Research Article

Liver Enzyme and Bilirubin Abnormalities and Associated Factors Among Patients with Liver Disease in a Tertiary Hospital, Northwest Ethiopia: A Cross-Sectional Study

Abateneh Melkamu[1], Yalew Much[1], Abebe Yensew[1], Melaku Laikemariam[2], Befikad Mandefro[3], Adane Adugna[1], Gashaw Azanaw Amare[1], Aytenew Atnaf[1]

1. Department of Medical Laboratory Science, College of Medicine and Health Sciences, Debre Markos University, Ethiopia; 2. Department of midwifery, College of Medicine and Health Sciences, Debre Markos University, Ethiopia; 3. Department of medical laboratory science, College of Medicine and Health Sciences, Arba Minch University, Ārba Minch', Ethiopia

Background: Liver disease is a disturbance of the normal and healthy functioning of the liver. It is directly linked to liver synthesis, excretion, and metabolism and results in liver dysfunction. Thus, this study aimed to evaluate the extent of liver function abnormalities and their related factors in patients with liver disease.

Methods: This cross-sectional study was conducted on 307 patients with liver disease via consecutive sampling from August 22, 2022, to October 24, 2022, at the University of Gondar Comprehensive Specialized Hospital. Approximately 3 ml of venous blood was collected and analysed via a *Beckman Coulter 700 chemistry analyser.* The data were analysed via the Statistical Package for Social Sciences version 25 software. Frequencies and proportions were used to characterize the results. Bivariable and multivariable logistic regression analyses were used to investigate factors associated with liver function abnormalities. Statistical significance was set at P <0.05.

Results: Among the 307 patients, 117 (38.11%, 95% CI: 32.64%, 43.57%), 212 (69.06%; 95% CI: 63.85%, 74.25%), and 168 (54.72%, 95% CI: 49.12%, 60.32%) had abnormal ALT, AST, and total bilirubin, respectively. Nearly one-fourth (25.40%) of the patients had all liver function test abnormalities. Male sex (AOR = 0.17; 95% CI: 0.08, 0.38) and the presence of viral hepatitis (AOR = 3.85; 95% CI: 1.23, 12.02) were significantly associated with abnormal liver ALT levels. A history of blood transfusion (AOR=0.45; 95% CI: 0.21, 0.95), lack of vegetable feeding habits (AOR=2.73; 95% CI: 1.34, 5.59), lack of physical

exercise habits (AOR=2.97; 95% CI: 1.44, 6.11), and alcoholic liver disease (AOR=17.09; 95% CI: 1.96, 148.98) were significantly associated with AST abnormalities. Anaemia (AOR=3.33; 95% CI: 1.58, 7.08), a lack of vegetable feeding habits (AOR=1.98; 95% CI: 1.06, 3.69), and a lack of physical exercise habits (AOR=4.03; 95% CI: 1.90, 8.57) were significantly associated with total bilirubin abnormalities. Conclusion: In this study, patients with liver disease presented substantial liver function abnormalities. Viral hepatitis was associated with increased ALT levels, whereas alcoholic liver disease was only associated with increased AST levels. Blood transfusion, lack of physical activity, and lack of vegetables are associated with increased bilirubin levels. Therefore, clinicians should consider these factors in the management and treatment of patients with liver disease.

Corresponding Author: Abateneh Melkamu, abatenehmelkamu@gmail.com

Background

The liver, which is located in the right upper quadrant below the diaphragm, is the largest organ of the body. It performs approximately 5,000 different physiological activities. The liver detoxifies different metabolites, produces digestive enzymes, and synthesizes proteins to keep other body systems operational[1].

Liver disease is one of the world's most critical public health problems[2] and can affect liver cells and impair normal liver function[3]. It is characterized by increased liver biochemistry, coagulopathy, and hepatic encephalopathy without underlying chronic liver disease[4]. The most common cause of the increasing prevalence of liver disease is nonalcoholic fatty liver disease (NAFLD), which is caused by obesity, diabetes, autoimmunity, hemochromatosis, and chronic viral hepatitis, primarily hepatitis B and hepatitis C viruses. Other causes and types of liver disease are caused by medication and chemicals[2].

The liver function test (LFT) is among the most commonly used laboratory tests to measure normality. Abnormal results indicate liver disease, even when a person does not have symptoms. However, LFTs can detect the severity of liver diseases, the effects of therapies, and drug-induced liver injury[5]. The most common causes of the increasing burden of abnormal liver function tests in patients with liver disease are nonalcoholic fatty liver disease, alcohol-related liver disease, and viral hepatitis[6].

Liver function tests are groups of blood, urine, and stool tests that provide information about a patient's liver condition. Blood LFTs include liver enzymes such as aspartate aminotransferase (AST) and alanine

aminotransferase (ALT), and total bilirubin is the main valuable biomarker of liver injury in patients with some degree of abnormal liver function[7].

Liver illness is becoming increasingly widespread globally, with an estimated two million fatalities each year and accounting for 4% of all deaths[8]. In 2019, cirrhosis and other chronic liver disorders caused 2.5% of deaths and 1.3% of total disability-adjusted life-years in sub-Saharan Africa[9]. In Ethiopia, it is the 7th leading cause of death, accounting for approximately 24 deaths per 100000 people in 2019[10]. Research has been conducted on the prevalence of liver disease in Ethiopia; despite its consequences, information on liver function test abnormalities and associated factors among liver disease patients in the study area is scarce. In this study, the authors aimed to evaluate the extent of liver function abnormalities and associated factors among liver disease patients at the University of Gondar Comprehensive Specialized Hospital Northwest, Ethiopia, in 2022.

Methods and materials

Study design, area, and period

Cross-sectional research was carried out at the University of Gondar Comprehensive Specialized Hospital (UoG-CSH) from August 22,2022, to October 24, 2022. The hospital is located in Gondar. Gondar is located 727 kilometers northwest of Ethiopia's main city, Addis Ababa, and 175 kilometers from Bahir Dar, the seat of the Amhara National Regional State. According to the 2015 report of the Central Statistical Agency of Ethiopia, Gondar has a population of 323,900[11]. The town has one public comprehensive specialty hospital, which is one of the oldest teaching hospitals in the country and offers health services for more than 7 million people in Gondar town and its catchment regions[12].

Operational definitions

- **Habit of drinking tea or coffee**: Habitual tea/coffee drinkers are defined as those who drink 120 mL or more of tea/coffee each day for at least a year[13].
- **Alcohol consumption habits:** Three or more drinks per day for men and two or more drinks per day for women[14].
- **AST levels are normal** if the serum levels range from 8 to 35 IU/L for females and from 6 to 31 IU/L for males[15].

- **ALT is normal** if the serum levels range from 4 to 45 IU/L for males and 2 to 34 IU/L for females[15].
- **Normal serum total bilirubin**: If the reference range is from 0.1 to 1.2 mg/dl[15].
- **Physical exercise**: Participants who engage in physical exercise for approximately 30 minutes each day[16].
- **Habit of feeding vegetables**: A consistent action is to integrate a variety of vegetables into one's diet or meal plan[17].
- **The habit of feeding meat** involves the use of animal-derived proteins, such as fish, chicken, cattle, or other meats, as the main source of food in a person's diet[18].

Sample size determination and sampling techniques

The sample size required for this study was calculated via the single population proportion formula with the following assumption. Since no study has been conducted to determine the magnitude of basic coagulation abnormalities in Ethiopia, the sample size was calculated using a 50% proportion with a 95% confidence interval and a 5% margin of error. The sample size (n) was determined via the following statistical formula.

$$\mathrm{n} = \frac{z^2 p(1-p)}{d^2} = \frac{(1.96)^2 * 0.5(1-0.5)}{(0.05)^2} = 384$$

Since the population at UoG-CSH was 1509, which is less than 10,000, the sample size was corrected by using the correction formula and given to 307.

$$no = \frac{n}{1+\frac{n}{N}} = \frac{384}{1+\frac{384}{1509}} \approx 307$$

where

- d = Margin of error between the sample and the population (d=5%)
- n_o= minimum sample size
- N=Population size
- n = uncorrected sample size
- $Z_{\alpha/2}$ = 95% confidence interval (1.96)

Study participants were recruited via the consecutive sampling method from patients with liver disease.

Population and variables

Patients with liver illness who attended the UoG-CSH during the data collection period and met the inclusion criteria were considered the study population. Although the liver function parameters (ALT, AST, and total bilirubin) were used as dependent variables, the sociodemographic variables, clinical variables and behaviour-related variables were used as independent variables.

Inclusion and exclusion criteria

All liver disease pathogens detected at UoG-CSH during data collection were included in the study. Study participants who were critically ill patients or pregnant women were excluded from the study.

Data collection methods and data quality management

A structured questionnaire was pretested at Maraki Health Center, Gondar, after pretest sociodemographic, lifestyle, and nutritional information was collected via face–to–face interviews by trained nurses from all wards in UoG-CSH. A data extraction sheet was used to obtain the clinical data from the patients' medical files. Three litres of venous blood were collected via the needle and syringe method and dispensed in a serum separator tube by medical laboratory technologist professionals. Liver function tests (ALT, AST, and total bilirubin) were performed with an automated clinical chemistry analyser (Beckman Coulter DXC 700, United States of America). The bilirubin level was determined via the diazo method for bilirubin determination. The indirect portion of bilirubin requires a solubilizing agent, such as a surfactant. A stabilized diazonium salt, 3,5-dichlorophenyldiazonium tetrafluoroborate, reacts with bilirubin to form azobilirubin. Caffeine and a surfactant are reaction accelerators, and reactions absorb at 570/660 nm absorbance, which is converted into a concentration via the spectrophotometry method[19]. The principle of measuring ALT activity is based on the fact that ALT catalyzes the reversible conversion of L-alanine and L-ketoglutarate to pyruvate and L-glutamate. In the presence of lactate dehydrogenase (LDH), pyruvate is reduced to lactate, whereas nicotinamide adenine dinucleotide (NAD + hydrogen H (NADH)) is simultaneously oxidized to nicotinamide adenine dinucleotide (NAD). The system monitors the absorbance change rate at 340 nm over a fixed time interval. The absorbance change rate is directly proportional to the ALT activity in a sample[20]. AST catalyzes the reversible transamination of L-aspartate and α-ketoglutarate to oxaloacetate and L-glutamate. The oxaloacetate is then reduced to malate in the presence of malate dehydrogenase with the concurrent oxidation of NADH to NAD. The system monitors the absorbance change rate at 340 nm over a

fixed time interval. The absorbance change rate is directly proportional to the AST activity in a sample[20].

Data quality management

To maintain the quality of the data, quality control testing was performed for each procedure. Furthermore, standard operating procedures were strictly followed. All the data collectors were trained prior to the actual data collection. The investigator strictly controls the data collector and general activity during the data collection period.

Statistical analysis

Epidata version 3.1 was utilized for data entry, coding, and cleaning. The statistical package for the social sciences (SPSS) version 25 software was used to import and analyse the data. To summarize the data, summary statistics, proportions, and frequencies were employed. The Pearson rank chi-square test was used to assess categorical variables. Bivariable and multivariable logistic regression were used to determine factors associated with liver function abnormalities. To verify the model fitness assumption, the Hosmer–Lemeshow goodness-of-fit test was performed, which requires a p value greater than 0.05. Finally, the odds ratio with a 95% confidence interval was used to express the strength of the association. The multivariable analyses with p values < 0.05 indicated that variables had a significant association with the results.

Results

Sociodemographic and clinical characteristics of the study participants

This research included 307 individuals. Among them, 220 (71.66%), 213 (69.38%), 181 (59.28%), and 143 (46.58%) were male, from rural areas, married, and unable to read and write, respectively. Furthermore, the average age of the research participants was 38.38 ± 15.13 years, with a range of 6--82 years.

Among the study participants, 157 (51.14%), 87 (28.34%), 37 (12.05%), and 26 (8.47%) had chronic liver disease (CLD), viral hepatitis, acute liver disease, and alcoholic liver disease (ALD), respectively. Among the viral hepatitis study participants, approximately 71.26% and 28.74% had HBV and HCV, respectively. On the other hand, approximately 51 (16.61%), 39 (12.70%), and 33 (10.75%) patients were anaemic, had

blood transfusions, and had heart disease, respectively, and approximately 86 (28.01%) of the study participants had taken medications other than drugs for liver disease. (Table 1).

Variable	Category	Frequency	Percent (%)
Use of medication other than liver disease	Yes	86	28.01
	No	221	71.99
Presence of anemia	Yes	51	16.66
	No	256	83.34
History of tuberculosis	Yes	12	3.90
	No	295	96.10
Presence of DM	Yes	13	4.20
	No	294	95.80
Presence of cardiac disease	Yes	31	10.10
	No	276	89.90
History of blood transfusion	Yes	39	12.70
	No	268	87.30
History of surgery	Yes	10	3.30
	No	297	96.70
Presence of cancer	Yes	8	2.60
	No	299	97.40
Presence of hypertension	Yes	21	6.80
	No	286	93.2
Presence of HIV/AIDS	Yes	6	2.0
	No	301	98.0
Types of liver disease	Acute liver disease	37	12.05
	CLD	157	51.14
	ALD	26	8.47
	Viral hepatitis	87	28.34
Presence of viral hepatitis	Yes	87	28.34

Variable	Category	Frequency	Percent (%)
	No	220	71.66

Table 1. Clinical characteristics of liver disease patients in UoG-CSH Northwest Ethiopia (n =307).

***Abbreviations**: **ALD**: alcoholic liver disease; CLD: chronic liver disease; HIV: human immunodeficiency virus; DM: diabetes mellitus*

Nutritional and lifestyle characteristics of the study participants

Among the study participants, approximately 269 (87.91%), 287 (93.49%), and 237 (77.1%) had a habit of feeding meat, drinking tea or coffee, and consuming vegetables, respectively. Despite these findings, many of the study participants (approximately 262 (85.34%) did not have regular physical exercise habits), and only 11 (3.58%) of the study participants had smoking habits (Table 2).

Variable	Category	Frequency	Percent (%)
Tea or coffee drinking habit	Yes	270	88.24
	No	37	11.76
Meat feeding habit	Yes	284	92.51
	No	23	7.49
Vegetable feeding habit	Yes	237	7.2
	No	70	22.8
Alcohol drinking habit	Yes	205	66.8
	No	102	33.2
Cigarette smoking habit	Yes	11	3.58
	No	296	96.42
Physical exercise habit	Yes	45	14.66
	No	262	85.34

Table 2. Lifestyle characteristics of liver disease patients in UoG-CSH, Northwest Ethiopia (n=307).

Magnitude of liver function abnormalities

Among the total study participants, 117 (38.11%, 95% CI: 32.64% - 43.57%), 212 (69.06%; 95% CI: 63.85% - 74.25%), and 168 (54.72%, 95% CI: 49.12% - 60.32%) had abnormal ALT, AST, and total bilirubin, respectively. Furthermore, 78 (25.40%) study participants had all liver function abnormalities (Figure 1).

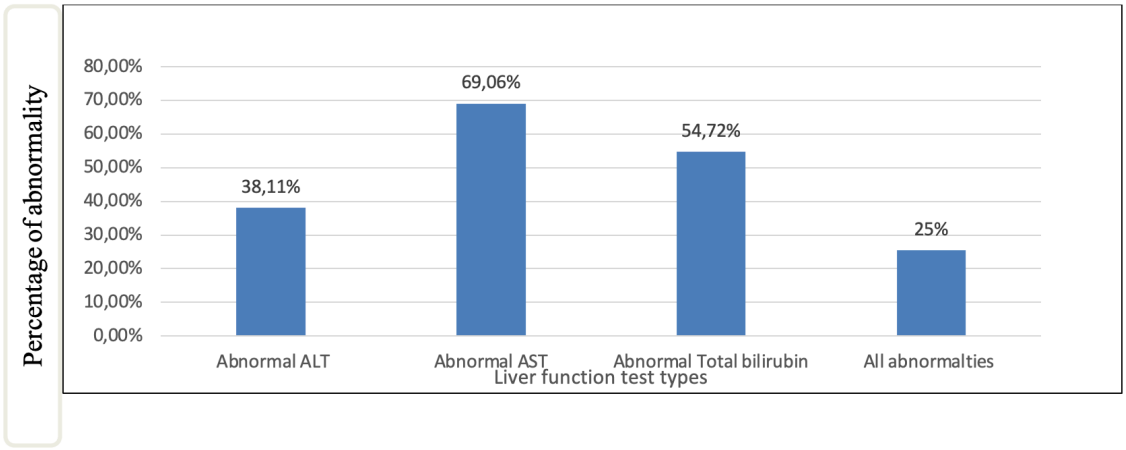

Figure 1. Magnitude of liver function test abnormalities among liver disease patients at the UoG-CSH, Northwest Ethiopia (n=307)

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Variables	Category	ALT		Bivariable analysis		Multivariable
		Abnormal (%)	Normal (%)	COR (95%CI)	P value	AOR (95%CI)
Sex	Male	70 (31.82)	150(61.18)	0.39 (0.23,0.66)	<0.001	0.17(0.08,0.38) *
	Female	47(54.02)	40(45.98)	1		1
Age	<18 (children)	4(16.66)	24(83.34)	1		1
	18-45 (young adult)	70(37.24)	118(62.76)	3.55(1.18,10.68)	0.024	2.92(0.49,17.24)
	>45 (old adult)	43(47.23)	48(52.77)	5.35(1.72,16.73)	0.004	4.66(0.73,29.68)
Residence	Rural	36(38.29)	58(61.71)	0.98(0.59,1.62)	0.964	NA
	Urban	81(38.02)	132(61.98)	1		
Occupation of study participants	Farmer	74(41.81)	103(58.19)	2.29(0.80,6.55)	0.119	3.21(0.53,19.2)
	Housewife	16(48.49)	17(51.51)	3.01(0.89,10.14)	0.075	0.84(0.11,6.24)
	Merchant	5(21.74)	18(78.26)	0.88(0.21,3.64)	0.870	1.11(0.14,8.45)
	Private employee	10(52.63)	9(47.37)	3.55(0.92,13.69)	0.065	2.95(0.40,21.52)
	Other	7(20.59)	27(79.41)	0.82(0.22,3.05)	0.779	1.46(0.20,10.34)
	Government employee	5(23.81)	16(76.19)	1		1
Educational level	No education	60(41.95)	83(58.05)	2.02(0.69,5.92)	0.198	1.48(0.21,10.13)
	Primary school	41(34.45)	78(65.55)	1.47(0.49,4.37)	0.752	1.84(0.27,12.43)
	High school	11(42.31)	15(57.69)	2.05(0.56,7.41)	0.272	2.73(0.37,20.08)
	University & college	5(26.32)	14(73.68)	1		1
Marital status	Unmarried	66(36.46)	115(63.54)	0.84(0.52,1.34)	0.477	NA
	Married	51(40.47)	75(59.53)	1		

Variables	Category	ALT		Bivariable analysis		Multivariable
		Abnormal (%)	Normal (%)	COR (95%CI)	P value	AOR (95%CI)
Use of medication other than liver disease	Yes	33(38.37)	53(61.63)	1.01(0.60,1.69)	0.953	NA
	No	84(38.01)	137(61.99)	1		
Presence of anemia	Yes	26(50.98)	25(49.02)	1.88(1.02,3.45)	0.040	1.53(0.76,3.10)
	No	91(35.55)	165(64.45)	1		1
Presence of DM	Yes	5(41.66)	7(58.34)	0.71(0.21,2.36)	0.579	NA
	No	112(37.96)	183(62.04)	1		
Presence of cardiac disease	Yes	9(29.04)	22(70.96)	0.63(0.28,1.43)	0.275	NA
	No	108(39.14)	168(60.86)	1		
History of blood transfusion	Yes	11(28.21)	28(71.79)	0.60(0.28,1.25)	0.176	0.70(0.30,1.61)
	No	106(39.55)	162(60.45)	1		1
Presence of hypertension	Yes	7(33.34)	14(66.66)	0.8(0.31,2.04)	0.641	NA
	No	110(38.46)	176(61.54)	1		
Tea or coffee drinking habit	No	104(38.52)	166(61.48)	0.86 (0.42,1.77)	0.691	NA
	Yes	13(35.14)	24(64.86)	1		
Meat feeding habit	Yes	107(37.67)	177(63.33)	0.78(0.33,1.85)	0.582	NA
	No	10(43.47)	13(56.53)	1		
Vegetable feeding habit	No	35(50.00)	35(50.00)	1.89(1.10,3.24)	0.021	1.54(0.83,2.86)
	Yes	82(34.60)	155(65.40)	1		1
Alcohol drinking habit	Yes	73(35.61)	132(64.39)	0.72(0.44,1.18)	0.202	0.65(0.37,1.16)
	No	44(43.14)	58(56.86)	1		1
Cigarette smoking habit	Yes	4(36.36)	7(63.64)	0.92(0.26,3.23)	0.903	NA
	No	113(38.18)	183(61.82)	1		
Physical exercise habit	No	15(33.33)	30(66.67)	0.78(0.40,1.52)	0.476	NA

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Variables	Category	ALT		Bivariable analysis		Multivariable
		Abnormal (%)	Normal (%)	COR (95%CI)	P value	AOR (95%CI)
	Yes	102(38.93)	160(61.07)	1		
Types of liver disease	CLD	48(30.57)	109(69.43)	1.59(0.68,3.74)	0.283	0.99(0.33,2.98)
	ALD	7(26.93)	19(73.07)	1.33(0.41,4.29)	0.627	1.38(0.32,5.83)
	Viral hepatitis	54(62.06)	33(37.94)	5.93(2.42,14.51)	<0.001	3.85(1.23,12.02) *
	Acute liver disease	8(21.62)	29(78.38)	1		1
Presence of virus hepatitis (HBV and HCV)	Yes	30(34.48)	57(65.52)	0.80 (0.47,1.35)	0.411	NA
	No	87(39.54)	133(60.46)	1		

Table 3. Bivariable and multivariable logistic regression of ALT among liver disease patients attending the UoG-CSH in Northwest China, Ethiopia (n=307)

Abbreviations: ***= *significant variable, ALD= alcoholic liver disease, CLD= chronic liver disease, DM=diabetes millets, AOR= adjusted odds ratio, COR= crude odds ratio, CI= confidence interval, 1= reference group other= includes students and has no jobs,* ***NA****=not applicable*

Factors associated with liver function abnormalities

The bivariable logistic regression analysis revealed that patient age, sex, habit of eating vegetables, viral hepatitis, and anaemia were linked to abnormal liver ALT levels. After multivariable logistic regression analysis, being male (AOR = 0.17; 95% CI: 0.08-0.38) and having viral hepatitis (AOR = 3.85; 95% CI: 1.23-12.02) were significantly associated with sex[3].

Through bivariable regression analysis, AST abnormalities were linked to independent factors such as the presence of blood transfusions, vegetable consumption habits, physical activity, and ALD. After multivariable logistic regression analysis, a history of blood transfusion (AOR=0.45; 95% CI: 0.21--0.95), a lack of vegetable-feeding habits (AOR=2.73; 95% CI: 1.34--5.59), and not engaging in physical exercise

(AOR=2.97; 95% CI: 1.44--6.11) and ALD (AOR=17.09; 95% CI: 1.96--148.98) remained significantly associated (Table 4).

Variable	Category	AST		Bivariable analysis		Multivariable analysis
		Abnormal (%)	Normal (%)	P value	COR (95%CI)	AOR (95%CI)
Sex	Male	148(67.27)	72(32.73)	0.284	0.73 (0.42,1.28)	NA
	Female	64(73.56)	23(26.44)		1	
Age	<18 (children)	18(64.29)	10(35.71)		1	NA
	18-45 (young adult)	127(67.55)	61(32.45)	0.731	1.15(0.50,2.65)	
	>45 (old adult)	67(73.63)	24(26.37)	0.341	1.55 (0.62,3.82)	
Residence	Rural	148(69.48)	65(30.52)	0.807	1.06(0.63,1.79)	NA
	Urban	64(68.09)	30(31.91)		1	
Occupation	Farmer	126(71.18)	51(28.81)	0.382	1.52(0.59,3.88)	NA
	Housewife	25(75.75)	8(24.25)	0.280	1.92(0.58,6.30)	
	Merchant	13(56.53)	10(43.47)	0.717	0.8(0.23,2.67)	
	Private employee	13(68.42)	6(31.58)	0.666	1.33(0.36,4.93)	
	Other	22(64.70)	12(35.30)	0.834	1.12(0.36,3.48)	
	Government employee	13(61.90)	8(38.10)		1	
Educational level	No education	96(67.13)	47(32.87)	0.426	1.48(0.56,3.93)	1.40(0.42,4.62)
	Primary school	87(73.10)	32(26.90)	0.180	1.97(0.72,5.35)	2.11(0.63,7.06)
	High school	18(69.23)	8(30.77)	0.434	1.63(0.47,5.62)	1.50(0.35,6.29)
	University& College	11(57.90)	8(42.10)		1	1
Marital status	Unmarried	121(66.85)	60(33.15)	0.317	1.12(0.78,2.12)	NA
	Married	91(72.22)	35(27.78)		1	

Variable	Category	AST		Bivariable analysis		Multivariable analysis
		Abnormal (%)	Normal (%)	P value	COR (95%CI)	AOR (95%CI)
Use of medication other than liver disease	Yes	60(69.77)	26(30.23)	0.866	1.04(0.60,1.79)	
	No	152(68.78)	69(31.22)		1	
Presence of anemia	Yes	41(80.40)	10(19.60)	0.059	2.03(0.97,4.26)	2.11(0.96,4.61)
	No	171(66.80)	85(32.20)		1	1
Presence of DM	Yes	11(84.61)	2(15.39)	0.230	2.54(0.55,11.71)	NA
	No	201(68.36)	93(31.64)		1	
Presence of cardiac disease	Yes	23(74.20)	8(25.80)	0.515	1.32(0.56,3.07)	NA
	No	189(68.47)	87(31.52)		1	
History of blood transfusion	Yes	21(53.85)	18(46.15)	0.030	0.47(0.23,0.93)	0.45(0.21‡0.95) *
	No	191(71.27)	77(28.73)		1	1
Presence of hypertension	Yes	17(80.95)	4(19.05)	0.230	1.98(0.64,6.06)	NA
	No	195(68.18)	91(31.82)		1	
Tea or coffee drinking habit	No	189(70.00)	81(30.00)	0.335	0.70(0.34,1.43)	NA
	Yes	23(62.16)	14(37.84)		1	
Meat feeding habit	Yes	195(68.66)	89(31.34)	0.601	0.77(0.29,2.02)	NA
	No	17(73.91)	6(26.09)		1	
Vegetable feeding habit	No	155(65.40)	82(34.60)	0.012	2.31(1.19,4.48)	2.73(1.34,5.59) *
	Yes	57(81.43)	13(18.57)		1	1
Alcohol drinking habit	Yes	146(71.22)	59 (28.78)	0.246	1.34(0.81,2.23)	NA
	No	66(64.70)	36(35.30)		1	
Cigarette smoking habit	Yes	7(63.64)	4(36.36)	0.693	0.77(0.22,2.71)	NA
	No	205(69.26	91(30.74)		1	
Physical exercise habit	No	22(48.89)	23(51.11)	0.002	2.75(1.44,5.25)	2.97(1.44,6.11) *

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Variable	Category	AST		Bivariable analysis		Multivariable analysis
		Abnormal (%)	Normal (%)	P value	COR (95%CI)	AOR (95%CI)
	Yes	190(72.52)	72(27.48)		1	1
Type of liver disease	CLD	95(60.50)	62(39.50)	0.428	0.73(0.44,1.57)	0.83(0.36,1.89)
	ALD	25(96.15)	1(3.85)	0.021	11.99(1.44,99.37)	17.09(1.96,148.98) *
	Viral hepatitis	67(77.01)	20(22.99)	0.274	1.60(0.68,3.76)	1.75(0.70,4.38)
	Acute liver disease	25(67.57)	12(32.43)		1	1
Presence of virus hepatitis (HBV and HCV)	Yes	55(63.22)	32(36.78)	0.165	0.68(0.40,1.16)	0.74(0.41,1.33)
	No	157(71.36)	63(28.64)		1	1

Table 4. Bivariable and multivariable logistic regression of abnormal AST among liver disease patients attending UoG-CSH, Northwest China, Ethiopia, 2022 (n=307)

*Abbreviations: *= significant variable, ALD= alcoholic liver disease, CLD= chronic liver disease, DM=diabetes millets, AOR= adjusted odds ratio, COR=crude odds ratio, CI=confidence interval, 1= the reference group, other= includes students and has no jobs, **NA**=not applicable*

Bivariable logistic regression analysis revealed associations between total bilirubin elevation and independent factors such as lack of education, anaemia, vegetable consumption habits, and physical activity. After multivariable logistic regression analysis, being anaemic (AOR=3.33; 95% CI: 1.58--7.08), not consuming vegetables (AOR=1.98; 95% CI: 1.06--3.69), and not engaging in physical exercise (AOR=4.03; 95% CI: 1.90--8.57) remained significantly associated (Table 5).

Variable	Category	Total Bilirubin		Bivariable analysis		Multivariable analysis
		Abnormal (%)	Normal (%)	P value	COR (95%CI)	AOR (95%CI)
Sex	Male	122(55.45)	98(44.55)	0.682	1.10 (0.67,1.82)	NA
	Female	46(52.87)	41(47.13)		1	
Age	<18 (children)	14(50.00)	14(50.00)		1	NA
	18-45 (young adult)	106(56.38)	82(47.62)	0.527	1.29(0.58,2.86)	
	>45 (old adult)	48(52.75)	43(47.25)	0.799	1.11 (0.47,2.60)	
Residence	Rural	117(54.93)	96(45.07)	0.913	1.02(0.63,1.67)	NA
	Urban	51(54.26)	43(45.74)		1	
Occupation	Farmer	98(55.37)	79(44.63)	0.280	1.65(0.66,4.12)	0.44(0.07,2.74)
	Housewife	16(48.48)	17(51.52)	0.686	1.25(0.41,3.77)	0.28(0.04,2.01)
	Merchant	12(52.17)	11(47.83)	0.537	1.45(0.44,4.78)	0.45(0.64,3.22)
	Private employee	14(73.68)	5(26.32)	0.054	3.73(0.97,14.22)	1.33(0.16,10.94)
	Other	19(55.88)	15(44.12)	0.349	1.68(0.56,5.06)	0.71(0.10,4.75)
	Government employee	9(42.86)	12(57.14)		1	1
Educational level	No education	82(57.34)	61(42.66)	0.040	2.91(1.04,8.09)	4.91(0.72,33.55)
	Primary school	64(53.78)	55(46.22)	0.079	2.52(0.89,7.07)	4.53(0.68,30.11)
	High school	16(61.54)	10(38.46)	0.051	3.46(0.99,12.08)	5.42(0.74,39.68)
	University& College	6(31.58)	13(68.42)		1	1
Marital status	Unmarried	95(52.49)	86(47.51)	0.346	1.24(0.78,1.97)	NA
	Married	73(57.94)	53(42.06)		1	

Variable	Category	Total Bilirubin		Bivariable analysis		Multivariable analysis
		Abnormal (%)	Normal (%)	P value	COR (95%CI)	AOR (95%CI)
Use of medication other than liver disease	Yes	44(51.16)	42(48.84)	0.435	0.81(0.49,1.35)	
	No	124(56.10)	97(43.90)		1	
Presence of anemia	Yes	38(74.50)	13(25.50)	0.003	2.83(1.44,5.56)	3.33(1.58,7.08) *
	No	130(50.78)	126(49.22)		1	1
Presence of DM	Yes	7(58.33)	5(41.67)	0.528	0.69(0.22,2.12)	NA
	No	161(54.58)	134(45.42)		1	
Presence of cardiac disease	Yes	16(51.61)	15(48.39)	0.714	0.87(0.41,1.82)	NA
	No	152(55.07)	124(44.93)		1	
History of blood transfusion	Yes	17(43.59)	22(56.41)	0.138	0.59(0.30,1.17)	0.62(0.29,1.29)
	No	151(56.34)	117(43.66)		1	1
Presence of hypertension	Yes	10(47.62)	11(52.38)	0.499	0.73(0.30,1.78)	NA
	No	158(55.24)	128(44.76)		1	
Tea or coffee drinking habit	No	149(55.19)	121(44.81)	0.661	0.85(0.43,1.70)	NA
	Yes	19(51.35)	18(48.65)		1	
Meat feeding habit	Yes	155(54.58)	129(45.42)	0.857	0.92(0.39,2.17)	NA
	No	13(56.52)	10(43.48)		1	
Vegetable feeding habit	No	122(51.48)	115(48.52)	0.037	1.80(1.03,3.14)	1.98(1.06,3.69) *
	Yes	46(65.71)	24(34.29)		1	1
Alcohol drinking habit	Yes	119(58.05)	86(41.95)	0.098	1.49(0.92,2.41)	1.21(0.71,2.07)
	No	49(48.04)	53(51.96)		1	1
Cigarette smoking habit	Yes	4(36.36)	7(63.64)	0.223	0.45(0.13,1.60)	NA
	No	164(55.40)	132(44.60)		1	
Physical exercise habit	No	13(28.89)	32(71.11)	0.000	3.56(1.78,7.10)	4.03(1.90,8.57) *

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Variable	Category	Total Bilirubin		Bivariable analysis		Multivariable analysis
		Abnormal (%)	Normal (%)	P value	COR (95%CI)	AOR (95%CI)
	Yes	155(59.16)	107(40.84)		1	1
Type of liver disease	CLD	80(50.96)	77(49.04)	0.801	1.09(0.53,2.24)	1.42(0.58,3.48)
	ALD	18(69.23)	8(30.77)	0.107	2.37(0.82,6.80)	3.21(0.90,11.36)
	Viral hepatitis	52(61.90)	32(38.10)	0.255	1.56(0.72,3.40)	1.88(0.72,4.93)
	Acute liver disease	18(48.65)	19(51.35)		1	1
Presence of virus hepatitis (HBV and HCV)	Yes	44(50.57)	43(49.43)	0.359	0.79(0.48,1.30)	NA
	No	124(56.36)	96(43.64)		1	

Table 5. Bivariable and multivariable logistic regression of abnormal total bilirubin among liver disease patients attending UoG-CSH, Northwest China, Ethiopia (n=307)

*Abbreviations: *= significant variable, ALD= alcoholic liver disease, CLD= chronic liver disease, DM=diabetes millets, AOR= adjusted odds ratio, COR=crude odds ratio, CI=confidence interval, 1= the reference group, other= includes students and has no jobs, **NA**=not applicable*

Discussion

Liver disease is a global public health issue that causes mortality and morbidity. It is one of the most common causes of coagulopathy and impaired liver function in both developed and developing countries. This study investigated the extent and associated factors influencing liver function abnormalities in patients with liver disease visiting UoG-CSH.

The findings of this study revealed that the overall prevalence of abnormal liver function test results was 38.11%, 69.06%, and 54.72%, respectively, among the study participants with abnormal ALT, AST, and total bilirubin levels. Furthermore, 25.40% of the study participants had all liver function abnormalities. When liver cells are damaged, they release ALT and AST and increase bilirubin levels in the bloodstream.

ALT is a preferable specific indicator over AST for active hepatic cell damage because of its location. An increase in blood AST indicates the occurrence of events other than liver damage[21].

In this study, patient sex and hepatic virus status were significantly associated with increased ALT. The likelihood of a patient's ALT abnormality occurrence being male was reduced by 83%, which contradicts the findings of studies performed in China[22] and Taiwan[23]. This could be associated with a high BMI, which is significantly associated with fewer liver function test abnormalities. A previous study revealed that males have a greater risk of abnormal liver function when hepatitis B and obesity are controlled. Given that patients are infected by hepatic virus(s), the odds of developing ALT abnormalities are 3.85 (95% CI: 1.23−−12.02) times greater than those associated with other types of hepatic disease, similar to previous studies in China[22][24], Serbia[6], and Korea[25]. The virus can multiply in the host, and more tissue is damaged in a short time, leading to the release of more ALT enzymes[26].

Patient blood transfusion history, vegetable dietary habits, regular physical exercise, and ALD were significantly associated with increased AST. Patients with a history of blood transfusion were 55% (95% CI: 0.21-0.95) less likely to have AST abnormalities than nontransfused patients were, which was similar to the findings of a study conducted in the USA[27]. The AST of liver disease patients who lacked a vegetable-feeding habit was 2.73 (95% CI: 1.34-5.59) times greater than that of the study participants who had a habit of consuming vegetables, which is similar to the findings of a study performed in Iran[28]. Vegetables containing antioxidants may reduce the value of AST. The odds of developing AST increase were 2.97 (95% CI: 1.44-6.11) greater among patients who did not exercise regularly than among those who did. Diet and weight loss are essential for enhancing liver enzymes, with antioxidants provided by vegetables[29]. Exercise decreases stress on the liver and fat content, increases energy levels and helps prevent obesity, which is a risk factor for liver disease[30]. Finally, ALD patients were 17.09 (95% CI: 1.96-148.98) times more likely to have increased AST than other patients were, similar to the findings of a study in Sweden[31]. Although vitamin B6 is used as a coenzyme for liver activities, alcoholism reduces the level of vitamin B6[32].

Patient status, anaemia, vegetable dietary habits, physical exercise and blood transfusion were significantly associated with increased total bilirubin. The odds of rising total bilirubin were 3.33 (95% CI: 1.58-7.08) times greater in anaemic patients than in nonanaemic patients. Bilirubin is formed when hemoglobin is broken down. High bilirubin levels in the circulation may indicate hemolytic anemia. High amounts of this chemical are also associated with certain liver and gallbladder illnesses. Erythrocyte

abnormalities are clinically important and frequent findings in patients with chronic diseases[33]. In this study, patients who lacked vegetables in their dietary habits were 1.98 (95% CI: 1.06– 3.69) times more likely to have increased total bilirubin, which may be a marker associated with cardiovascular problems. The controversial concepts of vegetables and bilirubin. When vegetables and balance data are abnormal, red blood cells and immunity are affected, resulting in cellular damage, infection, and protein abnormalities. Therefore, a balanced diet and vegetarian lifestyle are associated with a good prognosis among liver disease patients[34]. A lack of physical exercise increased total bilirubin by 4.03 (95% CI: 1.90-8.57) times compared with its counterpart, which contradicts the findings of a study performed in Columbia[35].

Strengths and limitations of the study

This study has strengths and limitations. The strength of this study is that it is the first study on the determination of the magnitude and associated factors of liver function abnormalities in liver disease patients in Ethiopia. However, the limitation of this study was that we could not perform parasitic infection screening, which may have interfered with the findings of the study. In addition, detailed liver function tests, such as total protein, albumin, urea and other proteins, were not performed due to budget scarcity.

Conclusion and recommendation

In patients with liver disease, AST followed by bilirubin is increased in the majority of patients. All liver enzyme abnormalities were detected in approximately 1/4 of the patients. In females, a history of hepatic virus infection, blood transfusion, a lack of vegetable dietary habits, a lack of regular physical exercise, and ALD are risk factors for liver function tests. We recommend that healthcare providers monitor and consider these factors to improve the drug of choice.

List of abbreviations

ALD: alcoholic liver disease, ALT: alanine transaminase, AST: aspartate transaminase, CLD: chronic liver disease, HBV: hepatitis B virus, HCV: hepatitis C virus, LFT: liver function test, **SPSS:** Statistical Package for the Social Sciences, **UoG-CSH**: University of Gondar Comprehensive Specialized Hospital.

Statements and Declarations

Ethical approval and consent to participate

This research was carried out in accordance with the Helsinki Declaration[36]. Ethics approval was obtained from the Ethics Review Committee of the School of Biomedical and Laboratory Science, College of Medicine and Health Science, University of Gondar Research, with reference number SBMLS/384/2022. A permission letter was then secured from the UoG-CSH medical director. Before starting data collection, the data collectors were informed to ask permission, explain the purpose of the study and its importance and benefits, and they offered to answer all the participants' questions to confirm their willingness. Written informed consent, or assent, was subsequently obtained. Participation in the study and refusals were possible. To ensure the confidentiality of the data, the study participants were identified via codes, and unauthorized persons had no access to the data. All abnormal laboratory findings were linked to health professionals for proper management and treatment of patients.

Conflict of interest

The authors declare that there are no conflicts of interest related to the publication of this manuscript.

Authors' contributions

AM: data collection, feeding, performing the statistical analysis, drafting the manuscript; YM: data analysis, drafting and editing the manuscript; AY, ML, BM, GA, AA, AA: review and editing the manuscript. All the authors read and approved the final manuscript.

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Availability of data and materials

All the data supporting these findings are contained within the manuscript.

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Declarations

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