

RESEARCH ARTICLE

The sensitivity of Chest CT for the diagnosis of COVID-19 pneumonia and imaging patterns as seen on Chest CT: a cross-sectional prospective study done in Addis Ababa, 2021

Ermias Assefa^{1*}, Azmera Gissila², Tesfaye Kebede², and Aschalew Worku³

Received: 04 June 2024

Accepted: 07 July 2024

DOI:10.20372/ajhsm.v03i01.01

Published: 10 July 2024



Suggested Citation: Assefa E., Gissila A., Kebede T, and Worku A. The sensitivity of Chest CT for the diagnosis of COVID-19 pneumonia and imaging patterns as seen on Chest CT: a cross-sectional prospective study done in Addis Ababa, 2021. *Afri. J. Heal. Sci. Med*; 2024, 03(01).

Copyright: ©2024 DU (Dilla University). This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Coronavirus disease 2019 (COVID-19) is a respiratory illness caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). While the RT-PCR test is considered the gold standard for diagnosis, chest imaging plays an important adjunct role in diagnosing and assessing the severity of the disease, as well as identifying complications. Distinguishing COVID-19 from other infectious processes can be challenging; thus, recognizing typical imaging patterns and degrees of involvement is crucial for guiding treatment. **Objective:** This study aimed to assess the sensitivity of chest CT scans in comparison to the standard RT-PCR for diagnosing COVID-19.

Method: Hospital based cross-sectional study design was employed using information collected from various diagnostic and treatment centers between July 1, 2021 and October 1, 2021. The chest CT scans of patients were reviewed, and a structured questionnaire was completed using a Google form. The data were exported and analyzed using SPSS version 26.

Results: Chest CT analysis revealed that 95.9% of cases exhibited bilateral involvement, with 51.3% showing a peripheral distribution. Among the typical chest CT patterns, ground-glass opacities (GGO) were observed in 157 (83%) cases, consolidation in 152 (80.4%), and broncho vascular thickening in 68 (35.4%). The mean chest CT severity score was 13.6 ± 6.2 , with 95 patients (49.2%) scoring above 18 (indicating severe disease). A positive correlation was found between the CT severity score and both age and diabetes, with a p-value < 0.01. There was a high probability of severe disease on chest CT among patients with diabetes mellitus (AOR = 1.6, 95% CI: 0.4-6.8).

Conclusion: This study demonstrated that chest CT has a high sensitivity (82.9%) for diagnosing COVID-19 pneumonia. The predominant imaging features included ground-glass opacity, consolidation, and bronchovascular thickening, with a notable bilateral, basal, and peripheral distribution. Additionally, the study revealed a positive correlation between the chest CT severity score and both age and diabetes comorbidity.

Keywords: Chest CT, COVID-19, RT-PCR

*Correspondence: ermiasassefa30@gmail.com

¹ Department of Radiology, Dilla University, Dilla, Ethiopia.

Full list of author information is available at the end of the article

1 Introduction

Background

Corona virus is an illness caused by corona virus designated severe acute respiratory syndrome SARS-CoV-2, primarily identified during an outbreak of respiratory illness in Wuhan city, Hubei province, China in December 2019 [1].

Coronaviruses are non-segmented, enveloped RNA viruses with a single-strand linear positive-sense RNA. Six types of coronaviruses have been identified that cause human disease; four of these cause mild respiratory symptoms, while the other two—Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV-1)—have previously resulted in epidemics with high mortality rates [2]. Respiratory illness is commonly associated clinical feature of SARS-CoV-2 due to abundant ACE2 receptor expression in the lung parenchyma, specifically on the acinar side of the lung epithelial cell within the alveolar space facilitating viral entry [2, 3].

Following the identification of the coronavirus as the cause of a cluster of pneumonia cases in Wuhan, it rapidly spread, resulting in an epidemic throughout China [4]. On January 30, 2020, the World Health Organization (WHO) declared a global public health emergency in response to the outbreak of COVID-19, and on March 11, 2020, the WHO classified the coronavirus outbreak as a global pandemic [5].

The primary mode of transmission of the virus is person-to-person, occurring mainly through respiratory droplets released during coughing, sneezing, or conversation. Environmental contamination also plays a role in viral transmission, with droplets accumulating on frequently touched surfaces, leading to subsequent spread to susceptible mucous membranes in the mouth, nose, and eyes [2, 3].

The clinical presentation of COVID-19 varies widely, with approximately 80% of cases experiencing mild to moderate symptoms, 14%–15% presenting with severe symptoms, and 5% classified as critical illness. The most common symptoms at presentation include fever, cough, and

shortness of breath. Mild to moderate disease is generally characterized by constitutional symptoms and the potential development of mild pneumonia, while severe disease symptoms include dyspnea and hypoxia [2, 3].

The SARS-CoV-2 virus has the potential to cause complications across all organ systems. Acute respiratory distress syndrome (ARDS) is a major complication of severe COVID-19, affecting 20%–40% of patients with severe symptoms. Other complications may include cardiac issues such as arrhythmias (including atrial fibrillation), acute myocarditis, cardiomyopathy, and shock. Thromboembolic phenomena can also occur, including pulmonary embolism (PE), peripheral venous and arterial thrombosis, and acute stroke [2].

Reverse-transcription polymerase chain reaction (RT-PCR) tests are currently the gold standard for diagnosing COVID-19. These assays are performed on nasopharyngeal and/or oropharyngeal swabs [3]. However, false-negative results may occur due to various factors, including insufficient viral load, improper sample collection, and technical errors during the swabbing procedure [2, 6].

Chest imaging plays an adjunct role in cases where an initial RT-PCR test returns negative results but there is a persistent high clinical suspicion of disease, as well as in patients with worsening symptoms or in resource-constrained environments where RT-PCR testing may be limited. The American College of Radiology advises against using CT as a first-line diagnostic tool for COVID-19, recommending its use be reserved for symptomatic hospitalized patients with specific clinical indications, such as the assessment of complications [2].

Among pulmonary imaging modalities, chest radiography is less sensitive for detecting COVID-19 lung disease compared to CT, with a reported baseline sensitivity of 69% [2, 6]. Pulmonary ultrasound is another useful imaging modality for evaluating critically ill patients with COVID-19, as it can be performed at the bedside and allows for the detection of pneumonia and complica-

tions such as pneumothorax [2].

CT has played a crucial role in the diagnosis and management of patients with viral pneumonia, as evidenced by large-scale outbreaks of Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV) [7]. The primary chest CT findings in patients with COVID-19 pneumonia include ground-glass opacities (GGO), crazy paving, consolidation, bronchovascular thickening, and traction bronchiectasis. Ground-glass and/or consolidative opacities are typically bilateral, peripheral, and basal in distribution, which are considered suggestive of the disease. Atypical findings include mediastinal lymphadenopathy, pleural effusions, pulmonary nodules, tree-in-bud patterns, pneumothorax, cavitation, the atoll sign, and pneumomediastinum [8].

While RT-PCR is the gold standard for definitive diagnosis, it has limitations regarding availability, sensitivity for detecting COVID-19, and extended waiting times for results. Additionally, inter-operator variability can affect sample quality, leading to false negatives [9]. CT has become a standard of care in diagnosing and assessing various respiratory conditions, such as interstitial lung disease and lung cancer, optimizing the management process. Although CT scans are not routinely used to diagnose ARDS, they can identify complications related to mechanical ventilation, including pneumonia, pneumothorax, and emphysema, which may not be evident on chest radiography [3].

Chest CT serves as a rapid and cost-effective alternative to RT-PCR, providing a highly specific diagnosis for COVID-19 when there is high clinical suspicion (9). In patients with high clinical suspicion and repeated negative RT-PCR tests, chest CT can facilitate early diagnosis, patient isolation, and contact tracing. A significant number of patients with typical imaging features have also been diagnosed incidentally when imaging is performed for other indications [6, 10].

Imaging is beneficial for differentiating patients with COVID-19 pneumonia from those with

other infectious and non-infectious pulmonary pathologies presenting acutely [10]. The significance of this study lies in assessing the diagnostic capacity of chest imaging, particularly chest CT, in diagnosing COVID-19 pneumonia, by identifying its sensitivity compared to RT-PCR and outlining typical chest imaging patterns.

2 Methods and Materials

2.1 Operational Definitions

Clinically Suspicious Case: A patient presenting with acute upper or lower respiratory symptoms, with or without fever, or having close contact with a confirmed COVID-19 patient [9].

Suspicious Imaging Feature: A patient exhibiting chest CT features of consolidation or ground-glass opacity (GGO) with a peripheral, bilateral, and basal distribution [2].

Unrelated Illness: A disease condition not attributed to the infection or complications of COVID-19 [9].

CT Severity Score: A semi-quantitative CT severity scoring system was used to assess the involvement of the five lobes of the lungs. Each lobe's involvement is scored as follows:

- 0: no involvement
- 1: < 5% involvement
- 2: 5–25% involvement
- 3: 26–50% involvement
- 4: 51–75% involvement
- 5: > 75% involvement

The global CT score is the sum of each lobar score, resulting in a total score ranging from 0 to 25. A score of < 7 is considered mild, 8–17 is moderate, and > 18 is severe [11].

2.2 Study Area and Period

Imaging for the study participants was primarily conducted at two institutions: Pioneer Diagnostic Center and Wudassie Diagnostic Center. Pioneer Diagnostic Center is one of the largest imaging facilities in Addis Ababa, providing dedicated imaging services for patients with suspected and confirmed COVID-19 using a

128-slice CT scanner. Wudassie Diagnostic Center also offers imaging services for all referred patients, regardless of their clinical diagnosis.

Additional data were collected from Tikur Anbessa Specialized Hospital (TASH), the largest tertiary hospital in the country, with over 700 beds and multiple outpatient services. TASH has an isolation ward and ICU for COVID-19 patients and provides imaging services using two CT scan machines with 128 and 64-slice capabilities. The treatment centers are dedicated care units that offer inpatient medical services, including intensive care for patients with moderate to severe COVID-19 pneumonia requiring admission.

Patients admitted to the treatment centers and those scanned at the aforementioned institutions between July 1, 2021, and October 1, 2021, were enrolled in the study.

2.3 Study Design

A cross-sectional study was performed to collect data on patients with clinically suspected or confirmed COVID-19 who underwent chest CT imaging and patients imaged for unrelated illnesses with incidental findings suggestive of COVID-19 pneumonia

2.4 Population

2.5 Source Population

All patients with clinical suspicion or confirmed COVID-19 infection underwent chest CT scanning and patients scanned for unrelated illness with imaging suspicion during the study period.

2.6 Study Population

All patients with clinical suspicion or confirmed COVID-19 patients who underwent chest CT and patients with suspicious imaging features were scanned for unrelated illnesses and had RT-PCR tests done during the study period.

2.7 Eligibility criteria

Inclusion criteria

- All patients with clinically suspected or confirmed COVID-19 infection underwent chest CT scan evaluation.

Exclusion criteria

- Patients with suspected COVID-19 pneumonia whose RT-PCR test is unknown or lost
- Those patients underwent chest imaging but were not reviewed due to poor quality (artifacts or not completely inclusive of the whole chest)

2.8 Sampling Technique and Sample Size

A convenience sampling method was employed in this study. All patients with laboratory-confirmed or clinically suspected COVID-19 infections who underwent chest CT scanning and RT-PCR testing during the study period (from July 1, 2021, to October 1, 2021) were enrolled.

2.9 Data Collection Instruments, Techniques, and Data Collectors

Data were collected from over eight COVID-19 treatment centers in Addis Ababa, which varied in the number of inpatient beds and services. These included Millennium Hall Treatment Center, Eka Kotebe General Hospital, St. Peter Hospital, Bulbula COVID-19 dedicated hospital, Sint Paul, Zewditu Memorial, and Hallelujah hospital. Most of these treatment centers do not have dedicated CT scan facilities for imaging their patients; those requiring cross-sectional imaging are referred to diagnostic centers.

Chest CT scans of patients who met the inclusion criteria were reviewed using an open-source DICOM viewer. The initial cases were reviewed in collaboration with the principal investigator and an experienced senior radiologist specializing in cardiothoracic imaging to standardize data collection. Important patient data, including COVID-19 RT-PCR results, demographic information, and clinical conditions (such as patient presentation and any underlying illnesses),

were collected from patient imaging requests and the national COVID registry.

The Principal Investigator collected the data using a structured questionnaire, which was then reviewed by two senior radiologists to minimize bias. The data were subsequently exported to SPSS for analysis.

2.10 Data Analysis

The data collected from the Google Form questionnaire were exported to SPSS version 26.0 for analysis, after checking for missing values. Various analytical methods, including tables and graphs, were used to present demographic data, clinical findings, and CT findings and patterns. Pearson correlation and binary logistic regression analyses were conducted to explore associations between demographic variables, clinical characteristics, and chest CT findings, as well as to assess associations with disease severity. A p-value of < 0.05 was considered statistically significant for testing associations between variables.

2.11 Ethical Considerations

Ethical clearance was obtained from the Review Board of the College of Health Sciences (IRB-CHS), allowing for data collection. To protect patient privacy, identifiers were used to maintain the anonymity of study subjects.

3 Results

3.1 Patient Characteristics

A total of 193 patients were included in the study, of which 116 (60.1%) were male and 77 (39.9%) were female. The age of the patients ranged from 23 to 85 years, with a mean age of 50 ± 14.2 years. Most of the patients (92, or 47.7%) were over the age of 51.

Among the 193 patients, 42 (21.8%) had one or more known comorbidities. Specifically, 26 (61.9%) had hypertension, 25 (59.5%) had diabetes mellitus, 4 had known HIV/AIDS, and 2 had a history of lung disease. Notably, a third of the patients with known comorbidities (14, or 33.3%) had both diabetes and hypertension (Table 1).

Table 1 Underlying comorbidities of the patient

Variable (n=42)	Number(percent)
Co-morbidity	
DM	25(59.5)
Hypertension	26(61.9)
HIV/AIDS	4(9.5)
Underlying lung disease	2(4.7)
Cardiac disease	1(2.3)
Malignancy	1(2.3)
Renal disease	1(2.3)

Clinical presentations were documented for 84 (43.5%) of the study participants. Among those with a known presentation, only one patient was asymptomatic. Of the symptomatic patients, cough was the most common complaint, reported by 82 (76%) patients, followed by short-

ness of breath in 65 (60.7%), chest pain in 36 (33.6%), and fatigue in 26 (24.3%). The majority of symptomatic patients reported a duration of symptoms between 5 and 8 days, accounting for 46 (43%) of the cases (Table 2).

Table 2 Clinical presentation of patients

Variable(n=107)		Frequency (percent)
Patients presenting symptoms	Cough	82(76.6)
	SOB	65(60.7)
	Chest pain	36(33.6)
	Fatigue	26(24.3)
	Fever	20(18.7)
	Headache	14(13)
	Arthralgia/myalgia	4(3.7)
	Loss of taste	4(3.7)
	Sore throat	2(1.9)
Duration of symptoms	< 4 days	19(17.7)
	5-8 days	46(43)
	9-14 days	15(14)
	>15 days	28(26.1)

Among the total number of patients included in this study, COVID-19 RT-PCR positivity was 93.8% (181 patients). Most of the patients who underwent chest CT evaluation had CT angiography (101 patients, or 52.3%), while 63 patients (32.6%) underwent non-contrast CT; the remainder had conventional post-contrast CT. Among those who had chest CT scans, 190 patients (98.4%) exhibited positive chest findings, and only 3 patients had unremarkable chest CT results. Considering chest CT findings with CORAD scores of 4 and 5 as suggestive of COVID-19 infection, 160 patients (82.9%) were diagnosed with COVID-19 pneumonia based on chest CT. Using RT-PCR results as the gold standard, the sensitivity and specificity of chest CT were found to be 82.9% and 16.7%, respectively.

3.2 Chest CT Findings, Distribution, and Severity

In this study, chest CT pattern distribution revealed that 95.9% of cases had bilateral lung involvement, 51.3% had a peripheral distribution, and 45.6% had a diffuse distribution. The disease process involved all lobes in approximately 90% of cases. The anterior-posterior distribution showed that 64.2% of cases had diffuse involvement, while 34.5% exhibited a predominant

dorsal distribution.

The chest CT findings displayed both typical and atypical patterns for COVID-19 pneumonia, with a typical pattern observed in 189 patients (97.9%) and atypical features in 30 patients (15.5%). Among patients with typical chest CT patterns, 157 (83%) showed ground-glass opacities (GGO), 152 (80.4%) had consolidation, 68 (35.4%) presented with bronchovascular thickening, and subpleural curved fibrosis was seen in 67 patients (35.4%). In patients with overlapping atypical chest CT features, mediastinal lymphadenopathy was noted in 18 patients (60%), pleural effusion in 16 patients (53.3%), and non-specific nodular opacity in 3 patients (10%).

The imaging patterns among symptomatic patients varied according to the duration of symptoms. Among those presenting with symptoms lasting less than 4 days, consolidation was found in 18 patients (94.7%) and GGO in 15 patients (78.9%). Of the 44 patients who presented with symptoms lasting between 5 to 8 days, 38 (86.3%) had GGO, 34 (77%) had consolidation, 14 (31.8%) exhibited bronchovascular thickening, and 15 (34%) had curved peripheral fibrosis. Among patients who presented with symptoms lasting 9 to 14 days, 14 (93.3%) had consolida-

tion, 13 (86.6%) had GGO, 8 (53.3%) showed bronchovascular thickening, and 5 had curved peripheral fibrosis. Of the 28 patients whose symptoms persisted for more than 15 days, 25 (89.3%) had consolidation, 24 (85.7%) had GGO, 14 (50%) had bronchovascular thickening, and 12 (42.8%) exhibited curved peripheral fibrosis (Table 3, Table 4, Figure 1).

Table 3 Imaging patterns of patients

Variable(n=193)		Number(percent)
Typical feature (189)	GGO	157(83)
	Consolidation	152(80.4)
	Broncho-vascular thickening	68(36)
	Peripheral curved fibrosis	67(35.4)
	Crazy paving	10(5.2)
	Traction bronchiectasis	15(7.9)
	Halo sign	14(7.4)
Atypical feature (30)	Mediastinal lymphadenopathy	18(60)
	Pleural effusion	16(53.3)
	Nodular opacities	3(10)

Table 4 Frequency of combined typical imaging feature

Variable(n=193)	Number(percent)
GGO and consolidation	120(62.1)
GGO and bronchovascular thickening	55(28.5)
Consolidation and bronchovascular thickening	55(28.5)
GGO, Consolidation and bronchovascular thickening	44(22.8)

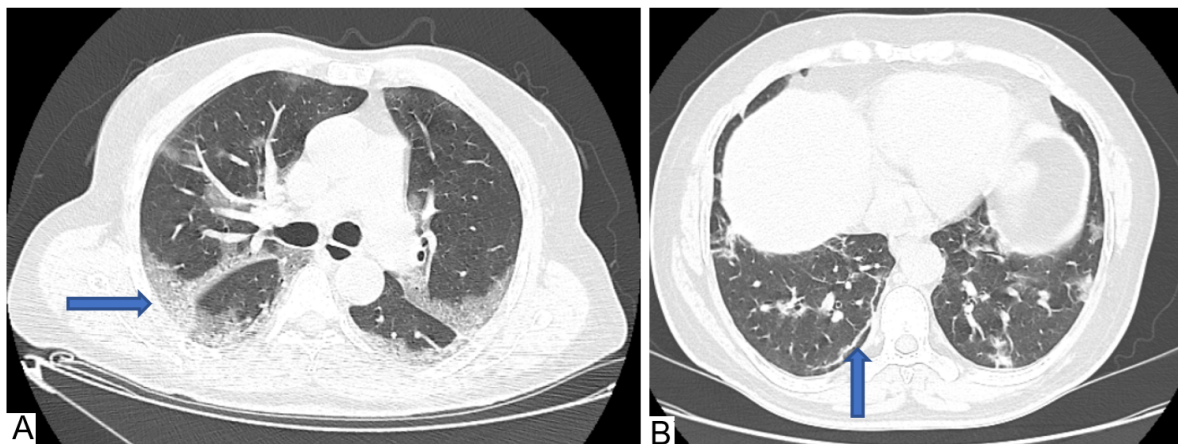


Figure 1 A) A 60 years old male patient with bilateral ground glass opacity (arrow) with peripheral and dorsal distribution B) A 51 years old male patient with positive COVID PCR test with a right basal lung peripheral curved fibrosis (arrow)

Among the 157 patients with ground-glass opacity (GGO), 85 (54.1%) exhibited a peripheral distribution and 68 (43.3%) displayed a diffuse distribution. Of the 152 patients with consolidation, 110 (72.4%) had a predominantly peripheral pattern, while 39 (25.6%) had a diffuse pattern.

Acute pulmonary embolism was identified in 8

patients. Among those with underlying lung diseases not attributed to COVID-19, lung fibrosis was observed in 11 patients, emphysema in 7, and cystic lung disease in 6 patients.

The mean (SD) chest CT severity score was 13.6 ± 6.2, with a median score of 14. A total of 95 patients (49.2%) had a severity score greater than 18 (Table 5).

Table 5 CT severity score grading (Francone et al, 2020)

CT severity	Frequency (Percent)
Mild (<7)	59(30.6%)
Moderate (8-17)	59(30.6%)
Severe (>18)	95(49.2%)

In this study, the association of variables was assessed using Pearson’s correlation. The relationships between age, sex, comorbidities, symptoms, and the duration of symptoms were evaluated in relation to the CT severity score. The analysis revealed a positive correlation between the CT severity score and both age and diabetes mellitus, with a p-value of < 0.01. The bivariate logistic regression indicated that diabetic patients had a 1.6 times higher risk of developing severe COVID-19 pneumonia (Table 6, Table 7).

Table 6 Correlation of age and DM with chest CT severity score

Variables	Mean	SD	1	2
1. Age	50	14.2		
2. DM			.413	
3. CT severity score	13.6	6.2	.0001*	.003*

* P<0.01(2-tailed); N= 193, SD: Standard deviation

Table 7 Association of severe CT score with age of the patient and DM

	Severe CT score (>18) Frequency(percentage)	COR 95% CI	AOR 95% CI
40-49 years	18(41.9)	2.16[0.39-11.9]	1.6[0.1-25.7]
50-64 years	20(33.9)	1.54[0.28-8.3]	2.8[0.26-31.6]
64-84 years	9(32.1)	1.42[0.23-8.5]	2.5[0.2-32.6]
DM	11(78.6)	2.01[0.56-7.31]	1.6[0.4-6.8]

4 Discussions

This study aimed to explore the demographic characteristics, clinical presentations, and imaging patterns among patients with suspected and confirmed COVID-19 pneumonia. The findings indicate a slight male predominance, with a male-to-female ratio of 1.5:1. The mean age of patients was 50 ± 14.2 years, and nearly half (47.7%) were over the age of 51. While many studies do not document a significant gender predilection, the older age distribution aligns with findings from a study conducted in Tehran, Iran [12], which reported the highest incidence of the disease among individuals aged 50-59 years. Similarly, a study in China [13] found a median age of 47 years, with 47% of patients over the age of 51.

In our study, among participants with known comorbidities, 62% had hypertension and 59.5% had diabetes mellitus, representing the most common underlying conditions in COVID-19 patients. This is comparable to a study involving 2012 patients in Pakistan [14], which identified uncontrolled diabetes with hypertension ($n = 56$; 26.4%) and controlled diabetes ($n = 22$; 10.37%) as prevalent comorbidities.

Cough and SOB are frequently reported findings, occurring in 76% and 60.7% of participants, respectively. Fever as a presenting symptom was noted in only 18.75% of patients in this study. This symptom pattern is consistent with findings from a study in China [13] involving 1099 patients, which reported cough (67.8%) and fever (43.8%) as the most common symptoms. In contrast, an Italian study [15] indicated that fever was the predominant symptom in 97 (61%) of patients, followed by cough and dyspnea in 88 (56%) and 52 (33%) patients, respectively. The discrepancy may be due to treatment interventions, such as antipyretics, affecting symptom presentation in our cohort, most of whom were admitted to COVID-19 treatment centers.

RT-PCR is considered the gold standard for assessing the diagnostic sensitivity of imaging modalities, including chest CT scans. In our study, using CO-RAD scores of 4 and 5 as criteria for diagnosing COVID-19 pneumonia via CT,

the overall positivity rate was 93.8%. The sensitivity and specificity of chest CT were found to be 82.9% and 16.7%, respectively, when compared to RT-PCR results. These figures are lower than those reported in studies from China and Italy. A study conducted in China [16] found chest CT sensitivity and specificity for COVID-19 infection to be 97% and 25%, respectively, while an Italian study [17] involving 773 patients reported sensitivity and specificity rates of 90.7% and 78.8%. A large meta-analysis of 1431 patients also indicated pooled sensitivity and specificity rates of 94.6% and 46.5%, respectively. Though these studies have methodological limitations that may have led to an overestimation of sensitivity [18], the lower sensitivity observed in our study may be attributed to selection bias; most patients had positive PCR results upon admission, and the majority of those imaged were confirmed cases undergoing evaluation for complications. The lower specificity in our study may also be due to the small number of RT-PCR negative cases that underwent chest CT imaging.

Our study revealed that the predominant chest CT findings were GGO and consolidation, observed in 83% and 80.4% of patients, respectively, followed by bronchovascular thickening (35.4%). These findings are consistent with multiple studies conducted in China [14, 18-20] and Italy [13], which reported multifocal ground-glass opacities and consolidations as the primary chest CT features in patients with COVID-19 pneumonia.

Our study examined the variation in imaging appearances among symptomatic patients based on the duration of their symptoms. Patients presenting with symptoms for less than 4 days predominantly exhibited consolidation (94.7%) and ground-glass opacity (GGO) (78.9%). Among those whose symptoms lasted 5 to 8 days, consolidation (86.3%) and GGO (77%) remained the predominant CT features, with bronchovascular thickening and curved peripheral fibrosis observed in 31.8% and 34% of cases, respectively. In patients with symptoms lasting 9 to 14 days, as well as those with symptoms exceeding 14 days, although consolidation and GGO remained the typical CT features, there was a

higher prevalence of bronchovascular thickening and curved peripheral fibrosis. The predominance of consolidation and GGO, followed by the development of bronchovascular thickening, has also been described by Jin *et al.* [21].

The bilateral, peripheral distribution with multilobar involvement seen in our study is consistent with findings from multiple publications, including a review by Salehi *et al.*, which analyzed various publications and case reports involving a total of 919 patients [22].

Using a semi-quantitative CT severity scoring system [11], we found that lung pathologies predominantly affected the basal regions, with the right lower lobe involved in 186 patients (96.4%) and the left lower lobe in 183 patients (94.8%). The mean total CT severity score in our study was 13.6 ± 6.2 . In a related study using the same scoring system, it was reported that pathological involvement was mostly in the inferior lobes, with the right lower lobe (RLL) affected in 122 patients (93.8%) and the left lower lobe (LLL) in 123 patients (94.6%). The mean (SD) CT severity score in that study was 12.3 ± 11.1 .

In our study, the 25-point CT severity score showed a significant correlation with patient age and the presence of diabetes mellitus, suggesting that COVID-19 pneumonia is more severe in older patients and those with diabetes. Patients with diabetes had a 1.6 times higher risk of developing severe disease as indicated by chest CT.

Strengths and Limitations of the Study

A major strength of this study is its ability to identify typical imaging patterns of COVID-19 pneumonia, distinguishing them from other infectious processes affecting the lungs. Additionally, the study successfully implemented a severity score assessment and identified major risk factors. Most patients included were admitted to treatment centers, and chest CT was performed to assess complications such as pulmonary embolism and post-COVID fibrosis. Consequently, the majority of our patients were symptomatic, and since most were admitted with a positive PCR test and moderate to severe illness, this

may have created a sampling bias in assessing both CT sensitivity and severity scores.

Moreover, we noted that the presenting symptoms of 107 (55.4%) patients and underlying comorbidities of 144 (74.6%) patients were not documented, which complicates the generalization of common presenting symptoms and comorbidities.

5 Conclusion and Recommendations

Most patients referred for chest CT evaluation from various treatment centers exhibited positive CT findings suggestive of COVID-19 pneumonia, characterized by predominant GGO, consolidation, and bronchovascular thickening. The pathologies demonstrated a notable dorsal and basal distribution. These imaging features are considered typical for COVID-19 pneumonia and are crucial for differentiating it from other causes of pneumonia and acute respiratory distress syndrome (ARDS).

Among those with known clinical information, many patients had diabetes and hypertension, with the primary complaints being cough, shortness of breath, and chest pain. The average CT severity score was moderate (13.6), and there was a significant correlation between older age and diabetes with the chest CT severity score, indicating that these factors directly influence patient clinical outcomes.

The study primarily involved hospitalized patients and did not include asymptomatic patients or those with mild symptoms, limiting the identification of CT imaging patterns, distributions, and severity scores. Future research should include a larger cohort of patients with complete clinical presentations and assess clinical outcomes in relation to imaging evaluations. It is also recommended to follow patients after COVID-19 pneumonia to observe the imaging patterns associated with post-COVID sequelae.

Abbreviations

ACE	Angiotensin-converting enzyme
ARDS	Acute respiratory distress syndrome
CDC	Center for disease control
CT	Computed Tomography
DM	Diabetes Mellitus
GGO	Ground glass opacity
MS Excel	Microsoft Excel
PACS	Picture archiving and communication system
PPV	Positive predictive value
RNA	Ribonucleic Acid
RT- PCR	Reverse-transcription polymerase chain reaction
SPSS	Statistical Package for the Social Sciences
TASH	Tikur Anbessa specialized hospital
US	Ultrasound
WHO	World Health Organization

Acknowledgments

I would like to express my heartfelt gratitude to my advisors for their unwavering support and guidance throughout the research process. Their expertise, insights, and encouragement were invaluable in helping me complete this work. I also want to thank my colleagues at Addis Ababa University and Dilla University for their helpful feedback and support.

Competing Interests Declaration

None of the authors received any financial or non-financial benefits from the submitted work.

Ethical Approval

Ethical clearance was obtained from the Research and Ethics Committee of the Department of Radiology and the Institutional Review Board of the College of Health Sciences (IRB-CHS), granting permission to collect the data. To protect patient privacy, identifiers were used to maintain the anonymity of the study subjects.

Data Access

All authors of this manuscript had full access to all data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding Statement

This research was conducted with financial support from the Addis Ababa University College of Health Sciences.

Author's Details

¹ Department of Radiology, Dilla University, Dilla, Ethiopia;

² Department of Radiology, Addis Ababa University, Addis Ababa, Ethiopia;

³ Department of Internal Medicine, Addis Ababa University, Addis Ababa, Ethiopia.

References

1. Infectious Diseases-Medscape [Internet]. [cited 2020 Oct 31]. Available from: <https://www.medscape.com/infectiousdiseases>
2. Multisystem Imaging Manifestations of COVID-19, Part 1: Viral Pathogenesis and Pulmonary and Vascular System Complications. RadioGraphics [Internet]. [cited 2020 Oct 31]. Available from: <https://pubs.rsna.org/doi/10.1148/rg.2020200149>
3. Karam M. Chest CT versus RT-PCR for the Detection of COVID-19: Systematic Review and Meta-Analysis. :33.
4. Search-UpToDate [Internet]. [cited 2020 Oct 31]. Available from: <https://www.uptodate.com/contents/search>
5. Li Y, Xia L. Coronavirus Disease 2019 (COVID-19): Role of Chest CT in Diagnosis and Management. *Am J Roentgenol*. 2020 Jun;214(6):1280–6.
6. Larici AR, Cicchetti G, Marano R, Merlino B, Elia L, Calandriello L, et al. Multimodality imaging of COVID-19 pneumonia: from diagnosis to follow-up. A comprehensive review. *Eur J Radiol*. 2020 Oct; 131:109217.
7. He J-L, Luo L, Luo Z-D, Lyu J-X, Ng M-Y, Shen X-P, et al. Diagnostic performance between CT and initial real-time RT-PCR for clinically suspected 2019 coronavirus disease (COVID-19) patients outside Wuhan, China. *Respir Med*. 2020 Jul; 168:105980.
8. Bell DJ. COVID-19. Radiology Reference Article. [Radiopaedia.org](https://radiopaedia.org) [Internet]. Radiopaedia. [cited 2021 Oct 6]. Available from: <https://radiopaedia.org/articles/covid-19-4>
9. Chendrasekhar A. Chest CT versus RT-PCR for Diagnostic Accuracy of COVID-19 Detection: A Meta-Analysis. (392):4.
10. CDC. Coronavirus Disease 2019 (COVID-19) [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2020 Oct 31]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/index.html>
11. Francone M, Iafrate F, Masci GM, Coco S, Cilia F, Manganaro L, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *EurRadio1*. 2020 Jul 4;1–10.
12. Kalantari H, Tabrizi AHH, Foroohi F. Determination of COVID-19 prevalence with regards to age range of patients referring to the hospitals located in western Tehran, Iran. *Gene Rep*. 2020 Dec; 21:100910.
13. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020 Apr 30; 382(18):1708–20.

14. Hussain M, Iltaf S, Salman S, Ghuman F, Abbas S, Fatima M. Frequency of Comorbidities in Admitting COVID-19 Pneumonia Patients in a Tertiary Care Setup: An Observational Study. *Cureus*. 13(2):e13546.
15. Caruso D, Zerunian M, Polici M, Pucciarelli F, Polidori T, Rucci C, et al. Chest CT Features of COVID-19 in Rome, Italy. *Radiology*. 2020 Aug; 296(2):E79–85.
16. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology*. 2020 Aug; 296(2):E32–40.
17. Falaschi Z, Danna PSC, Arioli R, Pasché A, Zagaría D, Percivale I, et al. Chest CT accuracy in diagnosing COVID-19 during the peak of the Italian epidemic: A retrospective correlation with RT-PCR testing and analysis of discordant cases. *Eur J Radiol*. 2020 Sep; 130:109192.
18. Kwee TC, Kwee RM. Chest CT in COVID-19: What the Radiologist Needs to Know. *Radiographics*. 2020 Nov 1; 40(7):1848–65.
19. Fu F, Lou J, Xi D, Bai Y, Ma G, Zhao B, et al. Chest computed tomography findings of coronavirus disease 2019 (COVID-19) pneumonia. *Eur Radiol*. 2020;1.
20. Han R, Huang L, Jiang H, Dong J, Peng H, Zhang D. Early Clinical and CT Manifestations of Coronavirus Disease 2019 (COVID-19) Pneumonia. *Am J Roentgenol*. 2020 Aug; 215(2):338–43.
21. Jin Y-H, Cai L, Cheng Z-S, Cheng H, Deng T, Fan Y-P, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res*. 2020;7(1):4.
22. Sana Salehi, Aidin Abedi, Sudheer Balakrishnan, Ali Gholamrezanezhad Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients, doi.org/10.2214/AJR.20.23034

RESEARCH ARTICLE

Prevalence of Pseudoexfoliation Syndrome and Related Ocular Manifestations in Patients Scheduled for Cataract Surgery

Mintesnot Ayalew Abebe^{1*}, Argaw Aberra Shire², and Kindie Desta Alem²

Received: 12 February 2023

Accepted: 13 June 2024

DOI:10.20372/ajhsm.v03i01.02

Published: 25 June 2024



Suggested Citation: Ayalew MA., Aberra AS., & Desta KA. Prevalence of Pseudoexfoliation Syndrome and Related Ocular Manifestations in Patients Scheduled for Cataract Surgery. *Afri. J. Heal. Sci. Med*; 2024, 03(01).

Copyright: ©2024 Dilla University. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Pseudoexfoliation syndrome is an age-related condition marked by the deposition of a distinct fibrillar extracellular material in the eyes and other organs. Affecting nearly 70 million people worldwide, it is linked to various ocular conditions and complications that can impact long-term visual outcomes.

Purpose: To determine the prevalence of pseudoexfoliation syndrome and ocular manifestations related to it among patients who were scheduled for cataract surgery.

Methods and material: A hospital-based cross-sectional study was conducted on consecutive 222 patients aged ≥ 40 years who were scheduled for cataract surgery. A structured questionnaire and an abstraction formant for ocular examination were used to collect data. The collected data were coded and entered into SPSS version 25 for analysis. Both descriptive and inferential statistical analyses were performed to present the results.

Results: The prevalence of pseudoexfoliation syndrome was 38.7% (86/222) (95% CI, 32.3–45.5). In comparison to patients without pseudoexfoliation, patient with pseudoexfoliation had a higher mean age (67.7 ± 11.2 vs. 61.2 ± 10.1 ; $P < 0.001$). Significant association were found with working conditions ($P < 0.001$) and sex ($P = 0.008$), with outdoor workers and males being more affected. The mean intraocular pressure was higher in eyes with pseudoexfoliation (17.16 ± 3.83 vs. 15.63 ± 2.96 mmHg; $P = 0.001$) and mean pupillary diameter after dilation was smaller (5.72 ± 0.86 vs. 6.73 ± 0.9 mm; $P < 0.001$). All 24 eyes with phacodonesis or subluxation had pseudoexfoliation syndrome ($P < 0.001$).

Conclusion and Recommendation: This study revealed a high prevalence of pseudoexfoliation syndrome (38.7%) among cataract patients. The condition was significantly associated with older age, working outdoors, male sex, higher intraocular pressure, poor pupillary dilation, and the presence of phacodonesis or subluxated lenses. Population-based studies are recommended to evaluate the prevalence of pseudoexfoliation in the general population, and further studies on cataract surgical outcomes in patients with pseudoexfoliation are recommended.

Keywords: Cataract, Hawassa, Ethiopia, Pseudoexfoliation syndrome

*Correspondence: mintesnotayalew3@gmail.com, Tel. +251912860110

¹Department of Ophthalmology, College of Health Sciences and Medicine, Dilla University, Ethiopia.

Full list of author information is available at the end of the article

1 Background

Pseudoexfoliation syndrome (PEX) is an age-related disease in which abnormal fibrillar extracellular material is produced and deposited nearly in all structures of the anterior segment, as well as in conjunctiva and orbital structures [1]. Lindberg was the first to describe this syndrome in 1917 [2].

Up to 30% of the population over 60 years of age and approximately 60–70 million people globally are affected by PEX. Its prevalence varies significantly by region and ethnicity, with rates ranging from 0% among Eskimos to 40.6% in Nordic individuals over 80. In people over 60, PEX prevalence is 25% in Iceland, 20% in Finland, 4% in England, and 0% among Inuit. Additionally, the disease seems to affect some ethnic groups and geographical areas within nations more frequently than others. Ethnic and intraregional variations are exemplified by US prevalence estimates of 1.6% in southeastern habitats compared with 38% in Navajo Indians [3].

Although several epidemiological studies on PEX have been conducted worldwide, there are few prevalence studies in the African context, and the burden of PEX on the continent is not well understood. According to one review article (2014) on PEX in sub-Saharan Africa, there was variation in the prevalence of PEX, ranging from 5.1% to 7.7% among patients aged 40 and above in population-based studies, while clinical-based studies showed even much wider variation [4]. Clinical-based research in Egypt and Somalia has revealed that the prevalence of PEX varies greatly, with respective rates of 4.14% and 40.9% [6, 6]. In Ethiopia, there are a few clinical studies conducted to evaluate the prevalence of pseudoexfoliation. A study conducted at Menelik II and Jimma Hospitals, showed the prevalence of PEX was 39.3% and 35.82%, respectively [7,8].

PEX has several ocular impacts, notably its association with cataract development. This was demonstrated in findings where the patient with only one eye affected by PEX, cataract almost always begins in that same eye [9,10]. PEX is also a leading cause of glaucoma worldwide, contributing significantly to cases in certain coun-

tries. At Menelik Hospital, pseudoexfoliation glaucoma (PEXG) was the second most common glaucoma subtype (26.6%), following primary open-angle glaucoma (POAG) (37.7%) [11]. Additionally, PEX increase the risk of postoperative complications, including fibrinoid reaction, posterior synechiae, decentration or dislocation of the lens implant, and anterior capsule contraction. It also raises likelihood of intraoperative problems such as poorly dilated pupils, zonular weakness, and capsular break [12].

As mentioned, PEX is associated with various ocular conditions and complications that affect long-term visual outcomes. Given Ethiopia's diverse population with varying ethnic groups and geographical areas, assessing the prevalence of PEX and its ocular manifestation among cataract patients in southern Ethiopia, an area previously unexplored in this context, is crucial. This study aims to determine the prevalence of PEX and related ocular manifestations among patients scheduled for cataract surgery at the Hawassa University Comprehensive Hospital (HUCSH).

2 Material and methods

The study was a hospital-based cross-sectional study conducted from April 14 to October 14, 2022, in Hawassa University tertiary eye care center, which is located in Hawassa City, about 272 km away from the capital city of Ethiopia. The center was established in 2005 G.C and served over 12 million people from Sidama and its neighboring regions. The study was conducted on consecutive cataract patients aged \geq 40 years who were admitted for cataract surgery at the HUCSH during the study period. Eyes with cataract related to trauma or previous ocular inflammation were excluded from the study.

Data were collected by senior ophthalmology residents who scheduled patients for surgery, with all ocular examination findings were completed after evaluating the patients together with the supervising ophthalmologist. A structured questionnaire and abstraction format for ocular examination were used for data collection. Visual acuity tested at 6 meters using the 'Snellen E

chart' by trained nurses. The IOP was measured using a Schiøtz tonometer (Riester Schiøtz Tonometer, Germany), and all eyes were examined with a slit-lamp biomicroscope (Keeler, USA) before and after mydriasis. In a patient with bilateral cataract, the eye scheduled for the first surgery was included in the study. The fellow eyes of all patients were examined to determine the bilaterality of PEX and to select patients for postoperative fundus examination of the scheduled eye.

The presence of PEX was confirmed by looking for typical white, fluffy, or granular material at the pupillary margin or on the anterior lens capsule. Even subtle signs of fibrillar deposition were sufficient to diagnose PEX. ACD was assessed using the Van Herrick grading method; patients with grade II or less underwent gonioscopic examination with Goldman indirect gonioscopes. Tropicamide 1% eye drops administered twice at 5-minute intervals, and pupil assessed for maximum dilation after 15 – 20 min. Pupillary dilation was measured with a pupil gauge chart or penlight. Patients with abnormal pupillary reflex or relative afferent defect were excluded from the study of pupillary size. Poor pupillary dilatation was defined as a maximally dilated pupil size less than 6 mm.

Dilated examination of the optic nerve head (ONH) was performed preoperatively in both eyes whenever the ocular media allowed for examination of the posterior segment of the eye. In patients with IOP $>21\text{mmHg}$ in either eye or vertical cup-to-disc ratio (VCDR) greater than 0.6 in the fellow eye, ONH examination of the scheduled cataractous eye was done after surgery. Fundus examination was performed using a 90-diopter posterior pole lens (Volk, USA) and a slit lamp biomicroscope. A visual field test (VFT) was done for patients with suspicious optic nerve VCDR ratio between 0.6 – 0.85 in the scheduled eye. Glaucoma was diagnosed in eyes with VCDR ≥ 0.6 or asymmetry of VCDR ≥ 0.2 with a definite visual field defect consistent with glaucoma, or eyes with VCDR ≥ 0.85 without visual

field testing, or those with evidence of previous glaucoma surgery or treatment. Cataract morphology was classified as mainly nuclear, cortical, posterior subcapsular, and mixed cataract using a slit-lamp biomicroscope.

Data were coded, checked, and entered manually into the Statistical Package for Social Sciences (SPSS) version 25. All analyses were performed using the same statistical software. Categorical variables are summarized as frequencies and percentages, whereas normally distributed continuous variables are presented as means and standard deviations using descriptive statistics. Bivariate analysis was performed using the Pearson chi-square test and Student's *t*-test to determine the possible association between pseudoexfoliation and the study variables. Statistical significance was set at P-value <0.05 .

3 Results

A total of 222 eyes from 222 patients admitted for cataract surgery at HUCSH during the study period were included. The minimum and maximum ages of the study participants were 40 and 90 years, respectively, with a mean age of 63.59 ± 10.98 years. Males made up 56.3% of the study participants, with a male to female ratio of 1.3:1. Majority of study participants resided in Sidama region (60.4%), and most of them were either farmers (55.9%) or housewives (24.8%). Nearly 58% of the study subjects worked outdoors (See table 1).

Pseudoexfoliation syndrome was diagnosed in 86 eyes (38.7%) out of the 222 eyes included in the study (95% CI, 32.3– 45.5). Pseudoexfoliation material deposits were observed at pupillary border in 54 (62.8%) of eyes with PEX, over the lens capsule in 7 (8.1%) eyes, and at both the pupillary border and lens capsule in 25(29.1%) of eyes. Regarding laterality, 69 (80.2%) had PEX bilaterally whereas 17 (19.8%) exclusively had it in the study eye. Three patients had a history of enucleation in the fellow eye; however, none of them had PEX in the study eye.

Table 1 Sociodemographic characteristics of patients admitted for cataract surgery at Hawassa University comprehensive Specialized Hospital, Hawassa, 2022(N=222)

Characteristics		Frequency (n)	Percentage (%)
Sex	Male	125	56.3
	Female	97	43.7
Age	40-50	31	14
	51-60	76	34.2
	61-70	71	32
	>70	44	19.8
Ethnicity	Sidama	104	46.8
	Oromo	66	29.7
	Amhara	19	8.6
	Kembata	11	5
	Wolayita	6	2.7
	Other	16	7.2
Residence	Sidama	134	60.4
	Oromia	70	31.5
	SNNP	18	8.1
Occupation	Farmer	124	55.9
	Housewife	55	24.8
	Civil servant	24	10.8
	Merchant	15	6.8
	Other	4	1.8
Workplace	Outdoor	12	5.4
	Indoor	94	42.3

Glaucoma was diagnosed in 15 eyes (6.8%), with 13 cases PEX glaucoma and 2 cases of POAG. None of the eyes included in the study had an ACD of $\leq +2$ using the Van Herrick technique. In 75% surgical treated eyes, the preoperative maximally dilated pupillary diameter was adequate. One patient with PEXG and relative afferent pupillary defect observed over the scheduled eye was excluded from the study of pupillary size after dilation. A mixed type of cataract morphology was observed in 74.3 % of the eyes, followed by posterior subcapsular cataract (PSC) (22.5%). Phacodensitis/subluxation of cataractous lens were found in 24 (11%) eyes out of 222 studied (See table 2).

According to this study, the prevalence of PEX

increased considerably with age, rising from 25.8% in the 5th decade of life to 59% in individuals over 70 years ($P < 0.001$). The mean age of patients with PEX was 67.7 ± 11.2 years, while that of those without PEX was 61.2 ± 10.1 years. Statistical analysis revealed that the difference was statistically significant ($P < 0.001$). Male patients had a two-fold higher likelihood of having PEX than female patients (COR: 2.13, 95% CI; 1.2 – 3.74).

The study also showed 52.3% of study participants working outdoors had PEX, compared with only 20.2% of those working indoors. This difference was statistically significant ($P < 0.001$) (See table 3).

Table 2 Ocular findings of eyes scheduled for surgery among patients admitted for cataract surgery at Hawassa University comprehensive Specialized Hospital, Hawassa, 2022 (N=222)

Variable		Frequency, n	Percentage, %
Scheduled eye	OD	120	54.1
	OS	102	45.9
Preoperative uncorrected visual acuity	CF < 1m or LP	151	68
	CF @1m up to CF < @3m	51	23
	CF @3m up to < 6/60	16	7.2
	<6/18 up to 6/60	4	1.8
Preoperative IOP, mmHg	≤ 21	205	92.3
	> 21	17	7.7
Type of glaucoma	PEX glaucoma	13	5.9
	POAG	2	0.9
	Glaucoma suspect	4	1.8
	Ocular hypertension	2	0.9
Preoperative maximally dilated pupillary diameter*	Adequately dilated	166	75.1
	Poorly dilated	55	24.9
Cataract morphology	Mixed	165	74.3
	Posterior subcapsular	50	22.5
	Nuclear	6	2.7
	Cortical	1	0.5
Stability of lens	Stable	198	89.2
	Phacodonesis	23	10.4
	Subluxated	1	0.5

Preoperative maximally dilated pupillary diameter *N=221

Table 3 Relationship of Socio-demographic variables with ocular pseudoexfoliation syndrome among study participants admitted for cataract surgery at Hawassa University comprehensive Specialized Hospital, Hawassa, 2022

Independent variables	Presence of PEX		P value+	COR	
	Yes n (%)	No n (%)			
Age	40-50	8 (25.8)	23 (74.2)	< 0.001	
	51-60	18 (23.7)	58 (76.3)		
	61-70	34 (47.9)	37 (52.1)		
	>70	26 (59.1)	18 (40.9)		
Mean age	67.7±11.2	61.2±10.1	< 0.001*	4.15 (95% CI; 1.5 – 11.37)	
Sex	Male	58 (46.4)	67 (53.6)	0.008	2.13 (95% CI; 1.2 – 3.74)
	Female	28 (28.9)	69 (71.1)		
Ethnicity	Sidama	47 (45.2)	57 (54.8)	0.065	
	Oromo	25 (37.9)	41 (62.1)		
	Amhara	5 (26.3)	14 (73.7)		
	Kembata	1 (9.1)	10 (90.9)		
	Wolayita	4 (66.7)	2 (33.3)		
	Other	4 (25.0)	12 (75.0)		
Residence	Sidama	54 (40.3)	80 (59.7)	0.132	
	Oromia	29 (41.4)	41 (58.6)		
	SNNP	3 (16.7)	15 (83.3)		
	Other	1 (25.0)	3 (75.0)		
Workplace	Outdoor	67 (52.3)	61 (47.7)	<0.001	4.34(95% CI; 2.35 – 7.99)
	Indoor	19 (20.2)	75 (79.8)		

+Pearson’s chi-square test, *Student’s t-test, and COR – crude odds ratio

Compared to eyes without PEX, those with PEX had a significantly higher mean IOP ($17.16 \pm 3.83 \text{ mmHg}$ vs. $15.63 \pm 2.96 \text{ mmHg}$; $P = 0.001$). Furthermore, 15.1% of patients with PEX had glaucoma compared to 1.5% of patients without PEX, and 17.4% of patients with PEX had an IOP $>21 \text{ mmHg}$. These differences

between the two groups were statistically significant ($P < 0.001$). The mean pupillary diameter after dilation in eyes with PEX ($5.72 \pm 0.86 \text{ mmHg}$) was significantly smaller than that in eyes without PEX ($6.73 \pm 0.9 \text{ mmHg}$) ($P < 0.001$) (See table 4).

Table 4 Intraocular pressure, presence of glaucoma, and fully dilated pupillary size comparison between eyes with and without PEX among patients admitted for cataract surgery at Hawassa University Comprehensive and Specialized Hospital, Hawassa, 2022

Variables	Presence of pseudoexfoliation		Bivariate analysis P value+	
	Yes n (%)	No n (%)		
IOP, mmHg	> 21	15(17.4)	2(1.5)	< 0.001
	≤ 21	71(82.6)	134(98.5)	
Mean IOP, mmHg		17.16 ± 3.83	15.63 ± 2.96	0.001*
Glaucoma	Yes	13(15.1)	2(1.5)	< 0.001
	No	73(84.9)	134(98.5)	
Preoperative maximally dilated pupillary diameter, mm#	< 6	43(50)	12(8.8)	< 0.001
	≥ 6	43(50)	124(91.2)	
Mean fully dilated pupillary diameter, mm		5.72 ± 0.86	6.73 ± 0.9	$< 0.001^*$

+ Pearson chi-square test, * Student’s t-test, # preoperative dilated pupillary diameter=221

All 24 eyes with phacodonesis or subluxation included in the study had PEX, whereas none of the eyes without PEX had such findings. This

difference was statistically significant ($P < 0.001$) (See table 5).

Table 5 Preoperative uncorrected visual acuity and characteristic of cataract comparison between eyes with and without pseudoexfoliation among patients admitted for cataract surgery at Hawassa University Comprehensive and Specialized Hospital, Hawassa, 2022

Variables	Presence of pseudoexfoliation		Bivariate analysis P-value+	
	Yes n (%)	No n (%)		
Cataract morphology	Mixed	66 (76.7)	99 (72.8)	0.807
	PSC	18 (20.9)	32 (23.5)	
	Nuclear	2 (2.3)	4 (2.9)	
	Cortical	0	1 (0.7)	
Lens stability	Stable	62 (72.1)	136 (100)	< 0.001
	Phacodonesis	23 (26.7)	0	
	Subluxated	1 (1.2)	0	
Preoperative uncorrected VA	CF $< 1\text{m}$ or LP	65 (75.6)	86 (63.2)	0.268
	CF @1m up to CF $< @3\text{m}$	16 (18.6)	35 (25.7)	
	CF @3m up to $< 6/60$	4 (4.7)	12 (8.8)	
	$< 6/18$ up to $6/60$	1 (1.2)	3 (2.2)	

+ Pearson chi-square test, PSC - posterior subcapsular cataract

4 Discussions

In this study, the prevalence of PEX was 38.7% (95% CI, 32.3–45.5) among patients with cataract. This prevalence is consistent with studies from other parts of Ethiopia such as Menelik Hospital, which reported 39.3% prevalence, and studies from Jimma and Gonder, which reported 35.82% and 35% prevalence respectively [7,8,13]. A comparable result was also observed in Somalia (40.9%), where the prevalence of PEX was studied in cataract patients scheduled for surgery [5]. These similarities in prevalence rates might be due to a similar study setting. However, prevalence in this study was higher than similar hospital-based studies conducted in Finland (25%), Serbia (17.5%), Spain (21.6%), India (22.1%), Jordan (10.3%), Turkey (16.4%), and Nigeria (2.7%) [4,12,14-18]. These observed disparities in prevalence could be explained by ethnic/racial and environmental factors. Additionally, a community-based study conducted in Baso and Worena District, central Ethiopia found the prevalence of PEX to be 13.2% among individuals ≥ 40 years old (90/682), which is significantly lower than the present study [19]. This discrepancy may be explained by a pattern documented in numerous studies, which shows the prevalence of PEX increases as study population shifts from the general population to hospital settings.

Our study showed that the proportion of patients with PEX significantly increased with age, with the mean age of the PEX group was significantly higher than that of the non-PEX group (67.7 vs. 61.2 years). This finding aligns with studies done in Menelik hospital (63.7 vs. 60.3 years) and Gonder (66.2 vs. 60.1) [7,13]. Studies done in Serbia (79.4 vs. 73.5), Turkey (74.4 vs. 69.3), and Somalia (71.3 vs. 64.7) also showed a similar trend. The correlation between increasing age and higher prevalence of PEX may be attributed to long-term environmental exposure, decline in cellular function with age, and deposition of exfoliative material over time [5,12,20].

Additionally, this study demonstrated that working outdoors increased the likelihood of developing PEX. This finding is in accordance with

that of a study conducted in Gonder, Northern Ethiopia [13]. The fact that workplace conditions, not ethnicity, were significantly associated with the presence of PEX in this study may favor the findings of a study conducted in the USA that showed ambient temperature and sun exposure as more important environmental triggers of PEX than hereditary risk factors. This could be due to ultraviolet radiation up regulation of Lysyl oxidase homolog 1 (LOXL 1) gene expression, as well as elastic fiber proteins found in the exfoliation material [3,21].

Despite many studies showing no sex predilection or conflicting results regarding sex predilection in patients with PEX, our studies have shown proportion of males (46.4%) with PEX was higher than the proportion of females (28.9%) with PEX ($P = 0.008$) [7,9]. Similar male predilection was observed in studies conducted in Gonder, Ethiopia, and Nigeria [4,13]. Male preference for PEX in our study may be explained by the fact that more men than women (73.4% vs. 26.6%) employed in outdoor working conditions.

In this study, the incidence of glaucoma was significantly higher in eyes with PEX than without PEX (15.11% vs. 1.5%) ($P < 0.001$). Similar results were reported in other studies: 13.3% in Menelik Hospital (13.3% vs. 8.5%), 71% in Somalia (71% vs. 10.8%), 8.3% in Turkey (8.3% vs. 2.5%), and 17.4% in Spain (17.4% vs. 9.4%) [5,7,17,20]. Furthermore, the mean IOP in a patient with PEX was significantly higher than patients without PEX (17.16 ± 3.83 vs. 15.63 ± 2.96 , $P = 0.001$). This result is consistent with previous studies [7,17]. Although the exact mechanism of IOP elevation in PEX is debatable, increased outflow resistance in the trabecular meshwork is the most widely accepted hypothesis [3].

The primary risk factors for intraoperative complications during cataract surgery in eyes with PEX are poor pupillary dilation and preoperative phacodonesis or lens subluxation related to zonular weakness [3]. In this study, the mean pupillary size after dilation in eyes with PEX was significantly lower than in eyes without PEX

(5.72 ± 0.86 vs. 6.73 ± 0.9) ($P < 0.001$). The difference in the proportion of patients with poor pupillary dilation between eyes with and without PEX was also statistically significant (50% vs. 8.8%) ($P < 0.001$). Similar results were observed in India, where mean pupillary dilation was $5.1 (\pm 1.4)$ mm in PEX patients compared to $7.2 (\pm 1.6)$ mm in non PEX patients ($P = 0.03$) [14]. Furthermore, all 24 eyes included in the study with phacodonesis and subluxation had PEX ($P < 0.001$). Infiltration of exfoliative material into the iris stroma can create a mechanical barrier to mydriasis, resulting in poor pupillary dilation. This can lead to smaller capsulorhexis, leaving weakened zonules more vulnerable to the traumatic forces of intraocular manipulation [22].

Since the study was restricted to cataract patients scheduled for surgery, it does not provide insights into the prevalence of PEX in the general population. Additionally, the cross-sectional design of the study prevents establishing a cause-and-effect relationship between the variables.

5 Conclusion

A high prevalence of PEX (38.7%) among patients with cataract was seen in the present study. PEX incidence increased with age, was more common in patients working outdoors, and was more frequent in males. The study also showed significantly higher mean IOP and glaucoma rates in eyes with PEX compared to those without. Preoperative conditions such as poor pupillary dilatation, phacodonesis or subluxation were notably more prevalent in PEX cases, suggesting a higher probability of intraoperative complications. To better understand PEX prevalence and its link to cataract, population-based studies are recommended. Healthcare policymakers should raise awareness of PEX and the related ocular conditions. Moreover, cataract patients with PEX should be properly evaluated preoperatively, and patients should be informed about possible surgical complications. Surgeons are recommended to be prepared to encounter potential intraoperative complications associated with PEX. Further studies on cataract surgical outcomes in patients with pseu-

doexfoliation are recommended.

Disclosure

The authors declare that they have no conflicts of interest to disclose.

Authors' Information

¹Department of Ophthalmology, College of Medicine and Health Sciences, Dilla University, Dilla, Ethiopia

²Department of Ophthalmology and Optometry, College of Medicine and Health Sciences, Hawassa University, Hawassa, Ethiopia

References

1. Ringvold A. Epidemiology of the pseudoexfoliation syndrome. *Acta Ophthalmol Scand.* 1999 Aug; 77(4):371–5.
2. Khaimi M, Skuta G, Morgan R. *Duane's Clinical Ophthalmology.* Chapter 54B. 2012. 5412–5427 p.
3. Nazarali S, Damji F, Damji KF. What have we learned about exfoliation syndrome since its discovery by John Lindberg 100 years ago? *Br. J. Ophthalmol.* 2018; 102:1342–50.
4. Olawoye OO, Ashaye AO, Teng CC, Liebmann JM, Ritch R, Ajayi BG. Exfoliation syndrome in Nigeria. *Middle East Afr. J. Ophthalmol.* 2012 Oct; 19(4):402–5.
5. Kalaycı M. Pseudoexfoliation Syndrome Prevalence in Somali Patients with Senile Cataract. *Istanbul Med. J.* 2020 Sep; 21(5):380–3.
6. Shazly TA, Farrag AN, Kamel A, Al-Hussaini AK. Prevalence of Pseudoexfoliation Syndrome and Pseudoexfoliation Glaucoma in Upper Egypt. *BMC Ophthalmol.* 2011 Jun 27; 11(1):18.
7. Teshome T, Regassa K. Prevalence of pseudoexfoliation syndrome in Ethiopian patients scheduled for cataract surgery. *Acta Ophthalmol Scand.* 2004; 82(2004):254–8.
8. Gelaw Y, Tibebu Y. Clinical Characteristics of cataract in patients with pseudoexfoliation syndrome at Jimma University Specialized Hospital, South West, Ethiopia. *Ethiop. J. Health Sci.* 2012 Mar; 22(1):1–6.
9. Ritch R, Schlötzer-Schrehardt U. Exfoliation Syndrome. *Surv. Ophthalmol.* 2001; 45(4):4.
10. Yanoff M, Duke J s, editors. *Ophthalmology.* Fifth edition. Elsevier Inc; 2019. 1074–77 p.
11. Giorgis AT, Mulugeta A, Aga A, Deyassa N. The spectrum of glaucoma presentation at Menelik II Hospital, Addis Ababa. *Ethiop. Med. J.* 2012 Jul; 50(3):259–64.
12. Kovač B, Vukosavljević M, Janičević MP, Resan M, Janković J. The prevalence of pseudoexfoliation syndrome and possible systemic associations in patients scheduled for cataract surgery at the military medical academy in Belgrade. *Vojnosanit Pregl.* 2014 Sep; 71(9):839–44.

13. Yibekal BT, Adimassu NF, Ayele FA. Pseudoexfoliation syndrome and associated factors among adults at gondar university comprehensive specialized hospital tertiary eye care and training center: A cross-sectional study. *Clin. Optom.* 2021; 13:249–55.
14. Joshi R, Singanwad S. Frequency and surgical difficulties associated with pseudoexfoliation syndrome among Indian rural population scheduled for cataract surgery: Hospital-based data. *Indian J. Ophthalmol.* 2019 Feb; 67(2):221–6.
15. Sekeroglu MA, Bozkurt B, Irkec M, Ustunel S, Orhan M, Saracbası O. Systemic associations and prevalence of exfoliation syndrome in patients scheduled for cataract surgery. *Eur. J. Ophthalmol.* 2008 Aug; 18(4):551–5
16. Hietanen J, Kivelä T, Vesti E, Tarkkanen A. Exfoliation syndrome in patients scheduled for cataract surgery. *Acta Ophthalmol (Copenh).* 1992; 70(4):440–6.
17. Govetto A, Lorente R, Parga PVD, Rojas L, Moreno C, Lagoa F, et al. Frequency of pseudoexfoliation among patients scheduled for cataract surgery. *J. Cataract Refract Surg.* 2015 Jun; 41(6):1224–31.
18. Shihadeh WA, Jammal HM, Alkhatib SQ, Okour FM, Gharaibeh AM, Alqudah NM, et al. Prevalence of Exfoliation Syndrome in Patients Scheduled for Cataract Surgery: A Hospital-based Study in Northern Jordan; Vol. 46, *J. Med. J.* 2012 p. 216–20.
19. Berhanu YA, Giorgis AT, Alemu AM. Prevalence of ocular pseudoexfoliation in Baso and Worena District, central Ethiopia. *The Ethiopian Journal of Health Development*, 2020:34(1).
20. Gunes A, Yasar C, Tok L, Tok O. Prevalence of Pseudoexfoliation Syndrome in Turkish Patients with Senile Cataract. *Semin. Ophthalmol.* 2017 May; 32(3):297–301.
21. Stein JD, Pasquale LR, Talwar N, Kim DS, Reed DM, Nan B, et al. Geographic and Climatic Factors Associated With Exfoliation Syndrome. Vol. 129, *Arch Ophthalmol.* 2011 p. 1053–60.
22. Sangal N, Chen TC. Cataract surgery in pseudoexfoliation syndrome. *Semin Ophthalmol.* 2014 Nov; 29(5–6):403–8.

RESEARCH ARTICLE

Efficacy and safety of erector spinae plane block for postoperative analgesia after surgery: An Umbrella review protocol

Semagn Mekonnen Abate^{1*}, Haylemariam Mulugeta¹, Bedru Jemal, and Anmut Ayinie²

Received: 27 October 2023

Accepted: 20 May 2024

DOI:10.20372/ajhsm.v03i01.03

Published: 04 June 2024



Suggested Citation: Mekonnen SA., Mulugeta H., Jemal B., and Ayinie A. Efficacy and safety of erector spinae plane block for postoperative analgesia after surgery: An Umbrella review protocol. *Afri. J. Heal. Sci. Med*; 2024, 03(01).

Copyright: ©2024 Dilla University. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Poorly managed postoperative pain after thoraco-abdominal surgery has several consequences in the postoperative period. The postoperative pain after thoraco-abdominal surgery has been managed with systemic opioids and different regional anesthesia techniques. The erector spinae plane block is a relatively new method that is simple to perform and generally associated with few complications. Despite these advantages, the strength of the evidence supporting its effectiveness remains limited, and further studies are needed to confirm its clinical value.

Objective: This systematic review aimed to provide the quality of evidence on the efficacy and safety of erector spinae block after surgery.

Method: A comprehensive search was carried out in PubMed/Medline, Cochrane, Science Direct, CINAHL, and LILACS without restrictions on date or language. Only randomized trials assessing wound infiltration for postoperative pain after cesarean section were included, while observational studies and reviews were excluded. Data extraction was performed independently by two authors using a tailored format. Study quality was assessed with the AMSTAR tool, and overall evidence strength was rated through GRADEpro. The review followed PRISMA guidelines for systematic reviews and meta-analyses.

Discussion: Postoperative pain is common after thoraco-abdominal surgery and places a heavy burden on patients, families, and healthcare systems. This review evaluates the effectiveness and safety of both landmark-guided and ultrasound-assisted erector spinae plane block techniques for managing pain after surgery.

Keywords: Analgesia, Erector spinae, Paravertebral, Postoperative

*Correspondence: semmek17@gmail.com, Tel. +251913864605

¹Department of Anesthesiology, College of Health Sciences and Medicine, Dilla University, Ethiopia.

Full list of author information is available at the end of the article

1 Introduction

1.1 Description of the condition

Postoperative pain is considered a form of acute pain due to surgical trauma with an inflammatory reaction and contributed by sensitization of dorsal horn neurons. It is a combined constellation of several unpleasant sensory, emotional, and mental experiences precipitated by surgical trauma and associated with autonomic, endocrine-metabolic, physiological, and behavioral responses [1].

Predictors of postoperative pain can be categorized as preoperative, intraoperative, and postoperative factors. Several potential preoperative factors for postoperative pain have been reported, like pre-existing pain, anxiety, younger age, and female gender [2-8]. Identifying those at increased risk and treating their postoperative pain adequately facilitates early ambulation and enhances recovery may eventually reduce postoperative mortality and morbidity [9-11].

Postoperative factors, including the severity of postoperative pain, patient on radiotherapy/chemotherapy, and psychological vulnerability have been shown to predict postoperative pain [2,12].

Evidence showed that the prevalence of postoperative pain in patients undergoing major surgery ranges from 17%-82% and 75% of those who reported describing their pain as moderate to severe during the immediate postoperative period [13-18].

Moderate to severe post discharge pain was experienced in 25–65% of these patients depending on the type of surgical intervention, leading to dissatisfaction with overall care [14,19-21]. Most of poorly managed acute postoperative pain transforms into chronic pain. Based on literature persistent postoperative pain occurs in 10%-60% patients after common surgical procedure. Traditionally, treatment of postoperative pain is based mainly on opioids with the result that are

not quite satisfactory, however, advancement multimodal analgesia and enhanced recovery after surgery protocol lead to adjuvant modalities for postoperative management [14,19-21].

Postoperative pain may lead to a wide range of postoperative complications, like an increased risk of thrombo-embolic events, respiratory impairment, anxiety, sleep disturbance, prolonged hospital stay, chronic pain, impaired physical functioning, recovery, and quality of life after surgery, which increases a burden to the patient, health care providers, and community and increases healthcare-related costs [10,14,22-25]. In addition, inadequately treated postoperative pain might have significant physiological and psychological consequences, which may affect the quality of life along with a severe impact on organ dysfunction and increase postoperative mortality and morbidity [14,20,22,23,26].

1.2 Description of the intervention

The postoperative pain during or after thoracoabdominal surgery has been managed by systemic analgesic opioids for years; nevertheless, there is a wide range of adverse effects. Recent peer-reviewed published literature showed that regional blocks, including paravertebral, intercostal, pectoral, epidural, and erector spinae plane blocks, are gaining popularity [27-37]. However, epidural anesthesia requires resources and technical expertise, while landmark techniques are ineffective and also associated with complications. The Erector Spinae Plane Block is a relatively new technique of regional anesthesia where local anesthetic (LA) injection is performed into the fascial plane situated between the transverse process of the vertebra and the erector spinae muscles, and it is considered a relatively safe and easy technique to perform compared to other regional techniques [28,38].

1.3 How the intervention might work

The regional nerve block is considered an essential component of multimodal analgesia.

Ultrasound-guided erector spinae plane block is a novel technique that injects local anesthetics into the fascial space between the transverse process and erector spines, blocking the branches of the thoracic and abdominal spinal nerves. The exact mechanism of erector spinae nerve block is uncertain, but the most probable primary mechanism is a direct effect of local anesthetic via physical spread and diffusion to neural structures in the fascial plane deep to the erector spinae muscles and adjacent tissue compartments.

The cadaveric injection and computerized tomographic scan studies showed that the local anesthetics spread in a cephalocaudal direction within a fascial plane deep to the erector spinae muscle in the paraspinous region potentially spreads towards paravertebral space through the inter-transverse tissue [39,40].

Why is it important to do this review

Many postoperative pain management modalities have been practiced during or after thoracoabdominal surgery in recent years. However, systemic opioid-based analgesics and landmark intercostal and paravertebral techniques have several complications; the epidural regional analgesia technique requires resources and expertise, while erector spinae is a new technique with minimal side effects and is easy to administer.

Currently, erector spinae has been compared with other regional anesthesia techniques for postoperative pain management after thoracoabdominal surgery. However, the quality of the available evidence on the efficacy and safety of this technique is uncertain.

This umbrella review will provide quality evidence and recommendations on the efficacy and safety profile of erector spinae plane block to prevent undesirable adverse effects of opioids and other landmark techniques, particularly for the resource-limited environment. Besides, the output of this umbrella review is expected to contribute to the successful accomplishment of

sustainable development goals (SDGs) Article 3.2.2 [41].

2 Objective and Research Questions

2.1 Objective of the Study

The objective of this umbrella review is to summarize the evidence from a systematic review and meta-analysis regarding the efficacy and safety of erector spinae plane block for postoperative analgesia.

2.2 Research Questions

This umbrella review is intended to address the following questions.

- Do we have strong evidence on the efficacy and safety of erector spinae plane block after surgery?
- Can we recommend an erector spinae plane block for all thoracoabdominal and spine surgeries?
- What are the most commonly reported complications associated with erector spinae block?

3 Methods

3.1 Protocol and registration

This systematic review and meta-analysis will be carried out in accordance with PRISMA guidelines [42]. The study protocol was registered in PROSPERO (CRD42021270711) on August 5, 2021.

3.2 Eligibility criteria

3.2.1 Types of studies

All systematic reviews and meta-analyses comparing the efficacy and safety of erector spinae plane block with epidural anesthesia, paravertebral block, intercostal block, pectoral nerve block, systemic analgesics, and placebo for postoperative pain management after thoracoabdominal and spine surgery were included. However,

randomized controlled trials, observational studies, and clinical reviews were excluded.

3.2.2 Types of participants

All studies comparing erector spinae plane block against any of the regional anesthesia techniques for pain management during or after thoracoabdominal and spine surgery were included, and the rest were excluded.

3.2.3 Types of intervention

The treatment group was patients allocated to landmark or ultrasound-guided erector spinae plane blocks, which were as per the included studies, while the patients assigned to comparator defined by each included study were considered as controlled groups.

3.2.4 Outcome measures

The primary outcome of this review was postoperative pain severity, first analgesic request, total analgesic request, and patient satisfaction. The secondary outcomes of this review was postoperative nausea and vomiting, sedation, and mortality.

3.3 Search strategy

The search strategy aimed to identify all published and unpublished systematic reviews and meta-analyses on thoracoabdominal surgeries, comparing erector spinae plane block with paravertebral, intercostal, epidural blocks, systemic analgesics, and placebo for postoperative pain management, without restrictions on language or date of publication.

An extensive search was carried out in Cochrane Library, CINAHL, PubMed/Medline, Science Direct, and LILACS.

Keywords from titles, abstracts, and indexed terms were analyzed, followed by searches combining free text and indexed terms with Boolean operators. Reference lists of relevant studies

were also reviewed, and additional sources, including grey literature, were explored through Google Scholar. Duplicate records were removed using EndNote, and the remaining studies were screened against eligibility criteria. The search process was summarized in a PRISMA flow chart [43].

The PubMed/Medline database was searched, as thoracic surgery OR breast surgery OR breast cancer OR thoracotomy OR cholecystectomy OR upper abdominal surgery OR abdominal surgery OR spine surgery AND erector spinae OR epidural OR paravertebral OR Intercostal OR pectoral nerve OR systemic analgesics OR placebo AND postoperative pain OR analgesia OR analgesic consumption OR morphine consumption OR opioid consumption OR pain score OR VAS score AND complication OR pneumothorax OR Toxicity OR cardiac arrest OR mortality OR death AND systematic review OR meta-analysis.

Data extraction

Two independent reviewers extracted data from each systematic review and meta-analysis to summarize included studies and assess evidence quality. Any disagreements were resolved by a third reviewer.

Extracted information included author, publication year, number of RCTs, sample size, study quality, outcomes, event counts for intervention and comparator groups, and effect measures (Odds Ratio, Relative Risk, Mean Difference, with 95% confidence intervals). Evidence quality was graded using GRADEpro GDT software. The umbrella review was presented as per the Preferred Reporting Items for Systemic Reviews and Meta-Analysis (PRISMA) [44].

3.4 Methodological Quality Assessment

Each positive finding was given one point, and the total score determined the quality rating of each systematic review. Disagreements between

the two primary reviewers were resolved by a third reviewer. Reviews were classified using AMSTAR scores: high quality (8–11), moderate quality (4–7), and low quality (0–3). The AMSTAR tool was used to assess methodological quality.

3.4.1 Grading the quality of evidence

The overall quality of evidence for the studied outcome will be evaluated using the GRADE system (Grading of Recommendations, Assessment, Development, and Evaluation) [46,47]. The system evaluates evidence based on five factors: study quality (risk of bias), consistency of results across studies, relevance of population and interventions, precision of confidence intervals, and likelihood of publication bias.

By combining these criteria, the overall quality of evidence for maternal and neonatal outcomes was categorized.

The overall quality of evidence will be categorized as follows by evaluating and combining the above five parameters for maternal and neonatal outcomes.

- Effective interventions: Reviews showed strong evidence supporting effectiveness.
- Possibly effective interventions: Reviews found moderate evidence of benefit, but further research is needed.
- Ineffective interventions: Reviews provided strong evidence of no benefit or potential harm.
- Probably ineffective interventions: Reviews suggested moderate evidence of no benefit or harm, requiring more data.
- No conclusions: Reviews had low or insufficient evidence to determine effectiveness or safety.

4 Discussion

This systematic review is planned to investigate the efficacy and safety of erector spinae plane

blocks for postoperative pain management after thoracoabdominal surgeries.

Evidence from various peer-reviewed published literature showed that systemic opioid-based analgesics, neuraxial analgesia, paravertebral block, intercostal nerve block, and pectoral nerve block provide better postoperative pain relief after thoracic and chest wall surgeries [48-58]. However, systemic opioid-based analgesics are associated with several postoperative adverse events, including nausea, vomiting, respiratory depression, opioid addiction, and other gastrointestinal complications [57,59]; neuraxial and thoracoabdominal field block require resources and expertise and are also associated with complications including pneumothorax, hypotension, high spinal, bradycardia, nerve damage, and local anesthetics toxicity [60,61].

On the other hand, erector spinae plane block is a new technique that is safe and simple to administer despite discrepancies in effectiveness and superiority [33,34,36,38,40,62-66].

Published literature showed that the incidence of postoperative acute as well as chronic pain is very high after surgery, which has a tremendous impact on postoperative patient outcomes, family, healthcare providers, and healthcare delivery [3,7,8,10,12,14,23,67,68].

It is a basic human right to provide postoperative pain management to every patient, which is feasible for everyone in terms of resources, technique, cost, and adverse events profile [69,70].

Acknowledgments

The authors would like to acknowledge Dilla University for technical support and encouragement to carry out the project.

Ethical Concern

Not applicable.

Consent for Publication - Not applicable.

Availability of Data and Materials

Data and material can be available where appropriate.

Competing Interests

The authors declare that there are no competing interests.

Funding

No funding was obtained from any organization.

Author's Detail

¹Department of Anesthesiology, College of Health Sciences and Medicine, Dilla University, P.O. Box. 419, Dilla, Ethiopia.

²Departemnt of Surgery, College of Health Sciences and Medicine, Dilla University, P.O. Box. 419, Dilla Ethiopia.

Author's Contributions

SA and GM conceived the idea design of the project.

SA, HM, BJ, and AA were involved in searching strategy, data extraction, quality assessment, analysis, and manuscript preparation. All authors read and approved the manuscript.

References

1. Wall PD, McMahon SB, & Koltzenburg M. Wall and Melzack's textbook of pain: Elsevier/Churchill Livingstone; 2006.
2. Ip HYV, Abrishami A, Peng PW, Wong J, & Chung F. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. *The Journal of the American Society of Anesthesiologists*. 2009;111(3):657-77.
3. Khan RS, Ahmed K, Blakeway E, Skapinakis P, Nihoyannopoulos L, Macleod K, et al. Catastrophizing: a predictive factor for postoperative pain. *The American journal of surgery*. 2011;201(1):122-31.
4. Kalkman C, Visser K, Moen J, Bonsel G, Grobbee D, & Moons K. Preoperative prediction of severe postoperative pain. *Pain*. 2003;105(3):415-23.
5. Coppes OJM, Yong RJ, Kaye AD, & Urman RD. Patient and surgery-related predictors of acute postoperative pain. *Current pain and headache reports*. 2020;24(4):1-8.
6. Werner MU, Mjöbo HN, Nielsen PR, Rudin Å, & Warner DS. Prediction of postoperative pain: a systematic review of predictive experimental pain studies. *The Journal of the American Society of Anesthesiologists*. 2010;112(6):1494-502.
7. Yang MM, Hartley RL, Leung AA, Ronksley PE, Jetté N, Casha S, et al. Preoperative predictors of poor acute postoperative pain control: a systematic review and meta-analysis. *BMJ open*. 2019;9(4):e025091.
8. Lautenbacher S, Huber C, Schöfer D, Kunz M, Parthum A, Weber PG, et al. Attentional and emotional mechanisms related to pain as predictors of chronic postoperative pain: a comparison with other psychological and physiological predictors. *PAIN®*. 2010;151(3):722-31.
9. Kehlet H. Effect of postoperative pain treatment on outcome—current status and future strategies. *Langenbeck's archives of surgery*. 2004;389(4):244-9.
10. Taylor A. & Stanbury L. A review of postoperative pain management and the challenges. *Current Anaesthesia & Critical Care*. 2009;20(4):188-94.
11. Rawal N. Current issues in postoperative pain management. *European Journal of Anaesthesiology (EJA)*. 2016;33(3):160-71.
12. Katz J, Jackson M, Kavanagh BP, & Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *The Clinical journal of pain*. 1996;12(1):50-5.
13. Couceiro TCdM, Valença MM, Lima LC, Menezes TCd, & Raposo MCF. Prevalence and influence of gender, age, and type of surgery on postoperative pain. *Revista brasileira de anesthesiologia*. 2009;59:314-20.
14. Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *Journal of pain research*. 2017;10:2287.
15. Niraj G, Kelkar A, Kaushik V, Tang Y, Fleet D, Tait F, et al. Audit of postoperative pain management after open thoracotomy and the incidence of chronic postthoracotomy pain in more than 500 patients at a tertiary center. *Journal of clinical anesthesia*. 2017;36:174-7.
16. Sommer M, De Rijke J, Van Kleef M, Kessels A, Peters M, Geurts J, et al. The prevalence of postoperative pain in a sample of 1490 surgical inpatients. *European journal of anaesthesiology*. 2008;25(4):267-74.
17. Sommer M, de Rijke JM, van Kleef M, Kessels AG, Peters ML, Geurts JW, et al. Predictors of acute postoperative pain after elective surgery. *The Clinical journal of pain*. 2010;26(2):87-94.
18. Sugiyama Y, Iida H, Amaya F, Matsuo K, Matsuo Y, Kojima K, et al. Prevalence of chronic postsurgical pain after thoracotomy and total knee arthroplasty: a retrospective multicenter study in Japan (Japanese Study Group of Subacute Postoperative Pain). *Journal of anesthesia*. 2018;32(3):434-8.

19. Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, et al. Prevalence of chronic pain and high-impact chronic pain among adults—United States, 2016. *Morbidity and Mortality Weekly Report*. 2018;67(36):1001.
20. Fayaz A, Croft P, Langford R, Donaldson L, & Jones G. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ open*. 2016;6(6):e010364.
21. Saporito A, Aguirre J, Borgeat A, Perren A, Anselmi L, Poggi R, et al. Persistent postdischarge pain and chronic postoperative pain after breast cancer surgery under general anesthesia and single-shot paravertebral block: incidence, characteristics and impact on quality of life and healthcare costs. *Journal of pain research*. 2019;12:1193.
22. Fiorelli S, Cioffi L, Menna C, Ibrahim M, De Blasi RA, Rendina EA, et al. Chronic pain after lung resection: risk factors, neuropathic pain, and quality of life. *Journal of pain and symptom management*. 2020;60(2):326-35.
23. Joshi GP. & Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. *Anesthesiology Clinics of North America*. 2005;23(1):21-36.
24. Philip BK, Reese PR, & Burch SP. The economic impact of opioids on postoperative pain management. *Journal of clinical anesthesia*. 2002;14(5):354-64.
25. Wu CL, Naqibuddin M, Rowlingson AJ, Lietman SA, Jermyn RM, & Fleisher LA. The effect of pain on health-related quality of life in the immediate postoperative period. *Anesthesia & Analgesia*. 2003;97(4):1078-85.
26. Taenzer P, Melzack R, & Jeans ME. Influence of psychological factors on postoperative pain, mood and analgesic requirements. *Pain*. 1986;24(3):331-42.
27. Bailey JG, Morgan C, Christie R, Ke J, Kwofie K, & Uppal V. Continuous peripheral nerve blocks (CPNBs) compared to thoracic epidurals or multimodal analgesia for midline laparotomy: a systematic review and meta-analysis. *Korean Journal of Anesthesiology*. 2020.
28. Cai Q, Liu G-q, Huang L-s, Yang Z-x, Gao M-l, Jing R, et al. Effects of erector spinae plane block on postoperative pain and side-effects in adult patients underwent surgery: A systematic review and meta-analysis of randomized controlled trials. *International Journal of Surgery*. 2020;80:107-16.
29. Chekol WB, Melesse DY, Denu ZA, & Tawuye HY. Evidence-based thoracic epidural nerve block: A systematic review. *International Journal of Surgery Open*. 2020;24:151-5.
30. Chen T, Zhu Z, & Du J. Efficacy of intercostal nerve block for pain control after percutaneous nephrolithotomy: A systematic review and meta-analysis. *Frontiers in surgery*. 2021;8:2.
31. El-Boghdady K, Madjdpour C, & Chin K. Thoracic paravertebral blocks in abdominal surgery—a systematic review of randomized controlled trials. *BJA: British Journal of Anaesthesia*. 2016;117(3):297-308.
32. Huan S, Deng Y, Wang J, Ji Y, & Yin G. Efficacy and safety of paravertebral block versus intercostal nerve block in thoracic surgery and breast surgery: A systematic review and meta-analysis. *PloS one*. 2020;15(10):e0237363.
33. Huang J. & Liu J-C. Ultrasound-guided erector spinae plane block for postoperative analgesia: a meta-analysis of randomized controlled trials. *BMC anesthesiology*. 2020;20(1):1-8.
34. Hughes M, Yim I, Deans DC, Couper GW, Lamb PJ, & Skipworth RJ. Systematic review and meta-analysis of epidural analgesia versus different analgesic regimes following oesophagogastric resection. *World journal of surgery*. 2018;42(1):204-10.
35. Safan TF, Ibrahim WA, Belita MI, Abdalla Mohamed A, & Salem AE. Ultrasound guided paravertebral block versus intravenous lidocaine infusion for management of post-thoracotomy pain. *Egyptian Journal of Anaesthesia*. 2021;37(1):377-85.
36. Turhan Ö, Sivrikoz N, Sungur Z, Duman S, Özkan B, & Şentürk M. Thoracic paravertebral block achieves better pain control than erector spinae plane block and intercostal nerve block in thoracoscopic surgery: A randomized study. *Journal of Cardiothoracic and Vascular Anesthesia*. 2021;35(10):2920-7.
37. Visser E, Marsman M, van Rossum P, Cheong E, Al-Naimi K, van Klei W, et al. Postoperative pain management after esophagectomy: a systematic review and meta-analysis. *Dis Esophagus*. 2017;30(10):1-11.
38. Swisher MW, Wallace AM, Sztain JF, Said ET, Khatibi B, Abanobi M, et al. Erector spinae plane versus paravertebral nerve blocks for postoperative analgesia after breast surgery: a randomized clinical trial. *Regional Anesthesia & Pain Medicine*. 2020;45(4):260-6.
39. Diwan S. & Nair A. Is paravertebral-epidural spread the underlying mechanism of action of erector spinae plane block. *Turk J Anaesthesiol Reanim*. 2020;48(1):86-7.
40. Schwartzmann A, Peng P, Maciel MA, & Forero M. Mechanism of the erector spinae plane block: insights from a magnetic resonance imaging study. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*. 2018;65(10):1165-6.

41. Nino FS. Sustainable Development Goals—United Nations. United Nations Sustainable Development. 2015.
42. Moher D, Liberati A, Tetzlaff J, Altman DG, & Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS med.* 2009;6(7):e1000097.
43. Liao C-Y, Ganz J, Vannest K., Wattanawongwan S, Pierson L, Yllades V, et al. PRISMA Flow Diagram of the Search Process. 2019.
44. Moher D, Liberati A, Tetzlaff J, & Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of internal medicine.* 2009;151(4):264-9.
45. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC medical research methodology.* 2007;7(1):10.
46. Abd El-Hamid AM, Alrabiey MI, & Abd El-Fattah MH. A comparison of the postoperative analgesic effects of intravenous dexmedetomidine with a combination of dexmedetomidine and bupivacaine wound infiltration for lower segment cesarean section: A prospective, randomized study. *Ain-Shams Journal of Anaesthesiology.* 2016;9(2):235.
47. Guyatt GH, Oxman AD, Kunz R, Brozek J, Alonso-Coello P, Rind D, et al. GRADE guidelines 6. Rating the quality of evidence—imprecision. *Journal of clinical epidemiology.* 2011;64(12):1283-93.
48. Abdallah F, Halpern S, & Margarido C. Transversus abdominis plane block for postoperative analgesia after Caesarean delivery performed under spinal anaesthesia? A systematic review and meta-analysis. *British journal of anaesthesia.* 2012;109(5):679-87.
49. Tan HS, Taylor C, Weikel D, Barton K, & Habib AS. Quadratus lumborum block for postoperative analgesia after cesarean delivery: a systematic review with meta-analysis and trial-sequential analysis. *Journal of clinical Anesthesia.* 2020;67:110003.
50. Turan A. & Sessler DI. Steroids to ameliorate postoperative pain. *The Journal of the American Society of Anesthesiologists.* 2011;115(3):457-9.
51. Ventham N, Hughes M, O'neill S, Johns N, Brady R, & Wigmore S. Systematic review and meta-analysis of continuous local anaesthetic wound infiltration versus epidural analgesia for postoperative pain following abdominal surgery. *Journal of British Surgery.* 2013;100(10):1280-9.
52. Waldron N, Jones C, Gan T, Allen T, & Habib A. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. *British journal of anaesthesia.* 2013;110(2):191-200.
53. Wang P, Chen X, Chang Y, Wang Y, & Cui H. Analgesic efficacy of ultrasound-guided transversus abdominis plane block after cesarean delivery: A systematic review and meta-analysis. *Journal of Obstetrics and Gynaecology Research.* 2021.
54. Xu M, Tang Y, Wang J, & Yang J. Quadratus lumborum block for postoperative analgesia after cesarean delivery: a systematic review and meta-analysis. *International journal of obstetric anaesthesia.* 2020;42:87-98.
55. Zhao W-L, Ou X-F, Liu J, & Zhang W-S. Perineural versus intravenous dexamethasone as an adjuvant in regional anesthesia: a systematic review and meta-analysis. *Journal of pain research.* 2017;10:1529.
56. Fusco P, Scimia P, Paladini G, Fiorenzi M, Petrucci E, Pozzone T, et al. Transversus abdominis plane block for analgesia after Cesarean delivery. A systematic review. *Minerva anesthesiologica.* 2014;81(2):195-204.
57. Bonnet M-P, Mignon A, Mazoit J-X, Ozier Y, & Marret E. Analgesic efficacy and adverse effects of epidural morphine compared to parenteral opioids after elective caesarean section: a systematic review. *European Journal of Pain.* 2010;14(9):894.e1- e9.
58. Møiniche S, Kehlet H, & Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief: the role of timing of analgesia. *The Journal of the American Society of Anesthesiologists.* 2002;96(3):725-41.
59. Jaafarpour M, Taghizadeh Z, Shafiei E, Vasigh A, & Sayehmiri K. The effect of intrathecal meperidine on maternal and newborn outcomes after cesarean section: a systematic review and meta-analysis study. *Anesthesiology and Pain Medicine.* 2020;10(2).
60. Fischer B. Benefits, risks, and best practice in regional anesthesia: do we have the evidence we need? *Regional Anesthesia & Pain Medicine.* 2010;35(6):545-8-8.
61. Brull R, McCartney CJ, Chan VW, & El-Beheiry H. Neurological complications after regional anesthesia: contemporary estimates of risk. *Anesthesia & Analgesia.* 2007;104(4):965-74.
62. El Ghamry MR. & Amer AF. Role of erector spinae plane block versus paravertebral block in pain control after modified radical mastectomy. A prospective randomised trial. *Indian journal of anaesthesia.* 2019;63(12):1008.

63. Huang W, Wang W, Xie W, Chen Z, & Liu Y. Erector spinae plane block for postoperative analgesia in breast and thoracic surgery: a systematic review and meta-analysis. *Journal of clinical anesthesia*. 2020;66:109900.
64. Leong R, Tan E, Wong S, Tan K, & Liu C. Efficacy of erector spinae plane block for analgesia in breast surgery: a systematic review and meta-analysis. *Anaesthesia*. 2021;76(3):404-13.
65. Liu Y-C. Erector Spinae Plane Block Similar to Paravertebral Block for Perioperative Pain Control in Breast Surgery: A Meta-Analysis Study. *Pain Physician*. 2021;24:203-13.
66. Taketa Y, Irisawa Y, & Fujitani T. Comparison of ultrasound-guided erector spinae plane block and thoracic paravertebral block for postoperative analgesia after video-assisted thoracic surgery: a randomized controlled non-inferiority clinical trial. *Regional Anesthesia & Pain Medicine*. 2020;45(1):10-5.
67. Yimer H. & Woldie H. Incidence and associated factors of chronic pain after caesarean section: a systematic review. *Journal of Obstetrics and Gynaecology Canada*. 2019;41(6):840-54.
68. Taylor RS, Ullrich K, Regan S, Broussard C, Schwenkglens M, Taylor RJ, et al. The impact of early postoperative pain on health-related quality of life. *Pain practice*. 2013;13(7):515-23.
69. Brennan F, Lohman D, & Gwyther L. Access to pain management as a human right. *American Journal of Public Health*. 2019;109(1):61-5.
70. Pain IPSotIAftSo. Declaration of Montréal: declaration that access to pain management is a fundamental human right. *Journal of pain & palliative care pharmacotherapy*. 2011;25(1):29-31.

RESEARCH ARTICLE

Incidence of Diabetic Foot Ulcer and its Predictors among Diabetic Patients Attending in Gedeo Zone Hospitals, Southern Ethiopia, 2020/2021

Daniel Sisay^{1*}, Tizalegn Tesfaye², Bahiru Mantfardot³, Temesgen Muche⁴, Wondeson Molla⁵

Received: 17 November 2023

Accepted: 11 June 2024

DOI:10.20372/ajhsm.v03i01.04

Published: 26 June 2024



Suggested Citation: Sisay D., Tesfaye T., Mantfardot B., Muche T., and Molla W. Incidence of Diabetic Foot Ulcer and its Predictors among Diabetic Patients Attending in Gedeo Zone Hospitals, Southern Ethiopia, 2020/2021. *Afri. J. Heal. Sci. Med.* 2024, 03(01).

Copyright: ©2024 Dilla University. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: The incidence of diabetic foot ulcer is growing over earlier decade with an increasing magnitude of diabetes mellitus (DM). The prior work primarily concentrated on the magnitude of DFU but incapable to recognize average time it takes for diabetic patients to develop DFU and difficult for early identification, prevention and treatment of the cause of diabetic foot ulcer.

Objectives: To determine incidence of DFU and its predictors among diabetes mellitus (DM) patients who were attending at Gedeo zone hospitals, 2020/2021 GC.

Materials and Methods: Institution-based Prospective follow up study was conducted in Gedeo zone hospitals From Nov 8/2020 to Sep 25/2021; Simple random sampling (SRS) technique was utilized to select respondents. The data gathering was daily checked for entirety and regularity and it was entered into EPI data version 3.2 data and transferred to Stata version 16 for analysis. The Kaplan-Meier estimation method was used and Cox proportional hazard model was applied.

Results: A total of 208 patients were taken from 4 hospitals 1 referral hospital and 3 Primary hospitals. of the total of study participant diabetic foot ulcer was found to be 10.58% [6.40-14.76]. Age greater than 55 years old [AHR=1.90; 95% CI: 1.56, 3.24], type II diabetes mellitus [AHR=3.02; 95% CI: 1.08, 5.40], Retinopathy [AHR=2.30; 95% CI: 1.43, 5.02], Nephropathy [AHR=3.56; 95% CI: 2.47, 5.70] were significantly associated with diabetic foot ulcer.

Conclusion: This study decided that 10.58% DM patient have foot ulcer. The leading explanations to develop foot ulcer were being older age, retinopathy, and nephropathy were meaningfully connected with DFU.

Keywords: Incidence, Diabetic Foot Ulcer, Predictors, Diabetes Mellitus, Ethiopia

*Correspondence: danielsisay93@gmail.com, Tel. +251921680206

¹Department of Epidemiology & Biostatistics, College of Health Sciences and Medicine, Dilla University, Ethiopia. Full list of author information is available at the end of the article

1 Introduction

Diabetes mellitus (DM) is a cluster of disorders that distress how your body handles glucose. Because glucose is a substantial source of energy for the cells that create up your muscle and tissue, it is crucial to your health. It's also the primary source of energy for your brain [1,2] Diabetic ulcers are the most common foot injuries that lead to amputation of the lower extremity. Diabetic foot complications can be detected by family physicians early on. Diabetic foot management necessitates a thorough understanding of the major amputation risk factors, regular routine evaluation, and meticulous preventative measures [2]. Diabetic foot ulcers are the most common and much feared of complication of diabetes, with recent studies suggesting that the lifetime risk of developing a foot ulcer in diabetic patient may be as high as 14% [3].

Diabetes foot ulcer is a severe long-lasting diabetic consequence characterized by lesions in the deep tissues of the lower extremities, as well as neurological abnormalities and peripheral vascular disease (PVD). The new case of DFU has intensified due to the world frequency of DM and the increased life expectancy of DM patients. A previous study showed that a lower limb is amputated due to diabetes every 30s [2].

Patients whose diabetes was treated with food or oral hypoglycemic agents (OHA) were measured to have type II diabetes. Patients receiving insulin had their diabetes type assessed using a scientifically based methodology that took into account their age at onset, pre-setting weight and symptoms, family history, onset of insulin treatment, and previous ketoacidosis history [5].

Ethiopia is one of the developing country has been sowing change in the life style of people toward urbanization particularly in recent decades. This rapped changes led to the emergency of non-communicable diseases such as DM. According to IDF report in 2015 the estimated adulate population in Ethiopia with Diabetes mellitus is 2,567,900 [3].

2 Methods

2.1 Study area and time frame

The research was carried out in Gedeo Zone South.

March 1, 2020–September 25, 2021, Ethiopia. One of SNNPR's fifteen zones is Gedeo. The zone consists of two administration cities (Dilla and Yirgachefe) and six Woredas (Bule, Dilla Zuriya, Gedeb, Kochore, Wonago, and Yirgachefe Woreda). The administrative hub of the zone is Dilla Town, which is located 90 kilometers from Hawassa and 369 kilometers from Addis Ababa. There are 17 known private health facilities, 35 health centers, 146 health posts, 4 NGO clinics, 3 primary hospitals, and 1 referral hospital in the zone. The region's land size is estimated to be 1347.04 square kilometers based on the existing border delineation.

2.2 Study design

Diabetic patients in Gedeo Zone Hospitals participated in a facility-based prospective cohort follow-up study.

2.3 Population

Source of Population

Every patient with diabetes mellitus who comes to Gedeo Zone Hospitals' diabetic follow-up clinic.

Study population

This study includes DM patients who were follow up From March 1, 2020 to Sep 25, 2021 in Gedeo Zone Hospitals.

Eligibility criteria

Inclusion criteria

- Diagnosed with diabetes mellitus types 2
- Able to complete the consent form

Exclusion criteria

- Severe medical and mental illness
- Current foot ulcer

2.4 Sample size determination

After evaluating a Cox Proportional hazard model assumption, the sample size was estimated using STATA version 16. From population based Prospective cohort study done in south-west of Iran, the incidence of foot ulcer was 5.3% and peripheral neuropathy was the predictor of diabetic foot ulcer show that probability of survival among not having peripheral neuropathy (control) was 0.954, the probability of survival among having peripheral neuropathy (exposure) was 0.856 and the proportion of withdrawals is 0.056 [6]. The calculated sample size by log-rank method was 208.

2.5 Study Variables

Dependent variable: Time to develop of diabetic foot ulcer.

Independent variable:

- **Socio demographic factors:** includes age, sex, place of residence, and educational status.
- **Clinical factors:** HDL, LDL, triglyceride, total cholesterol, baseline proteinuria, BMI, DM duration, fast blood sugar level, type of DM and types of medication).
- **Comorbidities:** Hypertension, Diabetic Neuropathy, peripheral vascular diseases, diabetic nephropathy and diabetic retinopathy.

2.6 Operational definition and Term definition

Diabetic foot ulcer: Non traumatic wounds of the skin (incomplete or full thickness) blew the ankle of the patient who has DM [1].

Event of interest: The incidence of Diabetes Foot Ulcer with-in the follow up period.

Censored: Those who are not experiencing DFU until the end of the study or died before experiencing DFU within the study period, lost to follow up before experiencing the event of interest with in study period by reason not related to the event of interest are considered as censored [6].

Body Mass Index (BMI): is determined by dividing a patient's body weight by the square of their height. BMI ranges <18.5 kg/m^2 are considered underweight, BMI ranges 18.5 – 24.5 kg/m^2 are considered normal, BMI ranges 24.5 – 30 kg/m^2 are considered overweight, and BMI >30 kg/m^2 are considered obese [7].

Fast blood sugar level (FBS): A blood sample was taken after an overnight fast. A FBS level between 70 mg/dL to 126 mg/dL is normal [8].

Lipid profiles: Lipid profiles include total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL). The normal value of LDL, less than 100 mg/dL, the normal value of HDL above 40 mg/dL, the normal value of triglycerides less than 150 mg/dL and the normal value of total cholesterol is less than 200 mg/dL [8].

Proteinuria: Proteinuria is a condition characterized by the presence of greater than normal amount of protein in the urine (protein/creatinine ratio greater than 45 mg/mmol) [9].

2.7 Data collection tools and procedure

Diabetic foot ulcer was assessed by using standard scale adapted from different literatures. Questions about other variables including sociodemographic characteristics, clinical factors and comorbidities questioners were adapted from different literatures review. A structured questioner and a face-to-face interviewer process were conducted, with the questioner being adapted from several literature reviews and for data collection 4 BSc nurses was selected and they were supervised by the principal investigator.

2.8 Data Processing and Analysis

Data was entered into Epi-data version 7. Then exported to STATA version 16 statistical data base to check for any incompleteness, coding error and for further analysis. The data was edited, cleaned and coded to make it suitable for analysis. Descriptive statistics were employed to examine data in terms of frequency and percentage, while continuous variables were represented

in terms of mean/median value. The overall incident cases were divided by the total number of person-years (PY) of follow-up to calculate the total incidence rate DFU. Using Kaplan-Meier and log-rank test survival time was estimated and survival curves are compared between different exposure groups. To identify the underline baseline distribution Kaplan-Meier and log-log hazard plot are used. The proportional hazard hypothesis was tested by using Schoenfeld residuals method. Goodness of fit was evaluated by using cox-snell residual procedure. The Variables with $p < 0.2$ in the bi-variable analysis are candidates for multi-variable analysis using backward elimination method. Hazard ratio (HR) with its 95% ($\alpha = 0.05$) confidence level was calculated to display the strength of association.

2.9 Survival Analysis

Censoring is a significant analytical difficulty in most survival analyses. In essence, censorship happens when we have some knowledge about an individual's survival period but not the exact time. When diabetic patients are transferred to another hospital, they discontinue therapy, die, and are not cured by December 2021. (at the end of study). This means that the survival data is right filtered and random.

Non-parametric Survival Methods

Estimations of the survival function and hazard function are useful for summarizing survival data. The survival scattering estimate method produces descriptive numbers such as the median survival time. These approaches are denoted to as non-parametric meanwhile they do not mark any assumptions about the survival time distribution. Preliminary data analysis using non-parametric approaches reveals the shape of each group's survival function and determines whether the groups are proportional, that is, if the estimated survival functions for two groups are nearly parallel (do not cross).

Kaplan-Meier Estimator of Survival Function

The Kaplan-Meier (KM) estimator is the standard non parametric estimator of the survival

function, $S(t)$, proposed by Kaplan and Meier (1958) which is not based on the actual observed event and censoring times, but rather on the ordered in which events occur. It is also called the Product-Limit estimator. KM estimator incorporates information from all of the observations available, both censored and uncensored, by considering any point in time as a series of steps defined by the observed survival and censored times. When there is no censoring, the estimator is simply the sample proportion of observations with event times greater than t . The technique becomes a little more complicated but still manageable when censored times are included.

The Cox proportional Hazards Regression model

Survival models link one or more factors that may alter the proportionate quantity to the time that passes before recovery from severe acute malnutrition. The Cox proportional hazards regression model is one of the most prevalent types of regression models used in survival analysis. Ox (1972) presented a semi-parametric hazard function model that allows for the insertion of covariates while leaving the baseline hazards undefined and only taking positive values.

2.10 Ethical Consideration

Ethical approval was acquired from Institutional Review Board (IRB) of College of Health Sciences and medicine, Dilla University; throughout the data gathering, the aim of the study was elucidated to the study members. After interpretation the agreement form to the respondents, willingness to take part was inquired. The respondents were also informed that they can decline from the interview at any time. They were also informed to ask any question on unclear issues about the study. Participants name were not captured in the questionnaire and after taking consent the interview was conducted in a private setting and confidentiality of the information was maintained. The study won't have any anticipated harm for the study participants.

3 Results

3.1 Socio-demographic Characteristics of respondents

Of the total 214 diabetic patient initially planned for the study 208 (97%) of them participated. The median age of participants was 42(IQR=35-58) years. More than half of 125(60.10%) of

the study subjects were males and Regarding to the residence, 124(59.62%) of participants were urban dwellers, 80(38.46%) of adults were Unable to read and write. 115(55.29 %) were attended Primary school education. Majority 114(54.81%) of respondents were follow christen religion (Table 1).

Table 1 Socio demographic characteristics of participant at Gedeo zone hospital, Ethiopia (N = 208)

Variables		Frequency (208)	Percent (%)
Sex of patient	Male	125	60.10
	Female	83	39.90
Age category	15-24	43	20.67
	25-34	58	27.88
	35-44	20	9.62
	45-54	21	10.10
	55 and above	66	31.73
Residence	Urban	124	59.62
	Rural	84	40.38
Religion	Christian	114	54.81
	Muslim	74	35.58
	Others	20	9.62
Marital status	Single	67	32.21
	Married	108	51.92
	Divorced	13	6.25
	Died	20	9.62
Occupational status	Unemployment	80	38.46
	Gov't employment	66	31.73
	Private job	51	24.52
	Other	11	5.29

3.2 Clinical and Comorbidities Factors

Based on clinical factors and comorbidities 129 of 208 (62.02%) were type I diabetic mellitus patient. Regarding to comorbidities 139(66.83%)

had retinopathy and 126(60.58) had nephropathy, Almost half of study participant using treatment of insulin 102(49.04) and 148(68.75) Trygysride levels are <150 at baseline (Table 2).

Table 2 Baseline Clinical and Comorbidity Information of DM Patients on Follow-up at Gedeo zone hospitals, South Ethiopia, (N= 208)

Variables		Frequency (208)	Percent (%)
Type of DM	Type I	129	62.02
	Type II	79	37.98
Duration of DM	<5 Years	77	28.2
	≤5 Years	196	71.8
HDL level (mg/dl)	≤40	131	62.98
	>40	77	37.02
Triglyceride level (mg/dl)	<150	143	68.75
	≥150	65	31.25
LDL level(mg/dl)	<100	126	60.58
	≥100	82	39.42
Retinopathy	Yes	139	66.83
	No	69	33.17
Nephropathy	Yes	126	60.58
	No	82	39.42
Type of treatment	OHA	98	47.12
	Insulin	102	49.04
	Both OHA & Insulin	8	3.85

3.3 Incidence of diabetic foot ulcer

A total of 22 or 10.58% [6.40-14.76] developed DFU. The follow-up of participants were for a minimum of one month and a maximum of eight months with the median survival time of 4 months. Based on this the total person-time of observation was 816 person-month. The overall new occurrence rate of DFU was found to be 2.6 (95% CI: 6.40–14.76) per 1000 person-month.

3.4 Median time to relapse

The overall follow up period was 8 months and the Study participants were followed for a median of 4 months (inter quartile range (IQR): 2-4 months). Based on life table estimate the cumulative relapse within the first five months of follow up was 64% and in the next 5 months was 17.4% (Table 3).

Table 3 Life table estimate the cumulative relapse within the first four months of follow up was 6% and in the next 5 months

Interval (in months)	Beg. Total at Risk	Average number at Risk in interval	DFU	Censored	Proportion of relapse with in interval	Cumulative probability of relapse	[95%CI]
0 – 2	208	245	2	186	0.064	0.082	[0.912-0.973]
2 – 4	198	132	5	102	0.117	0.60	[0.506-0.640]
4 – 6	120	71	8	96	0.110	0.14	[0.121-0.222]
6 – 8	35	46	7	57	0.168	0.39	[0.300-0.491]

In the Kaplan Meier curve for diabetic foot ulcer patients, the probability of foot ulcer increases as the follow-up time increases. Most patients

terminate throughout 5 months of enrolment as indicated by the curve (Figure 2).

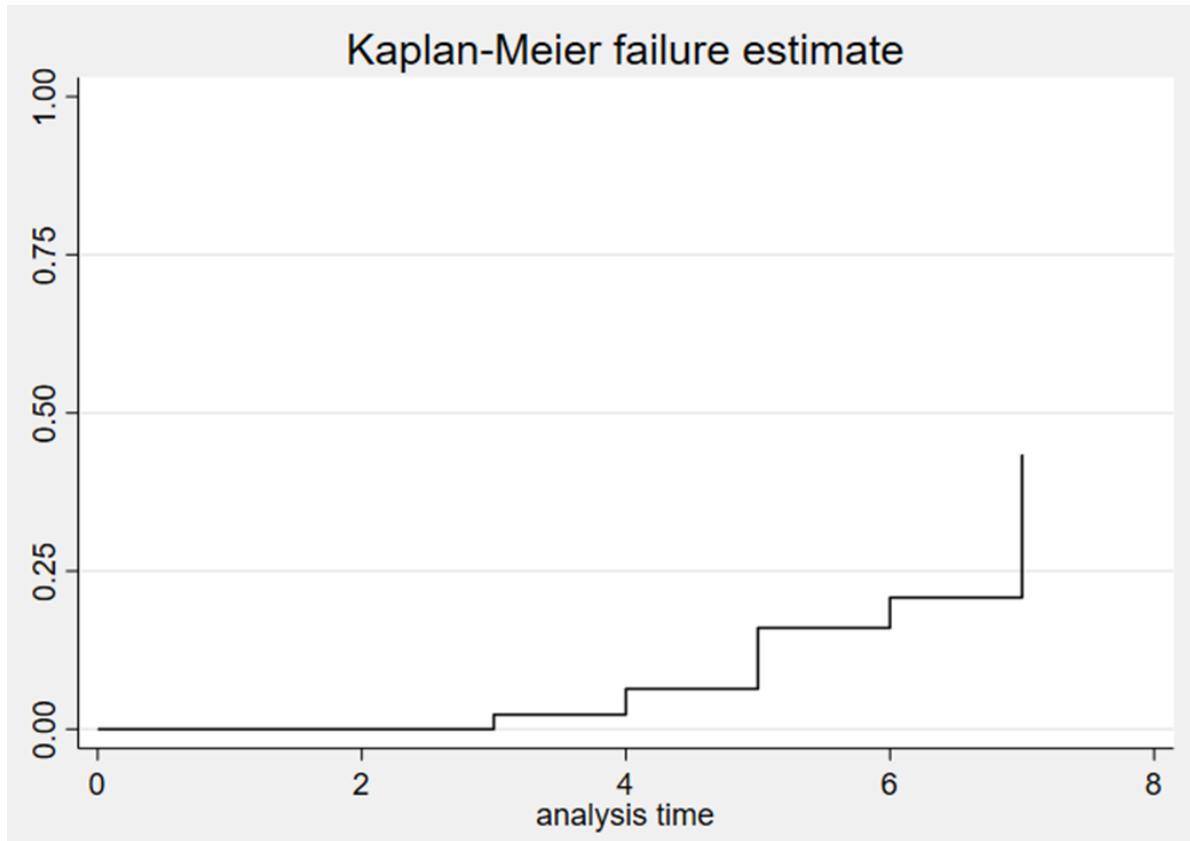


Figure 1 Kaplan meier curve for diabetic foot ulcer patient

3.5 Predictors of time to develop diabetic foot ulcer

In the Univariate analysis the Cox model identified potential predictors of diabetic foot ulcer at p -value ≤ 0.05 level. Consequently, the candidate variables for building a multivariable Cox model were: Sex, Residence, Occupation, Educational status, Religion, Region, Substance, Family history of diabetic mellitus, Comorbidity illness, Age of respondents, Type of treatment, Type of DM, Duration of illness, HDL, Triglyceride, LDL level, retinopathy and Nephropathy.

From the candidate variables considered for building multivariable Cox at 95% CI were Age of respondents, Educational status, Type of DM, retinopathy and nephropathy were statistically significant predictors used in the final Cox model after interaction and model diagnostics was checked. Also we have checked graphically the proportional hazard assumptions using Log-log plots for each predictor then parallel lines indicate proportional hazard assumption was fulfilled.

Therefore, each predictor satisfies the assumptions of proportional hazard regression. The interaction effect were checked among statistical significant variables in the final Cox model. Hence, no significant interactions were detected to consider in the final Cox model. The likelihood ratio test was also done for checking goodness of fit of the model. Hence, no interaction was detected so we can't consider it in the comparison of the models.

Therefore, the likelihood ratio test indicated the main effect model significantly predict diabetic foot ulcer (p -value < 0.001). Also the Cox-Snell residual plot shows the model was good fit. Finally, the interpretation of the AHR at 95% CI was done for the confirmed statistically significant predictors of diabetic foot ulcer in the final Cox model.

Results in this final model showed that, the risks of diabetic foot ulcer in Aged 50 and above patients were 2.9 times more risk as compared to in age 15-24 (AHR=2.9; 95% CI: 1.56-3.24).

Table 4 Cox regression analysis for predictors of diabetic foot ulcer among diabetic patient in Gedeo zone hospitals, Ethiopia 2019(N = 208)

Variables	Survival Status		BI-Variable Model		Multi variable model	
	Event	Censored	HR [95% CI]	p-value	HR [95% CI]	p-value
Sex	Male	12	113	1	1	
	Female	10	73	1.07[0.46-2.51]		0.86[0.78-3.29]
Age of respondents	15-24 years	6	37	2.47[1.46-2.61]		1.08[0.31-2.51]
	25-34 years	8	50	1.89[1.46-2.15]		1.68[0.60-3.55]
	35-44 years	2	18	1.95[1.46-2.28]		6.80[0.59-13.11]
	45-54 years	1	20	1.49[0.46-2.51]		4.00[0.48-4.60]
	55 and above	5	61	1.51[1.47-2.51]		1.90[1.56-3.24]
Residence	Urban	15	109	1	1	
	Rural	7	77	0.77 [0.31-1.89]		0.05[0.01-1.31]
Marital status	Single	8	59	1	1	
	Married	11	97	0.64[0.25-1.62]		0.81[0.75-1.22]
	Divorced	2	11	2.26[0.46-10.86]		4.35[0.19-12.47]
	Died	1	19	0.51[0.03-1.74]		0.02[0.01-5.02]
Type of DM	Type I	16	113	1	1	
	Type II	6	73	0.73[0.28-1.90]		3.02[1.08-5.40]
Duration of DM	<5 Years	14	129	1	1	
	≤5 Years	8	57	1.23[0.51-2.93]		0.35[0.13-2.02]
HDL level (mg/dl)	≤40	119	12	1	1	
	>40	67	10	1.12[0.48-2.61]		2.21[0.06-3.51]
LDL level(mg/dl)	<100	12	114	1	1	
	≤100	10	72	1.28[0.55-2.97]		0.35[0.23-1.02]
Retinopathy	Yes	12	114	1.79[0.73-4.40]		2.30[1.43-5.02]
	No	10	72	1	1	
Nephropathy	Yes	13	113	1.19[0.50-2.79]		3.56[2.47-5.70]
	No	9	73	1	1	
Type of treatment	OHA	10	88	1.26[0.54-2.93]		3.26[0.45-6.05]
	Insulin	12	90	0.89[0.54- 2.93]		0.77[0.42-3.90]
	Both OHA & Insulin	0	8	1	1	
Triglyceride level (mg/dl)	<150	18	125	1	1	
	≥150	4	61	0.50[0.04-1.50]		0.35[0.23-1.02]
Educational level	No education	15	100	1	1	
	Primary education	3	33	0.74[0.21-2.57]		5.10[0.50-7.13]
	Secondary and Above	4	53	0.52[0.17-1.58]		0.40[0.20-1.09]
Substance use	None	9	83	1	1	
	Kchat	0	12	0.64[0.04-0.87]		7.69[0.23-9.86]
	Alcohol	4	43	0.20[0.06-0.88]		0.13[0.03-1.88]
	Tobacco	4	13	0.26[0.07- 0.90]		0.11[0.01-3.02]
	Other	5	35	1	1	
Family history of DM	Yes	17	125	0.61[0.22-1.67]		0.67[0.52-1.99]
	No	5	61	1	1	
Comorbidity	Hypertension	14	96	1.96[0.78-4.92]		0.43[0.16-2.53]
	HIV	7	72	0.77[0.09-6.27]		0.17[0.15-1.27]
	Asthma	1	12	0.56[0.09-4.37]		0.66[0.16-1.95]
	Other	0	6	1	1	

Those participants who had type II DM were 3.03 times more likely to develop DFU than those who had type I DM [AHR=3.02; 95% CI: 1.08-5.40]. The risks of diabetic foot ulcer among

who had Retinopathy were 2.9 times higher than the corresponding reference group (AHR=2.9; 95% CI: 1.43-5.02).

The risks of diabetic foot ulcer among who had Nephropathy were 3.56 times more risk than the corresponding reference group (AHR=3.56; 95% CI: 2.47-5.70) (Table 4)

4 Discussions

This study investigated the incidence and predictors of diabetic foot ulcer among diabetic mellitus patients at Gedeo zone hospitals. In this study of 208 individual diabetic mellitus patients 10.58% of study participants had a diabetic foot ulcer. This finding is in line with studies done in Ethiopia [10]. But it was higher than the studies conducted in Nigeria [11]. This variance might be because of the difference in the inhabitants and the study area because all the matched studies were population based but the current study was institution based hospital-based study. And also, diabetic care in these countries and other developed countries might be well structured than evolving countries like Ethiopia. Besides, in low and middle-income countries many factors such as variation of health care services, limited resource allocation and low health literacy among diabetic mellitus patients contribute to high DFU [12].

Concerning incidence rate (IR) of diabetic foot ulcer, in this study, the incidence rate was 11 per 1000 person-year which means in 1000 Diabetes patients there was 11 Diabetic Foot Ulcer patients per year or if we follow 1000 persons with DM for one year 11 patients will develop the case, diabetic foot ulcer. This result was comparable with the study done in Japan [13] which found the incidence rate of 4 per 100 person-year.

Respondent age was independently associated with an increased hazard of diabetic foot ulcer in this study. Results in this final model showed that, the risks of diabetic foot ulcer in Aged 50 and above patients were 2.9 times higher as compared to in age 15-24 (AHR=2.9; 95% CI: 1.56-3.24). This is consistent with a cross-sectional study in Addis Ababa and Case control study done in Japan [14]. This might be because of hypertension, visual disturbance, and neuropathy increased with increasing age of the patient.

Type of diabetes mellitus was one of the most

predictors of diabetic foot ulcer occurrence. Those diabetic patients who had type II diabetes mellitus were 3.03 times more likely to develop diabetic foot ulcer than those who had type I diabetes mellitus [AOR=3.03; 95% CI: 1.08-5.40]. This finding is similar with the studies conducted in Sudan [11] which indicated type II diabetes mellitus was associated with the development of diabetic foot ulcer. The possible explanation could be in type II diabetic patients; there are related complications of the disease, such as peripheral neuropathy and atherosclerotic peripheral arterial disease; as a result, the patient may have less consumption of oxygen, nutrient transportation and cell detoxification consequence in ulceration in the extremities.

The risks of diabetic foot ulcer among who had retinopathy were 2.9 times higher than the corresponding reference group (AHR=2.9; 95% CI: 1.43-5.02) respectively. The hazard of developing diabetic foot ulcer among DM patients with retinopathy was higher than DM patients who have no diabetic retinopathy. A similar association was found with a cross-sectional study done in Iran [9]. This might be due to retinopathy patients had decreased visual activities, so it is challenging to give foot care activities such as scrutinizing their feet daily and exerting good foot sanitation and these upsurges the risk of DFU.

The risks of diabetic foot ulcer among who had nephropathy were 3.56 times higher than the corresponding reference group (AHR=3.56; 95% CI: 2.47-5.70). Diabetic nephropathy was significantly associated with an increased hazard of DFU in this study. This is consistent with a cross-sectional study in Brazil [15]. This might be due to vascular insufficiency and peripheral neuropathy are more common in patient with diabetic nephropathy, which in turn results in ischemic ulceration or foot ulcer [7]. This presence of vascular insufficiency, which is common in a patient with nephropathy, significantly increases the risk of chronic inflammation, fluid retention, rennin-angiotensin system alterations, and ischemic ulcerations that eventually ends up with foot ulcer.

Since cohort study it has the benefit of showing time-based associations. Because of the secondary nature of the data and in turn the excellence of data, some important variables like self-care practices and main traditional risk factors for DFU such as foot abnormality were not considered.

5 Conclusion

This finding showed that taking Type of DM, nephropathy, retinopathy, and being older age positively associated with DFU. Therefore, proper interventions to DM patient self-care exercise, way of life amendment, and constant follow up to avert DFU. Health service providers have to play their role in undertaking DFU through appropriate health information dissemination and patient's treatment.

Declarations

Acknowledgements

First of all, we would like to acknowledge Dilla University College of health and medicine for giving us the chance to conduct this research project. Second we would like to acknowledge data collectors for their faithfulness to collect the data. The last, but not the least, our gratitude goes to study participants for being involved in the study.

Consent to Publication: Not applicable.

Availability of Data and Materials: Data will be made available whenever requested for research purpose.

Conflict of interests: The authors declared that they have no competing interests.

Funding:

Dilla University and NORHED project fund the research but does not have a role in study design, collection and analysis of the study.

Authors' contributions:

All the authors had participated in the title selection, design, proposal preparation, statistical analysis, and interpretation of results, manuscript preparation. They approved this manuscript to be published.

Authors' Information

¹Department of Ophthalmology, College of Medicine and Health Sciences, Dilla University, Dilla, Ethiopia

² Department of Ophthalmology and Optometry, College of Medicine and Health Sciences, Hawassa University, Hawassa, Ethiopia

References

1. Association AD. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014; 37(Supplement_1):S81–90.
2. Consultation WHO. Definition, diagnosis and classification of diabetes mellitus and its complications. Part; 1999.
3. Atlas D. International diabetes federation. IDF Diabetes Atlas, 7th edn. Brussels, Belgium *Int. Diabetes Fed.* 2015; 33(2).
4. Agwu E, Dafiewhare EO, Ekanem PE. Possible diabetic-foot complications in Sub-Saharan Africa. *Glob Perspect Diabet Foot Ulcerations*. 2010; 2007:3–15.
5. Zimmermann MB, Boelaert K. Iodine deficiency and thyroid disorders. *Lancet Diabetes Endocrinol*. 2015; 3(4):286–95.
6. Shahbazian H, Yazdanpanah L, Latifi SM. Risk assessment of patients with diabetes for foot ulcers according to risk classification consensus of International Working Group on Diabetic Foot (IWGDF). *Pakistan J. Med. Sci.* 2013; 29(3):730.
7. Wolde HF, Atsedeweyen A, Jember A, Awoke T, Mequanent M, Tsegaye AT, et al. Predictors of vascular complications among type 2 diabetes mellitus patients at University of Gondar Referral Hospital: a retrospective follow-up study. *BMC Endocr Disord*. 2018; 18:1-8.
8. Khan MIH, Azhar U, Zubair F, Khan ZA. Can we link foot ulcer with risk factors in diabetics? A study in a tertiary care hospital. *Pakistan J. Med. Sci.* 2018; 34(6):1375.
9. Nongmaithem M, Bawa APS, Pithwa AK, Bhatia SK, Singh G, Gooptu S. A study of risk factors and foot care behavior among diabetics. *J. Fam. Med. Prim care*. 2016; 5(2):399–403.
10. McEvoy CT, Cardwell CR, Woodside J V., Young IS, Hunter SJ, McKinley MC. A Posteriori Dietary Patterns Are Related to Risk of Type 2 Diabetes: Findings from a Systematic Review and Meta-Analysis. *J Acad Nutr Diet [Internet]*. 2014; 114(11):1759-1775.e4. Available from: <http://dx.doi.org/10.1016/j.jand.2014.05.001>
11. Almobarak AO, Awadalla H, Osman M, Ahmed MH. Prevalence of diabetic foot ulceration and associated risk factors: an old and still major public health problem in Khartoum, Sudan? *Ann Transl Med*. 2017; 5(17).
12. Balducci S, Iacobellis G, Parisi L, Di Biase N, Candriello E, Leonetti F, et al. Exercise training can modify the natural history of diabetic peripheral neuropathy. *J Diabetes Complications*. 2006; 20(4):216–23.
13. Jiang Y, Wang X, Xia L, Fu X, Xu Z, Ran X, et al. A cohort study of diabetic patients and diabetic foot ulceration patients in China. *Wound Repair Regen*. 2015; 23(2):222–30.

14. Iwase M, Fujii H, Nakamura U, Ohkuma T, Ide H, Jodai-Kitamura T, et al. Incidence of diabetic foot ulcer in Japanese patients with type 2 diabetes mellitus: the Fukuoka diabetes registry. *Diabetes Res Clin Pract.* 2018; 137:183–9.
15. Arkkila PET, Kantola IM, Viikari JSA. Limited Joint Mobility in Non–Insulin-Dependent Diabetic (NIDDM) Patients: Correlation to Control of Diabetes, Atherosclerotic Vascular Disease, and Other Diabetic Complications. *J Diabetes Complications.* 1997; 11(4):208–17.

RESEARCH ARTICLE

Short term Outcomes of Patients with Decompensated Cirrhosis on Follow up at Tikur Anbessa Specialized Hospital: a 1-Year Retrospective Cohort Study

Edom Gebremedhin^{1*} and Amir Sultan²

Received: 31 May 2024

Accepted: 30 June 2024

DOI:10.20372/ajhsm.v03i01.05

Published: 10 July 2024



Suggested Citation: Gebremedhin E. & Sultan A. Short term Outcomes of Patients with Decompensated Cirrhosis on Follow up at Tikur Anbessa Specialized Hospital: a 1-Year Retrospective Cohort Study. *Afri. J. Heal. Sci. Med*; 2024, 03(01).

Copyright: ©2024 Dilla University. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Cirrhosis is the leading cause of liver-related mortality worldwide, with the highest age-standardized death rates found in low-income countries, particularly in Sub-Saharan Africa. In Ethiopia, studies evaluating the short-term outcomes of patients with chronic liver diseases, especially decompensated cirrhosis, are limited.

Objectives: This study aimed to assess the short-term outcomes of patients with decompensated cirrhosis at Tikur Anbessa Specialized Hospital and to identify the prevalence and factors associated with poor outcomes among these patients.

Methods: A retrospective cohort study was conducted over one year, including data from medical records of 110 patients with decompensated cirrhosis admitted to the emergency department, intensive care unit, medical wards, or seen as outpatients at the Gastroenterology clinic from March 2020 to March 2021. Participants were selected consecutively using a convenience sampling technique. Chi-square statistics and binary logistic regression were employed to examine associations between categorical variables, while the Cox proportional hazard model assessed the probability of poor outcomes. Statistical significance was set at $P < 0.05$.

Results: Among the 110 participants, 82 (74.5%) were male, with a mean age of 40.35 (± 13.5) years. The median duration of known chronic liver disease was 20.5 months (IQR 33). Chronic hepatitis B infection was the most common etiology of cirrhosis (46.36%), followed by alcohol-related cirrhosis (24.55%) and cryptogenic cirrhosis (20.9%). The prevalence of poor outcomes—defined as readmission, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, and/or death—was 16.3%, 14.4%, and 22% at 1, 3, and 6 months, respectively. Sixty-one hospital admissions were documented, with 49 (44.5%) participants admitted at the index visit. Upper GI bleeding, hepatic encephalopathy, and hepatocellular carcinoma were the leading causes of hospitalization. During the study, 16 (14.54%) participants died in the hospital. Chronic HBV infection significantly contributed to poor outcomes [AOR=4.4; 95% CI: 1.15-16.93]. Age over 40 years was associated with upper GI bleeding [AOR=2.8; 95% CI: 0.76-5.44], but not with other complications of portal hypertension.

Conclusion: Chronic HBV infection was the predominant etiology of cirrhosis and a strong predictor of poor outcomes. Age over 40 was significantly linked to upper GI bleeding, while hepatic encephalopathy and upper GI bleeding predicted hospitalization. Enhancing access to HBV vaccines and treatments could improve overall prognosis. A national multicenter study is recommended to further investigate the outcomes of cirrhosis patients, focusing on specific causes and treatments to identify predictors of poor outcomes.

Keywords: Chronic liver disease, Decompensated cirrhosis

*Correspondence: edomggebreegziabher@gmail.com, Tel. +251913931297

¹Department of Internal Medicine, Dilla University, Ethiopia.

Full list of author information is available at the end of the article

1 Introduction

1.1 Background

Chronic hepatitis encompasses a range of liver disorders with various causes and severities, characterized by ongoing hepatic inflammation and necrosis for at least six months, ultimately leading to fibrosis of the liver parenchyma [1]. Cirrhosis represents the final pathway for all chronic liver diseases (CLD), regardless of etiology, and is a pathological condition marked by late-stage progressive hepatic fibrosis, resulting in the replacement of normal liver architecture with regenerative nodules [1,2]. The most common causes of cirrhosis-related morbidity and mortality worldwide include chronic hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol-related liver disease, and non-alcoholic steatohepatitis (NASH) [3].

The clinical features of cirrhosis arise from pathological changes and reflect the severity of liver disease [1]. In the early stages, patients may maintain synthetic and excretory functions of the liver, often remaining asymptomatic. This stage is termed 'compensated' cirrhosis, during which patients can experience median survival times exceeding 12 years [4,5]. However, as hepatic architecture progressively distorts, patients develop complications related to portal hypertension and/or liver dysfunction, leading to decompensated cirrhosis [1,2,5]. Decompensated cirrhosis is defined by the presence (or history) of ascites, variceal bleeding, encephalopathy, and/or jaundice [4,6,7].

Variable pathophysiological mechanisms, including increased portal venous pressure, bacterial translocation, inflammation, and hyperdynamic circulation, are believed to contribute to decompensation in patients with cirrhosis [8].

The transition from compensated to decompensated cirrhosis is associated with a decline in quality of life and a significant reduction in survival rates, approximately two years [4,5,9]. Common causes of death in patients with cirrhosis include liver failure, bleeding, hepatocellular carcinoma (HCC), infections, hepatorenal syndrome, and acute-on-chronic liver failure (ACLF) [4].

According to the Global Burden of Disease (GBD) Study, in 2017, there were 10.6 million prevalent cases of decompensated cirrhosis and 112 million prevalent cases of compensated cirrhosis globally. That year, cirrhosis caused over 1.32 million deaths, accounting for 2.4% of total deaths worldwide. Sub-Saharan Africa reported the highest age-standardized death rate among GBD super-regions, with 32.2 (25.8–38.6) deaths per 100,000 population in 2017 [3].

While liver biopsy remains the gold standard for diagnosing cirrhosis, various clinical, laboratory, and imaging findings can aid in diagnosing and prognostic stratification across different etiologies [2,5,10]. These include physical examination signs such as jaundice, ascites, splenomegaly, hepatic encephalopathy, dilated abdominal veins, spider angiomas, and gynecomastia; laboratory findings like thrombocytopenia, elevated bilirubin, decreased serum albumin, deranged coagulation parameters, and altered creatinine levels; and imaging evidence of liver fibrosis or complications related to portal hypertension, assessed through ultrasound, transient elastography, or magnetic resonance elastography [1,2,11,12].

Among the various clinical and laboratory parameters influencing prognosis in cirrhosis, the presence of ascites, hepatic encephalopathy, and coagulation abnormalities, along with derangements in serum albumin, bilirubin, creatinine, and sodium levels, significantly increase the risk of mortality [2,4,5,13]. These parameters are incorporated into prognostic scoring models such as the Child-Pugh score, Model for End-Stage Liver Disease (MELD) score, and MELD-Sodium (MELD-*Na*) score, which are utilized to assess patients' eligibility for liver transplantation [7,11,14,15]. Each scoring system has distinct advantages and limitations for clinical application.

According to the Global Burden of Disease (GBD) Study, in 2017, low-income countries in the Sub-Saharan Africa region exhibited higher age-standardized death rates from cirrhosis compared to other GBD super-regions [3]. This may be attributed to limited access to standard medical care, reduced health-seeking behavior, and

a lack of advanced diagnostic services and therapeutic interventions for decompensated cirrhosis in these regions [16].

Studies assessing the short- and long-term outcomes of patients with chronic liver diseases, particularly decompensated cirrhosis, are limited in Ethiopia. A study conducted 30 years ago by E. Tsega and colleagues among 334 hospitalized patients with chronic liver disease (CLD) found that 208 participants (62%) had cirrhosis. The most common initial clinical presentations included ascites, splenomegaly, hematemesis, or melena from esophageal varices, and mental changes due to hepatic encephalopathy. Hepatitis B virus infection was the most frequently diagnosed cause of chronic liver disease in this study [17]. These findings are comparable to studies evaluating the survival and prognosis of patients with compensated and decompensated cirrhosis conducted in Italy and England [6,18]. However, specific outcomes and causes of decompensation were not reported in this study.

Recent studies among hospitalized CLD patients in Ethiopia indicated inpatient mortality rates ranging from 28.5% to 41%. [19,20] These figures may reflect a sampling bias, as participants were selected from advanced liver disease cases with high predicted mortality rates. Despite the reported high inpatient mortality rates, there is a lack of data on the specific causes of decompensation and predictors of mortality and complications.

This study aimed to assess the short-term outcomes of patients with decompensated cirrhosis at Tikur Anbessa Specialized Hospital (TASH), the largest tertiary hospital in the country, within six months of their index hospital visit or admission. Sociodemographic, clinical, and laboratory parameters of the participants were stratified to identify predictors of mortality, hospital admissions, and complications of portal hypertension. The findings of this study can serve as a baseline for future research aimed at identifying predictors of poor outcomes and developing pathways to improve clinical care for patients with chronic liver disease.

2 Methods

2.1 Study area and period

The study was conducted at Tikur Anbessa (Black Lion) Specialized Hospital, the largest tertiary hospital in Ethiopia, established in 1964 in Addis Ababa. This facility provides specialized clinical services to patients from all regions of the country through various departments and subspecialty units. It also serves as the primary teaching center for the College of Health Sciences at Addis Ababa University, offering both undergraduate and postgraduate clinical training in multiple disciplines.

The Gastroenterology unit within the Department of Internal Medicine offers both inpatient and outpatient services, including diagnostic and therapeutic endoscopic procedures. It features a dedicated 16-bed inpatient ward shared with the hospital's Pulmonary unit and serves approximately 180 outpatients weekly at the follow-up clinic, in addition to managing all emergent gastrointestinal cases in the emergency department. Consultants, fellows, and internal medicine residents actively participate in patient care. The study was conducted from August 2021 to October 2021.

2.2 Study design

A retrospective cohort study design was employed.

2.3 Study population

The study included all patients diagnosed with decompensated cirrhosis based on clinical and laboratory data. Participants were sourced from the emergency department (ED), medical wards, intensive care unit (ICU), and outpatients seen at the Gastroenterology (GI) clinic at Tikur Anbessa Specialized Hospital (TASH) from March 2020 to March 2021.

2.4 Inclusion and exclusion criteria

Inclusion criteria

- Age > 18 years
- Diagnosed with decompensated cirrhosis based on the operational definition of this study

- Admitted at ED, medical wards or ICU at TASH at least 06 months prior to the study period, or
- On follow up at GI clinic at TASH

Exclusion criteria

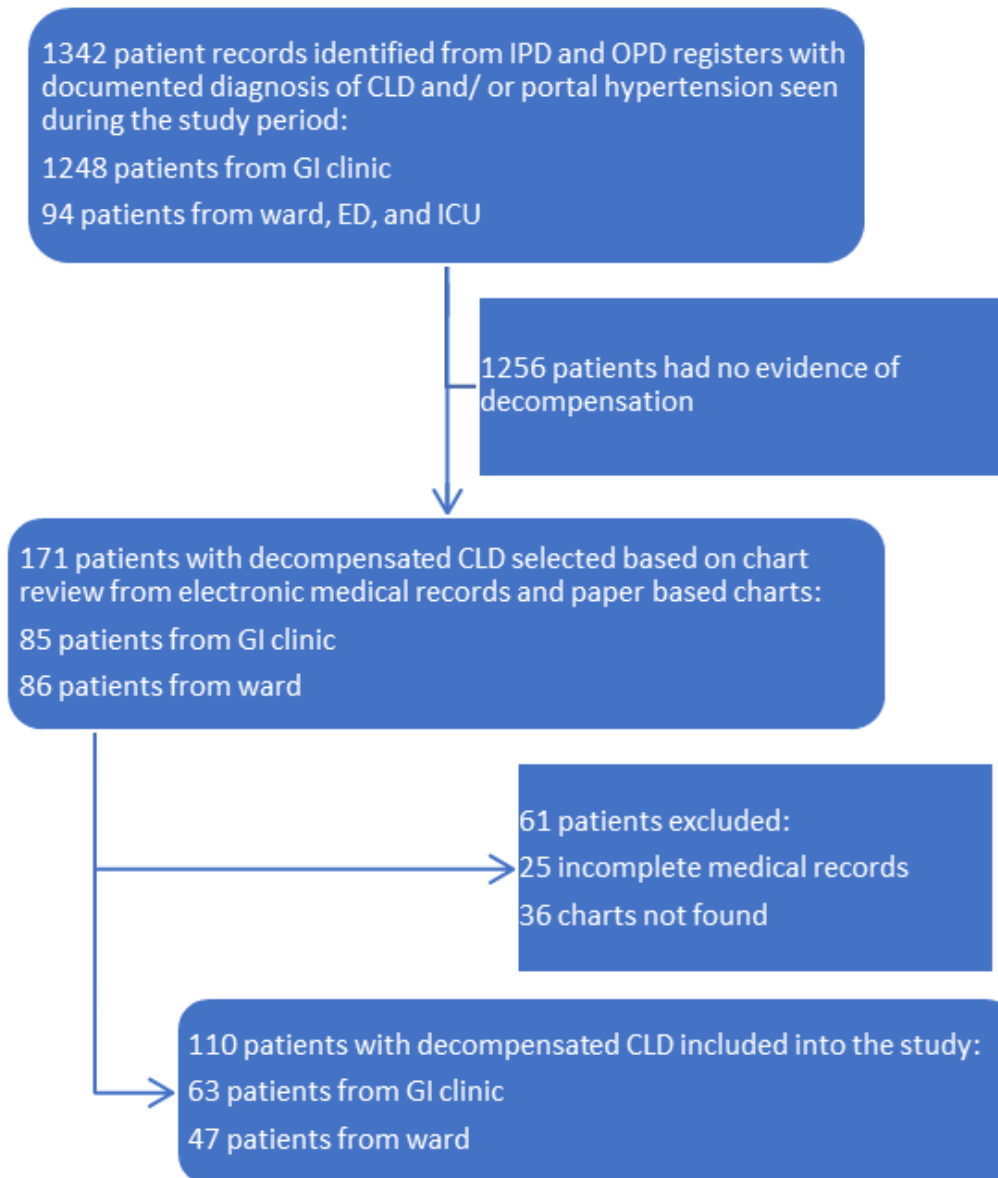
- Patients with decompensated cirrhosis with incomplete medical records or clinical assessment.
- Patients with portal hypertension resulting from disorders other than cirrhosis

2.5 Sampling procedure

Sample size calculation

The minimum sample size was initially calculated using a single population formula, followed by the finite population correction formula due to the limited number of patients with cirrhosis and complications (140) attending monthly follow-ups at the GI clinic or admitted to medical wards. The revised sample size was calculated to be 103, and with a 10% non-response rate included, the final sample size was set at 113.

Selection of participants



Sampling technique

Among adult patients with chronic liver disease (CLD), all individuals meeting the inclusion criteria were consecutively recruited using a convenient sampling technique.

2.6 Study variables

The independent variables in this study were:

- Age
- Sex
- Etiology of cirrhosis
- Child-Pugh score
- Renal function
- Presence of comorbidities

The dependent variables in this study were:

- Mortality at 01, 03, and 06 months of enrollment into the study
- Hospital admission
- Rate of occurrence of complications such as variceal bleeding, spontaneous bacterial peritonitis, hepatic encephalopathy, and hepatorenal syndrome

2.7 Operational definitions

Compensated Cirrhosis: A clinical stage of cirrhosis in which liver fibrosis is present, but complications of portal hypertension that indicate decompensation are absent.

Decompensated Cirrhosis: A clinical stage of cirrhosis characterized by the presence (or past history) of ascites, variceal bleeding, encephalopathy, and/or jaundice [4].

Poor Outcome: Defined as readmission to the hospital, development of variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, and/or death within 1, 3, and 6 months of enrollment in the study.

2.8 Data collection procedures

Patients admitted to the emergency department (ED), medical wards, or ICU, or seen as outpatients at the GI clinic at TASH with a diagnosis of decompensated cirrhosis from March 2020 to

March 2021 were identified from the admission and outpatient Health Management Information Systems (HMIS) registers and enrolled in the study. Medical record numbers (MRN) were used to retrieve patient medical records from both the electronic medical record system and paper charts.

A structured checklist was prepared in the Open Data Kit (ODK) format and pretested before data collection commenced. Data regarding demographic characteristics, clinical information—including etiology of cirrhosis, results of laboratory and imaging tests, management decisions, and outcomes documented in the patients' medical records—were reviewed and entered into the ODK by the primary investigator.

Eligible patients whose medical records were lost or incomplete (i.e., lacking documentation of clinical information, laboratory or radiographic investigations, and therapeutic interventions performed during the study period) were excluded from the final analysis.

2.9 Data Quality Assurance

The primary investigator checked the completeness and consistency of the data. The data were cleaned and edited before exporting the ODK questionnaires for analysis using SPSS version 26 software.

2.10 Data Analysis

Data from a total of 110 patients were used for the final analysis with SPSS version 26.0 statistical software. Descriptive statistics for demographic and clinical data were presented using means with standard deviations (SD) and medians with interquartile ranges (IQR) for continuous data, and frequency and percentage tables for categorical data.

Chi-square statistics and binary logistic regression were employed to examine the presence and strength of associations between categorical variables. The Cox proportional hazards model was used to assess the probability of poor outcomes among the study participants. Statistical significance was set at $p < 0.05$.

2.11 Ethical Considerations

To respect patients' rights and comply with the regulations of the hospital where the study was conducted, permission to undertake the study was obtained from the Ethical Review Committee of the Department of Internal Medicine to access patient medical records. All personal data of participants were de-identified.

3 Results

3.1 Demographic characteristics of the study participants

A total of 110 participants were included in the final analysis of this study, resulting in a response rate of 97.3%. Of these, 82 participants (74.5%) were male, with a median age of 40 years (IQR: 18) (Table 1).

Table 1 Demographic characteristics of patients with decompensated cirrhosis at TASH

Variable (n = 110)	Number (percentage)	
Sex	Male	82 (74.5%)
	Female	28 (25.5%)
Age category	<35 years	39 (35.5%)
	35 – 44 years	26 (23.6%)
	45 – 54 years	27 (24.5%)
	55 – 65 years	11 (10%)
	>65 years	7 (6.04%)

3.2 Clinical characteristics of the study participants

Clinical profile of study participants

In this study, chronic hepatitis B virus infection was the most common identified etiology of cirrhosis, affecting 51 participants (46.36%). This was followed by alcohol-related cirrhosis in 27 participants (24.55%) and cirrhosis of unknown cause in 23 participants (20.9%). Chronic hepatitis C virus-related cirrhosis and autoimmune hepatitis were documented in 11 participants (10%) and 3 participants (2.73%), respectively.

The median duration of known chronic liver dis-

ease in this study was 20.5 months (IQR: 33), with the longest duration being 14 years for a participant with cryptogenic cirrhosis. Twenty-three participants (20.9%) were newly diagnosed with decompensated cirrhosis during the study period.

Additionally, thirty-four participants (30.9%) had a documented chronic medical illness other than chronic liver disease, with HIV being the most common comorbidity, followed by diabetes mellitus, hypertension, and chronic kidney disease. Table 2 summarizes the clinical characteristics of patients with decompensated cirrhosis at TASH.

Table 2 Clinical profile among patients with decompensated cirrhosis at TASH

Variable		Number (percentage)
Etiology of cirrhosis (n=110)	Chronic HBV related cirrhosis	51 (46.36%)
	Chronic HCV related cirrhosis	11 (10%)
	Alcohol related cirrhosis	27 (24.55%)
	Autoimmune hepatitis	3 (2.72%)
	Cirrhosis of unknown cause	23 (20.9%)
Duration of known CLD (n=110)	Newly diagnosed	23 (20.9%)
	<12 months	22 (22%)
	13 – 24 months	25 (22.7%)
	25 – 36 months	16 (14.5%)
	37 – 48 months	12 (10.9%)
	49 – 60 months	4 (3.6%)
	>60 months	8 (7.3%)
Comorbidities (n=34)	HIV	8 (7.27%)
	Diabetes Mellitus	6 (5.45%)
	Hypertension	4 (3.63%)
	Chronic kidney disease	3 (2.72%)
	Structural heart disease	2 (1.81%)
	Others	15 (13.63%)

Among the 31 participants (28.18%) with a documented positive history of alcohol intake, daily alcohol consumption was quantified in terms of standard drinks for only 25 participants. Nine participants consumed 3-4 standard drinks per day, while 8 participants consumed 5-6 standard drinks per day. Twenty-two participants (20%) had no history of alcohol consumption. Only 7 participants (6.36%) had a documented history of cigarette smoking, all of whom had smoked 5 or more pack-years.

Clinical presentation of participants

In this study, the most common presenting complaints among participants at enrollment included abdominal distension in 44 participants (40%), tarry stools in 40 participants (36.4%), and both bloody vomiting and abdominal pain in 35 participants (31.8%) each. Other complaints included fatigue and yellowish discoloration of the eyes/skin. Sleep disturbances and altered mental status were documented in 11 participants (10%) and 4 participants (3.6%), respectively.

Among the 95 study participants for whom physical examination findings were documented at the time of hospitalization or clinic visit, the most common finding was ascites, observed in 61 participants (64.2%). This was followed by splenomegaly, pallor, jaundice, and pleural effusions.

Hepatic encephalopathy was documented in 20 participants (18.18%) at the time of hospital admission or clinic visit, including 9 participants (8.18%) with grade I and 8 participants (7.27%) with grade II hepatic encephalopathy. At 1, 3, and 6 months into the study, hepatic encephalopathy was recorded in 4, 2, and 3 participants, respectively, with the majority exhibiting grade I hepatic encephalopathy.

Among the 61 participants with ascites at enrollment, 35 (31.8%) had moderate ascites and 15 (13.64%) had severe ascites. The relative frequency of subjective complaints and physical examination findings among the study participants was comparable at 1 month, 3 months, and 6 months after enrollment. Details are presented in Table 3.

Table 3 Comparison of clinical presentation among patients with decompensated CLD over 06 months at TASH

	At index hospital visit	At 01month	At 03months	At 06months
	Number (%)	Number (%)	Number (%)	Number (%)
History	(n=110)	(n=92)	(n=83)	(n=77)
Abdominal distension	44 (40%)	12 (11.8%)	11 (13.25%)	11 (14.29%)
Bloody vomiting	35 (31.8%)	4 (4.3%)	4 (4.8%)	8 (10.4%)
Tarry stools	40 (36.4%)	2 (2.1%)	4 (4.8%)	8 (10.4%)
Yellowish discoloration of eyes	29 (26.4%)	4 (4.3%)	3 (3.6%)	2 (2.6%)
Abdominal pain				
Fatigue	35 (31/8%)	7 (7.6%)	2 (2.4%)	1 (1.3%)
Sleep pattern disturbance	32 (29.1%)	9 (9.7%)	4 (4.8%)	2 (2.6%)
Altered mental status	11 (10%)	4 (4.3%)	2 (2.4%)	2 (2.6%)
Other	4 (3.6%)	1 (1.0%)	1 (1.2%)	1 (1.3%)
	34 (24.5%)	40 (43.4%)	55 (66.2%)	43 (55.8%)
Physical examination				
Ascites	61 (64.2%)	18 (19.5%)	18 (21.7%)	15 (19.5%)
Splenomegaly	41 (37.3%)	25 (27.1%)	25 (30.1%)	30 (38.9%)
Pallor	36 (32.9%)	11 (11.9%)	7 (8.4%)	8 (10.4%)
Jaundice	33 (30%)	11 (11.9%)	6 (7.2%)	4 (5.2%)
Peripheral edema	33 (30%)	8(8.7%)	6(6.5%)	5(5.4%)
Pleural effusion	24 (25.3%)	5 (5.4%)	1 (1.2%)	1 (1.3%)
Abdominal tenderness	13 (13.7%)	3 (3.2%)	1 (1.2%)	3 (3.9%)

3.3 Laboratory and imaging findings of participants

Moderate anemia and thrombocytopenia were the most common findings in complete blood count assessments at all time points of the study, with mild leukopenia documented in a few participants. The results of renal function tests and serum electrolytes were within the normal range for the majority of participants at the time of

hospitalization or clinic visit.

The performance and documentation of liver function tests and enzyme levels varied during the study period. Moderate hypoalbuminemia, hyperbilirubinemia, and modest elevations in transaminases (1.5-2.5 times the upper limit of normal) were observed in the majority of participants (Table 4).

Table 4 Laboratory profiles of patients with decompensated cirrhosis at TASH

	At index hospital visit Median (IQR)	At 01 month Median (IQR)	At 03 months Median (IQR)	At 06 months Median (IQR)
WBC (103/ μ L)	6.0 (5.58)	4.27 (3.55)	4.0 (2.55)	3.3 (2.6)
Hemoglobin (g/dL)	11.65 (4.12)	11.98 (3.55)	13.3 (3.68)	13 (4.3)
Platelet (103/ μ L)	109 (95.5)	90 (88)	79 (54)	71 (49)
Serum creatinine (mg/dL)	0.82 (0.71)	0.7 (0.39)	0.7 (0.12)	0.6 (0.3)
Total bilirubin (mg/dL)	2.7 (3.16)	1.7 (1.65)	1.24 (1.25)	1.15 (0.98)
Albumin (g/dL)	2.45 (0.98)	3.1 (1.13)	3.6 (1.46)	3.5 (1.1)
PT (sec)	21.55 (6.68)	25.6 (19.9)	16.2	20.8 (3.1)
INR	1.9 (0.74)	1.89 (0.49)	1.39 (1.24)	1.85 (0.43)
Serum sodium (mmol/L)	130.8 (10.4)	132.5 (6)	136.7 (6.9)	136.8 (4)
Serum potassium (mmol/L)	3.99 (1.02)	4.5 (1.02)	4.68 (0.84)	4.25 (0.56)

Child-Pugh scores were calculated for 47 participants (42.7%) at enrollment, with a median score of 11. Twenty-eight participants (25.4%) had Child scores greater than 10 (Child class C), while 12 participants (10.9%) had scores between 7 and 9 (Child class B). At 1, 3, and 6 months into the study, Child scores were documented for 6, 2, and 6 participants, respectively.

Among the 27 participants (24.5%) who underwent ascitic fluid analysis at the time of hospitalization, the median total white cell count was 700 cells/ μ L (IQR: 1471.8). However, a differential count was performed for only 19 participants (17.27%), with 8 samples showing absolute neutrophil counts greater than 250 cells/ μ L. Among the 16 peritoneal fluid samples for which ascitic fluid albumin levels were documented, 15 had a serum-ascites albumin gradient (SAAG) greater than 1.1 g/dL. In 11 participants, Gram stains of the peritoneal fluid showed no organisms, and no growth was documented for 2 participants for whom cultures were performed.

Ascitic fluid analysis was conducted for only 2 and 1 participants at 1 and 3 months of the study, respectively. For both samples, only total white cell count and glucose levels were documented, with no objective evidence of spontaneous bacterial peritonitis.

Among the 51 participants with chronic HBV infection, quantitative HBV DNA levels were determined for 17 participants, revealing a median

viral load of 6,670 IU/ml. Six participants had documented HCV RNA results, among whom 3 achieved viral clearance after therapy with direct-acting antivirals (DAAs).

Features of cirrhotic liver, ascites, and splenomegaly were the most common findings on various modalities of abdominal imaging performed for the study participants. Portal vein thrombosis was documented in 13 participants, the majority of which were identified as tumor thrombi. Variable-sized liver masses were reported on triphasic abdominal CT in 18 participants (16.3%).

Transient elastography was performed for 4 participants, with documented liver stiffness measurements in kPa ranging from 12 to 14.9. However, fat attenuation measurements were recorded for only one participant (270 UAP).

Liver biopsy was performed for only one participant; with the reported finding of cirrhosis (details of other pathological findings were not documented).

Results of upper GI endoscopy were documented for 68 participants (61.8%), with the most common findings being variable degrees of portal hypertensive gastropathy. This was followed by grade 3 and grade 2 esophageal varices observed in 37 participants (33.6%), 34 participants (30.9%), and 19 participants (17.3%), respectively. Three additional participants under-

went screening endoscopy, but specific findings were not documented in their medical records.

Duodenitis was diagnosed in 9 participants, and duodenal ulcers were reported in 4 participants. Stigmata of recent bleeding were documented in 22 participants (20%) with varices, and endoscopic variceal ligation was performed for 17 participants (15.45%).

3.4 Outcome of the participants over 06 months of index hospital admission/OPD visit

Forty-nine participants (44.5%) were admitted to the hospital at enrollment, with a mean du-

ration of hospital stay of 9.5 days (± 7). During follow-up, 5, 3, and 4 participants were admitted to the hospital at 1, 3, and 6 months into the study period, respectively.

The most common reasons for admission among the study participants at all time points were upper GI bleeding, hepatic encephalopathy, hepatocellular carcinoma, and spontaneous bacterial peritonitis. See Figure 1 for details.

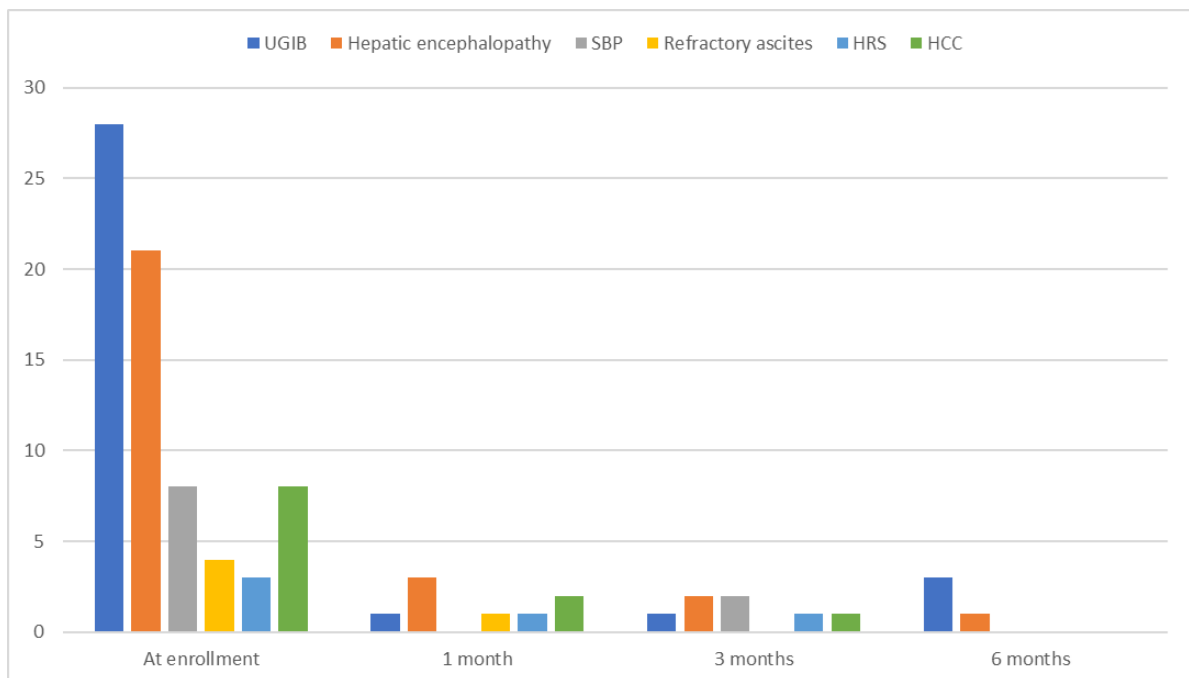


Figure 1 Reasons of hospital admission among patients with decompensated cirrhosis at TASH

The majority of participants received treatment with non-selective β -blockers, primarily Propranolol, at a maximum dose of 60 mg orally three times a day (PO TID). Diuretics were administered as indicated, with a maximum dose of Spironolactone at 200 mg PO daily and Furosemide at 80 mg PO/IV twice daily (BID). Additionally, proton pump inhibitors and antibiotics, mainly third-generation cephalosporins, were prescribed, with treatment escalation based

on clinical indications.

During the index admission, 12 participants experienced in-hospital death, while 6 participants left against medical advice. The median duration from hospital admission to death was 9 days (interquartile range (IQR): 8). An additional 4 deaths occurred during the remainder of the study period, and another 4 participants left against medical advice (see Table 5).

Table 5 Outcomes of patients with decompensated cirrhosis over 06 months of follow up at TASH

	At Index hospi- tal visit	1 month	3 months	6 months
	Number (%)	Number (%)	Number (%)	Number (%)
Documented hospitalization during the study period	49(44.54%)	5(5.4%)	3(3.6%)	4(5.1%)
Documented complications of portal hypertension during the study period:				
Upper gastrointestinal bleeding				
Hepatic encephalopathy	40(36.36%)	4(4.3%)	4(4.8%)	8(10.4%)
Spontaneous bacterial peritonitis (SBP)	22(20%)	5(5.4%)	2(2.4%)	3(3.9%)
Hepatorenal syndrome (HRS)	8(7.2%)	-	2(2.4%)	-
	3(2.72%)	1(1.0%)	1(1.2%)	-
Documented outcomes during the study period:				
Death				
Left against medical advice	12(10.9%)	1(1.0%)	1(1.2%)	2(2.6%)
Lost to follow up	6(5.4%)	3(3.2%)	-	1(1.3%)
Transferred to another health facility	-	4(4.3%)	5(6.0%)	10(12.9%)
Discharged alive and/or on follow up at TASH	-	1(1.0%)	-	5(6.5%)
	92(83.6%)	83(90.2%)	77(92.7%)	59(76.6%)

Among the 16 participants (14.54%) who died in the hospital during the study period, the most common immediate causes of death were sepsis or septic shock in 6 participants (5.45%) and multiorgan failure related to advanced liver failure in 5 participants (4.54%).

3.5 Predictors of poor outcome among patients with decompensated cirrhosis

Poor outcome in this study was defined by the presence of any readmission to the hospital, development of variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, and/or death within 1, 3, and 6 months of enrollment.

Binary logistic regression analysis revealed a statistically significant association between the presence of comorbidities and upper GI bleeding documented throughout the study period [COR=2.51; 95% CI: 0.97-6.50] (p=0.057). However, this association was not observed for individual comorbidities. Additionally, age above 40 years was found to have a statistically signifi-

cant association with upper GI bleeding when adjusted for comorbidity [AOR=2.8; 95% CI: 0.76-5.44] (p=0.017).

A statistically significant association was found between chronic HBV infection and overall mortality during the study period [COR=4.52; 95% CI: 1.2-16.9] (p=0.025), which persisted even when adjusted for upper GI bleeding [AOR=4.4; 95% CI: 1.1-16.9] (p=0.030).

Cryptogenic cirrhosis was associated with a statistically significant negative correlation with overall poor outcomes during the study period [COR=0.26; 95% CI: 0.08-0.82] (p=0.022).

Upper GI bleeding and hepatic encephalopathy were found to have a statistically significant association with hospital readmission at 1, 3, and 6 months into the study, with adjusted odds ratios (OR) of 10.59 (95% CI: 3.76-29.3) [p<0.0001] and 93.35 (95% CI: 11.13-782.8) [p<0.0001], respectively. Conversely, documented upper GI bleeding during the study period showed a negative but weak association with overall mortality [AOR=0.11; 95% CI: 0.014-0.88] (p=0.038).

The association between age, sex, other etiologies of cirrhosis, Child-Pugh score at enrollment, and renal function with poor outcome measures

during the study period was not found to be statistically significant (Table 6).

Table 6 Results of Pearson’s Chi-square test of factors associated with poor outcome in patients with decompensated cirrhosis at TASH

Poor outcome at any time during the study period			
	Value	df	Asymptotic significance (2-sided)
Sex	1.87	1	0.171
Age	4.49	1	0.343
Presence of comorbidities	0.09	1	0.764
Etiology of cirrhosis	7.54	4	0.110
Renal function test	21.76	27	0.749
Child Pugh score	4.85	2	0.088

In this study, multivariate analysis was performed using the Cox proportional hazards model to estimate the probability of inpatient mortality, hospital admission, and the development of new decompensating events (hepatic encephalopathy, upper GI bleeding, spontaneous bacterial peritonitis, and hepatorenal syndrome) among patients with decompensated cirrhosis. Age was found to have a statistically significant

association with a higher probability of developing upper GI bleeding, with a hazard ratio (HR) of 0.97 (95% CI: 0.94-0.99), but not with other poor outcome measures. There was no statistically significant difference in the risk of developing poor outcomes based on sex, comorbidity, or etiology of cirrhosis in patients with decompensated cirrhosis at TASH (Table 7).

Table 7 Probability of in patient mortality, hospitalization, hepatic encephalopathy, and upper GI bleeding at 1, 3, and 6 months in patients with decompensated cirrhosis at TASH

Variables	In patient Mortality	Hospitalization	Upper GI Bleeding	Hepatic Encephalopathy
Age	HR 1.00 (95% CI 0.96-1.05), p=0.847	HR 0.99 (95% CI 0.97-1.01), p=0.539	HR 0.97 (95% CI 0.94-0.99), p=0.03	HR 1.02 (95% CI 0.99-1.06), p=0.07
Sex	HR 0.61 (95% CI 0.19-1.93), p=0.847	HR 1.50 (95% CI 0.76-2.98), p=0.240	HR 1.62 (95% CI 0.66-3.98), p=0.288	HR 1.37 (95% CI 0.50-3.73), p=0.541
Comorbidity	HR 0.74 (95% CI 0.22-2.45), p=0.404	HR 0.78 (95% CI 0.42-1.45), p=0.435	HR 1.42 (95% CI 0.59-3.41), p=0.429	HR 1.26 (95% CI 0.48-3.35), p=0.637
Etiology of cirrhosis	HR 1.12 (95% CI 0.81-1.55), p=0.470	HR 1.09 (95% CI 0.92-1.29), p=0.303	HR 1.03 (95% CI 0.84-1.26), p=0.77	HR 1.09 (95% CI 0.83-1.43), p=0.511

4 Discussion

A total of 110 patients with decompensated cirrhosis admitted to medical wards, the emergency

department (ED), and the ICU, or seen as outpatients at the GI clinic at TASH from March 2020 to March 2021 were included in this study. The majority of participants (82 or 74.5%) were male, with a median age of 40 years (IQR: 18). This is comparable to a study by Terefe Tesfaye *et al.*, which included 109 admitted patients with chronic liver disease (CLD) across three selected teaching hospitals, where 85 participants (78%) were male, and the median age was 38 years (IQR: 30–48) [19].

Chronic hepatitis B virus infection was the most commonly identified etiology of cirrhosis, affecting 51 participants (46.36%), followed by alcohol-related cirrhosis in 27 participants (24.55%). Other hospital-based studies in Ethiopia also report a similar prevalence of HBV infection as a cause of CLD [17,19,20,21]. In a study conducted among 117 admitted patients at St. Paul's Hospital Millennium Medical College, hepatitis B virus was diagnosed in 44.4% of cases, while 18% were attributed to hepatitis C virus [20].

The most common presenting complaints among participants at the time of hospital admission were abdominal distension in 44 participants (40%), tarry stools in 40 participants (36.4%), and bloody vomiting in 35 participants (31.8%), with yellowish discoloration of the eyes or skin present in 29 participants (26.4%). These findings are comparable to other studies assessing the clinical profiles and outcomes of admitted CLD patients in Ethiopia [17,20].

Thirty-four participants (30.9%) in this study had documented comorbidities, primarily HIV and diabetes mellitus. Although the presence of these comorbidities has been associated with reduced survival and poor prognosis in patients with decompensated cirrhosis in studies from France and Spain, no statistically significant association was found between comorbidities and the overall prevalence of poor outcomes in this study [COR=0.88; 95% CI: 0.38-2.01] ($p=0.7640$) [22,23,24].

In this study, chronic HBV infection was found to have a moderate association with overall mor-

tality during the study period [AOR=4.4; 95% CI: 1.1-16.9]. Conversely, cryptogenic cirrhosis showed a statistically significant but negative association with overall poor outcomes [COR=0.26; 95% CI: 0.08-0.82].

The association between age, sex, etiologies of cirrhosis (other than HBV and cryptogenic cirrhosis), and renal function with poor outcome measures during the study period was not statistically significant. This contrasts with findings from a retrospective cohort study conducted by Kim *et al.*, which determined mean survival periods and cumulative survival rates by classifying patients into high-risk and low-risk groups based on MELD-*Na*. In that study, age and sex were found to be significant variables in the high-mortality group [15].

Complications of cirrhosis were found to have a significant association with poor outcomes in this study. Documented upper GI bleeding during the study period showed a moderate association with overall mortality and hospital readmission at 1, 3, and 6 months [AOR=0.11; 95% CI: 0.014-0.88] and [AOR=10.59; 95% CI: 3.76-29.3], respectively. Hepatic encephalopathy exhibited a relatively strong association with hospital readmission during the study period [AOR=93.35; 95% CI: 11.13-782.8].

In comparison, a study from India that explored predictors of hospital readmission in patients with decompensated cirrhosis found that MELD score at discharge and serum sodium independently predicted 1-month readmissions, while MELD score, serum sodium, and male gender independently predicted 3-month readmissions. However, neither etiology nor complications of cirrhosis emerged as risk factors [25].

The presence of renal failure in patients with decompensated cirrhosis is an important predictor of mortality, with common causes being hypovolemia, bacterial infections, and hepatorenal syndrome [13,26,27]. In contrast to findings from previous studies, renal function was not found to significantly increase the risk of death in this study, with a hazard ratio (HR) of 1.26 (95% CI: 0.98-1.61).

Although the accuracy of various prognostic models in predicting in-hospital mortality has been found to be high in other studies, [10] the association between baseline Child-Pugh scores and overall poor outcomes was statistically insignificant in this study.

Strengths and limitations of the study

This study aimed to assess the prevalence of poor outcomes in patients with decompensated cirrhosis and to identify predictors of these outcomes over a follow-up period longer than that of previous studies conducted in the country.

However, due to the retrospective design of the study, various confounders that could contribute to the development of poor outcomes could not be adequately explored. The utilization and documentation of laboratory and imaging investigations were inconsistent, as observed during data collection. This may limit the incorporation of these parameters into risk prediction models for this specific patient population.

Finally, since the study period coincided with the peak of the COVID-19 pandemic in our country, the use of virtual clinic services—where physical examinations and laboratory parameters were often not documented in the electronic medical record system—along with longer appointment times, may have affected the estimation of overall survival and the rates of loss to follow-up.

5 Conclusion

Chronic hepatitis B infection was identified as the most common etiological cause of cirrhosis among participants and a strong predictor of death during the study period. Age over 40 years significantly contributed to the development of upper GI bleeding. Hepatic encephalopathy and upper GI bleeding were identified as predictors of hospitalization among the study participants.

Recommendations

A prospective multicenter study is needed to assess the short- and long-term outcomes of pa-

tients with cirrhosis, focusing on specific etiologies and available therapeutic options in the country. This study would help fully explore the predictors of poor outcomes in this patient population.

Given that chronic HBV infection was identified as the most common etiology and a strong predictor of poor outcomes among patients with decompensated cirrhosis, enhancing the availability of vaccines and treatments for HBV could improve the overall outcomes for these groups.

The documentation of clinical data in both electronic and paper-based medical records should be standardized to include disease-specific parameters, ensuring that future data collection and analysis are thorough.

Ensuring the availability of routine laboratory and imaging tests without frequent interruptions, along with their appropriate utilization at recommended intervals, is essential for the follow-up and risk stratification of patients with decompensated cirrhosis.

Health professionals should actively engage in community awareness efforts regarding vaccines, moderation of alcohol intake, available treatment options for chronic liver diseases, and the importance of early health-seeking behavior in the event of decompensation.

The Ministry of Health and relevant stakeholders should strengthen efforts to expand access to treatment for patients with chronic liver diseases, particularly viral hepatitis.

Authors' Information

¹Department of Internal Medicine, Dilla University, Dilla, Ethiopia;

²Department of Internal Medicine, Addis Ababa University, Addis Ababa, Ethiopia

References

1. Jameson, J. Larry; Kasper, Dennis L.; Longo, Dan L.; Fauci, Anthony S.; Hauser, Stephen L.; Loscalzo J. Harrison's Principles of Internal Medicine. 20th ed. *McGraw-Hill Education*; 2018. 2405–2414 p.
2. Feldman, Mark; Friedman, Lawrence S.; Brandt, Lawrence J.; Chung RT., Rubin DT., Wilcox CM.

- Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management. 11th ed. Elsevier; 2021. 1164–1171, 1443–1498 p.
3. Sepanlou SG, Safiri S, Bisignano C, Ikuta KS, Merat S, Saberifiroozi M, *et al.* The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol.* 2020; 5(3):245–66.
 4. D'Amico G, Morabito A, D'Amico M, Pasta L, Malizia G, Rebora P, *et al.* Clinical states of cirrhosis and competing risks. *J. Hepatol.* [Internet]. 2018; 68(3):563–76. Available from: <https://doi.org/10.1016/j.jhep.2017.10.020>
 5. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies. *J. Hepatol.* 2006; 44(1):217–31.
 6. Davies P, Walters JRF, Paton A. A 20-year prospective study of cirrhosis. *Br. Med. J. (Clin Res Ed).* 1981; 282(6260):263–6.
 7. Ginés P, Quintero E, Arroyo V, Terés J, Bruguera M, Rimola A, *et al.* Compensated cirrhosis: Natural history and prognostic factors. *Hepatology.* 1987; 7(1):122–8.
 8. Bernardi M, Moreau R, Angeli P, Schnabl B, Arroyo V. Mechanisms of decompensation and organ failure in cirrhosis: From peripheral arterial vasodilation to systemic inflammation hypothesis. *J. Hepatol.* [Internet]. 2015; 63(5):1272–84. Available from: <http://dx.doi.org/10.1016/j.jhep.2015.07.004>
 9. Fleming KM, Aithal GP, Card TR, West J. All-cause mortality in people with cirrhosis compared with the general population: A population-based cohort study. *Liver Int.* 2012; 32(1):79–84.
 10. Fayad L, Narciso-Schiavon JL, Lazzarotto C, Ronsoni MF, Wildner LM, Bazzo ML, *et al.* The performance of prognostic models as predictors of mortality in patients with acute decompensation of cirrhosis. *Ann Hepatol.* 2015; 14(1):83–92.
 11. Singh S, Muir AJ, Dieterich DT, Falck-ytter YT. Review on the Role of Elastography in Chronic Liver Diseases. *Gastroenterology* [Internet]. 2017; 152(6):1544–77. Available from: <http://dx.doi.org/10.1053/j.gastro.2017.03.016>
 12. N. Gitau S, K. Menge I. Elastography in Chronic Liver Diseases. In: *Ultrasound Elastography*, [Internet]. Intech Open; 2020 [cited 2021 Jul 4]. Available from: www.intechopen.com
 13. Cullaro G, Verna EC, Lai JC. Association Between Renal Function Pattern and Mortality in Patients With Cirrhosis. *Clin. Gastroenterol Hepatol.* [Internet]. 2019; 17(11):2364–70. Available from: <https://doi.org/10.1016/j.cgh.2019.01.043>
 14. Cai Q, Zhu M, Duan J, Wang H, Sheng J. Establishment of prognostic scoring models for different etiologies of acute decompensation in hospitalized patients with cirrhosis. *J. Int. Med. Res.* 2019; 47(9):4492–504.
 15. Kim Y, Kim K, Jang I. Analysis of mortality prognostic factors using model for end-stage liver disease with incorporation of serum-sodium classification for liver cirrhosis complications: A retrospective cohort study. *Medicine*, (Baltimore). 2019; 98(45):e17862.
 16. Vento S, Dzudzor B, Cainelli F, Tachi K. Liver cirrhosis in sub-Saharan Africa: neglected, yet important. *Lancet Glob Heal.* [Internet]. 2018; 6(10):e1060–1. Available from: [http://dx.doi.org/10.1016/S2214-109X\(18\)30344-9](http://dx.doi.org/10.1016/S2214-109X(18)30344-9)
 17. Tsega E, Nordenfelt E, Hansson BG, Mengesha B, Lindberg J. Chronic liver disease in Ethiopia: a clinical study with emphasis on identifying common causes. *Ethiop. Med. J.* [Internet]. 1992 Apr [cited 2021 Jul 18]; 30(2 Suppl):1–33. Available from: <https://pubmed.ncbi.nlm.nih.gov/1319901/>
 18. D'Amico G, Morabito A, Pagliaro L, Marubini E. Survival and prognostic indicators in compensated and decompensated cirrhosis. *Dig Dis Sci.* 1986;31(5):468–75.
 19. Tesfaye BT, Gudina EK, Boshu DD, Mega TA. Short-term clinical outcomes of patients admitted with chronic liver disease to selected teaching hospitals in Ethiopia. *PLoS One.* 2019; 14(8):1–16.
 20. Adhanom M, Desalegn H. Magnitude, clinical profile and hospital outcome of chronic liver disease at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia. *Ethiop Med. J.* 2017; 55(4):267–72.
 21. Desu G. Clinicoepidemiological Pattern of Chronic Liver Disease among adult patients admitted to medical ward and those on follow up at Gastrointestinal Clinic, Jimma Medical Center, Jimma Town, South West of Ethiopia. 2019.
 22. Pineda JA, Romero-Gómez M, Díaz-García F, Girón-González JA, Montero JL, Torre-Cisneros J, *et al.* HIV coinfection shortens the survival of patients with hepatitis C virus-related decompensated cirrhosis. *Hepatology.* 2005; 41(4):779–89.
 23. Elkrief L, Chouinard P, Bendersky N, Hajage D, Larroque B, Babany G, *et al.* Diabetes mellitus is an independent prognostic factor for major liver-related outcomes in patients with cirrhosis and chronic hepatitis C. *Hepatology.* 2014; 60(3):823–31.
 24. Neff GW, Shire NJ, Rudich SM. Outcomes among patients with end-stage liver disease who are coinfecting with HIV and hepatitis C Virus. *Clin. Infect. Dis.* 2005; 41(1 SUPPL.).

25. Patel R, Poddar P, Choksi D, Pandey V, Ingle M, Khairnar H, *et al.* Predictors of 1-month and 3-months hospital readmissions in decompensated cirrhosis: A prospective study in a large Asian cohort. *Ann Hepatol.* 2019 Jan 1; 18(1):30–9.
26. de Carvalho GC, de Andrade Regis C, Kalil JR, Cerqueira LA, Barbosa DS, Motta MP, *et al.* Causes of renal failure in patients with decompensated cirrhosis and its impact in hospital mortality. *Ann Hepatol.* 2012; 11(1):90–5.
27. Al-Aly Z, Balasubramanian S, McDonald JR, Scherrer JF, O'Hare AM. Greater variability in kidney function is associated with an increased risk of death. *Kidney Int.* [Internet]. 2012; 82(11):1208–14. Available from: <http://dx.doi.org/10.1038/ki.2012.276>