ETHIOPIAN MEDICAL JOURNAL

OCTOBER 2024 VOLUME 62 NUMBER 4 ISSN0014-1755

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ETHIOPIAN MEDICAL ASSOCIATION

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

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

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Ethiopian Medical Journal 2024, 62 (4)
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ISSN 0014-1755 eISSN 2415-2420 Worku et al

Editorial

How to Minimize Common Biostatistical Errors in Clinical Research

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Biostatistics is essential for developing, interpreting, and drawing conclusions from clinical, biological, and epidemiological data. However, incorrect application of biostatistical methods can compromise the validity and reliability of study findings, leading to erroneous conclusions and misguided clinical practices. Clinicians and researchers must understand these pitfalls to ensure robust study design, accurate analysis, and meaningful interpretation of results. Many health researchers lack substantial biostatistical training and often do not collaborate with experts, leading to frequent errors in data analysis and presentation in published studies. Misusing biostatistics in health research is unethical and can result in severe clinical consequences, including incorrect conclusions, compromised study validity, and inaccurate treatment effect estimates (1,2). This editorial outlines the most frequent mistakes encountered in the biostatistical analysis process and offers tips to minimize these errors.

Many readers believe journal articles undergo thorough scrutiny by reviewers and editors, including a detailed examination of the biostatistical methods. However, this is often not the case. Common biostatistics errors includes: primary outcome measures are either not clearly stated or are ambiguous, no prior calculation of sample size or estimation of effect size, incorrect calculation of sample size, the study sample is not representative of the target population due to the use of inappropriate sampling techniques, use of an inappropriate control group, errors in summarizing data, insufficient graphical or numerical representation of essential data, employing an incorrect metric to describe the data, application of an inappropriate statistical test, using unpaired tests for paired data or vice versa, inappropriate multiple pairwise comparisons among more than two groups, using correlation as a measure of agreement, interpreting correlation as causation, failure to validate the assumptions of the test, inflation of Type I error, neglecting to adjust for multiple comparisons, over-interpreting results especially in small sample size studies, errors related with p-values, failure to use multivariable techniques to adjust for confounding, misunderstanding confounders and mediators, inappropriate interpretation and poor reporting of results, drawing conclusions not supported by the study data, and assuming that clinical significance is the same as statistical significance (1,3–7). These mistakes are well-documented and frequently discussed in numerous articles, yet persist in many journals. Identifying and addressing these errors can help authors, reviewers, and readers avoid them in the future, thereby improving the overall quality of manuscripts. By designing studies carefully and interpreting results within the context of clinical relevance and prior research objectives, we can overcome these pitfalls and ensure the accuracy and reliability of study findings. Raising awareness of these common mistakes will encourage authors and reviewers to be more vigilant, reducing their occurrence in the future (1,4).

While multifaceted statistical software packages make it easier for investigators with limited biostatistical skills to conduct their own data analysis, this can lead to significant problems due to a lack of understanding of the underlying statistical concepts (7). Since society relies on informed judgments supported by statistical methods, all practitioners must work professionally, competently, respectfully, and ethically regardless of their training, occupation, or job title. An ethical statistical practitioner is transparent about the assumptions made during the execution and interpretation of statistical practices, including the methods used, limitations, potential sources of error, and algorithmic biases (8).

Here are some approaches to minimize common biostatistical errors in clinical articles (1,2,5,7,9–11):

- Involve biostatisticians from the early study design phase, as errors at this stage can have significant repercussions, impacting all subsequent stages of health research, including data analysis and interpretation. Their expertise is invaluable in selecting appropriate study designs, calculating sample sizes, and planning analyses that strengthen the study methodology and ensure reliable results.

- Offer continuous training for researchers on biostatistical methods and common pitfalls.
- Utilize standard, reliable, and applicable instruments to evaluate the statistical rigor of manuscripts.
- Perform sensitivity analyses to evaluate the robustness of the study findings.
- Review submitted manuscripts for biostatistical aspects to prevent statistical and interpretation errors.
- Promote collaboration and peer review among multidisciplinary teams, including clinicians, epidemiolo gists, and biostatisticians

Journals play a crucial role in ensuring the quality and reliability of published health research. Since every journal aims to achieve a high scientific impact factor, maintaining research quality is essential. Researchers are responsible for understanding research methods, conducting the best possible studies, and publishing honest and unbiased results. By being aware of common pitfalls, researchers can enhance their studies' validity and contribute to advancing evidence-based medicine. Ultimately, by addressing these common mistakes and implementing the approaches mentioned above, researchers, reviewers, and editors can reduce the likelihood of biostatistical errors, significantly strengthening the rigor and credibility of clinical research articles. This leads to more accurate conclusions and improved patient outcomes (12,13).

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Ethiopian Medical Journal 2024, 62(4)
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ISSN 0014-1755 eISSN 2415-2420 Tsegaw et al.

Original Article

Treatment Outcomes and Prognostic Factors for Survival in Patients with Gastric Cancer: A Retrospective Study

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Abstract
Background: *Gastric cancer is the fifth most often diagnosed cancer and the third most frequent reason of cancer death worldwide. It is also associated with a lack of standard treatment strategies, particularly following first-line therapy. In Ethiopia, the survival status of gastric cancer patients was not well understood.*
Objective: *This study aimed to determine the clinical outcomes and prognostic factors for survival among gastric cancer (GC) patients in the adult oncology unit of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.*
Methods: *Hospital-based retrospective cohort study was conducted on 164 study participants recruited from patient registry between 1 January 2016 to 31 December 2020. Data was collected using a structured tool from medical records and telephone interviews Data analysis was performed using Descriptive and inferential statistics.*
Results: *The median (±SD) age of the study participants at diagnosis was 48.50 ±14.48 years. Adenocarcinoma accounted for 73.8% of the cases. Regarding clinical stage, 92 (56.1%) of the patients were diagnosed with stage IV and 84 (51.2%) of the cases had metastasized cancer, of which 47 (28.7%) participants presented with liver metastasis. About 40% (65) of the cases were treated with partial gastrectomy followed by bypass surgery. At the end of treatment follow-up, 110 (67.1%) of the patients were dead. A 5-year overall survival rate was 11% with a median survival time of 18.6 months. In multivariate logistic regression, ECOG ≥ 2 (AHR= 2.5, P=0.001)***, adenocarcinoma histologic type (AHR=0.4, P=0.004), ovary metastasis (AHR=2.9, P=0.035), liver + lung metastasis (AHR=2.4, P= 0.048), paclitaxel + carboplatin chemotherapy (AHR=0.3, P= 0.044) were found to significantly affect survival of the GC patients.*
Conclusion: *The survival outcome of gastric cancer is low and requires early detection in this study setting. The findings underscore the importance of early detection and tailored treatment approaches based on prognostic factors.*

Keywords: *Gastric cancer, treatment outcome, prognostic factor, Tikur Anbessa Specialized Hospital.*
Citation : *Tsegaw H, Beyene A, Tamiru M et al. Treatment Outcomes and Prognostic Factors for Survival in Patients with Gastric Cancer: A Retrospective Study Ethiop Med J 62 (4) 15-24*
Submission date : *21 August 2024 Accepted: 18 September 2024 Published: 01 October 2024*

Introduction

Gastric cancer is the fifth most often diagnosed cancer and the third most frequent reason for cancer death worldwide (1). It is also associated with a lack of standard treatment strategies, particularly following first-line therapy. In Ethiopia, the survival status of gastric cancer patients is not well understood. Gastric cancer (GC) is the fifth most often diagnosed cancer and the third most frequent cause of cancer death worldwide.

In 2020, more than 1,089,000 new cases and 770, 000 patients died of GC worldwide (2). This could be attributed to lack of standard treatment strategies, particularly following first-line therapy(2). Risk factors for GC include male gender (incidence is double), Helicobacter pylori infection, tobacco use, atrophic gastritis, partial gastrectomy, and Ménétriers disease (3).

There is a large variation in the incidence of GC in different geographical regions. While the incidence of GC is high in China, Japan, and Korea, it is relatively low in most of Europe, North America, and Africa (4). The World Health Organization (WHO) estimates a 15%

increase in non-communicable illnesses worldwide, with more than a 20% increase occurring in Africa between 2010 and 2020. Mali, West Africa, is ranked 15th (5).

The highest prevalence of GC is found in a region comprising Rwanda, Burundi, Southwestern Uganda, and Eastern Kivu province of the Democratic Republic of Congo (6). There is a great deal of variation in reported incidence and mortality among individual African countries. In Ethiopia, available works in the literature place GC 9th among all cancers in incidence (7).

GC is an aggressive malignancy whose management and early detection are challenging. There is no national or institutional guideline on GC in Ethiopia, and healthcare professionals use international guidelines. Moreover, no study was previously done on the treatment pattern, histologic types, survival status, and associated factors in GC patients in Tikur Anbessa Specialized Hospital (TASH), Ethiopia. Generating evidence on histologic types, treatment patterns, treatment outcomes of various cancers, survival status, and associated prognostic factors has important practical value for patients, healthcare providers, and researchers. Hence, the objective of the study is to determine the clinical outcomes and prognostic factors for survival among GC patients in the adult oncology unit of TASH, Addis Ababa, Ethiopia.

Materials and Method

A retrospective hospital-based study design was used. Data were extracted from March 10 to July 12, 2021, from the medical charts of GC patients who attended the adult oncology unit of TASH from January 1, 2016, to December 31, 2020. The hospital, established in 1972, serves as the main referral center for the nation. It is a teaching hospital for health science students and provides management services for more than 10,000 cancer patients, including chemotherapy and radiotherapy.

Eligibility criteria

Adult patients aged ≥ 18 years old with histologically confirmed GC and, on chemotherapy were included. Whereas, the patients who had incomplete information on registration and medical charts (no information about phone number, age, sex, and residency) and those with non-carcinomatous gastric tumors were excluded.

Study variables

Treatment outcome (Death/ survival) was the dependent variable. In addition, patient-related variables (age at diagnosis and sex), disease-related variables (stage of cancer at diagnosis, histologic type /grade, duration of symptoms, Initial cancer site, and Eastern Cooperative Oncology Group performance status, ECOG PS), and medication-related variables (duration of chemotherapy (number of cycles) and type of chemotherapy regimen) were the independent variables.

Sample size determination and sampling procedure

All GC patients receiving treatment during the study period and fulfilling the inclusion criteria were included in the study. Data (no report of histopathology, treatment, phone number, and cancer stage) were incomplete for 39 patients. Finally, the records of 164 patients were used for the final analysis.

Data Sources, Collection and Management

A data abstraction form was designed based on the availability of information on patient charts and reviewing the literature and utilized to collect information on socio-demographic features, clinical and pathological characteristics, and treatment approaches used. Phone interview of patients or their families was also performed to collect current event status, date of death if they died, and the presence of co-morbidities, which were not explicitly recorded in the patient charts. Data were collected by a trained pharmacist and nurse. The instruments were pretested on 5% of the sample and appropriate modifications were performed accordingly. Quality of the data was maintained through appropriate training of the data collectors and pretesting of the instrument. Additionally, daily follow-up was made by the supervisor to confirm accuracy and consistency of the collected data.

Data Analysis

Basic descriptive statistics like frequency, proportion, mean, and median were used, and data are presented using tables and graphs. Kaplan Meier analyses with a life table were used to identify the overall survival rates and median survival time. Variations in survival among different variables were compared using the log-rank test. Before running the Cox regression model, the assumption of proportional hazard was tested, and variables with a p-value > 0.05 were considered. All variables with $p<0.2$ in the bi-variable Cox regression model were included in a multivariable Cox regression model analysis. Variables in the multivariable Cox model with a p-value < 0.05 were considered to have a significant association with survival of patients at a 95% confidence interval.

Operational definitions

ECOG PS is a prognostic factor classified as : 0 - Fully active, able to carry out all pre-disease performance without restriction, 1- Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work, 2- Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours, 3- Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours, 4-Completely

disabled. Cannot carry on any self-care. Totally confined to bed or chair, 5- Dead (8)

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Ethics Committee of the School of Pharmacy, College of Health Sciences, Addis Ababa University (Ref No: ERB/ SOP/173/08/2020). Permission to conduct the study was also sought from the Oncology Unit of the Department of Internal Medicine, School of Medicine, College of Health Sciences, Addis Ababa University.

The School of Pharmacy Ethical Review Committee and the Oncology Unit of the Department of Internal Medicine granted waiver the need to obtain informed consent for the collection, analysis, and publication of the retrospectively obtained and anonymized data for this non-interventional study. All methods were carried out in accordance with the relevant guidelines and regulations. Only numerical identifications were used as a reference. Confidentiality and anonymity of subjects were maintained by excluding identifiers, such as names or any other personal identifiers. No disclosure of any names of the patients or healthcare providers was made in relation to the findings.

Results

Socio-Demographic Characteristics

The socio-demographic characteristics of the study participants are depicted in Table 1. Out of the 164 GC patients included in the study, males comprised 64% of the sex category with a male- to-female ratio of 1.8:1. The median age of the study participants at diagnosis was 48.50 years (with the youngest being 18 years and the oldest 87 years). Of these, 83 (50.6 %) were between 40-60 years of age, and 74 (45.1%) came from the Oromia Region. A sizable proportion of the study participants were married (143, 87.2%) (Table 1).

Table 1: Socio-demographic characteristics of gastric cancer patients treated at the Oncology Unit of Tikur Anbessa Specialized Hospital between 1 January 2016 and 31 December 2020, Addis Ababa, Ethiopia (n=164).

Variables	N (%)
Gender	
Male	105(64.0)
Female	59(36.0)
Age	
< 40 years	50(30.5)
40-60 years	83(50.6)
>60 years	31(18.9)
Region	
Oromia	74(45.2)
Addis Ababa	52(31.7)
SNNPR	24(14.6)
Amhara	12(7.3)
Dire Dawa	2(1.2)
Religion	
Orthodox	93(56.7)
Muslim	56(34.2)
Protestant	15(9.1)
Marital status	
Married	143(87.3)
Single	14(8.5)
Widowed	3(1.8)
Divorced	4(2.4)

Southern Nations, Nationalities, and Peoples' Region

Clinical and Pathological Characteristics

All the 164 GC patients had a documented initial functional status at the time of diagnosis. For instance, nearly two-third of the patients (113, 68.9%) had ECOG Performance Status score of 0-1, and almost half of the cases (87, 53%) had ⩾ 6 months since the first symptom started. The most common site of the tumors and cancer cell type were the antrum (101, 61.6%), and adenocarcinoma (AC) (121, 73.8%), respectively. As regards to pathological grading, half (82, 50.0%) of the participants had poorly-differentiated GC. Regarding clinical stage, 92 (56.1%) of the patients were diagnosed with stage IV, and 84 (51.2%) of the cases had metastasized cancer, of which 47 (28.7%) had liver metastasis (Table 2).

Table 2: Clinical and pathological characteristics of gastric cancer patients treated at the Oncology Unit of Tikur Anbessa Specialized Hospital between 1 January 2016 and 31 December 2020, Addis Ababa, Ethiopia (n=164).

Variables	N (%)
ECOG performance at diagnosis	
ECOG 0-1	113(68.9)
ECOG ⩾2	51(31.1)
Duration since the first symptom start	
<6month	77(47.0)
⩾6month	87(53.0)

Site of tumor	
Antrum	101(61.6)
Body	21(12.8)
Cardia	17(10.4)
Gastro-oesophageal junction	15(9.1)
Fundus	10(6.1)
Histopathology	
Adenocarcinoma	121(73.8)
Squamous cell carcinoma	30(18.3)
Lymphoma	13(7.9)
Pathological grading	
Poorly-Differentiated	82(50.0)
Moderately-Differentiated	45(27.4)
Well-Differentiated	37(22.6)
Stage	
4	92(56.1)
3	32(16.5)
2	27(17.7)
1	13(7.9)
Recurrences	
Yes	26(15.9)
No	138(84.1)
Metastasis of disease	
Yes	84(51.2)
No	80(48.8)
Site of Metastasis (n=84)	
Liver	47(28.7)
Lung	17(10.4)
Ovary	10(6.1)
Lung and liver	10(6.1)

Eastern Cooperative Oncology Group

Treatment Approaches Used

The approaches used for treating GC patients are depicted in Table 3. Out of the 164 patients with a confirmed diagnosis of GC, 80 (48.7%) were given palliative care. Whilst 68 (41.5%) patients did not undergo surgery, about 65 (40%) of the cases were treated with partial gastrectomy followed by bypass surgery. The duration between surgery and chemotherapy for almost half (83, 50.6%), of the patients was ⩾ 3 months. The commonest chemotherapy regimen was Cisplatin with paclitaxel (85, 51.8%) followed by Cisplatin with 5- Fluorouracil (5-FU) (49, 29.9%) (Table 3).

One hundred forty-nine (90.9%) of the cases took < 7 cycles of chemotherapy. Of the study participants, 36 (22.0%) had comorbidity and 110 (67.1%) patients died after 15.5 months of median follow-up.

Table 3: Description of the pattern of treatment used to treat gastric cancer patients at the Oncology Unit of Tikur Anbessa Specialized Hospital between 1 January

Variables	N (%)
Treatment aim	
Palliative	80(48.7)
Adjuvant	78(47.6)
Neo-adjuvant	6(3.7)
Type of surgery performed	
No surgery	68(41.5)
Partial Gastrectomy	65(39.6)
Bypass surgery	28(17.1)
Total Gastrectomy	3(1.8)
Duration between surgery and chemotherapy	
〈3 months	46(28.1)
⩾ 3 months	83(50.6)
Unknown	35(21.3)
Types of chemotherapy regimens taken	
Cisplatin + Paclitaxel	85(51.8)
Cisplatin + 5 FU	49(29.9)
Paclitaxel + carboplatin	17(10.4)
CHOP	13(7.9)
Treatment change	
No	130(79.3)
Yes	34(20.7)
Co-morbidity	
No	128(78.0)
Yes	36(22.0)
Discontinuing Chemotherapy cycles	
〈 7 cycles	149(90.9)
⩾ 7 cycles	15(9.1)
Follow up	
Yes	41(25.0)
No	123(75.0)
Treatment outcomes	
Dead	110(67.1)
Alive	54(32.9)

Overall Survival Rate

A 5-year overall survival rate was 11% with a median survival time of 18.6 months (1-54 months) (95% CI:16.4 -19.6). The estimated cumulative survival rates of GC patients at the 1st, 2nd, 3rd, and 4th months were 66%, 32%, 18%, and 13%, respectively. The probability of survival was highest on the first day of diagnosis of GC, but it decreased with increase in follow-up time (**Figure 1**).

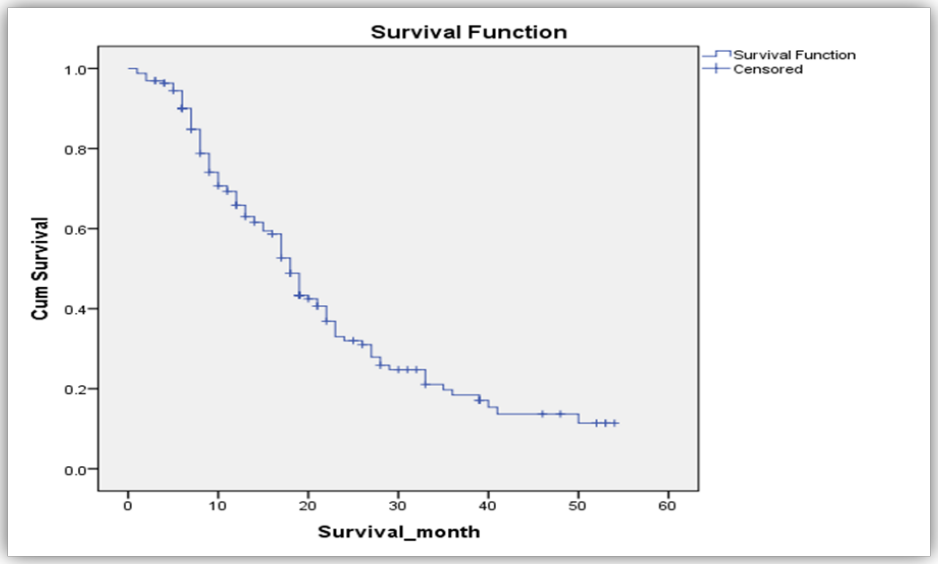

Figure 1: Kaplan Meier Plot for overall survival function in months of patients treated for gastric cancer at the Oncology Unit of Tikur Anbessa Specialized Hospital between 1 January 2016 to 31 December 2020 Addis Ababa, Ethiopia (n= 164).

Survival Estimates Among Associated Variables

(A)

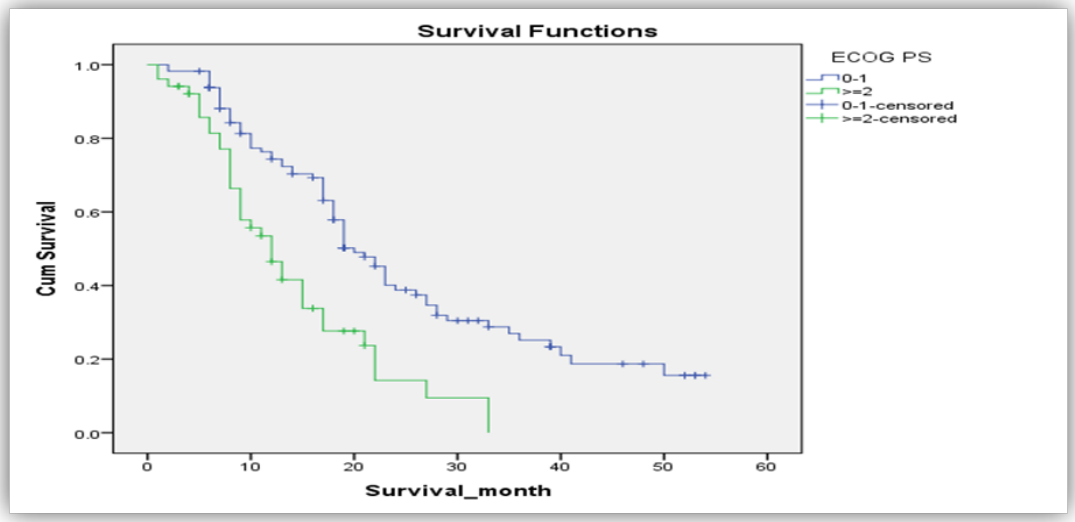

Figure 2A: The study found that the median survival time of GC having ECOG PS ≥ 2 was significantly ($p<0.001$) shorter than those with ECOG PS 0-1 (12.0 months 95% CI: 8.9-15.0).

(B).

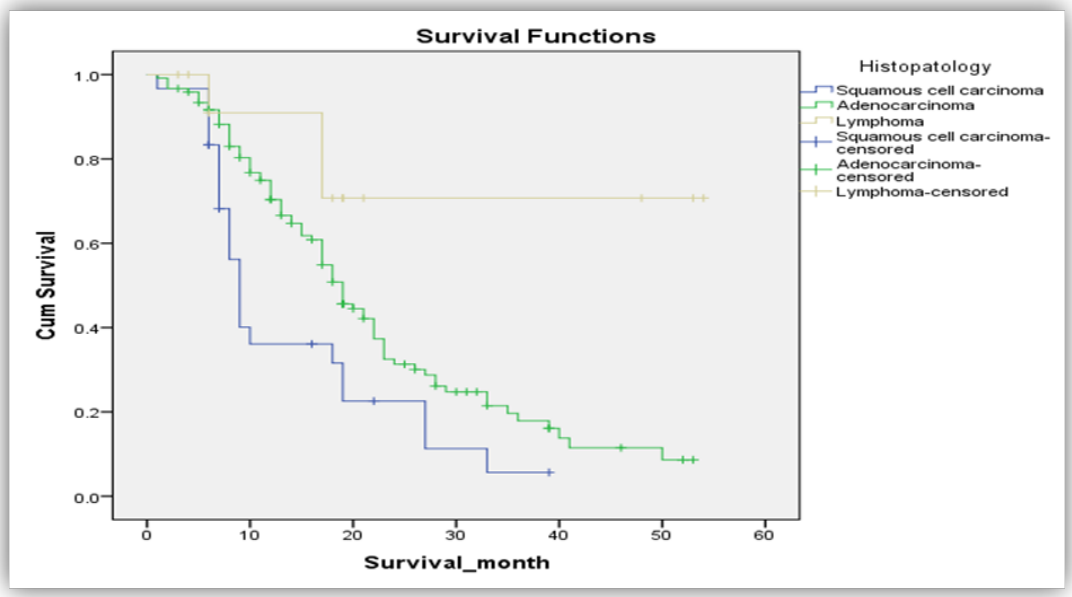

Figure 2B: Patients with AC had a shorter median survival time (22.0 months, 95% CI: 16.6- 21.3) (p< 0.004) than those with squamous cell carcinoma (SCC).

(C)

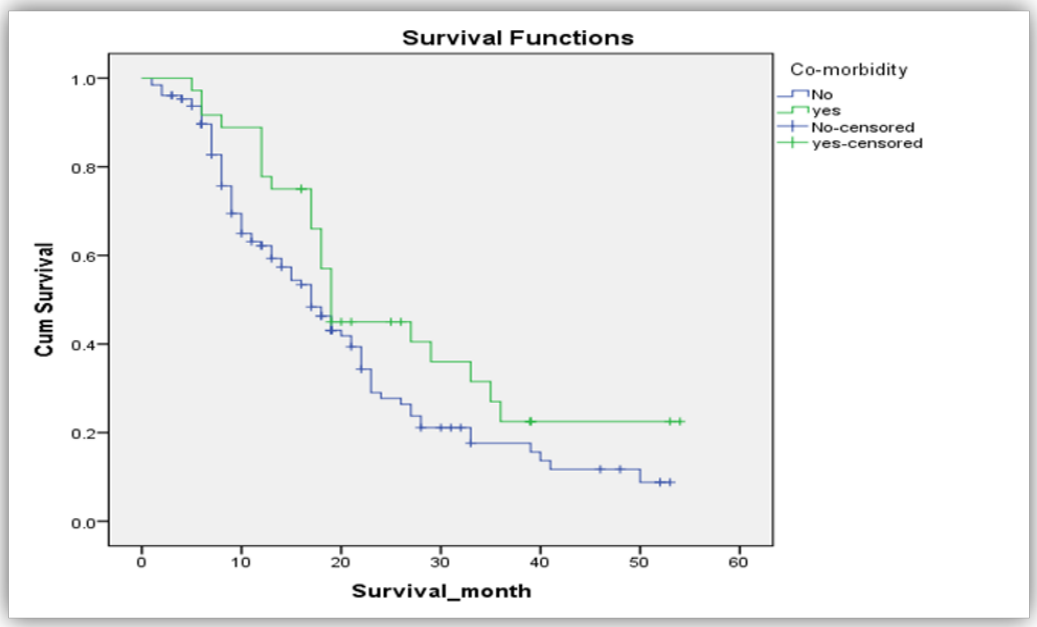

Figure 2C: Patients with comorbidity had less survival time as compared to those without comorbidity (17.0 months, 95% CI:17.6-20.4) (P < 0.037).

(D)

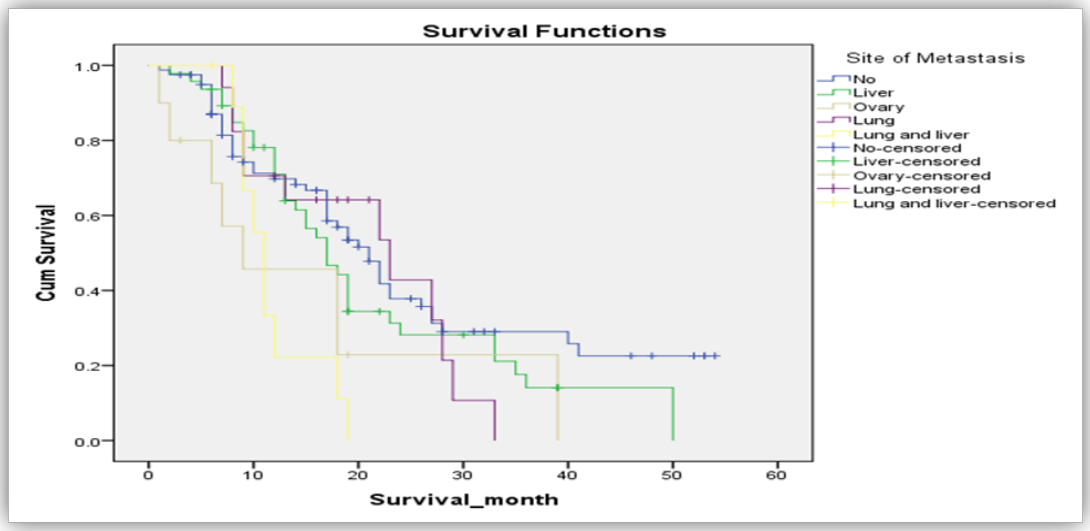

Figure 2D: Survival time for those with ovarian (9.0 months, 95% CI: 10.0-19.4) and liver + lung (11.0 months, 95% CI: 9.6-12.4) metastases was significantly lower compared to those with other sites of metastasis.

(E)

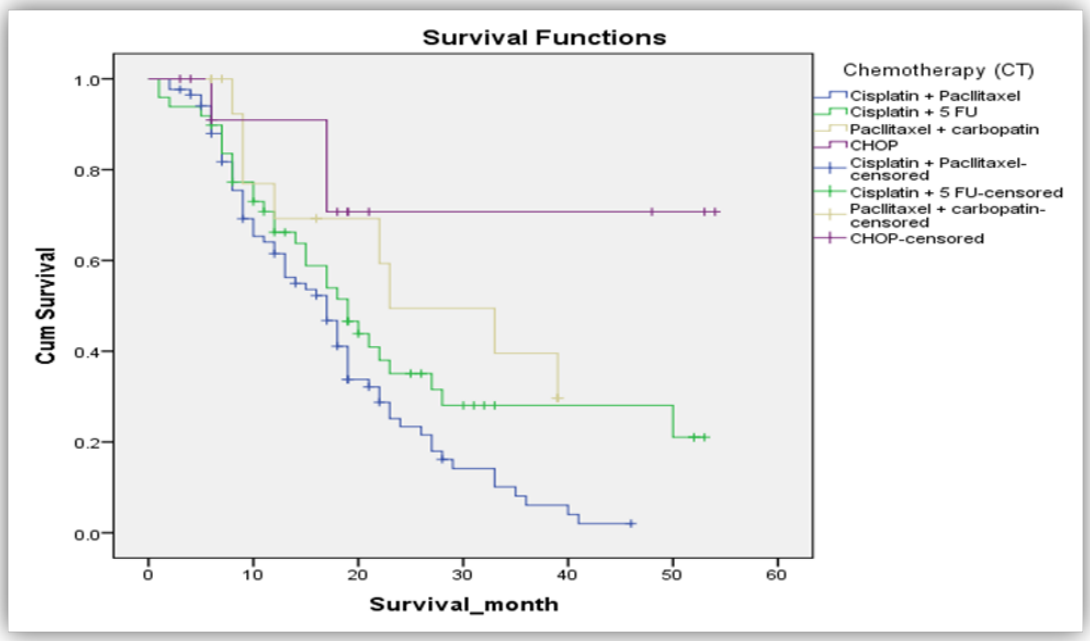

Figure 2E: Patients on paclitaxel + carboplatin had more survival time (23.0 months, 95% CI: 17.5-28.5) ($p < 0.006$) compared to those who received cisplatin + paclitaxel.

Figure 2: Kaplan-Meier survival function among different groups of gastric cancer patients: (A); ECOG PS (B); Histopathology (C); comorbidity (D); metastasis (E); Chemotherapy at Tikur Anbessa Specialized Hospital between 1 January 2016 to 31 December 2020, Addis Ababa, Ethiopia (n= 164).

Predictors of Gastric Cancer Mortality

Univariate analysis revealed that factors including age, sex, ECOG, histopathology, pathologic grading, stage, comorbidity, and metastasis site, surgical treatment modality, chemotherapy, and regimen change contribute to mortality. In multivariable analysis, ECOG PS, histopathology, comorbidity, metastasis site, and type of chemotherapy were found to have significant impact on survival ($p < 0.05$) (Table 4). Patients with ECOG PS ≥ 2 had 2.5 times higher risk of death (adjusted hazard ratio (AHR) =2.5, 95% CI: 1.4-4.5) as compared to those with ECOG PS 0-1 patients. Patients with AC had a 60% less chance to die (AHR = 0.4, 95% CI: 0.2-0.7) as compared to SCC. GC patients with comorbidities were 1.8-fold (AHR = 1.8, 95% CI:1.2-3.3) more likely to die compared to non-co-morbid conditions. Patients with ovarian metastasis as well as liver and lung metastases had 2.9 (AHR = 2.9, 95% CI:1.1-7.9) and 2.5 (AHR = 2.5, 95% CI:1. 9-6.5) times, respectively, higher risk of death than those with-out metastasis, . Patients on paclitaxel + carboplatin had a 70% less risk of death compared to those on cisplatin + paclitaxel (AHR = 0.3, 95% CI: 0.1-0.9) (Table 4).

Table 4: Univariate and multivariate analysis of factors contributing to survival in gastric cancer patients treated at the Oncology Unit of Tikur Anbessa Specialized Hospital between 1 January 2016 and 31 December 2020, Addis Ababa, Ethiopia (n=164).

Variable	Patients		Events		Median Survival Time	Crude HR (95% CI)	Adjusted HR (95% CI)	P-value
	N	%	N	%				
Age								
<40	50	30.5	30	18.3%	18.9	1	1	
40-60	83	50.6	56	34.1%	19.2	1.3(0.7-2.1)	0.7(0.4-1.4)	0.342
>60	31	18.9	24	14.6%	17.5	1.5(0.8-2.7)	0.8(0.4-1.8)	0.654
Sex								
Male	105	64.0	74	45.1	18.0	1	1	
Female	59	36.0	36	22.0	19.0	0.6(0.4-1.0)	0.6(0.4-1.2)	0.158
ECOG								
ECOG 0-1	113	68.9	72	43.9	20.0	1	1	
ECOG ≥2	51	31.1	38	23.2	12.0	2.4(1.5-3.5)	2.5(1.4-4.5)	0.001*
Histopathology								
Squamous cell carcinoma	30	18.3	23	14.0	14.0	1	1	
Adenocarcinoma	121	73.8	84	51.2	22.0	0.5(0.3-0.7)	0.4(0.2-0.7)	0.004*
Lymphoma	13	7.9	3	1.8	42.0	0.1(0.0-0.5)	0.4(0.1-2.1)	0.292

Pathological grading								
Well-Differentiated	37	22.6	22	13.4	21.0	1	1	
Moderately-Differentiated	45	27.4	26	15.9	19.0	0.9(0.5-1.7)	0.8(0.4-1.7)	0.522
Poorly-Differentiated	82	50.0	62	37.8	17.0	1.6(1.0-2.6)	0.9(0.5-1.9)	0.915
Stage								
Stage 1	13	7.9	8	4.9	20.0	1	1	
Stage 2	27	16.5	12	7.3	23.0	0.6(0.2-1.5)	0.2(0.0-1.6)	0.07
Stage 3	32	19.5	21	12.8	18.0	1.4(0.6-2.9)	0.4(0.1-1.3)	0.136
Stage 4	92	56.1	69	42.1	17.0	1.8(0.9-3.6)	0.5(0.2-1.4)	0.198
Co-morbidity								
No	128	78.0	86	52.4	19.0	1	1	
Yes	36	22.0	24	14.6	17.0	1.4(0.9-2.3)	1.8(1.2-3.3)	0.037*
Site of Metastasis								
No	80	48.8	46	28.0	21.0	1	1	
Liver	47	28.7	35	21.3	17.0	1.3(1.8-2.0)	0.9(0.5-1.8)	0.965
Ovary	10	6.1	8	4.9	9.0	2.1(1.0-4.6)	2.9(1.1-7.9)	0.035*
Lung	17	10.3	12	7.3	23.0	1.1(0.6-2.2)	0.4(0.2-1.1)	0.100
Lung and liver	10	6.1	9	5.5	11.0	2.9(1.4-6.1)	2.4(1.9-6.5)	0.048*
Surgical Treatment Modality								
No surgery	68	41.5	49	29.9	16.0	1	1	
Total Gastrecto-my	3	1.8	1	0.6	26.0	0.3(1.0-2.3)	0.3(0.0-4.5)	0.391
Partial Gastrecto-my	65	39.6	40	24.4	23.0	0.5(0.3-0.8)	0.3(0.1-1.1)	0.067
Bypass surgery	28	17.1	20	12.2	11.0	1.0(0.6-1.7)	0.4(0.1--1.3)	0.150

Types of chemotherapy regimens taken								
Cisplatin + Paclitaxel	85	51.8	68	41.5	17.0	1	1	
Cisplatin + 5 FU	49	29.9	31	18.9	19.0	0.6(0.4-1.0)	0.6(0.3-1.1)	0.081
Carboplatin + Paclitaxel	17	10.4	8	4.9	23.0	0.4(0.2-0.9)	0.3(0.1-0.9)	0.044*
CHOP	13	7.9	3	1.8	35.0	0.2(0.0-	0.6(0.3-1.2)	0.162
Regimen change								
No	130	79.3	82	50.0	19.0	1	1	
Yes	34	20.7	28	17.1	17.0	0.7(0.5-1.1)	1.6(0.7-3.4)	0.184

Variables showing significant association with mortality

Discussion

This study assessed the outcomes of GC patients in a tertiary care hospital in Ethiopia. The male predominance (1.8:1) aligns with other studies from various countries, including US-Mexico (4), Turkey (5), Taiwan(6), Nigeria(7), and Ethiopia(8) suggesting potential gender-related risk factors, including the protective role of estrogen(9).

The median age at diagnosis was 48.5 years, with 50.6 % of patients between 40-60 years. This is concordant with the Nigerian (7) and other Ethiopian studies (8), but lower than the Taiwan study (5). This discrepancy could be due to differences in life expectancy, socio-economic status, and dietary habits, including the consumption of raw red meat and high-fat content in Ethiopia, as well as the lack of birth registration in rural areas.

Most patients were from Oromia (45.1%), consistent with previous findings(8). The proximity to TASH and limited tertiary care facilities in the region may explain this distribution. The predominant tumor location was the antrum (61.6%), consistent with studies in Nigeria (64.8%)(7) and Ethiopia (40.7%)(8) but differing from US-Mexico(4), Turkey(6), and Taiwan(5), where proximal locations were more common. This variation might be due to geographical differences, genetic polymorphisms, time trends, and lifestyle factors.

AC was the most common histopathological type (73.8%), aligning with studies in Turkey (6) Iran(10), and China(11). Half of the patients had poorly differentiated carcinoma, similar to findings in China (12) and Korea(13), indicating a high prevalence of aggressive tumor types in these populations.

Contrary to some studies, the stage of GC was not significantly associated with survival in our study, possibly due to differences in sample size, study design, and follow-up period. For instance, the Italian study showed that the 5-year overall survival decreased from 75.0% for stage 0–I to 1.7% for stage IV(6,14). Around 51.2.% of patients had metastatic cancer at presentation, similar to reports from Turkey(15), Iran(16), and Ethiopia(8). Late presentation could be attributable to the asymptomatic nature of early-stage GC, lack of screening programs, and poor healthcare accessibility, especially for patients living far from TASH.

Partial gastrectomy was performed in 39.6% of the cases, consistent with reports from China (11) and US-Mexico(4). However, studies in Japan and Iran reported higher rates of complete resection(9, 10), likely due to differences in surgical practices and healthcare infrastructure. Our study showed a survival rate of 32.9%, with death occurring in 67.1% of patients, similar to studies in Latin America (4) , Italy(17), China (11), and Turkey(18, 6). This similarity may be due to delayed diagnosis, advanced lymph node metastasis, and frequent peritoneal dissemination at first operation.

The 1-, 3-, and 5-year survival rates of GC patients were 66%, 18%, and 11%, respectively. These findings are lower than other studies due to limited healthcare access, lack of early-stage cancer screening programs, and late-stage diagnosis(4, 10, 18). Variations in study design and local cancer care may also contribute to differences in survival rates. The Kaplan-Meier survival

curves stratified by AJCC staging, with the number at risk, are presented to address this aspect.

In the multivariable Cox regression model, ECOG PS ⩾ 2, AC histologic type, ovary metastasis, liver + lung metastasis, and paclitaxel + carboplatin were significant prognostic factors for poor survival. Patients with ECOG PS ⩾2 had a higher risk for death than those with ECOG performance 0-1 patients. This finding is supported by studies conducted in Italy(17), Korea(19), and Japan (20), indicating that high ECOG PS is associated with poor survival outcomes across different populations.

In the current study, patients with AC were 40% less likely to die than those with SCC. This is similar to studies done in the USA (21) and China (22), which revealed that SCC had a worse chance of survival compared to AC histology, possibly due to the aggressive nature and late-stage identification of SCC.

GC patients with a comorbid condition had a 1.8 times higher risk of death than non-comorbid conditions. This is in agreement with studies conducted in Canada(23) and Nigeria (7), suggesting that comorbidities significantly impact survival by limiting treatment options and increasing complications.

In the present study, patients with ovarian metastasis and liver + lung metastasis were more likely to die and this in line with other studies conducted in Japan, showing that GC metastasis to these sites is associated with poor prognosis [24]. In addition, Kim et al. (23) and Catalano et al. (20) confirmed that multiple metastatic sites increase the risk of death.

The finding of this study demonstrates that patients on paclitaxel + carboplatin had a decreased likelihood of death than those on cisplatin + paclitaxel. This is discordant with other studies in Italy (14), and Turkey (6) ,which could be due to differences in treatment protocols availability of anticancer agents and the toxicity profile of cisplatin.

Limitation of the study

Because the data were gathered retrospectively, it is possible that not all of the relevant information from the patients' charts could be extracted. It was also difficult to generalize the findings of a small sample size study conducted at a single facility. Patients with incomplete records were excluded, which may have induced selection bias during secondary data collection.

Despite the limitations listed above, the study's main strength was that it examined the entire treatment pattern for GC in Ethiopia as well as the median survival rate to determine the patients' status using chart review and a phone interview. This study was carried out at the TASH Radiotherapy Center, the country's first and largest radiotherapy facility, which may represent the majority of the country's population.

Recommendation

There is a need for additional research to be conducted using longitudinal designs, longer durations of follow-up, larger sample size and multicentre studies to better investigate the clinical outcomes and prognostic factors for survival among GC patients in Ethiopia.

Conclusions

Patients with GC had a low five-year overall survival rate. Significant predictors of mortality included ECOG PS ≥2, AC histology, comorbidities, ovary and liver + lung metastases, and carboplatin + paclitaxel. Early detection and improved treatment strategies are needed to enhance survival outcomes.

Abbreviation and Acronyms

AC: Adenocarcinoma;
AOR: Adjusted Odds Ratio;
CI: Confidence Interval;
COR: Crude Odds Ratio;
GC: Gastric Cancer;
OS: Overall Survival;
PFS: Progress Free Survival;
SCC: Squamous Cell Carcinoma;
SPSS: Statistical Package for the Social Sciences;
TASH: Tikur Anbessa Specialized Hospital;
WHO: World Health Organization
ECOG: Eastern Cooperative Oncology Group

Consent for Publication

Not applicable

Availability of data and material

All relevant data are included in the article and uploaded as supporting information files. Extra data can be accessed upon reasonable request from the corresponding author.

Competing interests

The authors declare that they have no competing interests.

Funding

The study was financially supported by Addis Ababa University to collect the data. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

H.T designed and conducted the study, analyzed, and interpreted results, and drafted the manuscript. E.E and

A.B.B contributed to the conception and design of the study, analysis, interpretation, supervision, drafting the manuscript, and its critical review. A.F contributed to study supervision and review the manuscript. M.T.T contributed to enriching the manuscript. All authors approved the final version of the manuscript to be published.

Acknowledgements

We would like to express our gratitude to all data collectors and support staff working in the medical record room of TASH and to the patients and family members

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https://dx.doi.org/10.4314/emj.v62i4.3

Ethiopian Medical Journal 2024, 62(4)
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ISSN 0014-1755 eISSN 2415-2420

Original Article

Prevalence of Asthma among Adults in Northwestern Ethiopia: Implications for Health Planning and Management

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Abstract

Background: *Bronchial asthma is a chronic inflammatory airway disease that substantially burdens individuals and healthcare systems. Regular investigation of its severity and identifying the factors that lead patients to seek medical care is crucial for effective health planning, management, and prevention to reduce healthcare costs and morbidity/mortality rates while fostering productive citizenship. The study aimed to assess the magnitude of asthma severity and associated factors that prompt adult patients to visit healthcare services in the Awi administrative zone of Northwestern Ethiopia.*

Method: *This study used a cross-sectional study design. Data from 662 asthma patients were collected using structured questionnaires and multistage sampling. The collected data were analyzed using the ordinal logistic regression model to determine how asthma status (the dependent variable) is affected by sociodemographic (independent) variables and the chi-square test of independence to determine the significance of the association between asthma status and the sociodemographic variables.*

Results: *Among the 662 asthma patients, the severity of 43.5%, 41.84%, and 14.65% of them was mild, moderate, and severe, respectively. The factors that affect the severity of asthma significantly are bad smells in the environment (AOR=0.02, $p<0.001$), marital status (AOR=0.003, $p<0.001$), educational level, physical exercise (AOR=5127.7, $p<0.001$), family history of asthma (AOR=90.05, $p<0.001$), presence of animals at home (AOR=0.0002, $p<0.001$), high asthma distribution season, limited daily activity (AOR=0.479, $p=0.027$), and energy source for cooking ($AOR=4.63x10^{-6}$, $p<0.001$).*

Conclusion: *The findings highlight the need for tailored interventions to promote asthma disease prevention strategies and the need to implement several interventions by the Awi Zone health office and non-governmental organizations to reduce asthma disease severity.*

Keywords: *Northwest Ethiopia, logistic regression model, bad smell, Bronchial asthma, Healthcare systems*
Citation : *Nigussie A, Atnkut B, Alemayehu GA et al. Prevalence of Asthma among Adults in Northwestern Ethiopia: Implications for Health Planning and Management. Ethiop Med J 62 (4) 15-24*
Submission date : *29 July 2024 Accepted: 18 September 2024 Published: 01 October 2024*

Introduction

Asthma is a chronic inflammatory disease of the airways that can cause shortness of breath, tightness in the chest, coughing, and wheezing symptoms (1). Asthma is one of the most prevalent chronic inflammatory illnesses of the airway, resulting in increased contractibility of the surrounding smooth muscles and worsened pulmonary function (2). If this inflammation is not treated, it will lead to an asthma attack and tightens the muscles around the bronchial tubes causing the airways to narrow. Mucus is produced within the bronchial tubes, further restricting airflow (3).

Asthma is considered a public health problem worldwide (4), negatively affecting patients, their families, and the community. It also creates a major economic and social burden (5). Asthma is documented as a common chronic disease that affected 5–10% of the population during the past 20 years (6).

The prevalence of asthma in Africa is estimated to be around 74 million people (11.7%) in 1990 and 120 million people (12.8%) in 2010 (4). During these years, the cumulative prevalence of asthma was the highest in South Africa (53%, 5-12 years) in 1997, followed by Egypt (26.5%, 11-15 years) in 2005, Nigeria (18.4%, 15 -35 years) in 1995, and Ethiopia (16.3%, >20 years) in 1997 (4).

Bronchial asthma is one of the public health problems in Ethiopia. The prevalence of bronchial asthma has increased recently with different contributing factors such as cigarette smoking (7), household economic status (8), occupational condition (9), type of residence (10), and a family history of asthma (11). Bronchial asthma is one of the diseases that cause chronic morbidity and mortality worldwide (12, 13). One of the significant causes of bronchial asthma-related morbidity is poor adherence to drug treatment (14).

Worldwide, the economic costs associated with asthma are estimated to exceed those of TB and HIV/AIDS combined (15). A study from Portugal showed that the use of tobacco, kerosene, paracetamol, and allergen skin sensitization to house dust mites was associated with an increased risk of wheezing (16).

Although asthma is a common problem in Ethiopia, it is not receiving the attention it deserves for proper management (17). Therefore, this study aimed to provide evidence-based information about the severity pattern of bronchial asthma and the associated risk factors in adult patients in the Awi administrative zone.

Materials and Methods

Study area

The study was conducted in the Awi administrative zone, Amhara Regional State of Ethiopia. This zone is 447 km from Addis Ababa and 118 km from Bahir Dar (18). It is situated in the northwestern part of the country, at an elevation of 700 to 2920 meters above sea level. The 2018 population of the zone was estimated to be 1,264,203 (1,057,604 rural, 206,599 urban residents), with 50.1% male and 49.9% female residents (19).

Variables of the study

The independent variables are sociodemographic characteristics: age, gender, educational status, income level, residence, occupation, type of fuel used for cooking, unpleasant odors, smoking cigarettes, family history of asthma, placement of the kitchen in the house, limitations on daily activities, season, presence of animals at home, exercise habits, experiencing drug discontinuation, house ownership, and marital status. The dependent variable is bronchial asthma level of severity, categorized as mild, moderate, and severe.

Study design and study period

A cross-sectional study was conducted from December 2022 to November 2023 to determine the factors associated with bronchial asthma among adult patients in Awi administrative Zone.

Sample size determination

The sample size (n) was determined using the formula described in (20).

The formula is $n = \frac{Z^2 p(1-p)}{d^2}$, where Z is the standard normal distribution value for a 95% confidence level (1.96), p is the expected severity (0.5), and d is the margin of error (0.04). Using these values in the formula and adding 10% for potential non-response, a final sample size of n=662 was calculated.

Sampling method

A two-stage sampling procedure was used. In the first stage, two strata of health services (5 hospitals, and 49 healthcare centers) were created based on the type of service they provide. Then 3 hospitals (Injibara General Hospital, Chagni Hospital, and Dangila Hospital) and 5 healthcare centers (Ayehu, Adiskedam, Kessa, Tilili, and Gemeja Bet) were randomly selected. In the second stage, n=662 was partitioned to the 8 hospitals and healthcare centers proportionally according to the number of adult bronchial asthma patients admitted, and the participants were randomly selected.

Data collection

This study utilized close-ended questionnaires, and the data were collected through face-to-face interviews. All participants of the survey provided informed consent.

Operational definition

Mild severity is defined as the subject not using accessory muscles, the subject's respiratory rate being between 12 and 20, the heart rate being between 60 and 100, and oxygen saturation being≥ 95%.

Moderate severity is defined as the subject using accessory muscles, speaking in phrases, having an agitated mental status, having a respiratory rate between 20 and 30, a heart rate between 100 and 120, and oxygen saturation between 90% and 95%.

Severe severity is defined as the subject using accessory muscles, the subject's speech being in words, the mental status being distressed, the respiratory rate being>30, the heart rate being>120, and oxygen saturation being <90%. These categories are based on GINA-pocket-2015 clinical methods.

Data analysis and process

Descriptive statistics were used to describe the sociodemographic characteristics. Ordinal logistic regression analysis with the Odds ratio model was utilized to determine the influence of the independent variables on the dependent variable.

Ethical considerations

Ethical approval was obtained from Injibara University's Institutional Research Ethics Review Committee (Ref. No. IU/IRERC/03/24). The participants were informed about the study's goals, and their verbal consent was obtained. Their right to refuse or to withdraw from participation was honored, and the confidentiality of the information provided by each participant was strictly maintained. The study did not involve using individual participants' names, images, or videos.

Results

Descriptive statistics

The severity of asthma in the different categories of socio-demographic and clinical characters is shown in Table 1.

Table 1: Severity of asthma in the different categories of socio-demographic characters.

Variable	Category	Status of bronchial asthma among adult patients n (% of severity within each category)			
		Mild	Moderate	Severe	Total n (%)
Gender	Female	121 (33.4)	234 (64.6)	7 (1.93)	362 (54.7)
	Male	156 (52.0)	54 (18.0)	90 (30.0)	300 (45.3)
Monthly income	<6000	120 (42.9)	127 (45.4)	33 (11.8)	280 (42.3)
	6000-10000	132 (45.2)	113 (36.7)	47 (16.1)	292 (44.2)
	>10000	36 (40.0)	37 (41.1)	17 (18.9)	90 (13.6)
Drug discontinuation	Yes	188 (47.5)	118 (29.8)	90 (22.7)	396 (59.8)
	No	100 (37.6)	159 (59.8)	7 (2.6)	266 (40.2)
Smoking cigarette	Yes	69 (41.6)	77 (46.4)	20 (12.1)	166 (25.1)
	No	219 (44.2)	200 (40.3)	77 (15.5)	496 (74.9)
Exercise habit	Yes	201 (57.1)	75 (21.3)	78 (22.2)	352 (53.2)
	No	87 (28.1)	202 (65.2)	21 (6.8)	310 (46.8)
Bad smell	Yes	165 (39.8)	157 (37.5)	97 (23.2)	419 (63.3)
	No	123 (50.6)	120 (49.4)	0 (0.0)	243 (36.7)
Residence	Rural	93 (30.2)	196 (63.6)	19 (6.2)	308 (46.5)
	Urban	195 (55.1)	81 (22.9)	78 (22.0)	354 (53.5)
Fuel for cooking	Electric	25 (35.7)	12 (17.1)	33 (47.1)	70 (10.6)
	Charcoal/wood	263 (44.4)	265 (44.8)	64 (10.8)	592 (89.4)
Marital status	Married	256 (57.3)	121 (27.1)	70 (15.7)	447 (67.5)
	Others	32 (14.9)	156 (72.6)	27 (12.6)	215 (32.5)
Age	<28	31 (42.5)	25 (34.3)	17 (23.3)	73 (11.0)
	28-38	173 (52.4)	114 (34.6)	43 (13.0)	330 (49.9)
	38-48	72 (34.0)	114 (53.8)	26 (12.3)	212 (32.0)
	>48	12 (25.5)	24 (51.1)	11 (23.4)	47 (7.1)
Layout of the kitchen	Inside	88 (43.8)	94 (6.8)	19 (9.5)	201 (30.4)
	Outside	200 (43.4)	183 (39.7)	78 (16.9)	461 (69.6)
Limited daily activities	Yes	165 (38.4)	181 (42.1)	84 (19.5)	430 (65.0)
	No	123 (53.0)	96 (41.4)	13 (5.6)	232 (35.0)
Presence of animals	Yes	221 (43.6)	252 (49.7)	34 (6.7)	507 (75.7)
	No	67 (43.2)	25 (16.1)	63 (40.7)	155 (23.4)
House ownership	Owned	168 (50.6)	136 (41.0)	28(8.43)	332 (50.2)
	Rented-Gov	4 (33.3)	6 (50.0)	2 (16.7)	12 (1.8)
	Rented-Private	120 (37.7)	129 (40.3)	97 (30.5)	318 (48.0)
Family history of asthma	Yes	85 (26.2)	150 (46.2)	90 (27.7)	325 (49.1)
	No	203 (60.2)	127 (37.7)	7 (2.1)	337 (50.9)
Season	Winter	1 (33.3)	0 (0.0)	2 (66.7)	3 (0.4)
	Summer	136 (39.4)	209 (60.6)	0 (0.0)	345 (52.1)
	Spring	0 (0.0)	43 (1.0)	0 (0.0)	43 (6.5)
	Autumn	151 (55.7)	25 (9.2)	95 (35.1)	271 (40.9)
Occupation	Farmer	74 (28.5)	162 (62.3)	21 (8.1)	260 (39.3)
	Trader	40 (75.5)	13 (24.5)	0 (0.0)	53 (8.0)
	G. employee	121 (68.8)	55 (31.3)	0 (0.0)	176 (26.6)
	Self-employee	53 (30.6)	44 (25.4)	76 (43.9)	173 (26.1)
Education level	Illiterate	74 (30.8)	145 (60.4)	21 (8.8)	240 (36.3)
	Reading/writing	175 (52.7)	81 (24.4)	76 (22.9)	332 (50.2)
	Others	39 (43.3)	51 (56.7)	0 (0.0)	90 (13.6)

Accordingly, 54.7% of the respondents were female and 45.3% male. However, there is a glaring difference between the severity level of males and females, where a higher percentage of females have moderate severity (64.6%). In comparison, only 18.0% of the males have moderate severity, and a higher proportion of the males (30.0%) have severe asthma compared to their female (1.9%) counterparts **(Figure 1).**

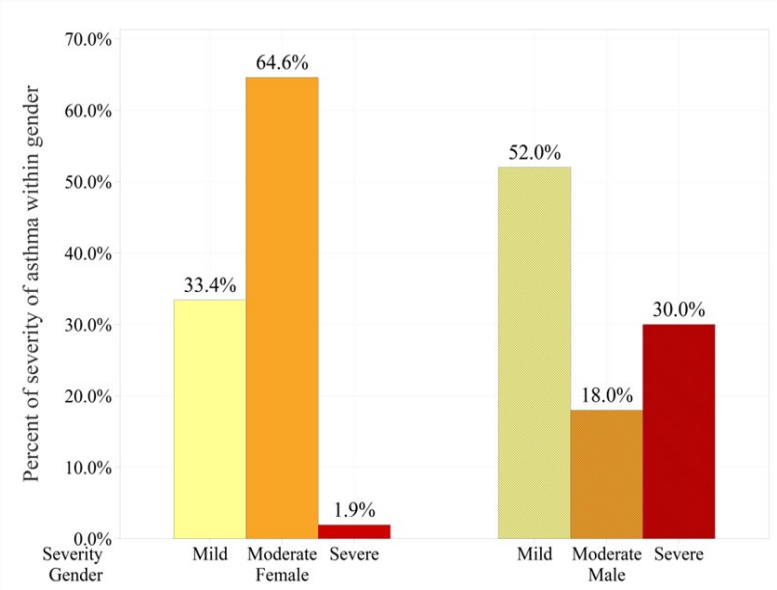

Figure 1: Status of bronchial asthma among adult male and female participants.

Regarding monthly income, 42.3%, 44.2%, and 13.6% of the respondents have income <60000, 6000 – 10000, and >10000, respectively, and respondents with >10000 income have more severe asthma. 59.8% of the respondents did not finish their drug, and 22.7% of those had severe asthma. Among all respondents, 25.1% smoked cigarettes, and 74.9% did not.

Among all asthma patients, 50.2% owned their house, and 48.0% rented from a private owner. Still, the severity level varied substantially, where 50.6% vs. 8.43% and 37.7% vs. 30.5% of the participants who lived in their own house and rented units have mild vs. severe severity, respectively. Regarding fuel for cooking, 10.6% and 89.4% of the respondents used electric and charcoal, respectively. There is no significant difference between the respondents with a family history of asthma (49.1%) and those without (50.9%).

Factors associated with the severity of asthma

The significance of the impact of the studied factors on the prevalence of asthma is shown in Table 2. Accordingly, smoking cigarettes, drug discontinuation, layout of the kitchen, and monthly income have no significant effect on the severity of asthma. However, exercise habits, family history of asthma, occupation, bad smell in the environment, education level, fuel used for cooking, seasons, limited daily activity, and marital status have a significant effect on the severity of asthma, and these factors are included in the multivariable ordinal logistic regression analysis.

The results showed that exercise habits, family history of asthma, occupation, bad smell in the environment, education level, fuel used for cooking, seasons, limited daily activity, and marital status significantly affect the severity of asthma. Asthma patients who do not smoke cigarettes were 0.00000175 times (AOR=0.00000175, very close to zero) more likely to have severe asthma than those who smoke cigarettes. Asthma patients who use electricity for cooking were $4.63x10^{-6}$ times (AOR=$4.63x10^{-6}$, 95%CI: $7.35x10^{-7}$, $2.9x10^{5}$) less likely to have severe asthma than those using charcoal and wood.

The odds of having severe asthma if a patient is not exposed to bad smells is < 45% less likely to have severe asthma. The odds of severe asthma level for patients not doing physical exercise is 5127.7 times (AOR: 5127.7, 95% CI: 188.2, 139728.1) more likely than their counterparts. The odds of having severe asthma for patients who have a family history of asthma is 90.05 times (AOR=90.05, 95% CI: 17.16, 472.48) more likely than that of those with a family history of asthma. Patients whose education level is at illiteracy and reading/writing levels have 0.001 (AOR=0.001, 95% CI: 0.00006, 0.315) and 0.016 (AOR=0.016, 95% CI: 0.001, 0.188) times higher odds of having severe asthma than patients whose education level is in the others category.

Table 2: Variables associated with the severity level of asthma, Crude Odds Ratio (COR), Adjusted Odds Ratio (AOR), and P-value of the ordinal logistic regression model.

Variable	COR (95% CI)	AOR (95% CI)	P-value
Severity level			
Mild		0.016 (1.6x10-5, 1.433)	0.071
Moderate		58.616 (0.607, 5.7x104)	0.081
Sever		1.00	
House ownership			
Private	0.510 (0.379, 0.686)	0.205 (0.100, 0.423)	<0.001
Rented from government	1.543 (0.606, 3.929)	1367.8 (33.5, 55825.0)	<0.001
Rented from a private owner	1.00	1.00	
Residence			
Urban	0.644 (0.482, 0.861)	7.254 (1.67, 31.55)	0.008
Rural	1.00	1.00	
Exercise habit			
No	1.808 (1.35, 2.42)	5127.7 (188.2, 139728.1)	<0.001
Yes	1.00	1.00	
Drug discontinuation			
No	0.904 (0.677, 1.207) [a]		
Yes	1.00		
Family history of asthma			
Yes	5.381 (3.91, 7.40)	90.05 (17.16, 472.48)	<0.001
No	1.00	1.00	
Gender			
Male	9.893 (6.98, 14.03)	15.876 (6.29,40.09)	<0.001
Female	1.00	1.00	
Occupation			
Farmer	0.374 (0.252, 0.556)	0.248 (0.015, 3.999)	0.326
Trader	0.060 (0.029, 0.123)	0.052 (0.007, 0.402)	0.005
Government employee	0.083 (0.052, 0.132)	0.005 (0.010, 0.031)	0.001
Self-employee	1.00	1.00	
Education level			
Illiterate	0.877 (0.570, 1.350)	0.001 (0.00006, 0.315)	0.001
Reading/writing	1.447 (1.057, 1.981)	0.016 (0.001, 0.188)	<0.001
Others	1.00	1.00	
Smoking cigarette			
No	0.992 (0.714, 1.377)		
Yes	1.00		
Presence of animals			
No	2.300 (1.583, 3.341)	0.0002 (0.00001, 0.002)	<0.001
Yes	1.00	1.00	
Bad smell			
No	0.450 (0.332, 0.608)	0.020 (0.007, 0.060)	<0.001
Yes	1.00	1.00	
Fuel for cooking			
Electricity	0.021 (0.012, 0.037)	4.63x10-6 (7.35x10-7, 2.9x105)	<0.001
Charcoal and wood	1.00	1.00	
Season			
Winter	6.886 (0.519, 91.423)	9.838 (0.08, 1293.8)	0.358
Summer	0.816 (0.594, 1.122)	3822.2 (812.6, 17977.8)	<0.001
Spring	2.030 (1.175, 3.508)	294694 (23273, 3731554)	<0.001
Autumn	1.00	1.00	
Limited daily activities			
Yes	2.076 (1.527, 2.822)	0.479 (0.250, 0.918)	0.027
No	1.00	1.00	
Layout of the kitchen			
Outside the house	1.173 (0.860, 1.599)		
Inside the house	1.00		

Age			
>28	0.615 (0.307, 1.231)	1.103 (0.367, 3.295)	0.861
29-38	0.358 (0.202, 0.634)	1.453 (0.571, 3.698)	0.433
39-48	0.619 (0.345, 1.110)	0.957 (0.376, 2.434)	0.927
>48	1.00	1.00	
Marital status			
Others	3.28 (2.40, 4.47)	0.003 (0.0003, 0.0299)	<0.001
Married	1.00	1.00	
Monthly income			
<6000	0.793 (0.506, 1.242)		
6001-10000	0.804 (0.513, 1.260)		
>10001	1.00		

[a]-AOR and p-value cells are blank because the COR value is not significant.

Discussion

This cross-sectional study assessed asthma's magnitude and associated risk factors among adult patients. The findings revealed that 41.8%, 43.5%, and 14.7% have mild, moderate, and severe asthma status, respectively. In contrast, a study conducted in Malaysia showed that 9.9% of the patients had moderate asthma, and 2.7% had severe asthma (21). However, the researchers used the clinical methods recommended by GINA to assess severity. In our study, the severity classification was not according to GINA's recommendation. Most of the patients were diagnosed only with acute exacerbation of asthma. The small number of physicians and the lack of enough training to assess the severity are partly the reasons for not following the recommendation of GINA.

The prevalence of bronchial asthma among adult patients in the selected healthcare centers was 4.3%. However, a study done in the adult emergency room of Addis Ababa Zewditu Memorial Hospital showed a 1.5% prevalence (17)). The prevalence of asthma among adult patients of the United Arab Emirates and Debre Berhan is 13% (22) and 29.6% (17), respectively. Relatively, the severity in our study is lower, which could be because the participants live in high-altitude areas with colder weather.

This study revealed that patients who come from a family with an asthma history are more likely to develop bronchial asthma. Similar findings have been reported in different countries (17, 22). In this study, the educational level of asthma patients is significantly associated with their asthma level. Educated patients have a lower risk of asthma disease because they have a better understanding of minimizing exposure to asthma than those who cannot read and write. However, this is not true in all countries; e.g., a study conducted in the United Arab Emirates (22) showed no association between asthma and the education level of the patients.

Asthma patients from a bad-smelling environment are more likely to develop bronchial asthma; a similar finding was reported in (23). Also, married patients have a lower chance of having severe asthma; however, patients who discontinued their drug have a higher chance of developing bronchial asthma, which was also reported in other studies (17, 21, 24). Using fuel instead of electricity as a source of energy for cooking significantly increases the chance of having severe asthma, which is consistent with the findings of (23). Charcoal and wood are widely used for cooking, which increases asthma status because they contain pollutants such as carbon monoxide (CO) and sulfur dioxide (SO2). Therefore, cleaner cooking technologies, such as solar power and electricity, could prevent or reduce asthma and other respiratory illnesses.

Conclusion

The severity of bronchial asthma among adult patients is relatively high. Exercise habits, drug discontinuity, education level, family history of asthma, bad smells around the house, the source of energy for cooking, and marital status increase the risk of bronchial asthma. Most asthma patients are urban dwellers. Most patients were classified as having moderate bronchial asthma, which differs from studies in other countries, highlighting the need for appropriate classification. Since adherence to GINA guidelines for treating and managing patients was low, a national guideline is needed for uniform classification and management of bronchial asthma.

Based on our findings, we recommend the following interventions to reduce the severity of asthma: (a) training and educating people about the significant variables identified in this study, (b) implementing guidelines for classifying asthma based on severity and according to GINA guidelines, and (c) prioritizing environmental hygiene to reduce the severity of asthma.

Acknowledgment

We thank Injibara University for the financial support and the healthcare professionals in the hospitals and the healthcare centers for their help. We also thank the study participants for their participation and for sharing valuable insights.

Consent for publication

Not applicable.

Authors' Contributions

Atalaye Nigussie (A.N.), Belsti Atnkut (B.A.), Gedif Mulat Alemayehu (G.M.A.), and Nigussie Adam Birhan (N.A.B.) prepared the survey tool, and supervised the data collection. A.N., B.A., and Destaw Mullualem (D.M.) conducted data entry to SPPS. A.N., B.A., G.M.A., and Tessema Astatkie (T.A.) analyzed the data. Zelalem Meraf Woldie, A.N. and B.A. wrote the draft manuscript and T.A. revised and prepared the final version of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Funding

Injibara University financed the study.

Data Availability

Data will be made available upon a reasonable request.

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Ethiopian Medical Journal 2024, 62(4)
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ISSN 0014-1755 eISSN 2415-2420 Mengesha et al.

Original Article

Assessing the Burden of Preventable Amputations in Hawassa: The Role of Health Care Access and Appropriate Early Interventions

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Background: *Limb amputation become one of the commonest procedures for various causes where the indications can be reduced by combination of public health interventions, improved public health access and early appropriate medical care. This study was aimed to highlight indications and patterns of amputation, compare to published data and provide possible ways in which the number can be reduced in Hawassa, Sidama region, Ethiopia.*
Method: *This was a retrospective study on 304 patients who underwent all types of amputations performed at Hawassa University Comprehensive Specialized Hospital from January 2019 to December 2021. Data was extracted from the operation registration log- book and patients' chart.*
Result: *There were 231 (75%) male patients with mean age 32.8 years. Main indications for amputation were trauma in 87 (28.6%) patients, peripheral arterial disease (PAD) in 69 (22.7%) and severe infection in 54 (17.8%). Complications due to treatment by traditional bone setters (TBS) was the most common cause of amputation in those under 18 years. 13.8% of amputations were deemed preventable, 14.1% potentially preventable, and 72% not preventable.*
Conclusion: *sixty six percent of observed amputations occurred in children and working-age adults under 40 years, giving rise to a massive societal cost. Through enhanced health education regarding severe trauma prevention as well as early severe infection treatment, fostering collaboration with TBS, data collection via trauma registries, and affordable, timely trauma services, the number of amputations could be significantly reduced.*

Keywords: *Hawassa, Ethiopia, Complication, Amputation, Low- and middle-income country (LMIC's), Traditional bone setter*
Citation : *Mengesha MG, Garikapati V,Adem EG et al. Assessing the burden of Preventable Amputations in Ha wassa: The role of health care access and Appropriate Early Interventions.Ethiop Med J 62 (4) 261-268*
Submission date : *26 July 2024 Accepted: 27 September 2024 Published: 01 October 2024*

Introduction

Amputation remains a standard orthopedic procedure in modern clinical practice, with a history dating back over 2500 years. Limb amputation is performed as a last option when limb salvage is impossible; the limb is viable but non-functional or has a high risk of mortality to the patient's life (1).

The indications for amputations vary from region to region, where peripheral vascular disease and diabetes are the leading causes in High-Income Countries (HICs) (2,3), whereas, in low-and-middle-Income Countries (LMICs), trauma is the leading cause (4,5). Also seen in LMICs is gangrene secondary to tight bamboo application by traditional bone setters (TBS), which may not be seen in HICs. Severe infection, which does not respond to aggressive repetitive debridement and culture-guided therapy, is another common indication to perform amputation in addition to high voltage electrical burn injury.

Within HICs, most patients undergoing amputation are over the age of 60 years (2,3,6), whereas in LMICs, the average age is much younger, specifically affecting those of working age (7,8).

Amputation within LMICs can have huge health, socio-economic, and psychological effects on the patients and their families. These operations have a high risk of mortality and morbidity, with disability representing a sig-

nificant burden to shoulder. Also, within these areas, a significant lack of prosthetic and rehabilitative services, leads to difficulty in rehabilitative and integrative challenges (9).

Here, we present a three-year (2019 to 2021) clinical experience showing the main reasons for amputation in our centre, one of the most prominent orthopaedic centres in the country and serves more than 20 million catchment population. We look to determine the patterns and indications of amputations in Hawassa, how this number can be reduced, and any strategies which could help to prevent and alleviate these complications that arise.

Material and Methods

Study design and Period

This is a retrospective study on 304 patients who underwent all types of amputations performed at Hawassa University Comprehensive Specialized Hospital (HU-CSH) from January 2019 to December 2021.

Study setting

HU-CSH is located in Hawassa, which is 275 km south of Addis Ababa, the capital city of Ethiopia. It is a 500-bed tertiary level Public University Hospital. It is the only referral hospital in the Sidama region serving a catchment population of approximately 20 million, including the nearby regions of Oromia, Central Ethiopia, and Somalia (10).

Sample size calculation and sampling

All of major amputation done at HU- CSH during the three-year period (2019 to 2021) were included without sampling.

Study population

The study population included all patients of all age groups and genders who underwent major amputations at HU-CSH within the study period.

Inclusion and Exclusion parameters

All age groups and genders who underwent major amputations at HU-CSH within the study period were included. Those amputations done in other departments and minor amputations (digital or finger amputations in both upper and lower extremities) were excluded.

Operational definition

Major amputation in this paper is defined as the surgical removal of the extremities by passing through the bone or joint, including upper and lower extremities; excluding amputation done through the digits or fingers.

Data Collection and statistical analysis

The dataset, including age, sex, primary diagnosis, immediate indication for amputation, and type of amputation, was collected from a hospital database of patients' acceptance logbook, operation theatre registry, and patient chart during the study period. All the data was collected by two trained third- and fourth-year orthopedic surgery residents under close supervision of the principal investigator and collected in open text form, which was coded later during data cleaning and analysis. In this study, we were not able to code diabetes mellitus as a primary cause of amputation, and cases that were listed as PAD or severe infection may also have had type 2 diabetes mellitus as a contributing diagnosis. The data was then retrospectively subdivided into whether the amputation was preventable, potentially preventable, or non-preventable by the researcher based on the diagnosis, causes, and risk of patients considering access to timely care (e.g., avoiding delays causing compartment syndrome, gangrene, severe infection), access to appropriate care (e.g., antibiotics for infection) as well as avoidance of harmful care (e.g., tight bamboo splints). We then defined preventable as those avoidable if appropriate steps had been taken; potentially preventable as amputations that could have been avoided with optimal care; and non-preventable as non-avoidable due to the injury or mechanism. We note that much trauma may be preventable, but our definition was applied only to the post-injury phase of care. All of the cases included in this study are those of major amputations performed by trauma and orthopedic surgeons where almost all of the amputations are being done under department of orthopedic surgery. The focus of this study is to describe the indications and patterns of amputations with possible explanation on how to reduce it. The data was entered onto Microsoft Excel software programme and descriptive analysis was performed. The results are presented in the form of text, figures, and tables.

Ethical Considerations

Since the study uses anonymized secondary data from the hospital registry, the study was approved by the orthopedics departmental ethical approval committee, and since it was considered a quality improvement audit, there was no need for further ethical approval.

Results

Three hundred four patients underwent amputation at HS-CSH from January 2019 to December 2021. Of these, 231 (76%) patients were male. The patients were aged eight days to 89 years, with mean age of 32.8 years and median age of 30 years. Most patients were under 40 years old (62.1%) (Table 1).

Table 1. Age group distribution of patients who underwent amputation at HU-CSH from 2019 to 2021

Age category	Number of Patients	Percentage (%)
< 18	91	29.9
19 – 39	98	32.2
40 - 59	74	24.3
> 60	41	13.5

The most common indication for amputation was trauma in 87 (28.6%) patients, followed by peripheral arterial disease in 69 (22.7%) patients and then severe Infection in 54 (17.8%) patients (Table 2). It is of note that only 4.2% of our data set have diabetes, leading to complications such as PAD or infection.

Table 2. Overall Indication for Amputation done at HU-CSH from 2019 to 2021

Indication for Amputation	Number	Percentage (%)
Trauma	87	28.6
Peripheral Arterial Disease	69	22.7
Severe Infection	54	17.8
Treatment from TBS	44	14.5
Malignancy	44	14.5
Electrical Burn	5	1.6
Congenital	1	0.3
Total	304	100

Complications due to treatment by TBS were the most common cause (33/91 patients) of amputation in those under 18. Trauma was the most common indication for amputation in those ages 19-39 (50/98 patients), whereas peripheral arterial disease was the most common in those aged 40-59 and greater than 60 (Table 3

Table 3. Age Groups of patients with Indication for amputation at HU-CSH from 2019 to 2021

Age group	Trauma	PAD	Infection	TBS	Malignancy	Burns	Congenital	Total
< 18	23 (7.6%)	6 (2%)	7 (2.3%)	33 (10.9%)	19 (6.3%)	2 (0.7%)	1 (0.3%)	91 (29.9%)
19 – 39	50 (16.4%)	16 (5.3%)	15 (4.9%)	6 (2%)	9 (3%)	2 (0.7%)	-	98 (32.3%)
40 - 59	9 (3%)	28 (9.2%)	17 (5.6&)	5 (1.6%)	14 (4.6%)	1 (0.3%)	-	74 (24.3%)
> 60	5 (1.6%)	19 (6.3%)	15 (4.9%)	-	2 (0.6%)	-	-	41 (13.5%)
Total	87 (28.6%)	69 (22.7%)	54 (17.8%)	44 (14.5%)	44 (14.5%)	5 (1.6%)	1 (0.3%)	304 (100%)

The types of amputations are shown in Table 4. The most common indications for lower limb amputation were trauma (25.1%) and peripheral arterial disease (25.1%). Trauma (33.7%) and treatment by TBS (28.1%) were the primary indications in upper limb cases.

Table 4. Type of Amputation at HU-CSH from 2019 to 2021

Type of Amputation	Number	Percentage (%)
Foot	24	7.9
Below-Knee	85	28
Through-Knee	10	3.3
Above-Knee	85	28
Hip Disarticulation	7	2.3
Other	2	0.6
Total Lower Limb	213	70.1
Hand	20	6.6
Wrist Disarticulation	3	1
Below-Elbow	12	3.9
Elbow Disarticulation	8	2.6
Above-Elbow	45	14.8
Shoulder Disarticulation	3	1
Total Upper Limb	91	29.9
Total	304	100

The causes of amputation were further subdivided into degrees of preventability. Of the cases that were presented, 13.8% of amputations were deemed preventable, 14.1% were potentially preventable, and 72% were not preventable.

Discussion

Amputation is associated with significant social, psychological, and economic effects on patients and their families. The indication and pattern of amputation can vary depending on the country, region, and the hospital. This is the largest series of amputations in an Ethiopian population within the literature. It was undertaken to describe our experience, compared to similar studies, allowing us to identify any patterns. It was also part of a quality improvement program aimed at identifying preventable amputation and addressing the underlying causes.

Similar to other studies, most patients undergoing amputation were male (75%) (11–13). In our study, the most common age group affected was those aged 19-39 years. Most LMICs have similar age group involvement because trauma is the leading cause of amputation in these age categories. This can be seen in similar studies done in Tanzania, Sudan, Nigeria, and Kenya (5,7,12–15). This is in contrast to high-income countries (HICs) where most amputated patients are aged 60 and above, as seen in The Netherlands, Canada, Hungary, and Sweden (2,3,6,16).

Despite a variation in causes of amputation between the different age groups, trauma was the most common cause, followed by PAD and severe infection. Trauma affected 28.6% of our population. This is a similar pattern noted by other studies (14,17–19). It is also seen that treatment by TBS was the most significant cause of amputation in those aged under 18.

Lower limb amputation was more common than amputation of the upper limbs. This is akin to other studies within Africa. We had an even distribution of above knee to below knee amputations. Studies show a varied distribution between above and below-knee amputations (4,7,12,13). The expected functional outcome varies hugely depending on above-knee to below-knee amputation, with above-knee amputees having increased morbidity and mortality (20,21).

Within LMIC, trauma is one of the leading causes of amputation. The decision to limb salvage versus amputation is a complex one that is influenced by patients' premorbid status, the nature of the injury, the location, contamination, the patient's wishes, and the resources available, including financial cost. There are many scoring systems, including the mangled extremity severity score (MESS), which can help guide decision-making. Most importantly, a multidisciplinary approach involving vascular, plastic, and orthopedic surgeons must be undertaken (22).

By improving the organization of trauma care, its management could become more sustainable and affordable, leading to lower morbidity and mortality rates (23). One such method is implementing trauma registries, which provide valuable data for injury surveillance, health system development, and resource allocation (24). Since 2019, HS-CSH has been collecting data through such a trauma registry, using the data to improve services and help reduce mortality by providing local data for decision-making (25).

Many studies have shown complications of diabetes mellitus to be a leading cause of amputation (8,15). Within our data set, only 4.2% were noted to have diabetes leading to complications such as PAD or severe infection. The prevalence within our population is likely to be underestimated due to a lack of diagnostics tools, preventative measures, and education (26,27). The rate of diabetes has been reported in Ethiopia between 2-6.5% (28). This is in comparison to India, another LMIC, where the prevalence is as high as between 9.3-24.5%. Across the globe, 10.4% of the population from high-income countries, 9.5% from middle-income and 4.0% from low-income countries were diabetic in 2019 (29). To help tackle diabetes, appropriate interventions towards patient self-care practice, lifestyle modification, and continuous follow-up are essential to prevent diabetic foot ulcers and subsequent amputations. Health care professionals are key to tackling diabetic foot ulcers through proper health education and patient treatment. To help control the amount of sugar in Ethiopia's diet, the Ministry of Finance of Ethiopia has implemented a 'sugar tax' of 20% on sugar products to help prevent the rise in diabetes mellitus that is seen in many other LMICs (30). In Ethiopia, 3.7% of the population are smokers, and 20.6% of Hawassa University undergraduate students smoke (31,32). Smoking and complications of Diabetes are common causes of PAD, which was the second most common cause of amputation in our study. This burden of smoking could be avoided through effective health promotion and disease prevention programs that tackle risk factors with low-cost and highly efficacious initiatives to curb tobacco. The taxation of tobacco products has also been effective in HICs.

Patronage towards TBS is a substantial reason for amputation in our study, particularly for those under 18. The main reasons for utilization of TBS included cheap fees, cultural beliefs, quick service, easy accessibility, and pressure from family and friends (33). Many strategies have been brought into place to help alleviate the complications that may arise from TBS treatment, including amputations. These strategies include educating TBS to provide training and recognize their limitations, formal engagement with orthodox services as well as a referral system, and providing regulation, certification, and licensing to TBS after preparation of the scope of practice with a monitoring and evaluation system. Many studies have shown that TBS are keen and willing to engage in such services and training courses (34,35). Within Ethiopia, a local initiative known as the BOne Setting Associated Disability (BOSAD) Study has been launched with its aim by 2025 to reduce complications by TBS to near zero prevalence by training practitioners, developing education materials, and producing a national database (36). In Hawassa, Trauma and Orthopaedics specialist service has only been available since 2016, and with this, patronage of TBS is expected to decrease as patients gain access to and understanding of safe, timely, and affordable care in the modern health sector.

Amputation represents the beginning of a new care journey for patients and their communities. While we considered that 28% of the amputations were preventable or potentially preventable, effective public health measures towards injury reduction, healthy lifestyle, and appropriate health seeking behaviour could also offer considerable reductions in the remaining 72% amputations. There is a need for post-amputation care and rehabilitation programs, including psychological support, physiotherapy, mobility devices, and prosthetics. Within Hawassa, there is only one such rehabilitation program, and it is difficult to access as it is funded by Non-Governmental Organisations (NGOs) and/or needs to be subsidized by the patient themselves, a far distance of travel and poor linkage of patients to centers. For those few who are able to access the program and be provided with prosthetics, many find they are not comfortable or fit for purpose. Due to this, most lower limb amputees will be crutch users (37). Within LMICs, there needs to be a holistic MDT approach combining the surgeons, physiotherapists, and prosthetists. An improved service can be achieved with collaboration between the patient, the doctors, and prosthetists in a regional rehabilitation hub and spoke model. Beyond the scope of this study, there is a need for analysis in subsequent studies into life after amputation in Hawassa.

In general, there are multiple studies done in different parts of Ethiopia that show nearly similar findings to our studies, specifically on the indication for amputation, pattern of amputation, and the age distribution. The studies done in Tikur Anbessa Specialized Hospital show that TBS-associated complications were the leading indication for amputation in the pediatric age group, which is similar to our current findings (38, 39). Similar findings were also reported from a study done by Mekelle specifically on the indication and patterns of amputation (40). A recent systematic review and meta-analysis done in Ethiopia show that different types of amputation, including for preventable causes, are being done throughout the country (41).

Although many publications are being produced in the country, there needs to be more effort to identify preventable and non-preventable causes of amputation. Furthermore, there has been a lack of initiatives to imple-

ment, such as awareness creation, improving access to modern orthopedic service, and focus on primordial prevention, all of which are crucial to reducing the number of amputations.

This study is limited by its retrospective methodology and absence of outcomes data. There are some gaps in our data set, including timing of amputation, significant comorbidities including diabetes, complications, re-operation rate, duration of hospital stay, and mortality rate. It is, therefore, difficult to fully assess the etiology of the patients or to review the patient outcomes.

This review had limited scope to study access prosthetics, return to school in children, and return to work in adults. An economic analysis including these societal costs would be beneficial.

The strengths of this study include its duration, number of cases, and our ability to ascertain various trends of amputation in Hawassa, and it provides a baseline against which to compare the impact of local TBS and trauma care initiatives.

Conclusion

Trauma, PAD, and severe infection are the leading causes of amputation for those over 18, whilst treatment by TBS is the leading indication in those under the age of 18 years. A significant number of these indications are potentially preventable. Eighty six percent of observed amputations occurred in children and working-age adults, giving rise to a massive societal cost. We have identified the need for public health and hospital improvements, which have proven effective in HICs to reduce this burden of human suffering and economic waste. Through good health education, collaboration with TBS, data collection via trauma registries, and affordable services, the number of amputations could be redacted, and for those that undergo amputation, an improved pre- and post-operative amputation rehabilitation program could improve outcomes.

Financial Support

There is no financial support since it was a quality improvement audit.

Conflict of Interest

The authors declared that there is no conflict of interest in this publication.

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Ethiopian Medical Journal 2024, 62(4)
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ISSN 0014-1755 eISSN 2415-2420 Fufa et al.

Original Article

Qualitative After-Action Review of Cholera in Ethiopia: Lessons Learnt, Best Practices, Challenges, and Perspectives for the Future

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Abstract

Background: *Cholera is a problem of public health importance worldwide. However, there was limited documentation of lessons learned from managing cholera outbreaks that could be applied to future improvements in Ethiopia. In October 2019, we assessed the overall cholera outbreak response and documented existing mechanisms and best practices in Ethiopia.*

Methods: *This After-Action Review (AAR) was conducted in Ethiopia from October 23rd to 25th, 2019 focused on the cholera outbreak from April 2019 to September 2019. A qualitative method with a participatory approach was used, using the standardized World Health Organization (WHO) guide for AAR. A total of 40 participants were from three regions (Afar, Amhara, and Oromia) and the Ethiopian Public Health Institute. The facilitators were from the Ministry of Health and WHO. Five working groups examined eight functional areas.*

Results: *The emergency operation center coordinated the national and regional cholera response. Social mobilization and reactive Oral Cholera Vaccine campaigns reduced financial burden and fostered trust in healthcare. Damaged water sources and pipeline maintenance helped control the outbreak. Redeployment of mobile health teams alleviated human resource shortages. Challenges during the response included late detection, weak multisectoral taskforce functionality, budget constraints, poor infrastructure, inadequate human resources, laboratory supplies, and delayed initial effective response.*

Conclusion: *Enhancing the surveillance system, operationalizing multisectoral coordination, and promoting community engagement and early risk communication can enhance the country's preparedness for future public emergency response, enhancing public health system responsiveness.*

Keywords: *After action review, Cholera, Outbreak response, Lessons learned, Core capacities, Ethiopia*
Citation : *Fufa Y, Abera N, Assefa* Y, *et al. Qualitative After-Action Review of Cholera in Ethiopia: Lessons Learnt, Best Practices, Challenges, and Perspectives for the Future..Ethiop Med J 62 (4) 269-275*
Submission date : *26 July 2024 Accepted: 27 September 2024 Published: 01 October 2024*

Introduction

Cholera is a diarrheal disease caused by toxigenic serogroups of the bacterium Vibrio cholerae, which can cause rapid dehydration and death. Severe disease manifests as acute, profuse, watery diarrhea ("rice water stools"), usually with vomiting. This leads to rapid dehydration, which can result in hypotensive shock, renal failure, and death within hours of onset (1). Prioritizing high-risk areas could substantially increase cholera control programs' efficiency and eliminate 50% of the region's cholera (2). Cholera remains a persistent health problem in sub-Saharan Africa and worldwide. Higher attack rates were associated with longer times to outbreak peak, longer epidemic durations, and lower case fatality risks (3).

This study provides detailed evidence of the cholera outbreak in Ethiopia, highlighting the effectiveness of interventions in affected regions and recommending strategies for local mitigation. This AAR aimed to assess the overall cholera outbreak response to validate existing mechanisms and best practices and identify areas for enhancement to strengthen emergency preparedness and improve future responses in Ethiopia.

Methods and materials

Study setting, period, and design

This after-action review assesses the overall cholera outbreak response in Ethiopia's three regions affected by the outbreak, particularly the Afar, Amhara, and Oromia regions. The review covered the period from April 24,

2019, to October 11, 2019, and was conducted in Ethiopia from October 23rd to 25th, 2019.

Sample size
A total of 40 participants from the working groups involved in the response, who possess relevant knowledge and experience related to the outbreak, from three outbreak-affected regions and the national team participated.

Data collection tools and procedures
All the review teams used the standardized WHO guide for AAR as a framework (11). Participants were divided into five groups to conduct an AAR, which involved a review of eight functional areas. The process began with introductory presentations on the methodology, objectives, agenda, and event. The groups were surveillance and laboratory, coordination, case management and infection prevention and control (IPC), water sanitation and hygiene (WASH), risk communication and community engagement (RCCE), and oral cholera vaccination (OCV). The after-action review process of the cholera outbreak response had five major sessions that is taken from WHO AAR guideline which are listed below
Session 1 – What was in place before the response?
Session 2 –What happened during the response?
Session 3 – What went well? What went less well?
Session 4 – What can we do to improve for next time?
Session 5 – Way forward

Data collection techniques
A multidisciplinary team from EPHI and MoH involved in the cholera outbreak response included epidemiologists, public health specialists, WASH experts, laboratory specialists, RCCE specialists, data analysts, and WHO representatives.

Data quality assurance
Data quality assurance was achieved through facilitation by experienced and trained facilitators and team leader leaders. The facilitators were trained for two days before the after-action review. Prior to the review format were developed to support data quality. Another method used were engaging all stakeholder so that were engaged during the response to the emergency to avoid information bias and crosschecking all information against credible source and facilitating open discussions to address potential inaccuracies. Sticky note was used during the discussion a visit round were made by each group to provide additional input and validate what has been done buy each group turn by turn until all group and thematic areas were addressed accordingly.

Data processing and analysis
Data analysis was conducted using a qualitative approach. Following the session, a compilation of all the notes, cleaning of all data and documentation was conducted The discussion's main ideas, takeaways, and suggestions are categorized and arranged methodically. Key information recorded in sticky note ,from the note taker of each group were and addition inputs were discussed and written one by one.

During analysis, the major pillars and sub-pillars of the response were topicalized to assign different categories of best practice strengths, weaknesses, and challenges for each pillar.

Results
A total of 40 participants of the working group who were involved in the response and possess relevant knowledge and experience related to the outbreak from three outbreak affected regions and the national team participated. Study participants are experts who were significantly contributed to response areas in key pillars like surveillance, laboratory, Coordination., Case management, WASH-IPC, RCCE and others at federal level and selected regions namely Amharas, Oromia and Afar Regions. The after-action review of the cholera outbreak in Ethiopia in 2019 assessed key functional areas of International Health Regulation (IHR) 2005 and presented them in five groups with best practices, challenges, and future improvement plans.

Surveillance and laboratory
An index case of cholera was reported on April 24th, 2019, in the Telemet Zone of the Amhara Region and gradually notified from the Afar and Oromia regions. Before the cholera outbreak, plans and policies were developed, including an early warning system, weekly bulletins, and continuous feedback. Vulnerability risk assessment, emergency preparedness, event-based surveillance, and indicator-based surveillance were performed. Region, zone, and woreda had designated Public Health Emergency Management (PHEM) officers and focal persons at health facility levels. Laboratory investigation formats, cholera guidelines, and case definitions were available at various levels.

.Some of the timelines are shown in the graph below (Figure 1).

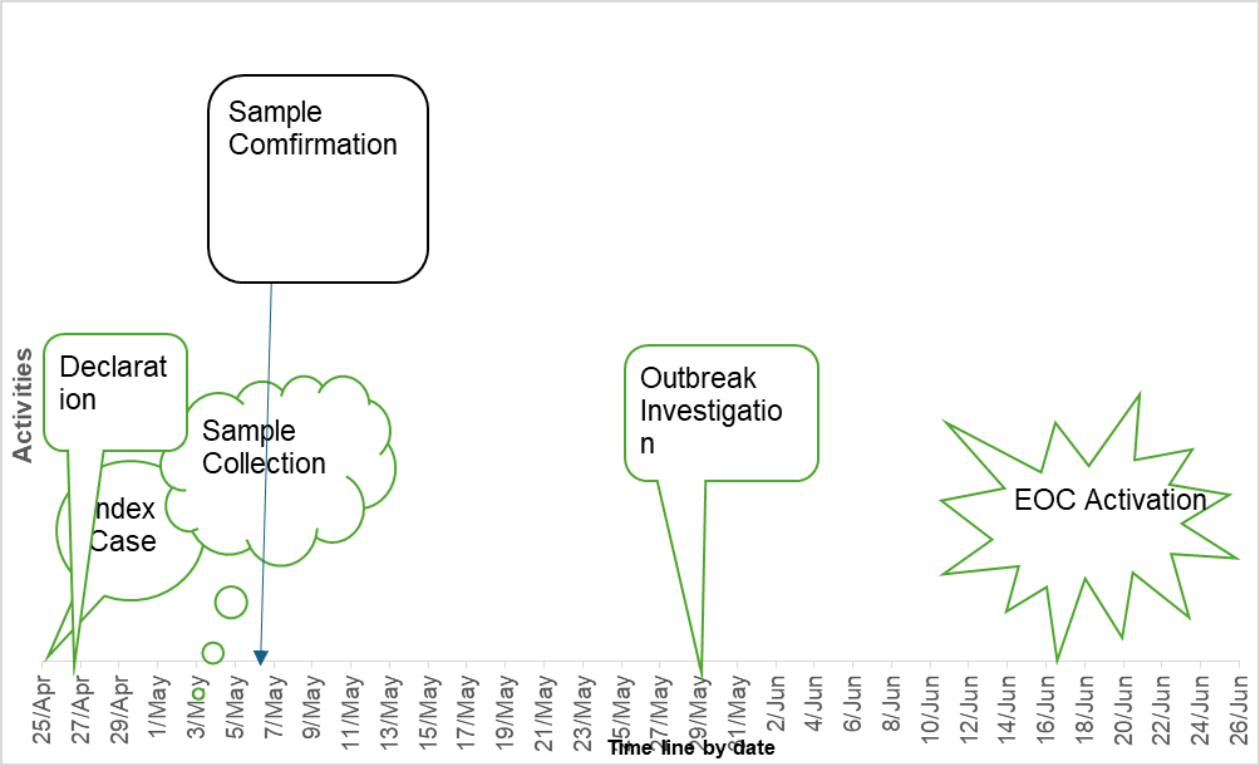

Figure 1: Timeline of Cholera outbreak and response activities in Ethiopia, April to June 2019

The cholera outbreak response faced numerous challenges, including delayed case detection, weak multisectoral task force, budget constraints, poor infrastructure, human resources shortages, and insufficient capacity to test food and water samples. These issues led to high morbidity, compromised surveillance activity, and outbreak control. Dagu, a traditional communication system for surveillance in the Afar region by clan leaders, has significantly reduced death rates and increased active surveillance by fostering trust among the community. The Emergency Operations Center leads cholera response at national and regional levels, improving coordination. Regular TWG meetings in the Amhara region enhance coordination and resource utilization. Best practices during response include regular bulletins and feedback, facilitated by the PHEM system.

Coordination

The cholera response was coordinated through an emergency preparedness plan, contingency plan, and national health emergency communication plan. Mechanisms of coordination included the Health Cluster Coordination Forum, National Public Health Emergency Operation Center (PHEOC), Sub-National EOC, Public Health Emergency Management System, region-cross-border forums, and National Cholera Task Force. Timelines of critical milestones and coordination activities during the cholera outbreak are shown in the table below (**Table 3**).

Case management and IPC

Before the cholera outbreak, contingency plans included mapping hospitals, transporting patients to CTCs, and identifying construction sites. An ORP was established, with 25% of emergency drugs allocated for outbreak responses and a task force was coordinated at regional and district levels. Essential preparedness mechanisms included a pre-positioned CTC kit, RRT, and health workers.

The cholera response faced several challenges, including delayed notification of cases due to poor community awareness, inadequate water supply, poor hygiene, sanitation, and IPC practices. Poor corpse management increased cross-contamination and prolonged outbreaks.

Risk communication and WASH

Before the cholera outbreak, plans and policies were developed, including joint plans with neighboring regions and emergency preparedness. Resources for cholera preparedness from national to district levels included a communication unit, guidelines, a women's development army, ICC/BCC materials, telegram channels, higher religious leaders, computers, and vehicles at regional and national levels. An emergency task force, partners, and rapid response

Table 3: Timelines of critical milestones and coordination activities during the cholera outbreak in Ethiopia, 2019

Date	Milestones	Location
03/01/2019	IDP EOC established	Addis Ababa, EPHI
28/04/2019	National Cholera EOC	Addis Ababa
20/05/2019	Oromia EOC	Oromia Health Bureau
03/06/2019	Tigray EOC	Mekelle, Tigray
15/06/2019	Addis Ababa EOC	AA
28/06/2019	RRT deployed for Amhara, CTC established, and	Amibara (Afar region)
24/06/2019	Afar EOC	Semera (Afar Region)
08/07/2019	On-job training for health workers	Amibara (Afar Region)
15/07/2019	Community-Based surveillance training	Addis Ababa
15/07/2019	Basic level training for health workers	Addis Ababa
15/07/2019	Community-Based surveillance training	Oromia, Hararghe
15/07/2019	Community-Based surveillance training	Amhara
19/07/2019	Prepositioning and coordination for the Qulube Gabriel holiday Mass gathering	Addis Ababa, Hararghe
19/07/2019	Hot spot mapping	Addis Ababa
25/08/2019	Cholera elimination and control plan launched	

Shortage of water supply in outbreak areas, poor wash infrastructure, and weak collaboration between health and the Ministry of Mine, Energy, and Water further exacerbated the situation.

team (RRT) were available from national to zonal levels. The leading cause of the cholera outbreak in the Amhara region was a damaged water pipe, which was repaired on June 28, 2019.

The response to the outbreak faced challenges such as a lack of trained human power, low community awareness, and inadequate resources. The outbreak led to delays in detection, increased morbidity and mortality, increased infection rates, human resource scarcity, and delayed case management. Limiting factors included high staff turnover and inadequate infrastructure budget,

The Dagu system in the Afar region was instrumental in reducing cholera transmission by promoting community engagement and trust through clan leaders. Identifying damaged water supplies and immediate maintenance of pipelines helped control the outbreak, while deploying mobile health teams relieved human resource shortages. Regular TWG meetings improved coordination and early mitigation. Health workers created awareness about hand washing and posted important messages around latrines, preventing person-to-person and feco-oral transmission.

Oral Cholera Vaccine

The EPRP plan was prepared before the outbreak, and human resources were in place but not trained for a specific OCV vaccine. The PHEOC, TWG, and task force were established for coordination at the national level. Major preparedness activities focused on using the existing cold chain system even though it wasn't adequate for OCV vaccines and training human power for vaccine-preventable diseases, especially cholera.

The national OCV plan was prepared in June 2019. The first OCV vaccine was requested on June 29, 2019. The first vaccination campaign for at-risk street children occurred in Addis Ababa, followed by the second campaign in the Afar region.

Challenges faced during the OCV campaign include the inability to coordinate vaccination, poor procurement procedures, the inability to target specific areas, and a shortage of OCV doses.

Discussion

The after-action review of the cholera outbreak in Ethiopia in 2019 has assessed some of IHR's key functional areas and discussed them in five groups with best practices and challenges.

Surveillance and laboratory

The first cholera case was reported in the Amhara region on April 24, 2019, and the notification was received on April 25, 2019, indicating a late notifi-

cation compared to the national PHEM Guidelines (7) that recommends notifications of immediately reportable disease to be within 30 minutes to the next higher levels. Despite this, it fulfilled the 7-1-7 target for detection, notification, and response to public health threats (12).

The cholera outbreak response faced challenges such as delayed case detection, budget constraints, infrastructure, inadequate human resources, and a shortage of laboratory supplies. These issues compromised surveillance activity, delayed response, and outbreak control. This is supported by the fact that early detection of outbreaks can reduce cases and deaths, while late detection results in a delayed response with limited opportunity for control (7).

Dagu, a traditional communication system in the Afar region, has strengthened community-based surveillance and fostered trust. This is supported by the evidence that utilizing the existing community structures in community and event-based surveillance systems in a well-organized way helps to engage the community in the identification and notification. This finding is consistent with the fact that the ability of Ethiopian laboratories to confirm cholera cases quickly and the degree to which local populations seek healthcare are closely related factors (14).

Coordination

The cholera response in regions and nationally faced challenges such as inadequate funding, partner fatigue, and medical, political, and IDP situations, leading to prolonged outbreaks and constraints for the OCV campaign. The absence of safe water supply in outbreak areas was due to natural causes, poor WASH infrastructure, and low collaboration between the health and water sectors. Difficulty of access to communities in hard-to-reach areas resulted in delayed referrals and a high CFR of 1.5%. When the fatality rates creep above 1 percent, it usually signals problems with the quality, access, and speed of treatment (15,16).

The National PHEOC Guideline highlights the importance of the media in preventing and controlling public health emergencies (17). Inadequate frontline human resources during the outbreak resulted in compromised case management and burnout among health workers; this strongly affects the quality of healthcare service in emergencies, as shown in studies conducted in Ethiopia (18)19). During the cholera outbreak, there is a weak subnational structure, and this finding is also highlighted in the national PHEM Guideline (20).

Weak cross-border collaboration was a problem due to a lack of prior relationships and the absence of collaboration forums, resulting in increased geographical spread and reduced information sharing. However, the national PHEM guideline principles recommended that emergency managers synchronize (coordinate) the activities of all relevant stakeholders to achieve a common purpose (7).

Case management and IPC

Inadequate water supply at households and the CTC resulted in poor hygiene, sanitation, and IPC practices in the CTC, resulting in prolonged outbreaks (16). Low clinical documentation and supervision led to difficulties in death reports, and poor management of corpses increased cross-contamination. Training gaps, lack of work experience, and inadequate staff contributed to poor case classification and management. A lack of skilled human resources hindered the closure and decontamination of CTC sites. The timely distribution of logistics and supplies was facilitated by dedicated leadership, a developed EPRP, and inter-sectoral solid coordination.

WASH and RCCE

Regular bulletins and feedback were effective for communication and decision-making practices during the cholera response. The cholera outbreak response faced challenges such as high staff turnover, inadequate infrastructure budget, and bureaucratic procurement processes. This is also relatively similar to the Dengue Fever outbreak, a public health emergency in Dire Dawa, Ethiopia that was challenged with a lack of budget allocation for risk communication and community engagement (22). However, the Dagu tradition in the Afar region contributed significantly to reducing transmission by promoting community engagement and trust through clan leaders. Identifying damaged water supplies and immediate pipeline maintenance also helped control the outbreak.

Oral Cholera Vaccination

The PHEOC, TWG, and task force were established at the national level for coordination. Several innovative OCV vaccination strategies have been introduced in different cholera epidemic and endemic countries, such as case-area targeted interventions (23), ring vaccination (24)(25), self-administration of the second dose of OCV (26), and integration of WASH intervention delivery at health facilities with vaccination programs (27). Challenges faced during the campaign included coordination issues, poor procurement procedures, targeting specific areas, and OCV dose shortages.

Limitations of the study

Limitations could be related to recall bias, which may have been introduced because some participants may forget the cholera outbreak preparedness and response details.

Conclusions and recommendations

The 2019 cholera outbreak in Ethiopia has led to several improvements. However, much work remains to ensure adequate preparedness for future outbreaks at national and subnational levels. The AAR has identified best practices that need to be institutionalized for continuity and challenges upon which preparedness activities have

been developed.
Major recommendations to better address the challenges and mitigate the impact of potential outbreaks include establishing a community-based surveillance system, conducting hot spot analysis and risk mapping, operationalizing multisectoral EOC/coordination forums, conducting inter-sectoral coordination meetings, and conducting regular water quality tests. Improving regular WASH service is very critical.

Acknowledgments
The authors express gratitude to all those involved in the article's realization, including Public Health England and WHO, for their technical support in drawing lessons for improving the healthcare system.

Author contributions
YF, YA, MA, and MB**:** designed the study, coordinated data collection, performed thematic analysis and interpretation of the data, and drafted the manuscript. NA, TS, AG, MB, JA, BM, MH, and ME, drafted the manuscript, reviewed the first draft, and interpreted the findings. All authors have read and approved the final manuscript for publication.

Declaration of conflict of interests
The authors declared no conflicts of interest concerning this article's findings, authorship, and publication.

Ethical approval and consent to participate
The EPHI has the power and duties to conduct on-site investigations during epidemics or public health emergencies, verify outbreaks, issue alerts, provide warnings, disseminate information, mobilize resources, support response activities at woredas, zones, and regional levels, and implement international health regulations on grave public health emergencies implying international crises, as per the Federal Negarit Gazeta of FDRE Regulation No.301–2013 (11). The working group consisted of government employees who were key players in the outbreak response. No ethical approval was required for their participation in the working group, and no human or animal samples were taken through any invasive procedure.

Consent for publication
Not applicable.

Acronyms

AAR	After Action Review
CTC	Cholera Treatment Center
EOC	Emergency Operation Center
IPC	Infection Prevention and Control
OCV	Oral Cholera Vaccine
PHEM	Public Health Emergency Management
RHB	Regional Health Bureau

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Ethiopian Medical Journal 2024, 62(4)
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ISSN 0014-1755 eISSN 2415-2420 Sheng et al.

Case Report

Severe Hypercalcemia as Paraneoplastic Syndrome of Hepatocellular Carcinoma

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Abstract:
Hypercalcemia is very unusual initial symptom of hepatocellular carcinoma (HCC). It commonly occurs as paraneoplastic syndrome after confirmed diagnosis of HCC. In our case report, we describe a 64–year–old gentleman who presented with symptoms of acute severe hypercalcemia and tested positive for hepatitis C. Initial investigation excluded upper and lower gastrointestinal malignancies. Further laboratory workup confirmed hypercalcemia (serum calcium 4.11 mmol/L) with normal intact parathyroid hormone (2.0 pmol/L). His alpha fetoprotein markedly raised to 16511 ug/L. Imaging investigations revealed hypervascular mass in the segment VIII of the liver. HCC can manifest as paraneoplastic syndrome like hypercalcemia due to the release of the PTHrP (parathyroid hormone related peptide), as seen in our patient. Thus, HCC should be considered part of the differential diagnosis in a hypercalcemic patient.

***Keywords**: hypercalcemia, hepatocellular carcinoma, paraneoplastic syndrome*
***Citation :** Sheng TS, Win KK.Severe Hypercalcemia as Paraneoplastic Syndrome of Hepatocellular Carcinoma. .Ethiop Med J 62 (4) 277-279*
***Submission date :** 8 June 2024 **Accepted:** 22 September 2024 **Published:** 1 October 2024*

Introduction

Hepatocellular carcinoma (HCC) is ranked as the fourth most common malignancy worldwide (1). In Malaysia, it ranked within the top ten of most frequently diagnosed cancers (2). Malaysia, being a country composed of multiple ethnicities, had its population estimated to be 34.3 million, with the majority being Malay (50.1%), followed by Chinese (22.6%), Indigenous (11.8%), and Indians (6.7%) (3). The majority of HCC cases are attributed to cirrhosis associated with chronic hepatitis B or C, alcoholism, or non –alcoholic steatohepatitis (NASH) (4). There was a report from a large multicenter study that revealed <2% of HCC are non-cirrhotic in origin (5). HCC development from cirrhotic liver is known to be from stepwise mutation, however, its progression from non –cirrhotic liver is not well understood, which is speculated to be from *de novo* carcinogenesis (6). It is rare to encounter HCC patients presented with hypercalcemia without bone metastasis, as one of its paraneoplastic syndromes, reported in 4–7% of patients (7).

There were some reported paraneoplastic syndromes associated with HCC, namely hypoglycemia (8), demyelination, pemphigus vulgaris (9), thrombocytosis (10), hypercalcemia, hypercholesterolemia, and erythrocytosis (11).

We would like to share our local experience, where our patient initially presented with symptoms of hypercalcemia and subsequent workup revealed HCC with hypercalcemia as paraneoplastic syndrome.

Case Presentation

A 64–year–old man with no prior medical problems presented with epigastric discomfort, constipations, loss of appetite, and weight loss of 10 kg in 1 month, with no known family history of malignancy. Physical examinations revealed palpable liver 2 cm below the costal margin. Laboratory results revealed elevated calcium 4.11 mmol/L (normal range 2.02-2.60), raised AFP (alpha fetoprotein) 16511 ug/L (normal range < 7.0), low albumin 34 g/L (35–50), positive for Hepatitis C screening. Other tumor markers and Hepatitis B screening were normal. He denied excessive intake of antacids or vitamins A and D. He was subsequently admitted to the general surgical ward.

Oesophagogastroduodenoscopy (OGDS) and colonoscopy did not reveal any abnormalities other than antral gastritis. Ultrasonography of abdomen revealed an ill-defined heterogenous mass at segment VIII of the liver (measuring approximately 6.8 x 7.3 x 7.0 cm). Computerized tomography (CT) scan showed solitary, well –defined liver mass in segment VIII (5.0 x 8.9 x 9.5

cm) in a non-cirrhotic background, with hepatic arterial enhancement and washout in the venous and delayed phase consistent with HCC, without evidence of bony metastasis (Figure 1).

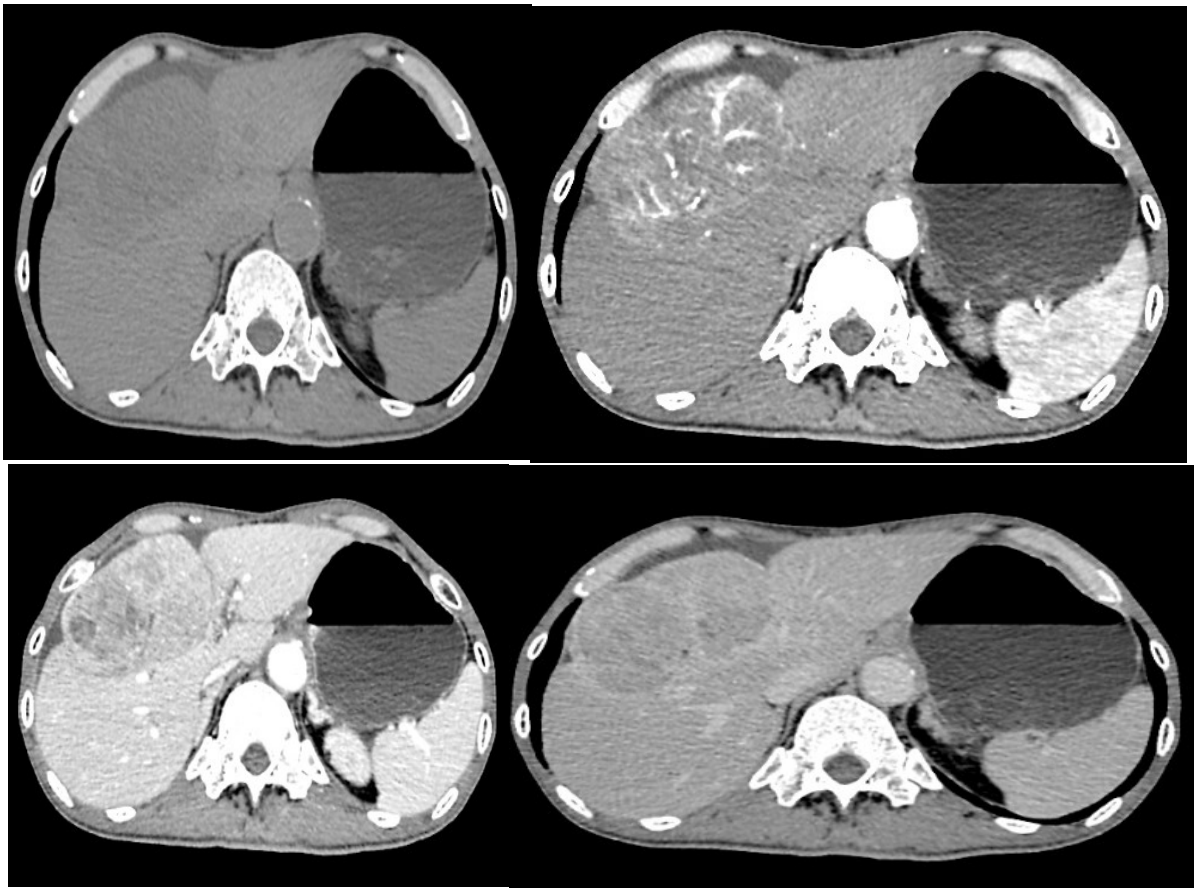

Figure 1. Axial CT images in (a) plain, (b) arterial, (c) porto-venous and (d) delayed phase. Hypervascular mass in segment VIII of liver which demonstrate arterial enhancement with washout in the porto venous and delayed phase.

His corrected calcium level was noted to be persistently high despite intravenous bisphosphonates and aggressive intravenous hydration with forced diuresis. Further workup for hypercalcemia revealed normal intact parathyroid hormone (PTH) 2.0 pmol/L (normal range 1.6-6.9), and a normal ultrasound neck (no sonographic evidence of parathyroid mass). A diagnosis of hypercalcemia as paraneoplastic syndrome associated with HCC (Barcelona Clinic Liver Cancer BCLC Stage B) was made. Diagnosis was revealed to the patient and his family members, where trans – arterial chemoembolization was offered; however, they were not keen. His clinical condition continued to deteriorate, and subsequently he expired after 2 months from the time of diagnosis.

Discussion

Identification of non–cirrhotic HCC generally was delayed due to its indolent nature of disease by virtue of being symptomatic at a later stage, as the case in our patient. Thus, they tend to have larger tumor burdens at initial presentation, with an average of 12 cm, in contrast to their cirrhotic counterparts with a smaller size range (12). Current literature suggests resection at the first step of treatment in those with good liver function (Child–Pugh score A), and a solitary mass (13).

There were four known mechanisms that lead to hypercalcemia in malignancy. About 80% of cases, commonly occur in squamous cell cancers, related to PTHrP (parathyroid hormone related peptide) secretion by cancer cells, also known as humoral hypercalcemia of malignancy. While 20% of cases are associated with osteolytic activity at sites of bone metastasis, most commonly seen in breast cancer, lymphomas, and multiple myelomas. There were unusual occasions where

some lymphomas were linked with vitamin D secretions from tumor cells or via ectopic tumor secretion of PTH (14).

Our patient was found to have hypercalcemia, normal intact parathyroid hormone, and a confirmed diagnosis of non–cirrhotic HCC, indicating humoral hypercalcemia of malignancy, while we do not have adequate resources to measure the PTHrP.
Our patient's unusual presentation of hypercalcemia leading to the diagnosis of non–cirrhotic HCC is challenging and tends to have a poor prognosis, as evidenced by a markedly high tumor marker (AFP > 10,000 ug/L) with the presence of paraneoplastic syndrome (hypercalcemia) (15).

Conclusion
Our patient had been diagnosed with non – cirrhotic HCC with accompanying hypercalcemia as paraneoplastic syndrome. Unfortunately, its detection carries a poor prognosis. HCC should be considered part of the differential diagnosis of hypercalcemia, though non –cirrhotic HCC tends to present late with isolated hypercalcemia.

Competing interests
There was no funding for the study and no conflicts of interest to disclose.

Consent
Patient's family members gave verbal consent for this case study.

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Ethiopian Medical Journal 2024, 62(4)
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ISSN 0014-1755 eISSN 2415-2420 Anbarasi et al.

Case Report

Management of Recalcitrant Case of Oral Pemphigus with Intralesional Corticosteroids: A case report

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Abstract:
Oral pemphigus is one of the prevalent autoimmune oral mucosal diseases. However, the recalcitrant variant is infrequent and challenging to manage. These shallow ulcers may persist for several months and interfere with the normal state of health. We present a case of a female patient with long standing ulcers in oral cavity involving multiple sites. She was referred from dermatologist. She was on conventional corticosteroids and immunosuppressants, but had no relief symptomatically for the past 6 months. We managed the patient with intralesional corticosteroids and within 3 months, resulted in disease-free state. The treatment methods followed in our case could be successful to implement by oral physicians when the situation demands.

***Keywords**: Oral Lesions, Intralesional corticosteroids, Pemphigus, Recalcitrant Type*
***Citation :** Anbarasi K[1],Warrier Aravind, Ramesh Preethi. Management of Recalcitrant Case of Oral Pemphigus with Intralesional Corticosteroids: A case report,Ethiop Med J 62 (4) 281-285*
***Submission date :** 25 August 2023 **Accepted:** 23 September 2024 **Published:** 1 October 2024*

Introduction

Pemphigus is an autoimmune blistering disease affecting middle-aged and elderly individuals, targeting skin and mucosal surfaces through IgG autoantibodies against desmoglein 3 and 1 proteins on keratinocytes. When both are involved, skin and mucosal surfaces are affected; if only dsg3 is involved, it primarily affects the mouth. Oral pemphigus presents as vesicles or bullae that rupture, forming chronic ulcers in areas like the buccal mucosa, gingiva, palate, and lips [1]. First-line treatment involves systemic corticosteroids, sometimes with agents like azathioprine or cyclophosphamide. This report details a rare case of oral pemphigus with an annual incidence of 0.1 to 0.5 per 100,000 [3]. The patient, unresponsive to six months of oral corticosteroids, was successfully treated with intralesional corticosteroid injections [4].

Case History

A 46-year-old woman presented with mouth ulcers, difficulty eating, bleeding while brushing, and increased salivation. She developed blisters that ruptured into ulcers and was diagnosed with oral pemphigus. Initially treated with topical Tenovate 0.05%, her condition worsened after 5-6 weeks, prompting systemic treatment with Omnacortil 20 mg and Endoxan 500 mg, twice daily. After six months with no improvement, she stopped taking Dexamethasone-Cyclophosphamide Pulse therapy due to cancer-phobia and was referred to our hospital.

Clinical Findings

On examination, the patient (161 cm, 49 kg) had multiple ulcers on the palate, buccal mucosa, and lower lip, with generalized gingival erythema [Figure 1]. Profuse bleeding and severe pain were noted. The pain score was 9 on the VAS. Recalcitrant pemphigus was diagnosed, with bullous pemphigoid and bullous lichen planus as differentials.

Investigations

The Tzanck test showed acantholytic cells, indicating pemphigus. [Figure 2A]. Histopathology revealed acanthosis with suprabasilar bullae and acantholytic cells, distinguishing pemphigus from sub-epithelial blistering diseases. [Figure 2B] Direct Immunofluorescence (DIF) showed IgG positivity on desmosomes, confirming pemphigus vulgaris. [Figure 2C]

Therapeutic intervention

Systemic immunosuppressants were stopped, and intralesional corticosteroid injections (ICSI) of dexamethasone and lignocaine hydrochloride were administered biweekly for six weeks. The patient had no adverse reactions. [Figure 2D] The treatment response is detailed in Table 1.

Figure 1: Multiple shallow irregular ulcers at the junction of hard & soft palate, lower lip and right buccal mucosa.

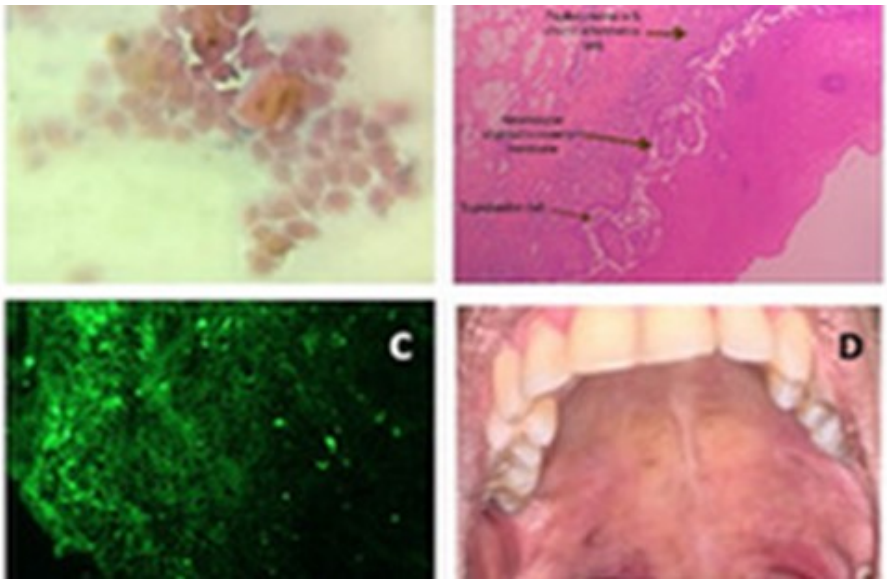

Figure 2A: Tzanck smear shows presence of acantholytic cells.

Figure 2B: Healing of lesion by 2nd week of ICSI

Figure 2C: Healing of lesion by 4th week of ICSI

Figure 2D: Healing of lesion by 6th week of ICSI

Figure 2E: Healing of lesion by 8th & 9th week of ICSI

Figure 2F: Complete resolution of lesions in the palate and lips by 12th week of ICSI & Patient remained free of oral ulceration without any relapse after 4 reviews

Table 1: Patients response to the ICSI, at Chennai, 2021(March – May).

Treatment	Review report			
	2nd week review	4th week review	6th week review	8th week review
ICSI – Twice weekly Syrup. Dexorange 0 - 1tsp-0 Tab. Zu- C 500mg 0-1 -0 Povidine iodine (Betadine) gargle, twice daily	Appreciable healing of the lesion in right buccal mucosa and gingiva, with symptomatic relief. No response in Lip and palatal lesions. [Figure 3] VAS score - 6.	Lesions on the buccal mucosa healed completely. significant healing of the gingival lesions. [Figure 4] Lip and palatal lesions remind the same. VAS score – 4	Gingival erythema subsided. signs of healing was noted in the lip and palate. [Figure 5] VAS score – 3	Lesions on the palate healed completely with the track-down of erythema. Lip lesion showed remarkable response. [Figure 6] VAS score - 0

Follow-up and Outcome

By the second week of therapy, new lesion formation stopped, and existing lesions began to heal. By the ninth week, 80% of lesions had healed, and no new lesions appeared. Intralesional corticosteroid injections (ICSI) were discontinued, and the patient was prescribed topical Tenovate 0.05% thrice daily. By week 12, significant healing was noted, with complete resolution of palatal lesions and lip lesions healing the following week. [Figure 7] As all symptoms resolved and no new lesions formed, topical therapy was withdrawn. The patient completed four follow-up visits and remained free of oral ulcerations. At a one-year follow-up, there was no relapse, and annual review visits were planned.

Discussion

Oral pemphigus causes chronic ulcers due to bullae formation and rupture [5]. The primary treatment goal is symptom relief using corticosteroids. Initially, the patient received low-dose prednisolone and cyclophosphamide. Dexamethasone-Cyclophosphamide Pulse (DCP) therapy, known for higher efficacy and rapid healing, was considered but

avoided due to its complications, such as diabetes and hypertension [6]. Instead, ICSI was chosen to deliver high local drug concentrations, accelerating healing and minimizing systemic absorption [7]. This approach reduces mucosal atrophy risk and ensures longer drug retention at the lesion site. Despite the potential side effects like bleeding and mucosal atrophy, the patient experienced none. The total dose was limited to 2 ml per session, and significant improvement was observed by the fourth week, with complete healing by the eighth week. There was no recurrence during the one-year follow-up, but sustained remission for at least five years is necessary to reduce recurrence risk.

Conclusion

Though systemic corticosteroids, with or without immunosuppressive drugs, are the standard treatment for pemphigus, a favorable response to intralesional steroid injections achievied a symptom-free, recurrence-free state one-year post-treatment in the present case.

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Ethiopian Medical Journal 2024, 62(4)
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ISSN 0014-1755 eISSN 2415-2420 Birhanu et al.

Original Article

Acute Gastrointestinal Bleeding from Gastric Dieulafoy's Lesion in a Pregnant Woman with Chronic Hepatitis B Infection

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Abstract

Background *Dieulafoy's lesion is a rare but important cause of upper gastrointestinal bleeding (UGIB). It is a dilated submucosal artery that erodes the overlying mucosa and bleeds without causing ulcerations. Dieulafoy's lesion can be a cause of life threatening UGIB which can be identified and controlled successfully by endoscopic therapy. We present a rare case of a 40-year-old mother, in her 3rd trimester of pregnancy, who presented with voluminous bloody vomiting and melena of five days duration. Her past medical history was notable for chronic HBV infection with suppressed viral load. After thorough evaluation, endoscopy revealed Dieulafoy's lesion along the greater curvature of body of stomach, identified as the source of her UGIB. She was successfully treated with hemoclipping. On subsequent follow up, her hemoglobin levels were stable and she had no obstetric complications or recurrence of her symptoms. This paper highlights the unusual occurrence of Dieulafoy's lesion as a cause of UGIB in pregnancy and reviews current diagnostic and therapeutic recommendations.*

Keywords*: Dieulafoy's lesion, Upper Gastrointestinal bleeding, Pregnancy, Endoscopy, clipping*
Citation : *Birhanu Y , Demissie Z, Zemedkun N et al. Acute gastrointestinal bleeding from gastric Dieulafoy's lesion in a pregnant woman with chronic hepatitis B infection Ethiop Med J 62 (4) 287=290*
Submission date : *10 April 2024 Accepted: 19 September 2024 Published: 1 October 2024*

Introduction

Upper gastrointestinal bleeding (UGIB) is a commonly encountered life-threatening medical emergency, with a bleeding PUD being the most common cause. During pregnancy, however, mucosal tears from Mallory-Weiss syndrome are the most common causes, pertaining to the physiologic changes of pregnancy. Notably, there have been only two documented occurrences of Dieulafoy's lesion causing UGIB in pregnancy in the literature [1, 2].

Dieulafoy's lesion (DL) is a vascular malformation causing a dilated submucosal blood vessel that bleeds without ulceration [3]. Although it's hard to determine its true incidence, it's believed to account for 1-2% of UGIB cases [4, 5]. The challenges in diagnosing Dieulafoy's lesion, along with its historically high mortality rate of up to 80%, make it an important differential diagnosis in UGIB. Endoscopic interventions have significantly reduced the mortality associated with this condition. However, its diagnosis still requires high level of clinical suspicion and expertise [5].

In this paper, we describe a case of a 40-year-old pregnant woman in her third trimester of pregnancy who presented with symptoms of hematemesis and melena. Her past medical history of chronic HBV infection, without clinical signs of cirrhosis and no other apparent cause of UGIB, posed a diagnostic challenge.

Case Presentation

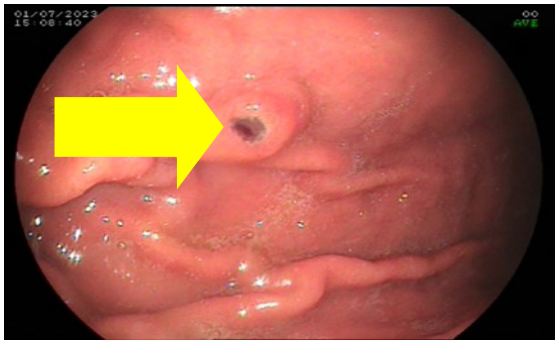
A 40-year-old woman in her third trimester of pregnancy, with a previous diagnosis of chronic hepatitis B infection under regular follow-up visited the Gastroenterology and Hepatology clinic at Lancet General Hospital after experiencing two episodes of voluminous coffee-ground vomiting and dark stools of five days duration. She had no history of nonsteroidal anti-inflammatory drugs (NSAIDs), antiplatelet, or anticoagulant use, no alcohol intake, and no prior treatment for PUD, nor did she have history of preceding vomiting, retching, or vascular disease in herself or family. Upon arrival, her vital signs were stable, and her physical examination was unremarkable except for pale conjunctiva and palmar pallor. There was no jaundice, palpable abdominal

organ, or signs of peritoneal fluid collection. Laboratory results showed hemoglobin was 9.1 g/dL, platelet count of 140,000 per microliter, and international normalized ratio (INR) of 1.19, with normal liver and renal function tests. Abdominal and obstetric ultrasound showed a normal third trimester pregnancy that was otherwise unremarkable. Her most recent HBV DNA level, done two months back, was 25 IU/mL.

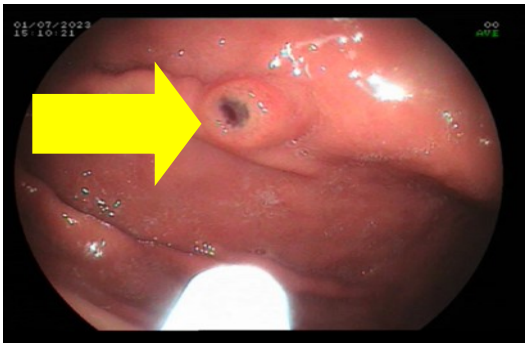
An esophagogastroduodenoscopy revealed a normal mucosa of the esophagus, fundus, antrum, and cardia of the stomach. However, a large protruding submucosal vessel with an overlying clot, but no active bleeding, was noted over the greater curvature of the stomach body. No ulcer or varices were identified. Endoscopic clipping was successfully performed at the base of the dilated vessel.

Obstetric evaluation performed on the same day of the procedure revealed normal findings, aside from the anemia. It was planned to shorten second stage of labor and to give iron supplements for the anemia. The patient was then started on daily oral doses of Esomeprazole 40 mg and Ferrous sulfate 325 mg. She was re-evaluated at the GI clinic two and four weeks post-discharge, with hemoglobin levels of 10 g/dL and 11 g/dL, respectively, and no further episodes of bleeding. She continued her ANC visit, and delivery was uneventful.

Endoscopic images showing the gastric Dieulafoy's lesion before and after clipping are shown in Figure 1.

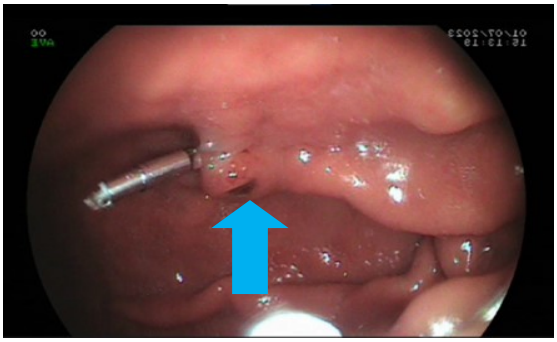


1A

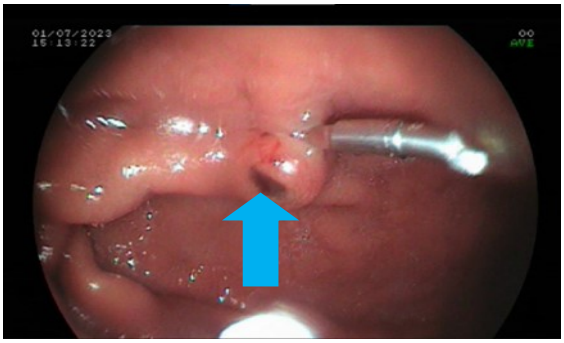


1B

Figures 1A and 1B show a big protruding submucosal vessel with an overlying clot over the greater curvature of the stomach body, without active bleeding (yellow arrow).



1C



1D

Figures 1C and 1D show the applied endoscopic clipping (blue arrow).

Discussion

Dieulafoy's lesion is a notable cause of UGIB, with the potential to cause severe, life-threatening, and recurrent episodes. It is characterized by a histologically normal tortuous submucosal vessel, measuring 1–3 mm in diameter, that protrudes through a small mucosal defect [5]. DLs account for 1% to 2% of all GI bleeding cases, with a recent mortality rate ranging from 9 to 13 % [6].

Although DL can develop anywhere along the GI tract, the gastric region is the commonest site representing 70% of cases, followed by duodenum (15%), esophagus (8%), colon, and rectum (2%) [5].

The etiologies and precipitating factors for DLs remain poorly understood. The lesions occur twice as commonly in males than females and are more common in the elderly population, though they can occur in any age group. Patients with DLs often have non-gastrointestinal

comorbidities such as cardiovascular disease, hypertension, diabetes, and chronic renal insufficiency.
While NSAIDs and anticoagulants are known to precipitate UGIB in individuals with DLs, no definitive causal link has been established between these medications, *Helicobacter pylori* infection, or PUD and the development of DLs[5, 6].

DL typically presents with acute GI bleeding in a patient with no prior history of gastric problems. About half of the patients with upper GI lesion present with both hematemesis and melena. The bleeding is arterial and therefore can be severe episodes, often causing hemodynamic instability and laboratory abnormalities [6].

Upper endoscopy is the first-line diagnostic modality to detect DLs. These lesions typically appear as a mucosal protuberance with a visible pigmented underlying vessel, without an associated ulcer. However, endoscopy detects the lesions in only 70% of cases. The lower diagnostic yield is attributable to small size of lesions, their challenging locations, and obscuration by active bleeding. Other diagnostic modalities include endoscopic ultrasonography (EUS), bleeding provocation, capsule endoscopy, and angiography [5-7].

The general treatment principle of UGIB should be followed in the management of DL bleeding. These include risk stratification, adequate resuscitation, blood product support, and securing hemostasis. Since patients with DLs are at risk of recurrent episodes of bleeding especially in the first 72 hours, securing hemostasis is critical. The methods include clipping, thermal or electrical coagulation, sclerotherapy, and Argon plasma coagulation. These techniques achieve initial hemostasis in about 90% of cases [5-7].

The safety of endoscopy during pregnancy remains uncertain. The major risks include fetal hypoxia, premature labor, trauma and teratogenesis due to sedative medications. In pregnant women, endoscopy should be performed only for strong indications and with strict fetomaternal monitoring. To minimize complications, it is recommended to delay the procedure until the third trimester, when possible, use the lowest effective dose of sedatives, and shortening the procedure time [8].

According to some reports, HBV DNA levels remain stable during pregnancy, and pregnancy is unlikely to affect the long-term course of chronic hepatitis B or its progression to decompensated liver disease and cirrhosis. Therefore, the primary focus during pregnancy remains taking necessary measures to reduce vertical transmission of the virus [9]. We could not find an association between hepatitis B infection and DL in our literature review.

The management of DL during pregnancy is similar to the general population [2]. In both reported cases of DL-induced UGIB during pregnancy, hemoclipping was used as the treatment modality. In our case, although the patient has chronic HBV infection and was at risk for variceal bleeding, the endoscopy identified DL on the greater curvature of the stomach and hemostasis was secured with clipping. The patient was discharged home with supportive treatment and experienced no obstetric complications or recurrence of bleeding.

Conclusion
Although rare in occurrence, Dieulafoy's lesion is an important cause of potentially severe, recurrent, and life -threatening UGIB. In patients with no identifiable cause of UGIB, DL should be considered including in pregnant women. Endoscopy is he cornerstone of both diagnosis and management, with high success rate. However, it requires a high level of clinical suspicion and expertise to identify these lesions. Early recognition and prompt intervention are crucial in managing UGIB caused by DL.

Ethical approval
Written consent was obtained from the patient for publication of this case report and associated images.

Acknowledgment
We express our gratitude to the patient for supplying all pertinent details and allowing the publication.

Funding
None

Disclosure
All authors declare no competing interests of any kind in this publication.

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https://dx.doi.org/10.4314/emj.v62i4.9

Ethiopian Medical Journal 2024, 62(4)
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ISSN 0014-1755 eISSN 2415-2420 Zahid et al.

Case Report

Infant Testicular Tumour in Maternal Ovarian Cancer

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Abstract:
Vertical transmission is a rare phenomenon that can occur during pregnancy with a mother diagnosed with cancer. We present a rare case of an infant with a testicular tumor with a history of a mother having ovarian cancer and undergoing surgery and chemotherapy during pregnancy. A five-month-old boy presented with a right testicular mass of 3 weeks duration. Ultrasound of the bilateral scrotum showed a homogenous mass with increased vascularity, and his Alpha-fetoprotein (AFP) result was high at 4300ng/ml. We performed a high ligation right orchidectomy. Computer Tomography of the thorax, abdomen, and pelvis was done, and no evidence of metastasis was found.

Keywords: *Infant Testicular Tumour; Ovarian Cancer; Pregnancy; Vertical Transmission*
Citation : *ZahidL SK,Shah MS ,Samad MR . Infant Testicular Tumour in Maternal Ovarian Cancer. Ethiop Med J 62 (4) 291-295*
Submission date : *23 June 2023 Accepted: 09 August 2024 Published: 1 October 2024*

Introduction

Cancer during pregnancy is not an uncommon condition; however, maternal to fetal transmission of cancer cells is a rare phenomenon; it is not unexpected due to uteroplacental blood flow representing 10% of maternal cardiac output (1) . There are approximately 100 reported cases, most representing metastasis confined to the placenta(2). It is a rare occurrence, given the placenta barrier and fetal immune system, that can prevent the possibility of tumour transmission to the placenta and fetus. However, the risk of transmission still can occur when the separation of the fetal and maternal blood systems is breached; maternal intravascular tumor cells can pass through the placenta and end up in the fetus (3).

This case report presents a rare case of a mother with ovarian cyst adenocarcinoma during pregnancy, then her infant develops a right testicular tumor (yolk sac tumor). To the best of our knowledge, there is no reported case regarding this condition with two different types of tumour cells.

Presentation of the case

A 5-month-old boy presented with right testicular swelling of 3 weeks; it was painless, with no redness, and there was no other complaint. On clinical examination, his right testis, size 3x3 cm, located in the scrotum, was regular and had no skin changes. His blood investigation results were AFP 4436 ng/ml, Lactate dehydrogenase 475 U/L, Beta Human Chorionic gonadotropin <0.1 ng/ml.

Further history, antenatally, his mother was diagnosed with right ovarian cancer at 16 weeks POA. Initially it was incidental finding during booking, USG at 8 weeks, there is right ovarian cystic multiloculated with thick septae. She has undergone a right cystectomy and omentectomy at 16 week period of amenorrhea (POA). The histopathological examination revealed low-grade cystoadenocarcinoma of the right ovary. Then, his mother was given intravenous chemotherapy with a total of 4 cycles started at 19 weeks of POA. He was delivered via emergency Caesarean section at 36 weeks since the mother had pre-eclampsia and leaking liquor. Post delivery, the baby was well and was monitored until day 7 of life and then was discharged well.

Further investigation by ultrasound of the scrotum and abdomen showed the right testis homogenously enlarged with increased vascularity with size 2.1 x2.6 x3.1 cm (Figure A). We performed a high-ligation right orchidectomy via an inguinal approach. Intraoperatively, the right testis size 4x3 cm, dilated and engorged testicular vessels, and no lymph node was

noted at the right inguinal region (Figures B and C). Subsequent histopathological examination showed the presence of a tumor replacing the testicular parenchyma infiltrating rete testis (Figure D). There are Schiller Duval bodies characterized by fibro vascular core within the cystic space, which is lined by neoplastic cells (Figure E). Immunohistochemical stains showed positive for CKAE1&3, AFP, and CD117 and harmful for CD30 (Figure F). The overall features are consistent with prepubertal type yolk sac tumours. His CT TAP showed no evidence of distant metastasis. His post-operative AFP is reducing, and the latest one is 345ng/ml. No chemotherapy is done in view of stage I disease, and only monitoring his condition and AFP level.

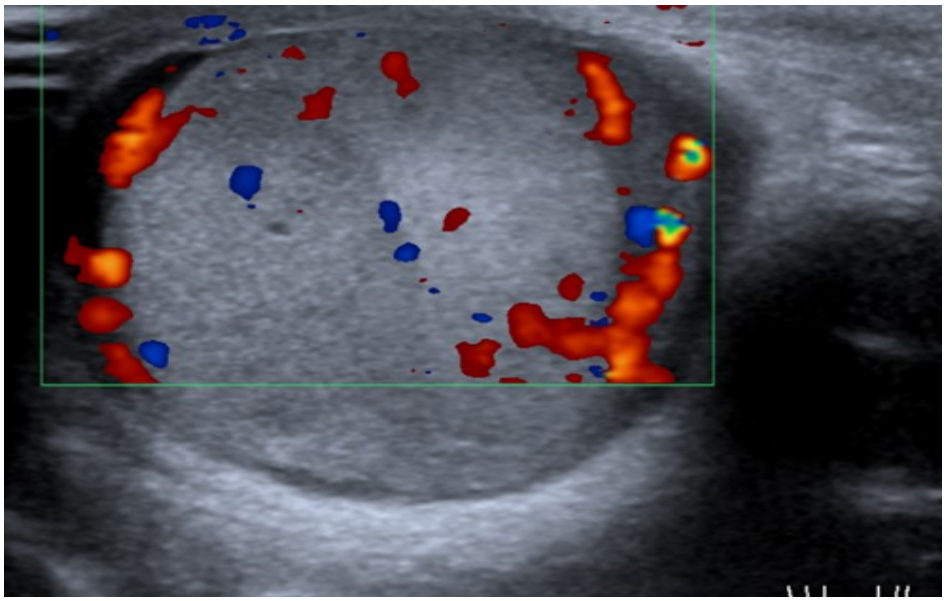

Figure A: showed right testis is homogenously enlarged and increased in vascularity. It is measuring 2.1cm x 2.6cm x 3.1cm (AP x W x CC).

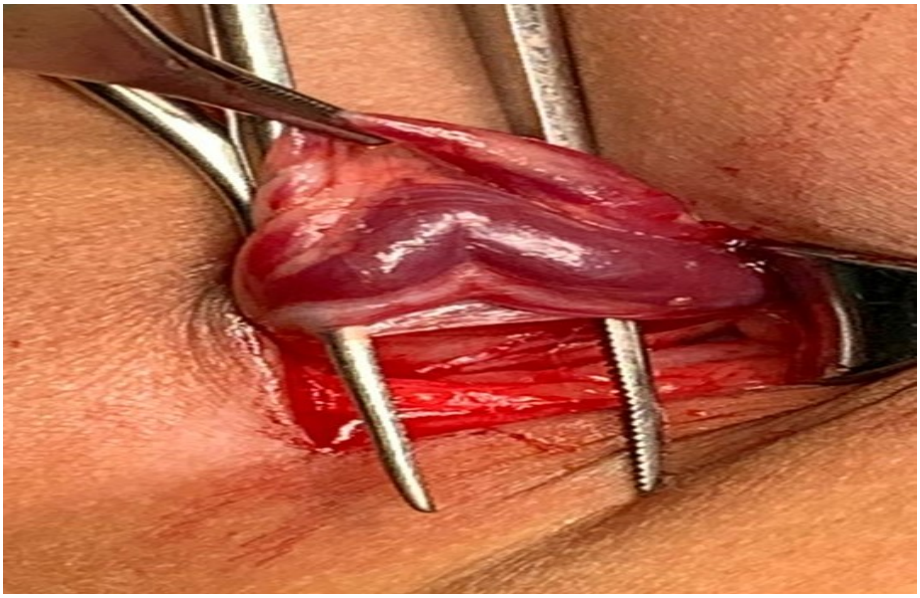

Figure B: showed engorgement of right testicular vessel

Figure C: showed the right testicular mass with spermatic cord that was removed during high ligation orchidectomy.

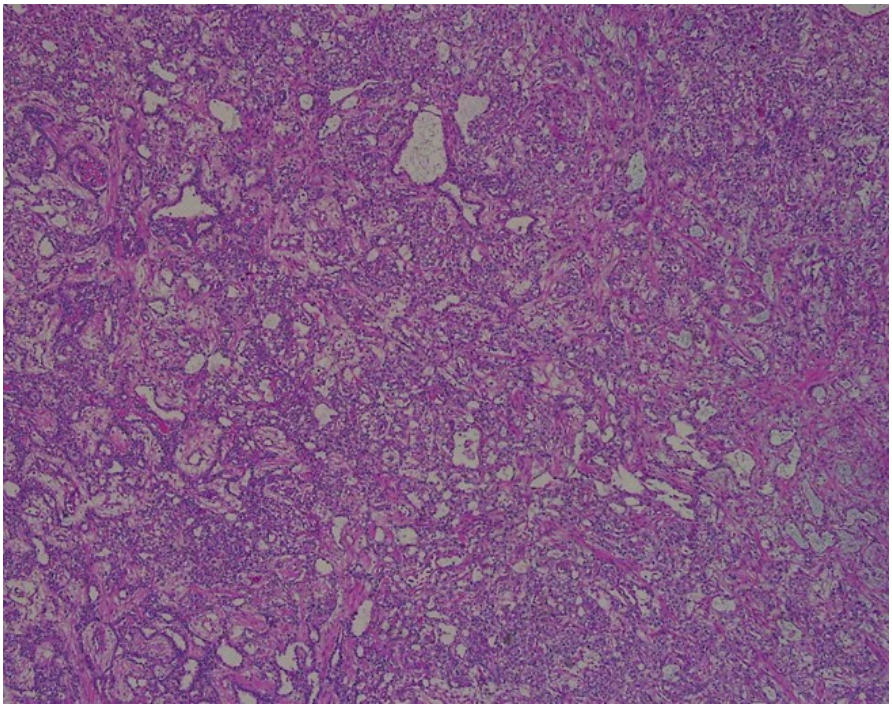

Figure D: Tumor arranged in microcystic reticular pattern admixed with macrocystic, alveolar, and solid sheet architecture. The tumor cells are moderately pleomorphic, with vesicular nuclei, some shows prominent nucleoli in clear to eosinophilic cytoplasm

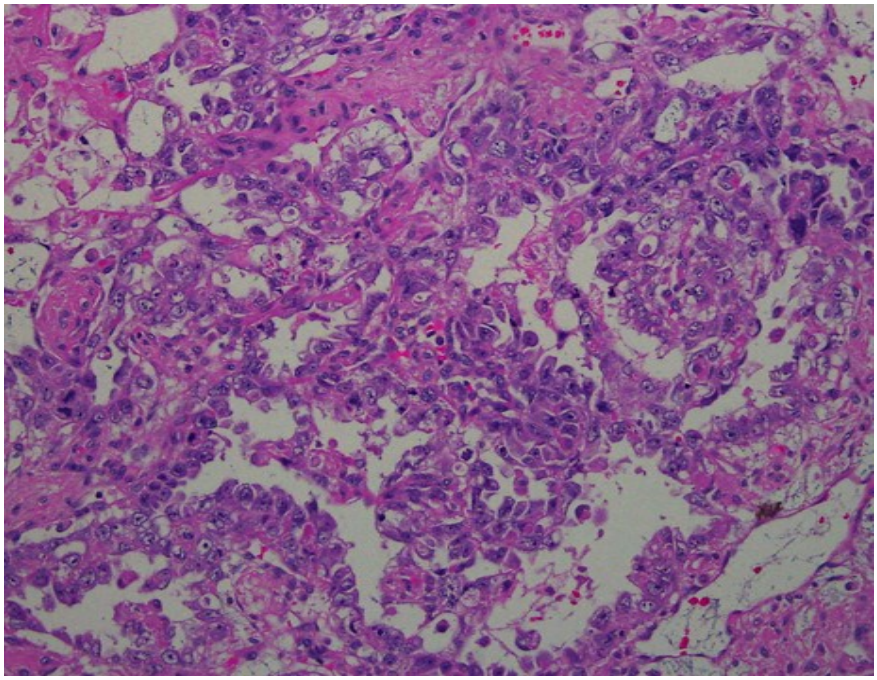

Figure E: Presence of Schiller Duval bodies.

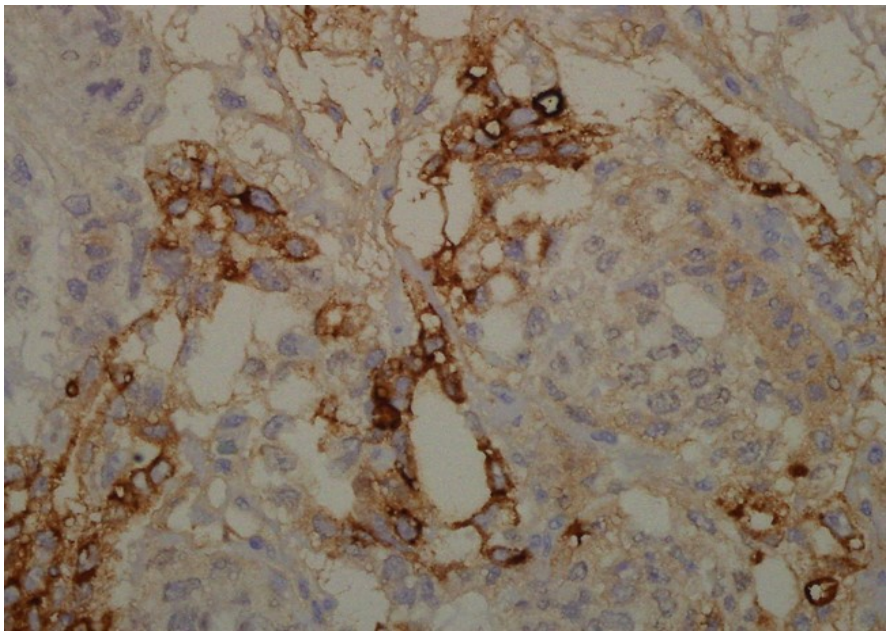

Figure F: Tumor cells are focally positive for AFP

Discussion

Cancer with coexistence of pregnancy is not uncommon, with a frequency of around 1 case of cancer every 1,000 gestation (4). Vertical transmission is a rare phenomenon that can occur during pregnancy. Vertical transmission is defined as the spread of tumor cells from mother to fetus through the placenta. It is rare, probably due to the placental barrier and fetal immune system. The Placenta barrier plays a role in the syncytiotrophoblast cells' recognition and rejection of foreign maternal antigens expressed by the cancer cells (4,5). The transmission is thought to be haematogenous spread, although lymphatic dissemination and contiguous invasion have also been considered(4).

The transmission to the placenta or fetus is most frequently seen in melanoma (30%), leukemias and lymphomas (15%), breast cancer (14%), and lung

cancer (13%), followed by bone or soft tissue sarcomas, gynaecological malignancies, gastric cancer or other tumors (6). Furthermore, the tumour in the fetus that was reported is the same type as a maternal tumour that is suggestive of metastasis. The average age of presentation of vertical transmission of maternal tumor is 4–5 months after delivery but ranges from birth to 20 months (5). A baby that was delivered via mother with malignancy during pregnancy needs to be properly examined and followed up to look for the risk of possibility to develop metastasis or malignancy (1).

Every reported case regarding fetus and placental metastasis showed evidence that cancer cells in the mother and infant are from the same types. However, in our case, the mother and infant had different types of cancer cells, so the possibility of metastasis is unlikely. The occurrence of testicular cancer in infants in correlation with the mother of ovarian cancer during pregnancy has not yet been reported with different types of tumors. There is need further evaluation or study need to be done to check the possibility genetic link between these two types of cancer.

Conflict of interest: Authors declare no conflict of interest involved.

Ethical Considerations: Verbal consent taken from the mother to take picture and to publish this case report.

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https://dx.doi.org/10.4314/emj.v62i4.10

Ethiopian Medical Journal 2024, 62(4)
ISSN 0014-1755 eISSN 2415-2420
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Brief Communication

Malaria Outbreak Resurgence in Ethiopia May Reverse Maternal and Perinatal Health Progress: Is This The Time to Implement Intermittent Preventive Treatment?

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Abstract:
Malaria remains a major public health challenge in Ethiopia. Despite earlier progress toward elimination, confirmed cases surged after 2021 due to disruptions from COVID-19, armed conflicts, displacement, climate change, and the emergence of insecticide-resistant mosquitoes.
Especially pregnant women are vulnerable to malaria and face increased risks of maternal anemia, preterm delivery, stillbirth, low birth weight, and neonatal death, which could reverse the effort made on the two decades' progress in maternal and perinatal health. Recent unpublished evidence from routine hospital perinatal audits highlights the potential impact.
Despite the World Health Organization's recommendation to use intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP), Ethiopia has not yet adopted this intervention, which relies on previous malaria control successes and assumes low-to-moderate transmission levels. However, the recent surge in malaria cases, coupled with the persistent nature of contributing factors, calls for an urgent reassessment of this policy, as it may take a prolonged period to regain control. This brief communication underscores the urgent need to implement IPTp-SP in high-risk populations and strengthen collaboration between maternal health and malaria control programs for the ongoing monitoring of pregnancy outcomes. It emphasizes prioritizing pregnant women for interventions and enhancing healthcare providers' awareness of preventive strategies. Immediate action is vital to protect vulnerable populations and reverse the harmful effects of malaria resurgence.

Keywords: *Malaria resurgence, pregnancy, intermittent preventive treatment, maternal and perinatal outcomes, Ethiopia*
Citation : *Gedefaw A. Malaria Outbreak Resurgence in Ethiopia May Reverse Maternal and Perinatal Health Progress: Is This The Time to Implement Intermittent Preventive Treatment? Ethiop Med J 62 (4) 297-300*
Submission date : *20 September 2024 Accepted: 29 September 2024 Published: 1 October 2024*

Resurgence of the Malaria outbreak in Ethiopia

Malaria remains a significant public health and socio-economic challenge in Ethiopia, affecting millions annually (1, 2) and varying across the country, with some regions experiencing more severe outbreaks(3). From 2000–2016, malaria control efforts led to a sharp decline in malaria-related morbidity and mortality (3-5). The number of confirmed cases decreased by 42.7% between 2017 and 2019, and the number of malaria-related deaths decreased by 40% (6, 7). However, this progress was interrupted by a resurgence in the last three years. Between 2021 and 2022, the number of confirmed cases increased by 32.5%. In 2022 alone, 5.1 million people were infected, and approximately 75 million people were at risk (8). In 2023, malaria cases increased by 150% and 120%, respectively, compared with the same periods in 2021 and 2022. In the first half of 2024, over 2.3 million cases and 554 deaths were reported(9).

This resurgence is driven by several factors, including programmatic disruptions due to the COVID-19 pandemic, armed conflicts, displacement, climate change-induced extreme weather events such as heavy rains and flooding, emerging insecticide resistant mosquitoes, and possibly increasing antimalarial drug resistance(1, 8). Additionally, prevention and control efforts have been hampered by limited funding for control and prevention programs(8).

Maternal and perinatal adverse outcomes of malaria infection

Ethiopia has experienced one of the fastest declines in maternal and perinatal mortality in sub-Saharan Africa

over the past two decades(10). The resurgence of malaria may threaten the maternal and perinatal health gains achieved over the past two decades(11). Pregnant women are vulnerable to malaria, which can result in severe complications such as maternal anaemia, preterm delivery, low birth weight, miscarriage, stillbirth, and neonatal death(12, 13). Pregnant women are three times more likely to develop severe malaria than non-pregnant ones, with mortality rates from severe disease reaching 50%(14, 15). While comprehensive data on the impact of recent outbreaks on maternal and perinatal outcomes in Ethiopia are lacking, recent audit reports from malaria-endemic regions, such as Hawassa University Hospital, highlight the severity of the issue. For example, perinatal mortality audits conducted in July and August 2024 revealed that malaria infection contributed to approximately 50% of perinatal deaths during this period (*unpublished but data can be shared upon request*). These findings underscore the urgent need for further investigation and intervention to mitigate the adverse effects of malaria epidemic on maternal and perinatal health.

Current global strategies for malaria prevention during pregnancy

Current strategies for preventing malaria during pregnancy rely on two main approaches. The World Health Organization (WHO) recommends effective vector control methods, such as insecticide-treated nets (ITNs) or indoor residual spraying, and intermittent preventive treatment during pregnancy with sulfadoxine-pyrimethamine (IPTp-SP) in areas of moderate to high malaria transmission(1, 16). IPTp-SP has been shown to reduce the incidence of malaria during pregnancy, placental parasitemia, as well as maternal anaemia, and improve birth outcomes(17, 18). However, in 2018, only 30% of pregnant women in sub-Saharan countries received the recommended three or more doses of IPTp at ANC facilities. Limited access to ANC services, the unavailability of IPTp at health facilities, and healthcare workers failing to prescribe treatment contribute to this low uptake(19).

Malaria prevention during pregnancy strategies in Ethiopia

In Ethiopia, the use of IPTp-SP is limited because the healthcare system has not adopted the policy(5, 20, 21), even though more than 37 sub-Saharan African countries, including neighbouring Kenya, have done so (22). The WHO estimates that current IPT coverage in Africa has prevented over 500,000 low-birthweight deliveries, highlighting its critical benefit in reducing perinatal mortality(1).

The 2021 National ANC guidelines(20) and the 2022 National Malaria guidelines (21) recommend only the use of insecticide-treated nets and the diagnosis and treatment of malaria for pregnant women attending ANC, assuming that Ethiopia has low-to-moderate malaria transmission. The decision may be based on the national achievements of the malaria control and prevention program before the recent outbreak(5). Although there was success at the national level, the implementation did not benefit high-transmission districts or seasonal outbreaks. IPTp-SP is mentioned only as a WHO recommendation for moderate -to-high transmission areas, relying on individual healthcare provider preferences to prescribe it in the ANC guidelines(20). Furthermore, the guidelines fail to specify recommended dosages, gestational ages, or administration intervals, which hinders utilization even at the individual level, even when healthcare providers recognize the threat of infection and wish to prescribe it(20). There are no published papers in Ethiopia that address the utilization status of IPTp-SP or healthcare providers' knowledge and practices, despite numerous studies available from other sub-Saharan African countries(19, 22). This lack of research indicates the limited IPTp-SP use even at the individual level.

In contrast to the national ANC guidelines(20), the national malaria guidelines recommend chloroquine prophylaxis for women infected with *P. vivax* during pregnancy and breastfeeding to suppress reactivation (21). A weekly single dose of chloroquine (250–300 mg) is advised to prevent malaria recurrence and its associated adverse pregnancy and perinatal outcomes (23, 24). This recommendation is also endorsed by the WHO(18). However, this crucial intervention is not included in the national ANC guidelines, and lack of awareness hampers its implementation. Consequently, the use of chloroquine prophylaxis may be limited primarily to tertiary facilities with sufficient expertise.

Call to action

Given the persistent factors contributing to the increased malaria incidence and the limited global funding for control and prevention programs, considerable time may be needed to return to previous success levels(25). During these prolonged epidemics, pregnant women and children remain the most at risk populations for severe malaria complications, which affect maternal and perinatal health outcomes. This urgent issue demands immediate attention as well as innovative and equitable solutions to mitigate its impact on maternal and perinatal mortality and morbidity. Some of the interventions to be considered at the national level include the following:

I. The collaboration between the maternal and child health directorate and the national malaria control and prevention program should be strengthened. This collaboration should focus on assessing the epidemic's impact on maternal and perinatal outcomes over the past three years for immediate intervention planning, ensuring continuous surveillance, and monitoring and evaluating implemented interventions.

II. Implementing IPTp-SP at the national level or at least in high-risk populations. The changing epidemiology of malaria requires the adaptation of interventions. IPTp-SP is a clinically proven malaria preventive therapy recommended by the WHO that can prevent adverse maternal and fetal outcomes(1, 18). While previous guidelines did not adopt IPTp-SP due to the assumption of low-to-moderate transmission, the resurgence over the past three years has resulted in high transmission in specific regions, necessitating IPTp-SP implementation. In addition to minimizing pregnancy complications, IPTp-SP can support overall malaria control efforts. With limited access to ITNs and inconsistent use of those available(4) and the emergence of insecticide-resistant mosquitoes(1), chemoprophylaxis could be a more viable prevention method. Opportunities for IPTp implementation exist, such as the recent 8-visit ANC schedule, which allows for the administration of at least three doses of SP. Experts can develop implementation strategies, considering the facilitators and barriers identified in other countries (22).

III. Prioritizing pregnant women for malaria control and prevention interventions, including the distribution and consistent use of insecticide-treated nets (ITNs), behavioural change communication, and access to diagnosis and treatment at facilities, should be strengthened. Interventions should also focus on promoting behavioural change, as evidence shows that both pregnant and non-pregnant women of reproductive age are often prioritized for net use within households(26). Primigravid women—those experiencing their first pregnancy—face a greater risk of poor outcomes than those with previous deliveries(27, 28). Therefore, in resource-constrained settings, interventions should specifically target and support first-time pregnant women and young individuals.

IV. Enhancing healthcare providers' knowledge of preventive strategies is crucial, especially since the outbreak now affects areas previously not endemic to malaria. Particular attention should be given to increasing awareness of weekly chloroquine (CQ) prophylaxis for pregnant women with *P. vivax* infections during pregnancy and breastfeeding. While CQ is included in the national malaria program(16), it is not addressed in the national ANC guidelines, which most maternal and child healthcare providers follow. The absence of published studies on CQ prophylaxis utilization indicates limited experience among healthcare providers, highlighting the urgent need for interventions to address this gap, given that nearly 30% of infections are caused by *P. vivax* alone or in mixed forms(29).

Conclusion

The resurgence of malaria in Ethiopia threatens to reverse the progress made in maternal and perinatal health. Given the proven benefits of IPTp-SP and the current high transmission rates, it is imperative to implement this preventive therapy in at least high-risk populations. Doing so will not only protect pregnant women and improve birth outcomes but also support Ethiopia's efforts to regain control over malaria transmission. A focused, equitable, and innovative response is urgently needed to mitigate the impact of this outbreak on maternal and child health.

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