groups the population were included. The findings of the present systematic review revealed that there were a number of determinants which hinder the utilization of COVID-19 vaccine in the world. According to this systematic review the major determinants were categorized in to three major themes namely: behavioral, socio-demographic and communication related.

Concerning the behavioral determinants, from the total 65 articles included in this systematic review, 22 studies have pointed out behavioral determinants play major role in shifting vaccine acceptance in the study population. From 22 studies pointed behavioral determinants 10 of them stressed on knowledge impacts the acceptance level of the population (3,5,6,11,12,16,23,25,40,43). Some of the studies showed that attitude (6,7,12,16), perception (6,14), and perceived ease of use (4,8) as major contributing determinants for the acceptance. This might be due to that knowledge/awareness plays vital role due to that knowing the advantage of vaccine enforces individuals to take the vaccine than their counter parts. Indeed, the knowledge level of individuals affect their decision on the vaccination and day to day activities. Favorable attitude has also effect on acceptance of the vaccine for the pandemic. Perception has also impact on the acceptance of the vaccine, this might be due to that individual need to have insight about the vaccine before immunization. Similarly, perceived benefit and ease of use has an impact of the acceptance of the vaccine, this might be due to that the vaccine has an advantage for protecting /keep them healthy.

Another major theme was socio-demographic determinants, studies have reported that sex (2,10,13),age (6,9 –11,13,17),educational status (2–4,10,11,13,18), residency (3,9,10,18), occupation (10,17) as determinants for the acceptance of the vaccine for COVID-19. This might be due to the fact that educational status plays important role in diverting the decision of individuals, vaccine acceptance needs understanding of the advantages of immunization specifically during pandemic.

Similarly, residency has an effect on the vaccine acceptance, those individuals in remote area may not get enough information regarding the pandemic and the available vaccines for tackling the spread and impact of the disease in general.

Location affects vaccination adoption; people living in distant areas might not receive enough information

about the pandemic and the immunizations that are available to stop its spread and lessen its effects generally.

Access to mass media and communication-related characteristic were previously identified as a key factor in vaccine acceptance (16,17). This may be because the general public receives timely information from the mass media about the pandemic's present state, the vaccinations that are available, the value of immunization, and related issues. Trust in the information source was another element in this category that contributed to the acceptance of the COVID-19 vaccine (69,75,77). This may be because the audiences' decision to use the vaccination depends on the accuracy and timeliness of the information sources. The acceptability of vaccines was also significantly influenced by media misrepresentation.

Access to mass media, a communication-related characteristic, was previously identified as a key factor in vaccine acceptance (2,3). This may be because the general public receives timely information from the mass media about the pandemic's present state, the vaccinations that are available, the value of immunization, and related issues. Trust in the information source was another element in this category that contributed to the acceptance of the COVID-19 vaccine (55,61,63). This may be because the audiences' decision to use the vaccination depends on the accuracy and timeliness of the information sources. The acceptability of vaccines was also significantly influenced by media misrepresentation (23), this might be due to that information has to be provided to understand the aim of the vaccination, advantages of having vaccine, and to improve the knowledge of the population on the vaccine.

Conclusion

This systematic review has focused on the vital determinants towards vaccination for health policy makers, non-governmental organization in health care, health facilities, health professionals, researchers and for the population in general. It has identified key factors that influence vaccine adoption and the achievement of national and international health organization targets. This comprehensive review revealed that behavioral, sociodemographic, and communication-related characteristics as the main factors. To vaccinate the largest possible population, these factors require prompt intervention. To this end, health offices, facilities, and medical personnel must develop health communication programs that specifically target both rural and urban citizens across the nation.

Based on the most recent data, it is essential to deliver timely information across a variety of media venues. The vaccine must also be administered quickly since it is a crucial method for halting the spread and minimizing the effects of the pandemic in the population.

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Abbreviations

COVID-19, coronavirus disease 2019; WHO, World Health Organization; PRISMA, Preferred Reporting Item for Systematic Review and Meta-Analyses;

Disclosure

No conflict of interest

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Case report

Huntington's disease in a 31-year-old Ethiopian patient: A case report and a brief literature review

Blen M. Gebresilassie[1], Biniyam A. Ayele[2], Guta Zenebe[3] , Abenet Tafese[4]

[1]Department of Neurology, College of Health Science Addis Ababa University, Addis Ababa, Ethiopia
[2]Global Brain Health Institute (GBHI) Atlantic Fellow, University of California, San Francisco

*Corresponding author; Email: mamoblen83@gmail.com

Abstract

Background: *Huntington's disease is an inherited progressive neurodegenerative disorder characterized by choreiform movements, neuropsychiatric features, and cognitive impairment which leads to significant functional disability and caregiver burden. It is caused by a cytosine-adenine-guanine (CAG) trinucleotide repeat expansion in the huntingtin (HTT) gene on chromosome 4p and inherited in an autosomal-dominant pattern. We report the clinical and genetic characteristics of a patient with Huntington's disease with strong family history.*

Case report: *We report a case of a 31-year-old female with two years history of involuntary limb and trunk movements which were exacerbated by stress and disappeared during sleep. The symptoms gradually worsened with associated dysarthria, behavioral and mood abnormalities. She had a strong positive family history of similar illness with the involvement of both her siblings and three deceased family members. Her routine laboratory investigations were unremarkable. Brain magnetic resonance image (MRI) showed severe bilateral caudate and putaminal atrophy with ballooning of the adjacent lateral ventricle. Her genetic test identified a CAG repeat expansion of 48. The patient was started on Valproate and began follow-up at a Psychiatric unit as well, but she has only mild improvement in symptoms.*

Conclusion: *The present case highlights, the importance of genetics tests in the early diagnosis of Huntington's disease in resource-limited settings and multidisciplinary intervention to improve patient's quality of life.*

Keywords: *Huntington's disease; chorea; penetrance; family history; Ethiopia*
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Background

Huntington's disease (HD) is a rare neurodegenerative disease characterized by a range of symptoms that involve motor, cognitive, and psychiatric functions. It is an inherited disease that involves progressive degeneration of nerve cells in the brain, specifically within the basal ganglia. Typical onset occurs at the age of 30 to 40 years and the median survival time is 15 to 18 years after onset [1-3]. It occurs in all racial groups, and its prevalence varies widely with worldwide prevalence ranging from 0.4 -5.7 cases per 100,000 persons [4, 5]. There is no nationwide epidemiologic study on the disease in Ethiopia, but the one-year prevalence of chorea was reported to be 7.3% [6]. Huntington's disease is a "trinucleotide repeat" disorder, which is caused by an increase in the number of CAG repeats in the *HD* gene.

The number of triplet repeats determines penetrance with 40 or more repeats cause full penetrance and are associated with disease expression. It also exhibits genetic anticipation; earlier onset in successive generations within a pedigree. There is an inverse relationship between repeat length and age at onset [7,8]. At present, no treatment has been found to delay the onset of HD or to treat it effectively. As far as our knowledge is concerned, this is the first reported case of a family with Huntington's disease from Ethiopia.

Case report

Our patient is a 31-year-old female who came to the clinic with complaints of 2 years history of uncontrollable, dance-like involuntary limb and trunk movements. The movement was exacerbated by stress and disappeared during sleep.

The symptoms gradually worsened with difficulty of performing her daily tasks, like cleaning, cooking, and washing. She also had reduced voice, dysarthria, slow responses, and mild difficulty of swallowing. She confirmed mild depressive symptoms, but no history of psychotic symptoms. She had no significant problem remembering things, and no history of fits, visual impairment, body weakness, or sensory symptoms. No history of known chronic illnesses, drug use history, or substance use. She is currently divorced and has two children (10 and 5 years old) both didn't have any symptoms. She has a family history consistent with autosomal dominant inheritance. Her great-grandmother, grandmother, mother, and her two surviving siblings (her elder sister and younger brother) suffered from similar diseases, but her mother died at the age of around 50, and her grandmother died at the age of around 55 (Figure 1). The age of onset became earlier with each new generation. Her sister (now age 35) had severe psychiatric and choreiform symptoms making her bedridden and currently resides in a nursing home. Her younger brother had the rigid form of the illness with predominant dysarthria.

On physical examination, the patient was alert and oriented to person, place, and time. Her vital signs and systemic assessments were normal.

Her neurological examination revealed that she had severe dementia with MOCA-B of 18, delayed initiation of the saccade, difficulty with anti-saccadic tasks, and mild dysarthria.

The abnormal movement was characterized as fidgeting with the difficulty of sitting still, random choreiform movements involving the hands, legs, and face (involved forehead with grimacing, eyebrow wiggling, and perioral twitching), and some dystonic posturing of the right arm. She had motor impersistance with milkmaid grip and darting tongue. Blood work results were all normal. Brain MRI confirmed the presence of bilateral, severe atrophy of the caudate and putamen (Figures 2A and 2B). With the informed consent of the patient's family, genetic testing for HD was performed by polymerase chain reaction (PCR) analysis of the region encompassing the CAG repeat in exon 1 of the huntingtin gene (*HTT*) followed by fragment sizing through capillary electrophoresis. The results of diagnostic testing revealed a normal allele with 22 CAG repeats and expanded as well as an unstable polyglutamine-encoding allele with 45 CAG repeats. Due to financial reasons, we couldn't send genetic tests for her siblings. A neuropathological study wasn't done. It was not possible to get the first-line medications targeting her symptoms, due to financial and availability issues, so she was started on valproate and later Fluoxetine was added but, she had no significant symptom improvement.

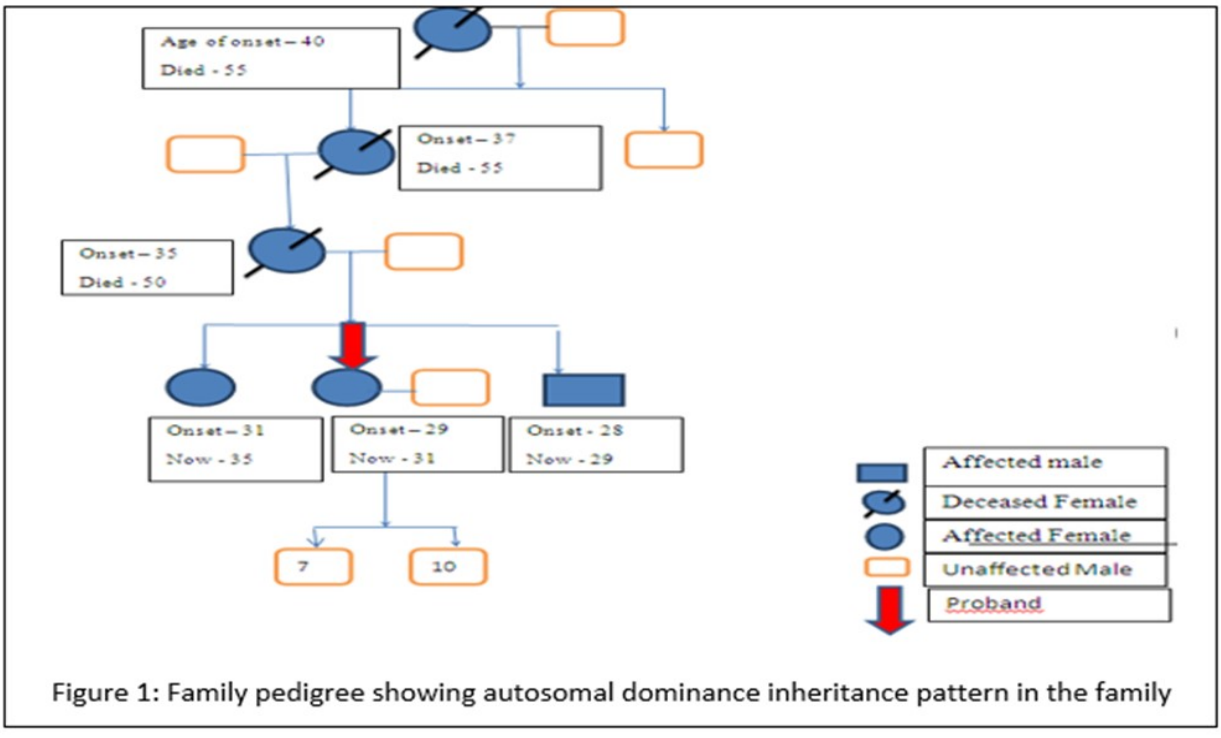

Figure 1: Family pedigree showing autosomal dominance inheritance pattern in the family

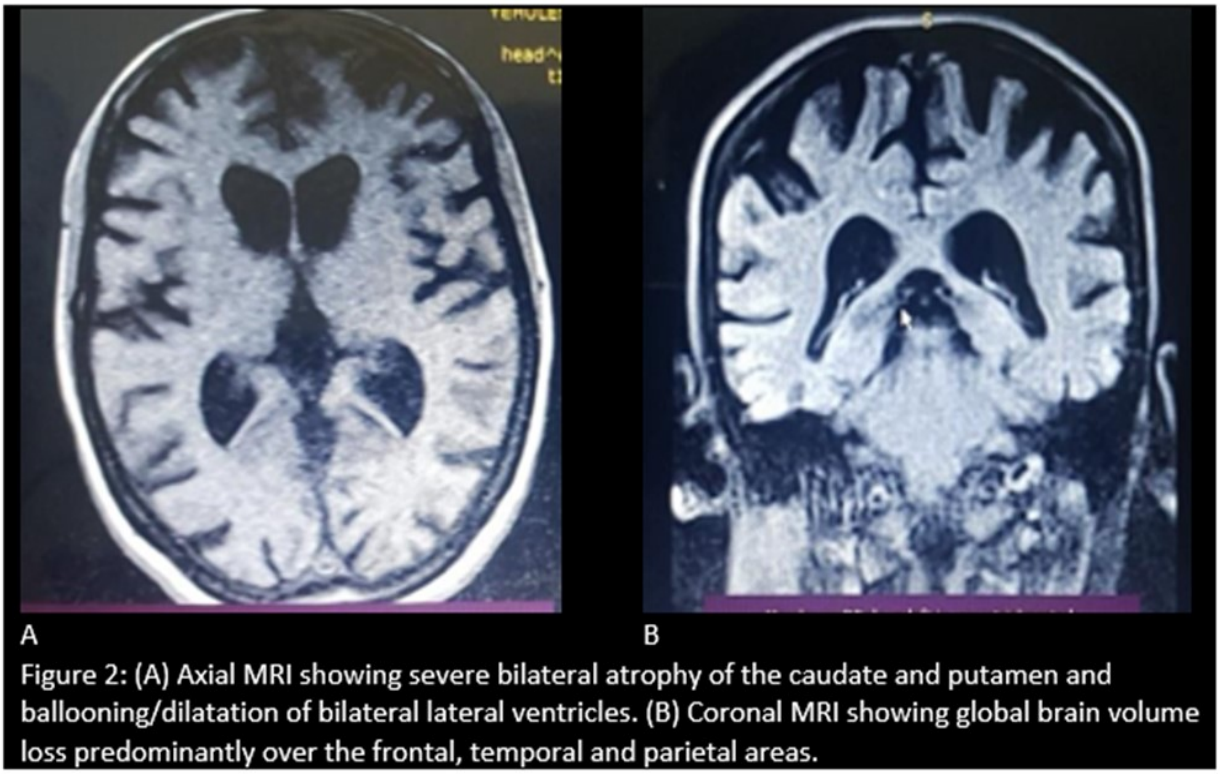

Figure 2: (A) Axial MRI showing severe bilateral atrophy of the caudate and putamen and ballooning/dilatation of bilateral lateral ventricles. (B) Coronal MRI showing global brain volume loss predominantly over the frontal, temporal and parietal areas.

Table 1: Summary of blood workups of the patient with Huntington's disease, on follow up at TASH, Addis Ababa, Ethiopia.

Investigation	Results
CBC	Normal
OFT	Normal
ELE	Normal
TFT	Normal

Abbreviations: CBC: complete blood count, OFT: organ function test, ELE: electrolytes, TFT: Thyroid function test, TASH: Tikur Anbessa Specialized Hospital

Discussion and conclusion

In this report, we describe a case of a patient diagnosed with Huntington's disease, a neurodegenerative condition caused by a dominantly inherited CAG trinucleotide repeat expansion in the huntingtin gene on chromosome 4.

The clinical information as well as the genetic results of our patient matched the typical HD presentation [2,9,12,14]. Our patient has expanded allele with 45 CAG repeats that cause full penetrance and is associated with disease expression.

Her presentation, the choreiform movements involving the hands, legs, especially the forehead with grimacing and eyebrow wiggling can be explained by the involvement of caudate and putamen. In addition, the presence of severe cognitive impairment and though mild, psychiatric symptoms are typical of adult-onset HD [7,8,13]. There was history of varying degrees of dementia and abnormal body movements in their mother, grandmother and great grandmother [figure 1]. Her surviving two siblings had also developed the symptoms. Her elder sister started to have symptoms at the age of 31, she was experiencing more severe psychiatric symptoms. She is now 35-year-old, overtime developed worsening of symptoms, became bed ridden and lives in nursing home. Apathy, irritability and depression are the most common and problematic neuropsychiatric symptoms in HD. An increased risk of suicide has been recognized since Huntington's seminal description of the condition. Non-motor features have greatest effect on functional independence and quality of life, so require recognition and management [3,9,15]. The younger sibling on the other hand had onset at the age of 26. His sister reported difficulties understanding his speech, and frequent throat clearing.

Motor symptoms such as rigidity and tremor were more prominent. In addition, examination revealed reduced voice, severe dysarthria, and mild choreiform movements. He also had mild depressive symptoms. Brain MRI revealed bilateral caudate atrophy. Due to financial reasons, a genetic test was not done for him. These types of HD are labeled as Westphal variants as rigidity is the dominant feature. However, based on previous studies, parkinsonian features are reported in juvenile cases, in which the father is the affected parent three to four times more frequently than is the mother and there is female preponderance and the age of onset is before 20 years of age [1,7,16].

Several other cases of HD have been reported but it is very rare to find cases of all siblings affected, similar to our presented cases. An earlier report from Oman had described three siblings (two girls and one boy) and their father who developed Huntington's disease. All the children developed the symptoms before the age of 12. Dystonia and severe & refractory seizures were the features in the children. the father had choreiform movements and emotional changes, but his symptoms occur after the symptoms appeared in his children [10, 11].

Though it has been suggested that the frequency of HD is probably low among people of African origin, documentation remains poor and evidence is inconclusive. A study in the South African population showed that the mean CAG-tract size in black South Africans was significantly lower than that in the Caucasian and mixed-race subpopulations, with most sizes falling in the range of 40 and 44 [4, 5,17]. HD is known to occur in most African countries, but short of confirmatory genetic tests, the epidemiological data is incomplete. Another study described that A new genetic variant- Huntington's disease-like 2 (HDL2)-occurring more frequently in blacks, and showed a tendency towards a later age of onset [18]. This serves as an important confirmation that HD can present in different forms, indicating the need to have a high index of suspicion in atypical presentations as well. Moreover, not many reports of three affected siblings and a parent are there in the literature[8, 11].

Because the disease inevitably affects the patient's closest ones, it is crucial to also provide adequate psychological and social support to all the family members.

When adequate multidisciplinary support is available, the diagnosis provides a possibility to ensure better elaborate support of quality of life for patients and their families

Ethics approval and consent to participate:

The authors' institution does not require ethical approval for the publication of a single case report.

Consent to publication:

The patient's family provided written informed consent for the publication of this report and any applicable materials and a copy of the consent form is accessible for review by the Editor-in-Chief of this journal.

Availability of data and materials:

All data sets on which the conclusions of the case report are based, are to be available as a medical record document and available from the corresponding author on reasonable request from the editors.

Funding: None

Competing interests: The authors declare that they have no competing interests.

Authors' contributions:

BMG, MG, WG, BAA, and GZ were involved in the concept design for the manuscript, manuscript preparation, critical analysis, and revision. They were also involved in the management of the patient.

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We extend our gratitude to the patient and her family, who agreed to the publication of this article, as well as to the medical professionals and supporting staff who participated in the patient's care.

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Case Report
Ectopic intranasal tooth in a child with labiopalatoschizis: A rare case

Rano Aditomo[1], Yayun Siti Rochmah[2], Gabrina Selvi Yanuarista[1]

[1]Otorhinolaryngology Department, Faculty of Medicine, Sultan Agung Islamic University Semarang, Indonesia
[2]Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Sultan Agung Islamic University Semarang, Indonesia

*Corresponding author email: ranoaditomo@unissula.ac.id

Abstract
Ectopic teeth is a rare case in clinical practice. Intranasal teeth is particularly related to osteomyelitis, traumatic impaction and squamous cell carcinoma. Surgery is chosen to prevent these complications. This case report presents a 16 year old boy with ectopic intranasal tooth and labiopalatoschizis. The patient came with epistaxis as the major symptom. Endoscopic endonasal approach is the most common technique in patients with ectopic intranasal teeth due to its safety and outcomes are cosmetically satisfying.

Keywords: *intranasal teeth, labiopalatoschizis, ectopic tooth*
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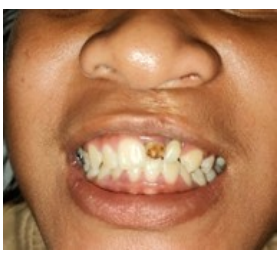
Submission date : *20 June 2018 Accepted: 27 June 2023 Published: 1 July 2023*

Introduction

Ectopic tooth is a rare case in clinical practice. The locations may vary and the most common site is maxillary sinus and palate. Some cases are found in mandibular condyle, coronoid process, orbits, intranasal and facial skin [1,4] Intranasal teeth is particularly related to osteomyelitis, traumatic impaction and squamous cell carcinoma. Signs and symptoms of intranasal ectopic teeth may vary from asymptomatic to chronic nasal obstruction and rhinosinusitis. Surgery is the main stay of treatment to prevent complications such as abscess, perforation or osteomyelitis [5]. The surgery chosen maybe either endoscopic endonasal, conventional endonasal or transoral approach. The endonasal method is the most preferred because of excellent lighting, shorter time of surgery, better visualization, and good dissection [6]. Here we present an intranasal ectopic tooth in child with labiopalatoschizis(Picture 1).

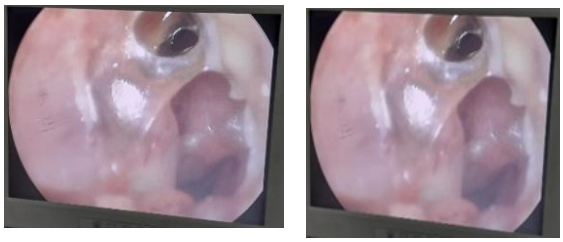


Picture 1. Abnormality shown during intraoral examination

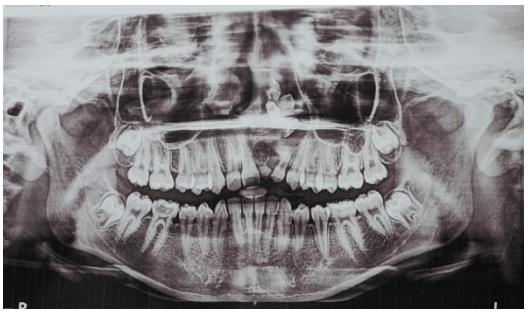
A 16- year- old male presented to our ENT clinic with symptom of recurrent epistaxis especially during cold weather. The patient had no other symptoms. He has no obvious facial abnormality. And he did not seek medical help. The patient has no history of trauma facial and head surgery, facial and head tumor or other relevant history related to his nose. During general examination, the patient looked healthy, had no difficulties in breathing, no fever and all of the vital signs were normal.

We performed intraoral and intranasal examination and we identified teeth in the nostril and defect in anterior maxilla. The patient was then referred panoramic x/ray (picture 2&3) and we could see teeth germs 21,22 and supernumerary teeth in superior aspect ofincisors61,62.

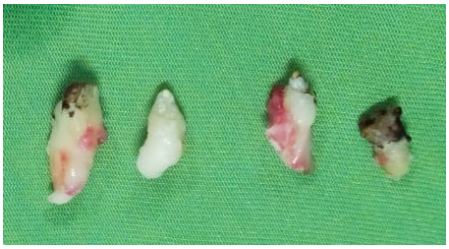
A B



Picture 2. Nasoendoscopy result. Nasoendoscopy showed four whitish foreign body (teeth) embedded in left nostril. A. Floor of the nasal cavitiy & anterior nasal septum. B. Posterior nasal septum.



Picture 3. Panoramic result. Panoramic showed teeth germs 21,22 and supernumerary teeth in superior aspect of incisors 61,62.



Picture 4. Extracted teeth from nasal cavity.

Due to repetitive epistaxis and aberration in the nasal mucosa, we performed surgery to extract the teeth. The teeth were extracted under general anesthesia. The teeth were found in the dental septum and the extraction process was guided by endoscopy. Before extraction, we infiltrated lidocaine and epinephrine around the teeth. Tooth extraction was then carried out from the nasal cavity by making a small incision in the nasal mucosa so that the teeth covered by the mucosa can be seen clearly. Extraction was carried out with forcep one by one until all were removed. After extraction, we sutured the incision with plain catgut size 3.0. The teeth in between the maxilla crest were extracted without endoscope and a concommittent oro-nasal defect could be seen. The defect was then sutured. The patient was then observed after the surgery, and there were no complications during post operative evaluation.

Discussion

The literature agrees that the most common treatment for intranasal teeth is early surgical extraction to prevent complications such as rhinosinusitis, osteomyelitis, dacryocystitis, nasal septal abscess or perforation, oronasal or intraoral fistula, aspergillosis, and nasal deformity. The extraction of intranasal teeth can be guided by endoscopy for clear visualization to minimize injury to nearby structures [7-9].

There are several approaches for surgery including endoscopic endonasal, conventional endonasal, or transoral approach. Choice of surgery depends on the experience of the surgeon, patient's age, presence of a bony socket, and depth of eruption. When endoscopic surgery is not feasible, the next choice must be conventional surgery. Endoscopic approach is widely known to be safer and more efficient technique than conventional surgery [10]

In our case, we used endoscopic endonasal approach for extracting the teeth. It provided excellent lighting, shorter time of surgery, better visualization, and precise dissection. It also offered better cosmetic outcome [10].

Conclusion

Endoscopy endonasal approach is the most common technique in patients with ectopic intranasal teeth due to its safety and outcomes. This technique is really helpful during surgery and the result is cosmetically satisfied.

Declaration

Ethical considerations

The study was conducted after securing ethical clearance from Bioethic Commision of Sultan Agung Islam University (UNISSULA) (letter no. 96/II/2023/ Komisi Bioetik). Since the study used secondary data, waiver of consent was obtained from Oral Surgery Department and Otolaryngology Head and Neck Department.

Competing interests:

The authors declare that they have no known competing interests.

Authors contributions

Data collection : Rano Aditomo, Yayun Siti Rochmah. Manuscript preparation : Gabrina Selvi Yanuarista. Translator: Rano Aditomo, Gabrina Selvi Yanuarista. Supervisor: Rano Aditomo, Yayun Siti Rochmah.

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ETHICAL CONSIDERATIONS

Researches Involving Human Participants

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

Explicitly:

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

Dealing with unethical behavior

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

- The Editor-in-Chief makes the decision regarding the initiation of an investigation.
- During an investigation, any evidence should be treated as confidential and only made available to those strictly involved in the process.
- The accused will always be given the chance to respond to any charges made against them.
- If it is judged at the end of the investigation that misconduct has occurred, then it will be classified as either minor or serious.
- Minor misconduct (with no influence on the integrity of the paper and the journal, for example, when it comes to misunderstanding or wrong application of publishing standards) will be dealt directly with authors and reviewers without involving any other parties. Outcomes include:
    - Sending a warning letter to authors and/or reviewers.-
    - Publishing correction of a paper, e.g. when sources properly quoted in the text are omitted from the reference list.
    - Publishing an erratum, e.g. if the error was made by editorial staff.
- In the case of major misconduct, the Editor-in-Chief may adopt different measures:
    - Publication of a formal announcement or editorial describing the misconduct.
    - nforming officially the author's/reviewer's affiliating institution.
    - The formal, announced retraction of publications from the journal in accordance with the Retraction Policy.
    - The formal, announced retraction of publications from the journal in accordance with the Retraction Policy.
    - A ban on submissions from an individual for a defined period.
    - Referring a case to a professional organization or legal authority for further investigation and action
    - The above actions may be taken separately or jointly. If necessary, in the process of resolving the case relevant expert organizations, bodies, or individuals may be consulted.
- When dealing with unethical behavior, the Editorial Board will rely on the guidelines and recommendations provided by the Committee on Publication Ethics (COPE).

Plagiarism prevention

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

- Self-plagiarism, which is using one's own previous work in another context without citing that it was used previously;
- Verbatim (word for word), or almost verbatim copying, or purposely paraphrasing portions of another author's work without clearly indicating the source or marking the copied fragment (for example, using quotation marks) in a way described under Responsibilities of authors;

* Copying equations, figures or tables from someone else's paper without properly citing the source and/or without permission from the original author or the copyright holder.

Any manuscript which shows obvious signs of plagiarism will be automatically rejected. In case plagiarism is discovered in a paper that has already been published by the journal, it will be retracted in accordance with the procedure described under Retraction policy, including blacklisting the author(s). To prevent plagiarism, submitted manuscripts will go through rigorous plagiarism detection process using standard software. The results obtained are verified by the Editorial Board in accordance with the guidelines and recommendations of the Committee on Publication Ethics (COPE).

Confidentiality

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

Conflict of interest

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

Retraction policy

Legal limitations of the publisher, copyright holder or author(s), infringements of professional ethical codes, such as multiple submissions, bogus claims of authorship, plagiarism, fraudulent use of data or any major misconduct require retraction of an article according to Retraction guidelines | COPE: Committee on Publication Ethics. Occasionally, a retraction can be used to correct numerous serious errors, which cannot be covered by publishing corrections. A retraction may be published by the Editor-in-Chief, the author(s), or both parties consensually. The retraction takes the form of a separate item listed in the contents and labeled as "Retraction". The original article is retained unchanged, except for a watermark on the PDF indicating on each page that it is "retracted".

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Self-archiving policy

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

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GUIDELINES FOR AUTHORS

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

Article types acceptable by EMJ

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

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

Content and format of articles:

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

1. Original Articles

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

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

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

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

c) Patients or (Materials) and Methods: should contain details to enable reproducibility of the study by others. This section must include a clear statement specifying that a free and informed consent of the subjects or their legal guardians was obtained. Corresponding author should submit a copy of institution review Board (IRB) clearance or letter of permission from the hospital or department (if IRB exempt)

with the manuscript. For manuscripts on clinical trials, a copy of ethical approval letter from the concerned body should be submitted with the Manuscript. If confidential data is being used for publication (such as student grades, medical board data, or federal ethics board data), then appropriate support/ agreement letter should be included. Photos of patients should disguise the identity or must have obtained their written consent. Reference number for ethical approval given by ethics committee should be stated. In general, the section should include only information that was available at the time the plan or protocol for the study was being written; all information obtained during the study belongs in the Results section.

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

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

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

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

h) References:

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

The following examples demonstrate the acceptable reference styles.

Articles:

- Gilbert C, Foster A. Childhood blindness in the context of Vision 2020: the right to sight. *Bull World Health Org 2001;79:227-32*
- Teklu B. Disease patterns amongst civil servants in Addis Ababa: an analysis of outpatient visits to a Bank employee's clinic. *Ethiop Med J 1980;18:1-6*

- Tsega E, Mengesha B, Nordenfelt E, Hansen B-G; Lindberg J. Serological survey of human immuno-deficiency virus infection in Ethiopia. *Ethiop Med J 1988; 26(4): 179-84*
- Laird M, Deen M, Brooks S, et al. Telemedicine diagnosis of diabetic retinopathy and glaucoma by direct ophthalmoscopy (Abstract). *Invest Ophthalmol Vis Sci 1996; 37:104-5*

Books and chapters from books:

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

Website:

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

2. Brief Communication

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

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

3. Case Series

Minimum of three and maximum of 20 cases

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

4. Case Report

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

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

5. Systematic review

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

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

6. Teaching Article

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

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

7. Editorial

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

8. Perspectives

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

9. Obituaries

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

Preparation of manuscripts

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

Submission of manuscripts

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

Conflict of interest

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

Manuscripts review procedures

The procedures for manuscripts review include:

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

General information

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

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

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

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THE ETHIOPIAN MEDICAL JOURNAL

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

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