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Prevalence of liver function disorder in a Tertiary Care Centre of Manipur

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Abstract:
Background: *The liver function test (LFT) is among the most commonly used clinical investigations to assess hepatic function and severity of liver diseases. There is paucity of health policy relevant data for prevalence of liver disease in India and prevalence varies widely on etiology and epidemiology of liver diseases.*
Aims: *The purpose of the study was to find out the prevalence of abnormal liver function tests in an adult population in Manipur.*
Materials and Methods: *This was a cross-sectional hospital based study done at Biochemistry Department of Jawaharlal Nehru Institute of Medical Sciences, Imphal in a total of 602 subjects aged above 20 years for a period of 6 months. The parameters included are Total Bilirubin, direct Bilirubin, Alkaline Phosphatase (ALP), ALT, AST, Total Protein, Albumin and Globulin. Data were analysed by using SPSS version 20.*
Results: *In this study, we found high total bilirubin in 19% (74 males and 40 female), high Direct Bilirubin in 23% (94 males, 42 female), high SGOT in 42% (154 males, 98 female), high SGPT in 20% (80 males, 44 female), high ALP in 34% (104 males, 102 female), high Globulin in 23% (70 males and 70 female). High levels of T. bilirubin, SGPT, ALP, Globulin are found in age group 40-49 years. The development of abnormal LFTs was correlated with age.*
Conclusions: *Abnormal LFT are associated with a range of health outcomes, the study is taken up to detect and prevent severe liver pathology which signifies the need for screening of Liver Function Test routinely.*
Keywords: *Elevated liver enzymes; Aminotransferase elevation; Liver function tests; Evaluation of abnormal liver enzymes.*

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I. Introduction

Liver Function Test is the blood test that indicates the abnormalities in the liver functioning and measures the levels of enzymes and proteins in the blood. They are useful in the evaluation and treatment of patients with hepatic dysfunction[1]. The liver carries out metabolism of carbohydrate, protein and fats. Some of the enzymes and the end products of the metabolic pathway which are very sensitive for the abnormality occurred may be considered as biochemical marker of liver dysfunction[2].

The liver function test (LFT) is among the most commonly used clinical investigations to assess hepatic function and severity of liver diseases. They are commonly performed to investigate asymptomatic individuals or those with specific symptoms[3].

Liver disease accounts for approximately 2 million deaths per year worldwide 1 million due to complications of cirrhosis and 1 million due to viral hepatitis and hepatocellular carcinoma[4]. The liver is a vital organ and has a very wide range of functions such as detoxification, protein synthesis, and production of biochemical, glycogen storage, decomposition of red blood cells and hormone production[5].

Because of its strategic location and multidimensional functions, the liver is prone to many diseases. Some of the enzymes and the end product of metabolic pathway which are very sensitive for the abnormality occurred may be considered as biochemical marker of liver dysfunction[2]. Some of the biochemical markers such as Serum Total Bilirubin, Direct bilirubin, Alkaline phosphatase (ALP), Alanine aminotransferase (ALT/SGPT), Aspartate Aminotransferase (AST/SGOT), Total protein, Albumin and Globulin are considered in this study.

Measurement of serum aminotransferases, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) serve as a marker of hepatocytes injury. ALP and bilirubin act as markers of biliary function and cholestasis whereas Total Protein and albumin reflect liver synthetic function[6].

The prevalence of elevated liver enzymes has geographic variations and they are rarely reported in

Manipur, a state in north-eastern India since Chronic Liver Disease (CLD) is a worldwide public health concern. There are various studies conducted regarding prevalence of liver function disorder in different parts of the world and also in India. This study of liver function disorder is first kind in State of Manipur.

II. Material and Methods

This was a cross sectional hospital-based study done at the Biochemistry Department of Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur. Liver function tests of subjects aged between 20-80 years from May 2020 – October 2020 were consecutively studied. We looked mainly at Total Bilirubin, Direct Bilirubin, ALP, ALT/SGPT, AST/SGOT, Total Protein, Albumin and Globulin in a total of 602 individuals.

Study Design: Hospital based cross sectional study

Study Location: The study was conducted in Department of Biochemistry at Jawaharlal Nehru Institute of Medical Sciences, Manipur, India.

Study Duration: May 2020 – October 2020

Sample Size**:** 602 individuals

Subjects & selection method: The individuals were selected from the population attending the tertiary care hospital, JNIMS, which is the only state funded medical college and hospital in Manipur. A total of 602 individuals between the age group 20 – 80 years were enrolled in this study. Patients of both sexes were included.

Inclusion criteria: All the subjects, male and female between the age group of 20 and 80 years who attended liver function test were considered for the study.

Exclusion criteria:

1. Patients with history of Type 2 diabetes mellitus
2. Patients with medical history of any type of malignancy
3. Patients with history of drug or alcohol abuse.
4. Patients with known case of HIV/AIDS, HCV infection.
5. Patients taking oral contraceptives, hormone replacement therapy, physically inactive and individuals with modified physiological states such as pregnancy, psychological and mental disorders were excluded.

Procedure methodology: The written informed consent of the patients or relatives were taken to participate in the study. After taking informed consent, about 5ml of venous blood was drawn under aseptic precautions from anti-cubital vein from selected subjects. The needle was removed from the syringe and the blood was immediately transferred carefully into clean, dry properly labelled vials. Plasma was obtained by centrifugation at 3000 revolutions per minute for 10 minutes in a centrifuge machine and serum was collected. The serum was processed within one hour of collection.

Liver function parameters were estimated using IFCC approved method. Total protein and Serum Albumin were estimated using Biuret[7,8] and Bromocresol Green method[9,10]. Total Bilirubin and Direct Bilirubin were estimated based on the modification of the Doumas reference method[11]. Transaminases (AST & ALT) methods are an adaptation of the recommended procedure of IFCC as described by Bergmeyer[12,13]. Alkaline phosphatase method is based on a procedure by Bowers and Mc Comb[14].

Statistical analysis: The statistical analysis was performed using the SPSS (version 24.0). Results were expressed as percentages and liver profile levels were expressed as the mean ± SD. The study protocol was approved by the Institutional Ethics Committee (IEC), JNIMS and informed consent was obtained from all the patients before enrolling into the study. Prevalence of liver function disorder by means of its determinants was calculated using the prevalence rate formula: number of patients per total number of all subjects at the time of study multiplied by 100. A p value <0.05 was considered statistically significant.

Preferred cut off values of liver tests: Abnormal liver tests, Total Bilirubin $\geq$ 1.3mg/dL and/ or Total Protein $\geq$ 8.2mg/dL and/ or Albumin $\geq$ 5 gm/dL and/or Globulin $\geq$ 3.5 gm/dL and/or AST $\geq$ 46 IU/L and / or ALT $\geq$ 69 IU/L and/ or ALP $\geq$ 126 IU/L. These values are consistent with the upper or lower limits of normal established by reference laboratory for the area**.**

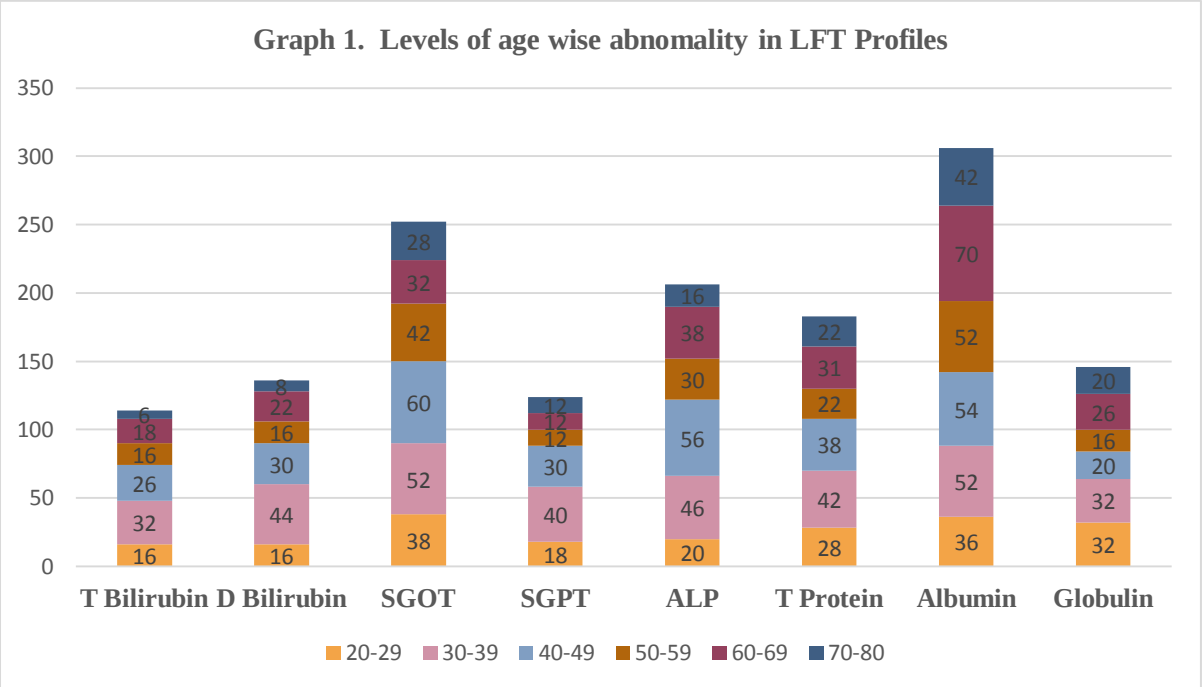
III. Result

The result obtained for the analytes used to measure the liver function is tabulated in the Table 1, 2 and 3. The reference interval, which has been utilized by the lab, is tabulated along with the results so as to enable us to compare the results obtained from the study.

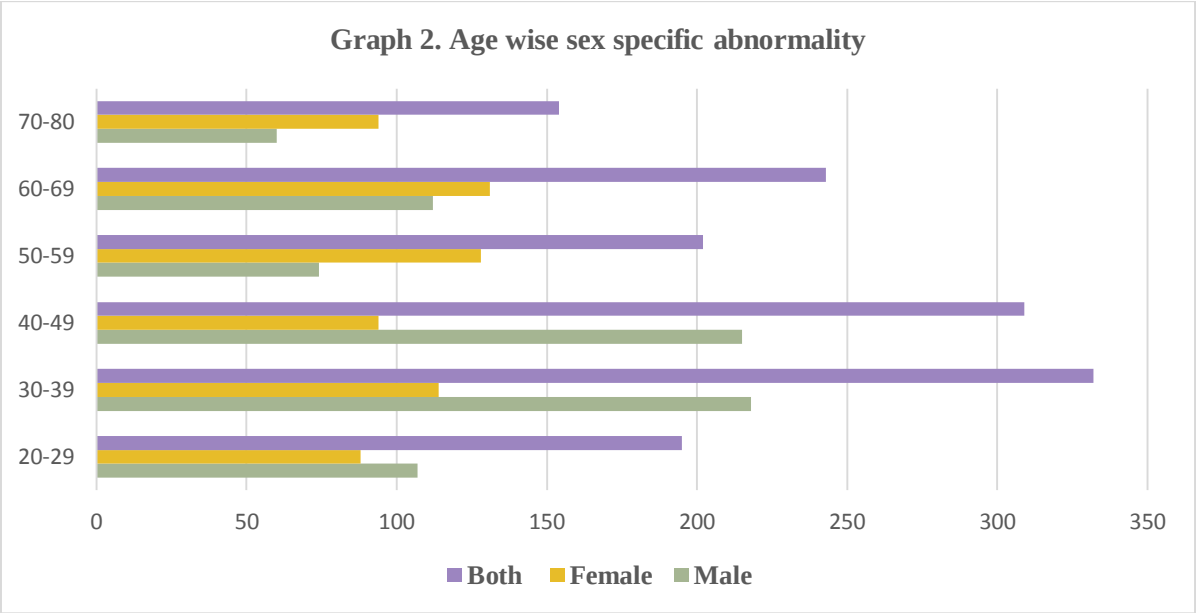
A total of 602 serum samples were collected from 274 males and 328 females in the age group 20-80 years. Mean year taken for the age group for Male is 45.12 and Female is 49.05. The clinical characteristics of the subjects are shown in Table 1.

Table 1. Clinical characteristics of study population			
	Sex	N	Mean±SD
Age	M	274	45.12±15.34
	F	328	49.05±16.49
T Bilirubin	M	274	1.94±3.98
	F	328	1.03±2.12
D Bilirubin	M	274	1.06±2.55
	F	328	0.47±1.24
SGOT	M	274	114.74±180.15
	F	328	61.08±110.84
SGPT	M	274	89.77±155.62
	F	328	51.41±79.70
ALP	M	274	134.89±82.99
	F	328	133.00±138.80
T Protein	M	274	8.28±10.10
	F	328	7.98±8.45
Albumin	M	274	3.65±0.73
	F	328	3.58±0.84
Globulin	M	274	3.36±0.43
	F	328	3.32±0.37

In the Table 1 mean of the total samples are relatively lower in all respects compare to Table 2, the mean of the abnormal profiles only. For instance, T Bilirubin has mean 1.94 and 1.03 for male and female respectively in Table 1 and in Table 2 the mean has value of 5.32 and 4.39 for male and female respectively. Similarly, in respect of SGOT mean values are 114.74 and 61.08 for male and female respectively in Table 1 and 216.87 and 183.00 for male and female respectively in Table 2. This shows there is high deviation in high LFT profiles.



In the Graph 1, highest level of LFT abnormality is found in SGOT and Albumin. In the age group 40-49 SGOT has the highest level of abnormality and in the age group 60-69 Albumin has highest level of abnormality. Age group 20-29 and 70-80 has generally lower level of LFT abnormality in all profiles. T Bilirubin and SGPT has lowest level of abnormality occurrence in the study.



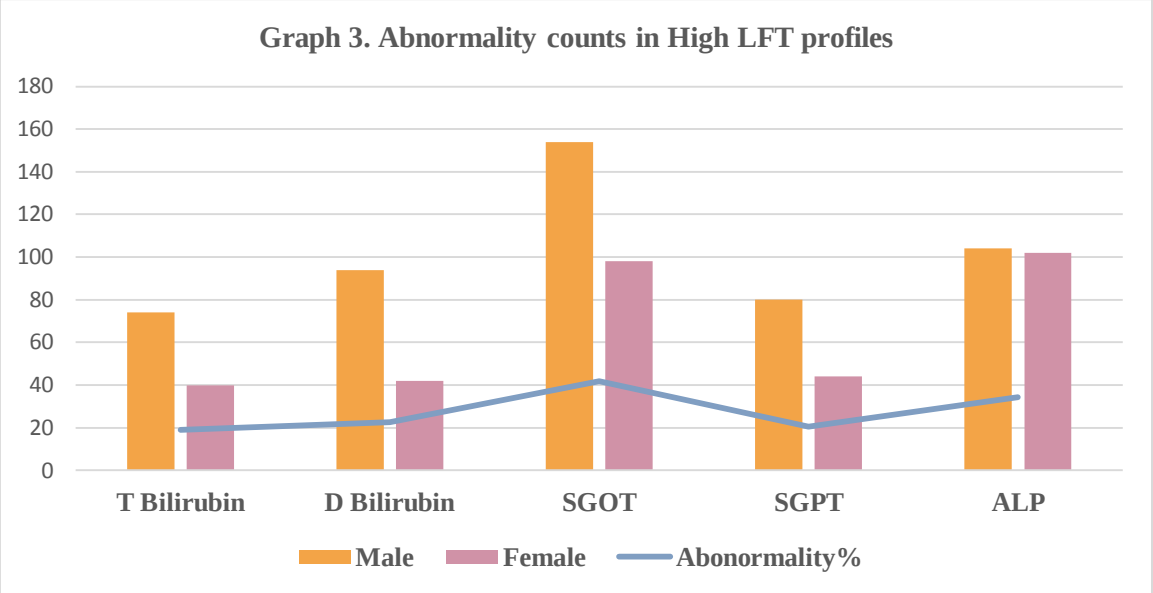
In the Graph 2 for Male the prevalence of highest abnormality is found in the age group 30-39 years and then next higher age group is 40-49 years. The prevalence of highest abnormality in Female is found in the age group 60-69 years and next higher age group is 50-59 years. For both the sex together highest prevalence is found in the 30-39 years of age group then next higher age group is 40-49 years.

Table 2. LFT Abnormality levels and parameters

Abnormal value	Mean±SD		Percentage
T Bilirubin >1.3	5.32±6.58	M=74	18.9%
	4.39±4.90	F=40	
D Bilirubin >0.4	2.67±3.89	M=94	22.5%
	2.24±2.93	F=42	
SGOT >46	178.48±220.25	M=154	41.8%
	136.32±245.23	F=98	
SGPT >69	216.87±155.62	M=80	20.5%
	183.00±163.91	F=44	
ALP >126	212.38±87.26	M=104	34.2%
	233.84±215.25	F=102	
T Protein <6.3/>8.2	5.42±1.01/30.31±32.80	M=54/18	26.4%
	5.71±0.46/29.73±30.31	F=70/17	
Albumin <3.5/ >5	2.95±0.38/7.80±0.00	M=120/2	45.8%
	2.99±0.39/8.65±1.09	F=150/4	
Globulin <0.2/>3.5	3.92±0.44	M=70	23.2%
	3.86±0.26	F=70	

In Table 2, high level abnormality is found in total Bilirubin in 18.9% (74 males and 40 female), direct Bilirubin in 22.5% (94 males, 42 female), SGOT in 41.8% (154 males, 98 female), SGPT in 20.5% (80 males, 44 female), ALP in 34.2% (104 males, 102 female), globulin in 23.2% (70 males and 70 females) and abnormality in lower and higher than range in T. Protein in 26.4% (72 males and 77 females) and albumin in 45.8%(122 males and 154 females). Low level abnormality is higher in both T Protein and Albumin for both male and female.

In the Table 1 mean value of T Protein is 8.28 and 7.98 for male and female respectively and in Table 2 mean value is 5.42 and 5.71 for male and female respectively, which is lower than preferred value. Similarly, for Albumin mean value is 3.65 and 3.58 for male and female respectively in the Table 1 and 2.95 and 2.99 for the male and female respectively in the Table 2.



As shown in Graph 3 and Table 2 High level abnormality profile is found in total bilirubin in 18.9%, high direct bilirubin in 22.5%, high SGOT in 41.8%, high SGPT and highest abnormality in SGOT for male and ALP for Female. Male has normally higher level of abnormality in T Bilirubin, D Bilirubin, SGOT, SGPT and ALP than Female.

Table 3. Correlation of age with various LFT parameters

		T Bilirubin	D Bilirubin	SOGT	SGPT	ALP	T Protein	Albumin	Globulin
Age Correlation coefficient	M	-0.043	-0.015	0.043	-0.018	0.016	-0.084	-0.043	-0.011
	F	-0.013	-0.010	-0.035	-0.081	-0.073	0.008	0.048	0.137
P value		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Pearson's correlation co-efficient test showed that age was significantly correlated ($p < 0.05$) with the liver profile parameters. Table 3 gives details about correlation of various variables with liver profile parameters.

*Pearson's correlation coefficient, T Bilirubin – total Bilirubin; D bilirubin – direct Bilirubin; SGOT – serum glutamic-oxaloacetic transaminase); SGPT – Serum glutamic-pyruvic transaminase; ALP – Alkaline Phosphatase; T protein – total protein.

IV. Discussion

There is paucity of health policy relevant data for liver disease from India, impeding formulation of an interventional strategy to address the issue. Care for liver disease is maximally effective if instituted early.

Most of the study population were females comprising of 54.4% in the age group 20-80 years, the peak prevalence was observed in females in the age group of 50-59 years, which was higher when compared with male of same age group, which might be due to menopausal status and lack of physical exercise in this period of time. For male the peak prevalence 30-39 and 40-49 age group which is far higher than females of same age group.

Mean values of ALP, AST, ALT total and Direct Bilirubin were significantly higher and was significantly correlated ($p < 0.05$) and this was in accordance with previous study done by G. Teshome et al[15]. In our study, we found highest abnormality on LFT profiles in SGOT and ALT as compared to normal value which is in coordination with earlier report studies done by Kalra S et al[16]. In the age group 40-49 years has the highest level of abnormality and age group 50-59 has next higher level of abnormality.

The overall prevalence of LFT abnormality was found to be 29% in the age group studied for both sexes combined. The prevalence of mildly abnormal LFTs, with one or more abnormal constituents in the LFT, was high at 10 – 21.7%[17]. Hong Zhang et al. also stated that the prevalence of abnormal LFTs was 14.77%[18]. In previous community-based studies in Italy, the percentage of individuals with persistently abnormal LFTs was 12.7%[19].

The reference population that is just identified might represent healthy individuals, non – healthy individuals without a disease, which is known to affect a particular vicinity.

The causes of abnormal liver tests may vary in different geographic areas. Abnormal liver tests may present in an asymptomatic patient. Liver tests often become abnormal in non-hepatic diseases. ALT is more specific for active hepatocellular damage. The prevalence of elevated AST reflects the incidence of other conditions besides liver damage[20]. Elevated ALT or AST above the upper limit of normal in a population without identifiable risk factors is associated with increase liver-related mortality. However, elevations in liver enzymes are physiological – example, ALP levels may be increased during the third trimester of pregnancy, and both AST and ALT may increase with vigorous exercise[21]. Albumin is synthesized in the liver; in our study, there was low level of albumin and T. Protein which might reflect on poor protein intake (malnutrition) or protein loss (nephrotic syndrome, malabsorption, or protein losing enteropathy)[22].

Marked elevation of ALT is observed in disease affecting with hepatocytes such as viral hepatitis, ischaemic liver injury (shock injury) and toxin – induced liver damage[23]. AST catalyze transamination reaction. AST exist in two different isoforms; the mitochondrial and cytosolic form. AST is found in highest concentration in heart compared with other other tissues in the body such as liver, skeletal muscle and kidney[24]. Rise in ALP is seen in infiltrative liver diseases, abscesses, granulomatous liver disease and amyloidosis[25].

V. Conclusion

The prevalence of liver function tests was found to be higher than previously reported. This study showed worrying prevalence of abnormal liver profile parameters among the population including younger population and both gender. Elevation of liver enzymes is one of the most common problems encountered. Abnormal LFT are associated with a range of health outcomes, the study was taken up to detect and prevent severe liver pathology which signifies the need for screening of Liver Function Test routinely.

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