

ORIGINAL RESEARCH

ABNORMALITIES OF PLATELET PARAMETERS, HAEMATOCRIT AND LIVER FUNCTION TESTS IN DENGUE- A HOSPITAL BASED CROSS-SECTIONAL STUDY

Dr. Oindrila Dhar¹, Dr. Nabanita Banerjee², Dr. Piyali Mitra³, Dr. Rajasree Chakrabarty⁴, Dr. Anjan Kumar Das⁵

¹Assistant Professor, Department of Pathology, Dr. B. C. Roy Multi-speciality Medical Research Centre, IIT Kharagpur, West Bengal, India.

²Assistant Professor, Department of Community Medicine, Maharaja Jitendra Narayan Medical College & Hospital, Vivekananda Street, Pilkhana, Cooch Behar, India.

³Assistant Professor, Department of Pathology, Maharaja Jitendra Narayan Medical College & Hospital, Vivekananda Street, Pilkhana, Cooch Behar, India.

⁴Assistant Professor, Department of Pathology, Maharaja Jitendra Narayan Medical College & Hospital, Vivekananda Street, Pilkhana, Cooch Behar, India.

⁵Professor, Department of Pathology, NRS Medical College and Hospital, Kolkata, West Bengal, India.

Corresponding Author: Dr. Anjan Kumar Das, Professor, Department of Pathology, NRS Medical College and Hospital, Kolkata, West Bengal.

ABSTRACT

Background: Dengue, an important cause of fever, spread by bite of infected Aedes mosquito. Sometimes changes of platelet parameters, haematocrit and liver function tests are found in dengue fever. The aims of this study are to find out the prevalence of liver function tests abnormalities in patients with dengue and to find out the abnormalities in platelet parameters in patients with dengue.

Methods: Total 300 patients with NS1 antigen and IgM positive or dengue IgG or IgM positive, having no preexisting liver diseases or other superadded infection i.e. hepatitis, malaria, enteric fever causing hepatitis (according to bed head tickets) from January'22 to December'23, admitted in the Sishu-o- Matrimongal Kendra hospital are included in this study.

Results: In this study, most of the patients are adults (>18 years to 60 years) male (56.67%). Majority (85.33%) have platelet count >1,00,000/cumm, 8.67% have platelet count <50,000/cumm. Majority of them (92%) have normal mean platelet volume, platelet distribution width and haematocrit. Most of them have plateletcrit lower than normal. Most of the males have aspartate aminotransferase level and alanine aminotransferase level between 40U/L -250U/L. Majority of the females have both aspartate aminotrasferase and alanine aminotransferase level <40U/L. Most of the patients (both males and females) have alkaline phosphatase level less than 128 IU/L. Majority of them (both males and females) have more than normal level of gamma-glutamyl transferase level. Most of the patients (both males and females) have total serum bilirubin level 20µmol/L or less. Majority of the patients (both males and females) have total serum protein level 64 gm/L or less and serum albumin level less than 35gm/L.

Conclusion: Dengue, a mosquito borne viral fever, is a condition very commonly encountered in all over India. Along with haematological changes, some liver function tests are also found

deranged in dengue patients. Liver involvement in the form of elevated transaminases, GGT, bilirubin, low protein, albumin were found in this study population. The spectrum of hepatic involvement in dengue can vary from asymptomatic biochemical changes to severe liver damage. The haematocrit level of dengue patients are increased significantly indicating the haemoconcentration of the patients. Platelet parameters give information about ongoing destruction of platelets in dengue patients. Limitation of this study is that no differentiation is examined between dengue fever and dengue haemorrhagic fever and coagulation profile is not assessed.

Keywords: Dengue fever, Haematocrit, Platelet parameters, Liver function tests

INTRODUCTION

Dengue or ‘break bone fever’, an important cause of fever in the tropical countries, spread by the bite of infected *Aedes* mosquito (mostly by *Aedes aegypti*, less commonly by *Aedes albopictus*). Currently, it is the most common cause of arboviral disease globally.^[1] Presenting with a wide range of severity, “severe” dengue (Group C) as categorized by World Health Organization (WHO) in 2009 includes the dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS)^[2]. Dengue virus (DENV) has 4 serotypes (DEN 1-4) and is a member of the Flaviviridae family and the genus *Flavivirus*^[3]. Infection with DENV results in asymptomatic disease or an undifferentiated viral fever like illness in the majority of infected individuals. However, in others, it may result in dengue fever (DF), dengue haemorrhagic fever (DHF) leading to shock (DSS)^[4]. Involvement of liver leading to hepatic dysfunction is a well-recognized complication of dengue. Dengue associated acute liver failure has a high mortality due to complications such as encephalopathy, severe bleeding, renal failure, metabolic acidosis^[5,6]. Since the frequency of liver involvement associated with dengue is increasing and since isolated liver involvement in the absence of shock and other dengue associated complications (expanded dengue syndrome) is also increasing^[4], now-a-days it is very important to know the causes of liver involvement in dengue along with the changes in liver function tests associated with acute dengue infection. Liver dysfunction as a result of dengue infection can be a direct viral effect on liver cells or an adverse consequence of dysregulated host immune response against the virus. Dengue fever is known to involve multiple systems sometimes resulting in multi organ dysfunction. Liver involvement is known to occur and of late there have been multiple reports of fulminant hepatitis in children with dengue fever. Liver dysfunction varies from mild injury with elevation of transaminases to severe hepatocyte injury, resulting in jaundice. Direct hepatotoxicity as well as deranged host immune response against the virus is responsible for the hepatic dysfunction. Though there have been isolated cases of fulminant hepatic failure, the derangements in the transaminases are usually self-limiting and may serve as a predictor for assessing the disease severity^[9,10]. The exact mechanism of liver damage is still not completely understood. However, there are several mechanisms postulated including direct viral damage, immunological injury and hypoxic injury due to reduced hepatic perfusion during shock. Evidence-based guidelines are sparse to manage acute liver failure in dengue. However, the use of N-acetyl cysteine (NAC) for non-acetaminophen-related liver injury in particularly dengue-related liver injury has gained importance in the recent past^[11, 12]. The CBC in dengue patients change by the day of the fever, specifically on days 3 to 8, starting with progressive leucopenia followed by thrombocytopenia and hemoconcentration due to plasma leakage.^[13,14]

Aims and Objectives

1. To find out the prevalence of liver function tests abnormalities in patients with dengue.

- 2. To find out the abnormalities in platelet parameters in patients with dengue.
- 3. To find out the changes in haematocrit in dengue patients.

Inclusion Criteria

All NS1 antigen and dengue Ig M positive or dengue Ig G positive patients irrespective of age and sex.

Exclusion Criteria

- 1. Patients with preexisting liver disease according to bed head ticket.
- 2. Patients with other superadded infection i.e. hepatitis, malaria, enteric fever causing hepatitis according to bed head ticket

MATERIALS & METHOD

Study Design: Cross-sectional study

Study Timeline- From January'22 to December'23

Period of Study- 24 months

Place of Study- Sishu- O- Matrimongal Kendra, Uttarpara, Hooghly, West Bengal

Study Population- Total 300 patients with NS1 antigen and dengue IgM positive or dengue IgG positive, having no preexisting liver diseases or other superadded infection i.e. hepatitis, malaria, enteric fever causing hepatitis, are included in this study.

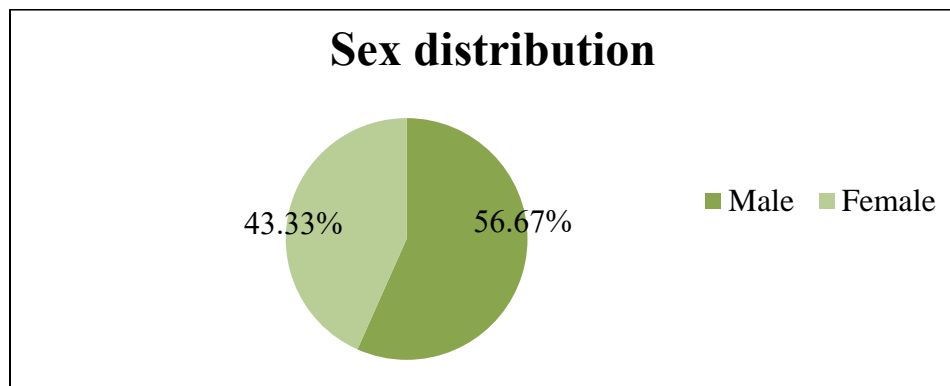
Medical Record Review: Patients with NS1 antigen and dengue IgM positive or dengue Ig G positive, having no preexisting liver diseases or other superadded infection i.e. hepatitis, malaria, enteric fever causing hepatitis, having all platelet parameters and liver function tests reports are included in this study.

Sampling Technique: Complete enumeration of all NS1 and dengue Ig M positive or dengue IgG positive patients.

RESULTS

Table No. 1: Sex distribution of the study population (n=300)

Sex	No. of patient	% of patient (n=300)
Male	170	56.67
Female	130	43.33
Total	300	100

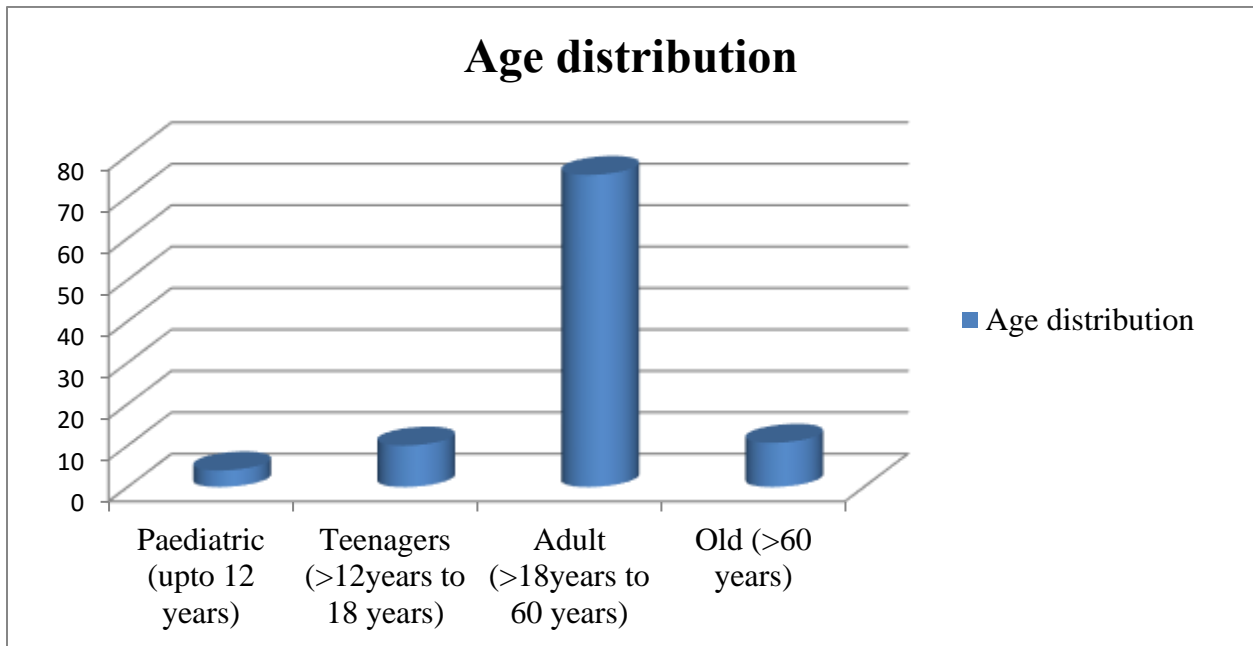


Graph no. 1- Sex distribution of the study population

Inference- Male patients are slightly more in number (56.67%) in this study population

Table No. 2- Age distribution of study population (n=300)

Age group	No. of patients	% of patients (n=300)
Paediatrics (upto 12 years)	12	4
Teenagers (>12 years – 18 years)	30	10
Adult (>18 years - 60 years)	226	75.33
Old (>60years)	32	10.67
Total	300	100

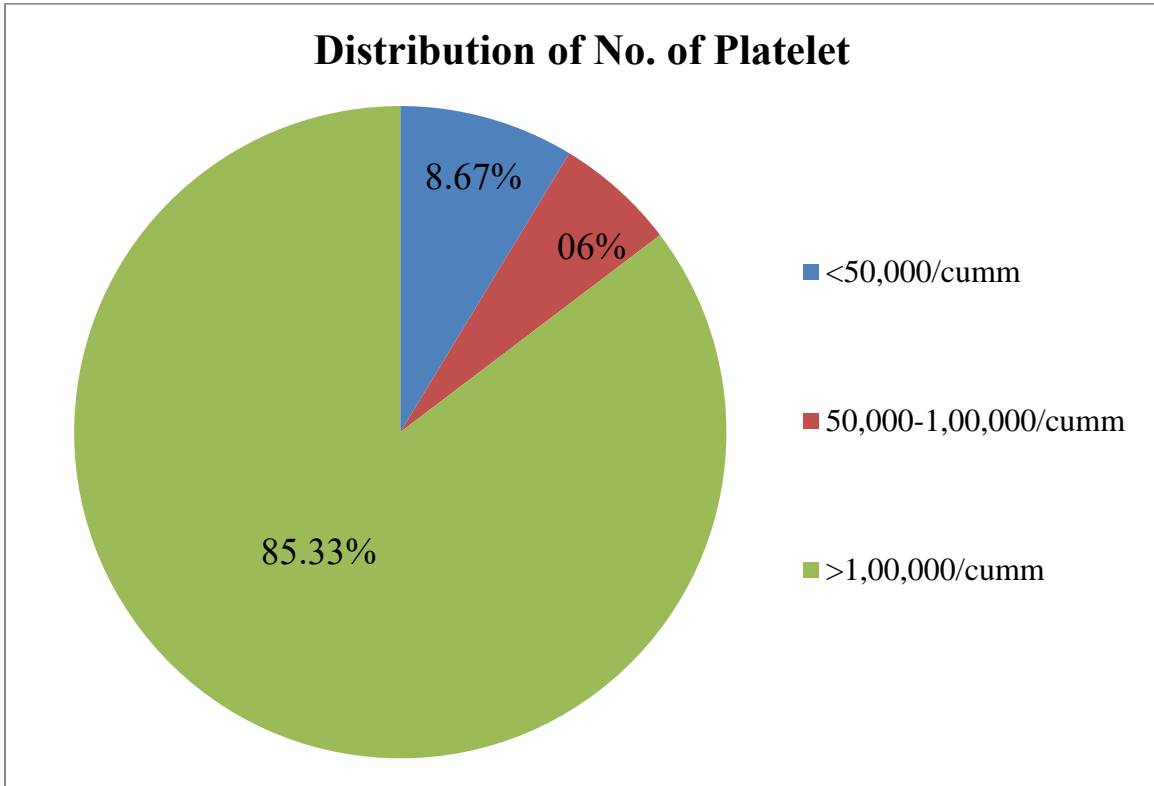


Graph no. 2: Age distribution of study population

Inference- Majority of the patients (75.33%) are adults (>18 years to 60 years)

Table no. 3(a)- Abnormalities in number of platelet in the study population (n=300)

No. of platelet (per cu.mm)	No. of patients	% of patients (n=300)
< 50,000	26	08.67
50,000 – 1,00,000	18	06
>1,00,000	256	85.33
Total	300	100

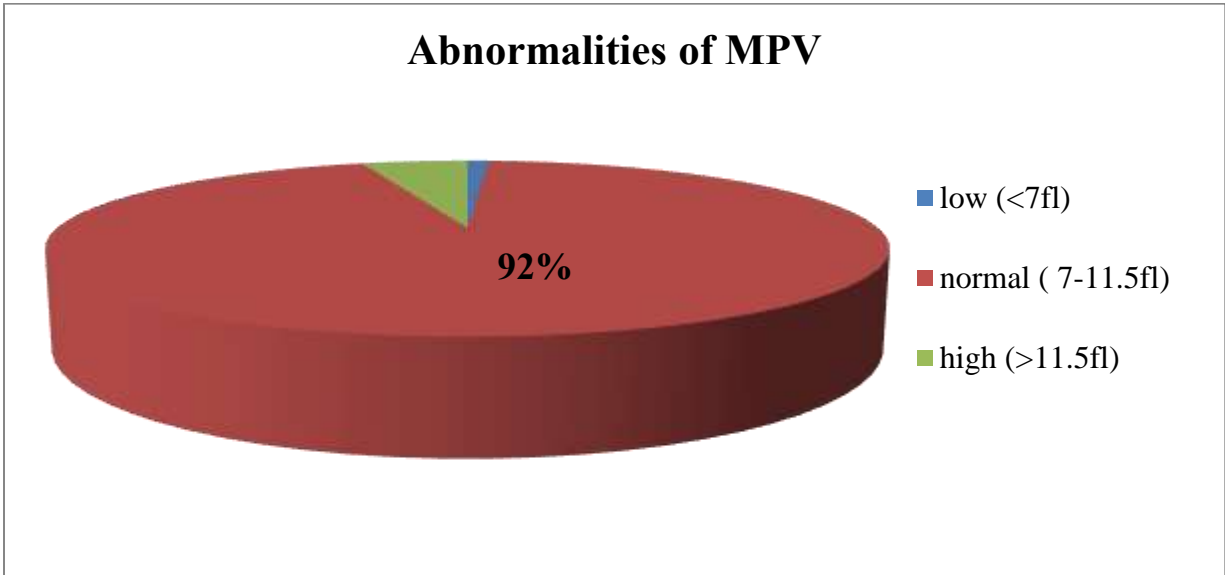


Graph no. 3(a)- Abnormalities in number of platelet in the study population

Inference- Out of 300 patients, 256 patients (85.33%) have platelet >1,00,000/cumm, 26 patients (8.67%) have platelet <50,000/cumm and 18 patients (06%) have 50,000-1,00,000/cumm platelet in blood

Tabale no. 3(b)- Abnormalities of Mean Platelet Volume (MPV) in the study population (n=300)

Mean Platelet Volume (MPV)	No. of patients	% of patients (n=300)
Low (< 7 fl)	09	03
Normal (7-11.5 fl)	276	92
High (> 11.5 fl)	15	05
Total	300	100

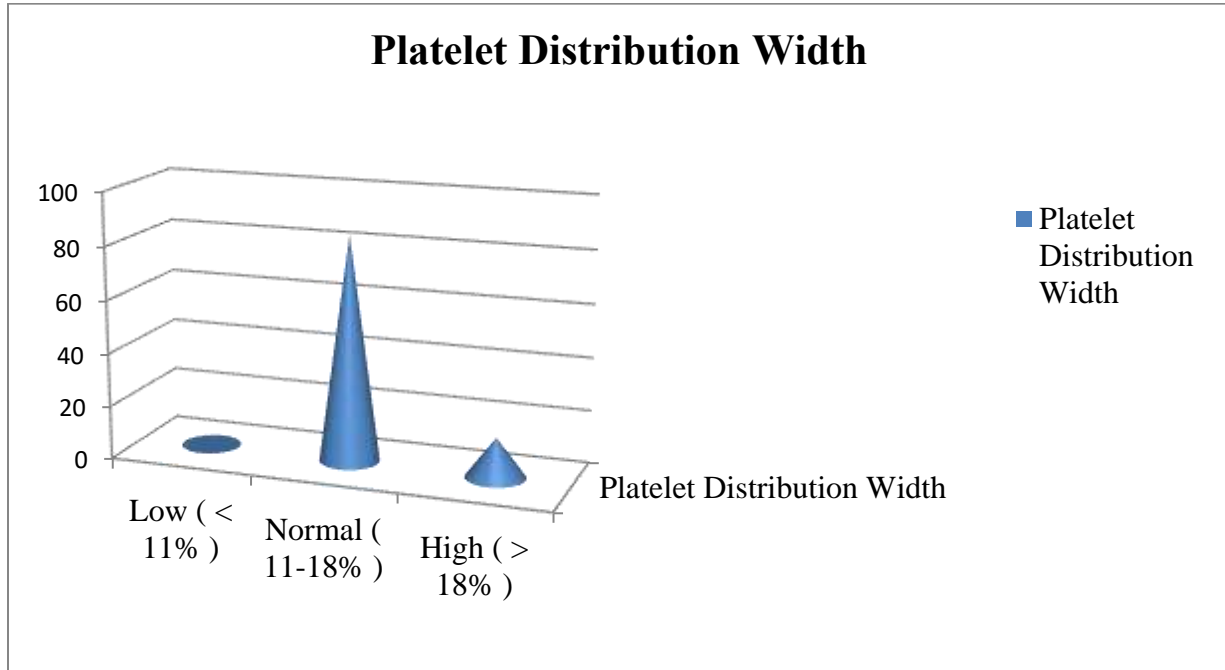


Graph no. 3(b) - Abnormalities of Mean Platelet Volume (MPV) in the study population

Inference- Most of the patients (92%) have normal MPV, 05% patients have high MPV and 03% have low MPV.

Table no. 3(c) – Abnormalities of Platelet Distribution Width (PDW) in the study population (n=300)

Platelet Distribution Width (PDW)	No. of patients	% of patients (n=300)
Low (<11%)	00	00
Normal (11-18%)	255	85
High (>18%)	45	15
Total	300	100

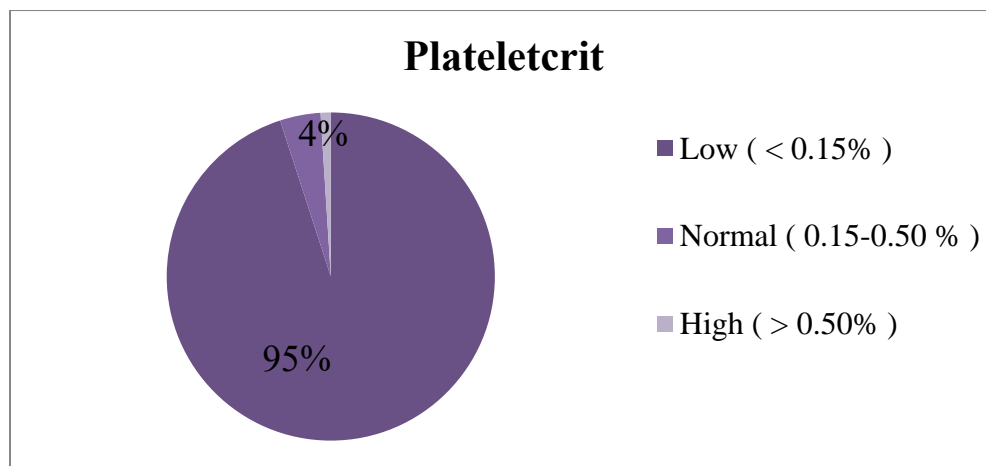


Graph no. 3(c) – Abnormalities of Platelet Distribution Width (PDW) in the study population

Inference- 85% patients have normal platelet distribution width and 15% have high platelet distribution width.

Table no. 3(d) – Abnormalities of Plateletcrit (PCT) in the study population (n=300)

Plateletcrit (PCT)	No. of patients	% of patients (n=300)
Low (< 0.15%)	285	95
Normal (0.15- 0.50%)	12	04
High (> 0.50%)	03	01
Total	300	100

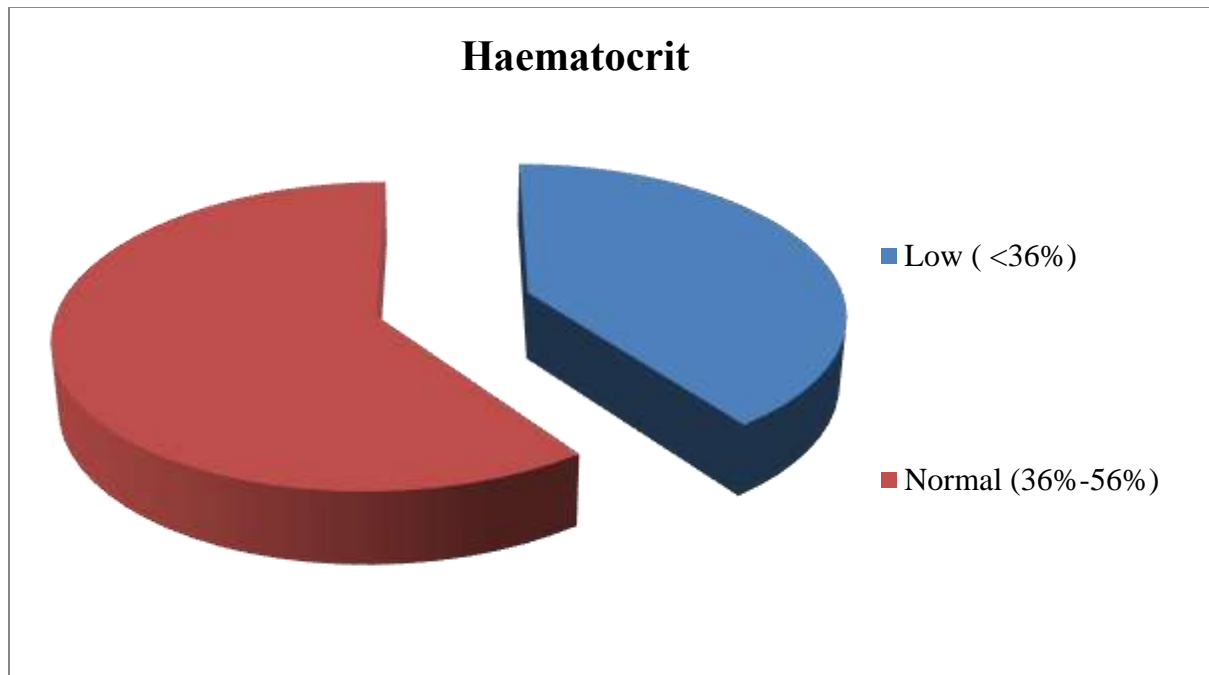


Graph no. 3(d) – Abnormalities of Plateletcrit (PCT) in the study population

Inference- 95% patients have low plateletcrit and 04% patients have normal plateletcrit and only 01% have high plateletcrit.

Table no. 4(a) – Abnormalities of Haematocrit (HCT) in the study population (n=300)

Haematocrit (HCT)	No. of patients	% of patients (n=300)
Low (< 36%)	120	40
Normal (36%-56%)	180	60
Raised (>56%)	00	00
Total	300	100

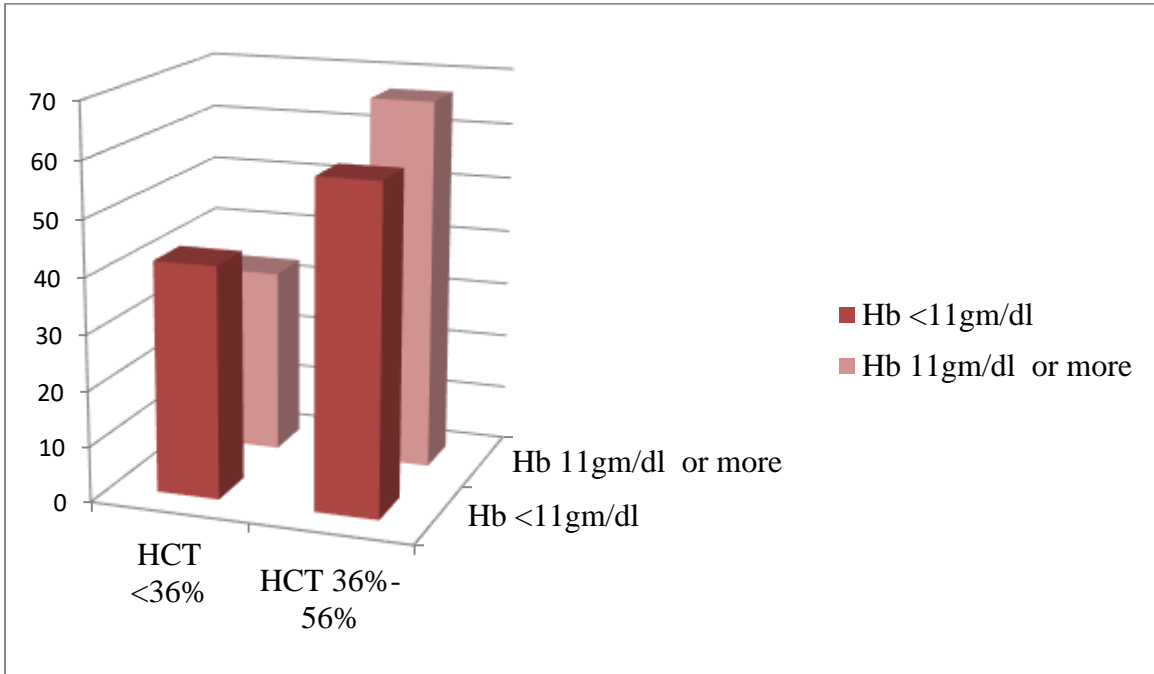


Graph no. 4(a) – Abnormalities of Haematocrit (HCT) in the study population

Inference- In this study, out of 300 patients, 180 patients (60%) have normal haematocrit and 120 patients (40%) have low haematocrit.

Table no. 4(b) – Abnormalities of Haemoglobin (gm/dl) in comparison to Haematocrit (HCT) in the study population (n=300)

Haematocrit (HCT)	Haemoglobin (gm/dl)			
	<11gm/dl		11gm/dl or more	
	No. of patients	% of patients (N=240)	No. of patients	% of patients (N=60)
<36%	100	41.67	20	33.33
36%-56%	140	58.33	40	66.67
Total	240	100	60	100
Total patient (n) = (240+60) = 300				

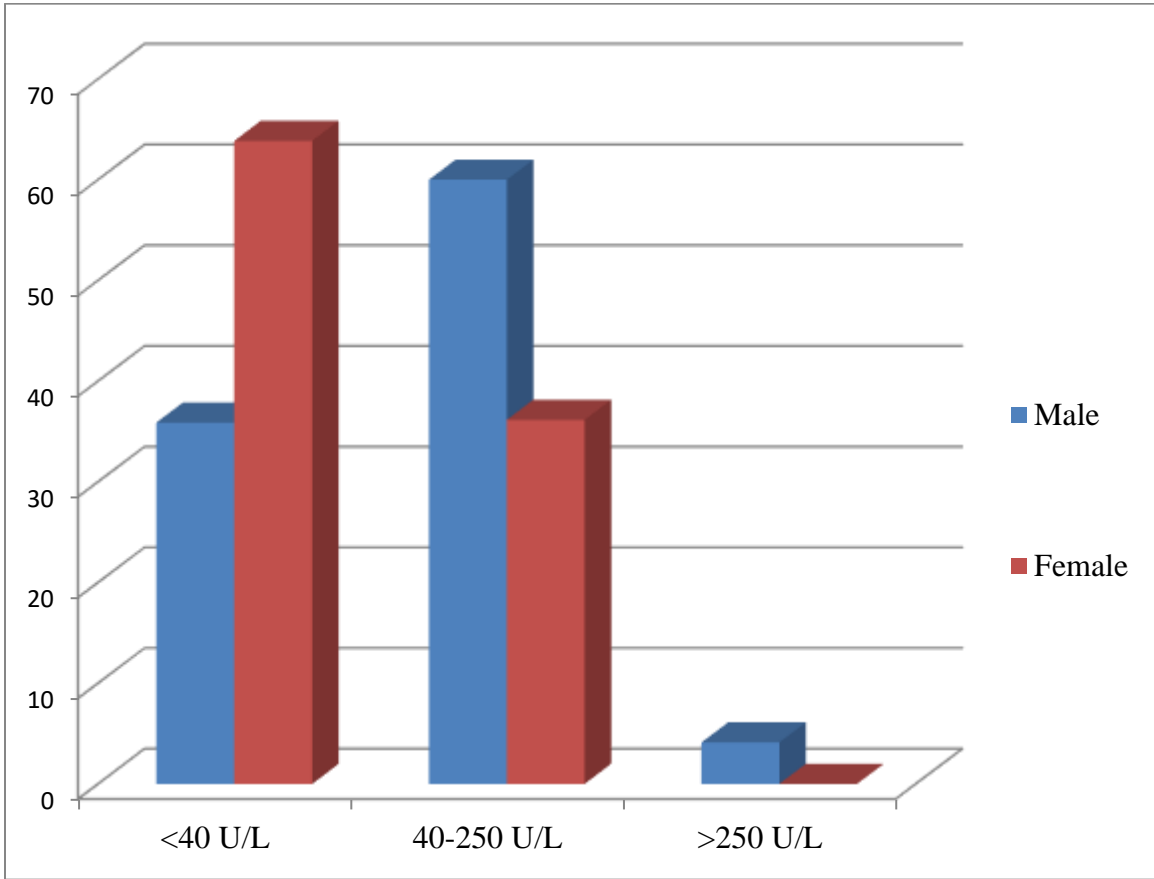


Graph no. 4(b) – Abnormalities of Haemoglobin (gm/dl) in comparison to Haematocrit (HCT) in the study population

Impression- Out of 240 patients with haemoglobin level <11gm/dl, 140 patients (58.33%) have haematocrit level 36%-56% and 100 patients (41.67%) have haematocrit level <36%. Out of 60 patients with haemoglobin level 11gm/dl or more, 20 patients (33.33%) have haematocrit <36% and 40 patients (66.67%) have haematocrit level 36%-56%.

Table no. 5(a) – Abnormalities of Aspartate aminotransferase (AST) in the study population (n=300)

Aspartate aminotransferase (AST) (U/L)	Male		Female	
	No. of patients	% of patients (N=170)	No. of patients	% of patients (N=130)
< 40	61	35.88	83	63.85
40-250	102	60	47	36.15
>250	07	4.12	00	00
Total	170	100	130	100
Total patients (n) = (170+130) = 300				

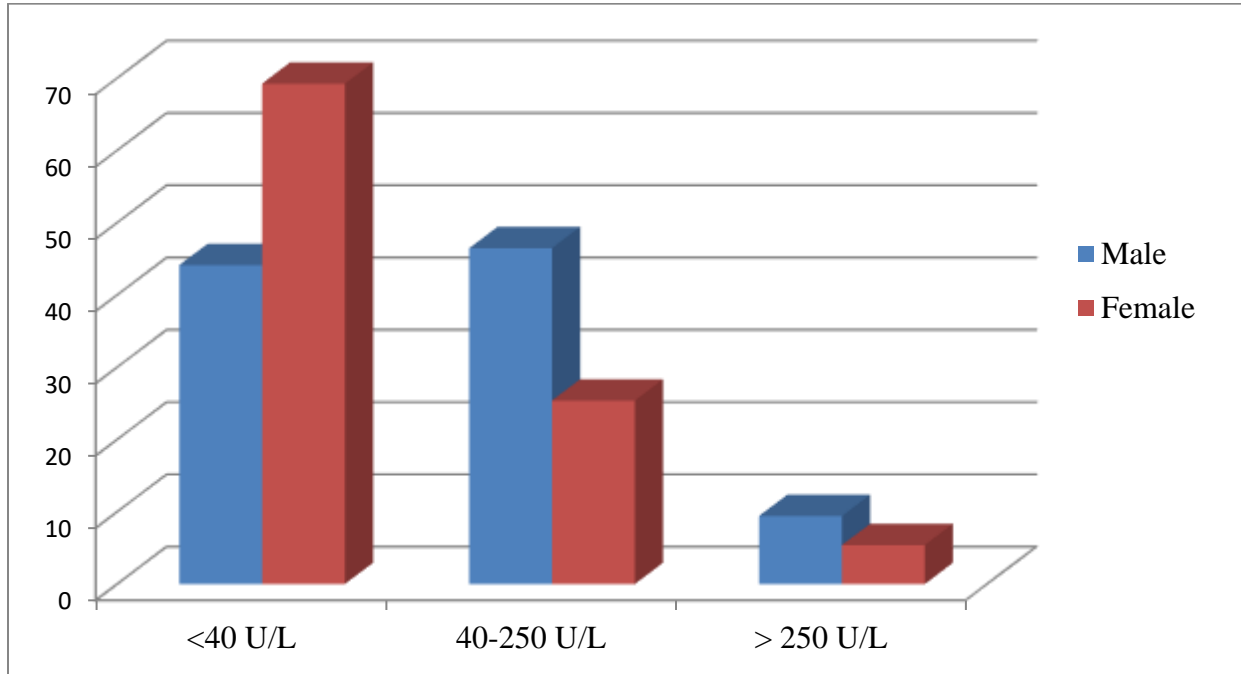


Graph no. 5(a) – Abnormalities of Aspartate aminotransferase (AST) in the study population

Inference- Out of 170 male patients, 102 (60%) have AST level 40-250 U/L, 07 patients (4.12%) have AST level > 250 U/L and out of 130 female patients, 83 patients (63.85%) have AST level < 40U/L.

Table no. 5(b) – Abnormalities of Alanine aminotransferase (ALT) level in the study population (n=300)

Alanine aminotransferase (ALT) (U/L)	Male		Female	
	No. of patients	% of patients (N=170)	No. of patients	% of patients (N=130)
< 40	75	44.12	90	69.23
40-250	79	46.47	33	25.38
>250	16	09.41	07	05.39
Total	170	100	130	100
Total population (n) = (170+130) = 300				

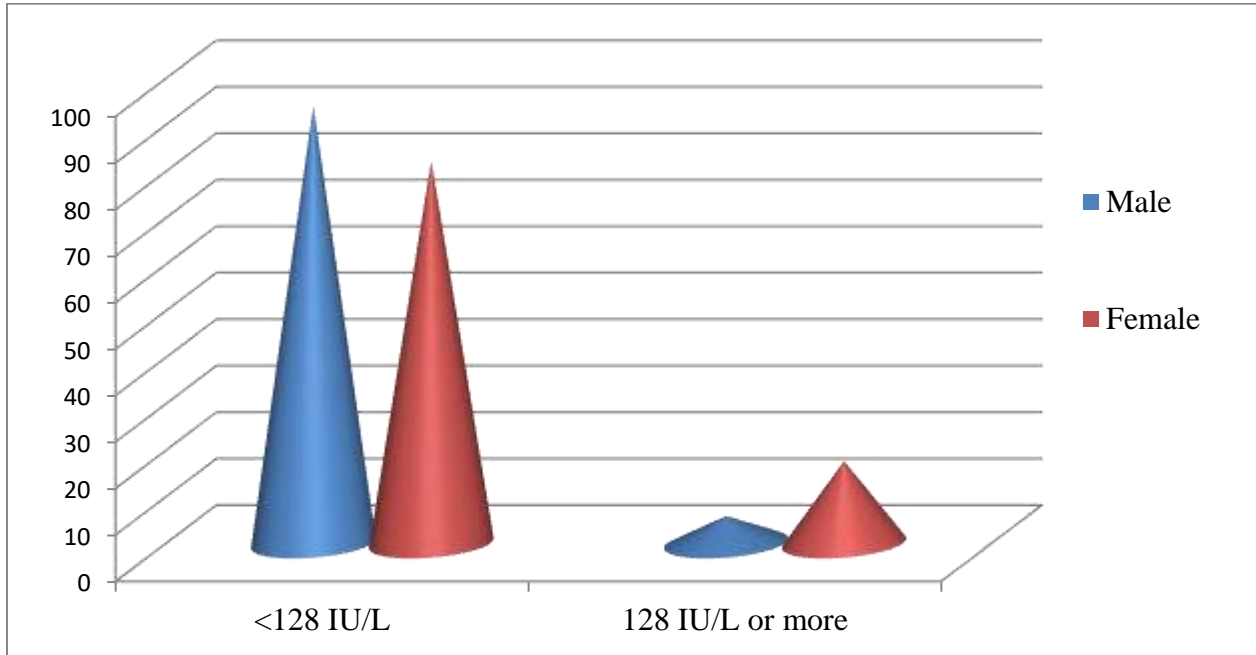


Graph no. 5(b) – Abnormalities of Alanine aminotransferase (ALT) in the study population

Inference- Out of 170 male patients, 79 patients (46.47%) have ALT level within 40-250 U/L, 75 (44.12%) have ALT < 40U/L and 16 patients (09.41%) have ALT > 250 U/L. Out of 130 female patients, 90 patients (69.23%) have ALT level <40 U/L and 07 (05.39%) have ALT level >250 U/L.

Table no. 5(c) – Abnormalities of Alkaline phosphatase (ALP) in the study population (n=300)

Alkaline phosphatase (ALP) (IU/L)	Male		Female	
	No. of patients	% of patients (N=170)	No. of patients	% of patients (N=130)
< 128	160	94.12	107	82.31
128 or more	10	05.88	23	17.69
Total	170	100	130	100
Total patients(n) = (170+130) = 300				

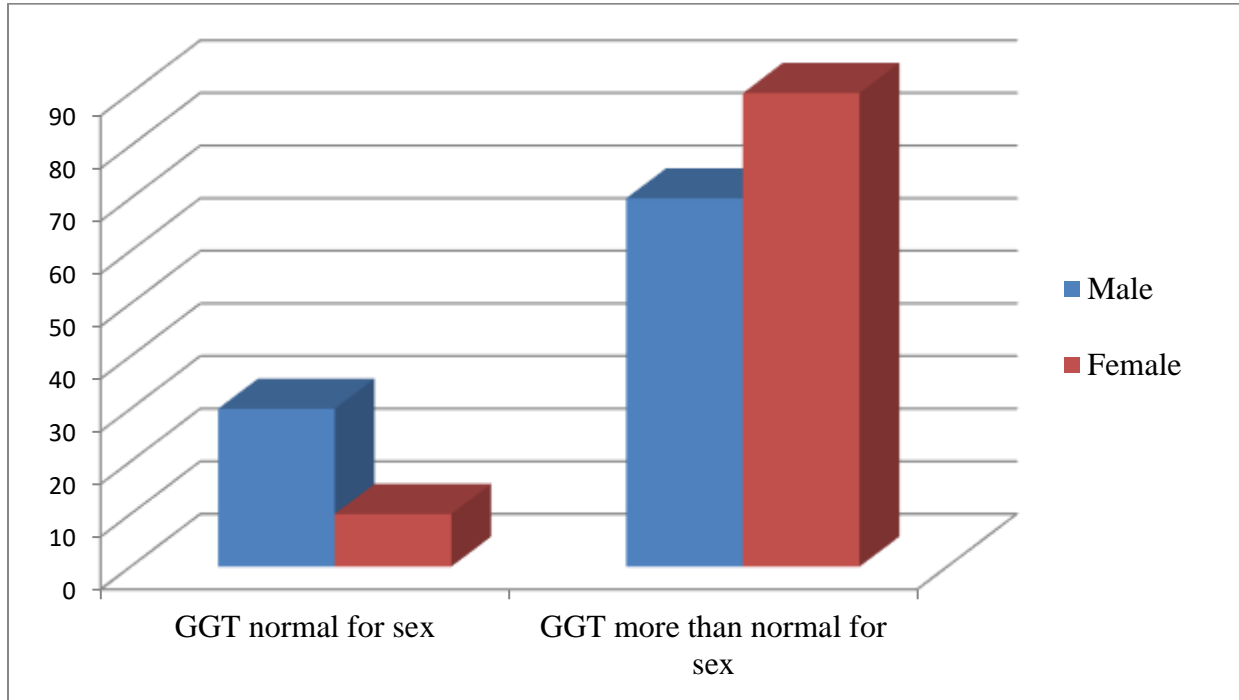


Graph no. 5(c) – Abnormalities of Alkaline phosphatase (ALP) in the study population

Inference- Out of 170 male patients, 160 patients (94.12%) and out of 130 female patients, 107 patients (82.31%) have alkaline phosphatase level <128 IU/L.

Table no. 5(d) – Abnormalities of Gamma-glutamyl transferase (GGT) in the study population (n=300)

Gamma-glutamyl transferase (GGT) (IU/L) Normal for male – 55 IU/L or less , for female- 30 IU/L or less	Male		Female	
	No. of patients	% of patients (N=170)	No. of patients	% of patients (N=130)
Normal for sex	51	30	13	10
More than normal for sex	119	70	117	90
Total	170	100	130	100
Total patients (n) = (170+130) = 300				



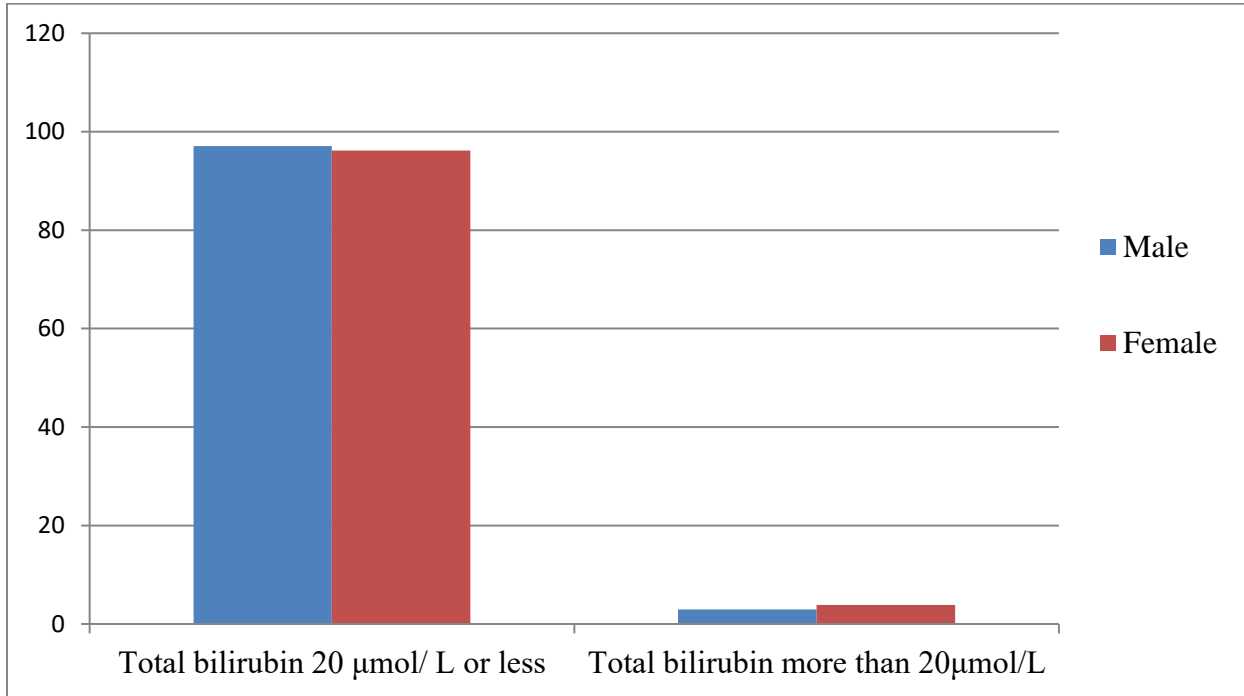
Graph no. 5(d) – Abnormalities of Gamma-glutamyl transferase (GGT) in the study population

Inference- Out of 170 male patients, 119 (70%) have GGT level more than normal value for sex (i.e. 55IU/L or more) and out of 130 female patients, 117 (90%) have GGT level more than normal value for sex (i.e. 30IU/L or more).

Table no. 5(e) – Abnormalities of total bilirubin level in the study population (n=300)

Total bilirubin (µmol/L)	Male		Female	
	No. of patients	% of patients (N=170)	No. of patients	% of patients (N=130)
20 or <20	165	97.06	125	96.15
>20	05	2.94	05	3.85
Total	170	100	130	100

Total patients (n) = (170+130) = 300



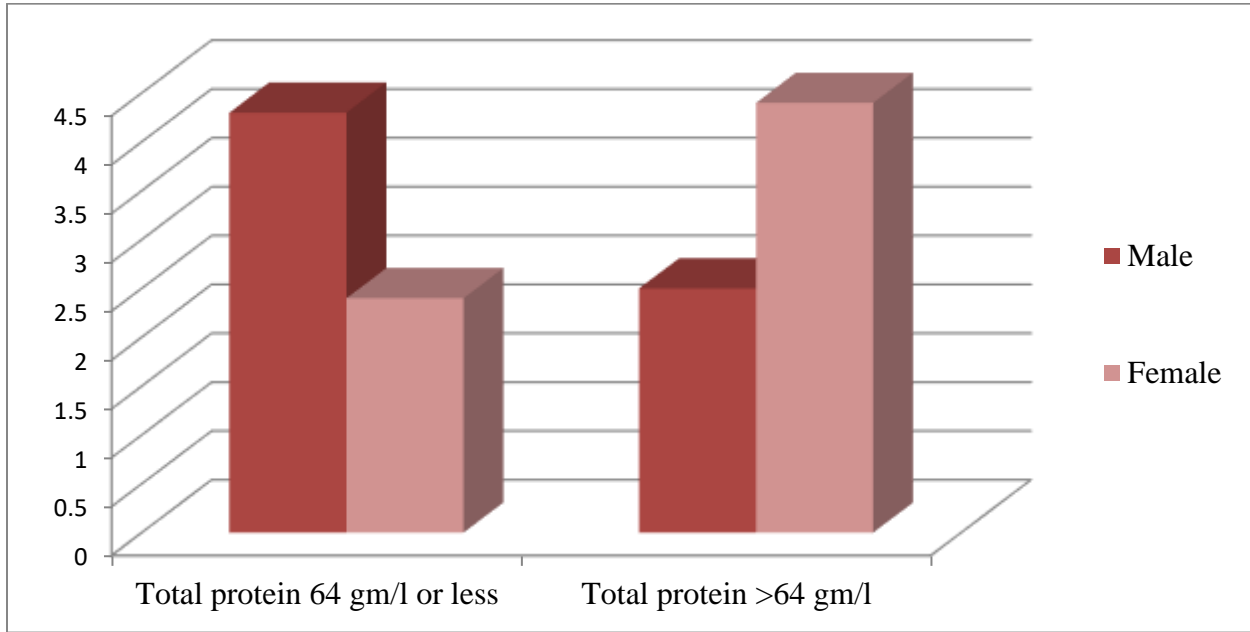
Graph no. 5(e) – Abnormalities of total bilirubin level in the study population

Inference- Out of 170 male patients, 165 males (97.06%) and out of 130 female patients, 125 females (96.15%) have total bilirubin 20 µmol/L or less.

Table no. 5(f) – Abnormalities of total protein level in the study population (n=300)

Total protein (gm/L)	Male		Female	
	No. of patients	% of patients (N=170)	No. of patients	% of patients (N=130)
64 or less	111	65.29	120	92.31
>64	59	34.71	10	07.69
Total	170	100	130	100

Total patients (n) = (170+130) = 300



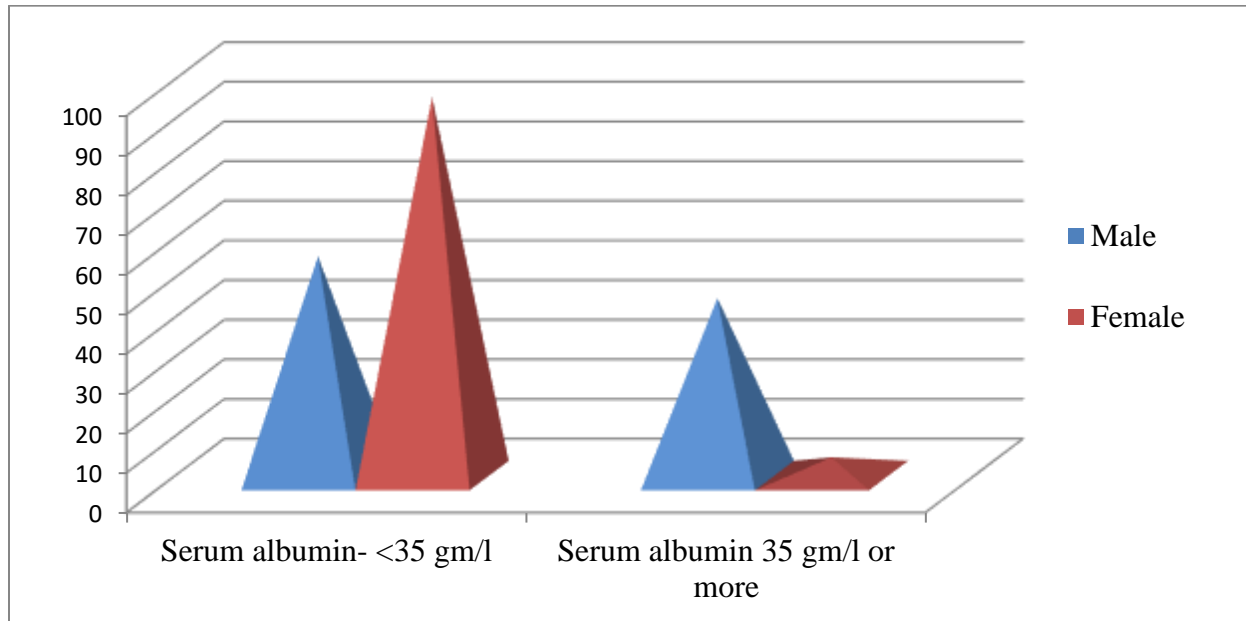
Graph no. 5(f) – Abnormalities of total protein level in the study population

Inference- Out of 170 male patients, 111 males (65.29%) and out of 130 female patients, 120 females (92.31%) have total protein 64 gm/l or less.

Table no. 5(g) – Abnormalities of serum albumin level in the study population (n=300)

Serum albumin (gm/l)	Male		Female	
	No. of patients	% of patients (N=170)	No. of patients	% of patients (N=130)
< 35	94	55.29	124	95.38
35 or more	76	44.71	06	04.62
Total	170	100	130	100

Total patients (n) = (170 +130) = 300



Graph no. 5(g) – Abnormalities of serum albumin level in the study population

Inference- Out of 170 male patients, 94 (55.29%) have serum albumin < 35gm/l and out of 130 female patients, 124 patients (95.38%) have serum albumin level 35 gm/l or more.

DISCUSSION

Dengue is a mosquito borne viral infection can cause mild to moderate and sometimes severe illness and death. In this study, out of 300 patients 170 patients (56.67%) are male and 130 patients (43.33%) are female. Muhammad Aamir et al have showed that out of the total, 77 (81.1%) were males. Agarwal *et al.*, Ray *et al.*, and Wali *et al.*, found a higher number of male patients infected with dengue compared to females, sex ratio (M:F) being 1.9:1, 1:0.57, and 2.5:1, respectively.^[15,16,17] In this study, 71 patients (23.67%) are in 31-40 years, followed by 59 patients (19.67%) are in 41-50 years and 55 patients (18.33%) are in 21-30 years. Muhammad Haroon et al have showed that in the dengue positive patients, the highest prevalence was observed in the age group of 21-40years with 160 (38%) followed by the age group of 1-20years with 89 (21%) patients.^[18] In this study, most of the patients (85.33%) have platelet >1,00,000/cumm, 08.67% patients have platelet <50,000/cu mm. A kinetic description of platelet count in DHF/DF showed a significant decrease on the 4th day of the illness. In fact, previous studies reported DHF in adults without shock, in which platelet counts mildly to moderately decreased on the 3rd day until the 7th day of illness and reached normal levels on the 8th or 9th day.^[19] Out of 300 patients, 276 patients (92%) have mean platelet volume within normal limit (7-11.5fl) and 15 patients (05%) have mean platelet volume > 11.5fl. Kritika Sharma et al shows in their study that no significant difference was observed in mean between MPV at the time of minimal platelet counts and at discharge in dengue cases except in dengue fever cases.^[20] Wiwanitkit et al have showed that MPV for patients with DHF is not decreased & appears to be similar to that for the general healthy population.^[21] In this study, out of 300 patients 255 patients (85%) have normal platelet distribution width (11-18%) and 45 patients (15%) have platelet distribution width >18%. J Asha et al have showed in their study that the majority (99.6%) of patients had normal PDW value as the baseline.^[22] In this study, 285 patients (95%) have plateletcrit(PCT) <0.15% and 12 patients

(04%) have normal PCT (0.15-0.50%) and 3 patients (1%) have PCT > 0.50%. J Asha et al have also found that the majority (98%) of patients have low PCT as the baseline value.^[22] In this study 180 patients (60%) have normal haematocrit (36-56%) and 120 patients (40%) have haematocrit <36%. Out of 240 patients with haemoglobin <11gm/dl, 140 patients (58.33%) have normal haematocrit and 100 patients (41.67%) have haematocrit <36%. Out of the 60 patients with haemoglobin level 11gm/dl or more 40 patients (66.67%) have normal haematocrit and 20 patients (33.33%) have low haematocrit. In a study by S. Balasubramanian et al hemoconcentration (>20%) was detected in 20 (57.14%) out of 35 cases of DHF. Hemoconcentration based on the area specific hematocrit cut off values was observed in 32 cases(91.42%) and it had a better sensitivity and negative predictive value as an indicator of plasma leakage.^[23] Duangjai Sahassananda et al have found that the Hct calculated via the three- fold conversion method had an excellent relationship with the Hct calculated via the automated hematology analyzer, except when the Hgb was <12 g/dl or ≥16g/dl.^[24] Sharma S et al have found that raised Hct > 48% were present in 6 (6.12%) cases and Hct > 20% in 14 (14.28%) cases.^[25] In this study, out of 170 male patients, 102 patients (60%) have Aspartate aminotransferase (AST) level 40-250 U/L and 61 patients (35.88%) have AST level <40U/L and 7 patients (4.12%) have AST level >250 U/L. Out of 130 female patients, 83 patients (63.85%) have AST <40U/L, 47 females (36.15%) have AST level 40-250U/L. Out of 170 male patients, 79 patients (46.47%) have Alanine aminotransferase (ALT) level 40-250 U/L, 75 patients (44.12%) have ALT level < 40U/L, 16 patients (09.41%) have ALT level >250 U/L. Out of 130 female patients, 90 patients(69.23%) have ALT < 40U/L, 33 patients (25.38%) have ALT 40-250 U/L and 7 patients (5.39%) patients have ALT >250 U/L. Shreemoyee Palmal et al have found that in the case of AST, 60% in males and 36.8% in females, and for ALT, 46.7% males and 23.6% females showed high levels of serum expression.^[26] In this study, out of 170 male patients, 160 males (94.12%) have alkaline phosphatase (ALP) level <128 IU/L and 10 males (5.88%) have ALP 128 IU/L or more. Out of 130 female patients, 107 patients (82.31%) have ALP level <128 IU/L and 23 patients (17.69%) have ALP 128 IU/L or more. In a study by Rajoo Singh Chhina et al, alkaline phosphatase levels were elevated in 30.3% of cases with dengue fever and 40% of cases with dengue hemorrhagic fever.^[27] In this study, out of 170 male patients, 119 males (70%) have gamma-glutamyl transferase (GGT) more than normal for sex (i.e. >55 IU/L) and 51 patients (30%) have GGT level normal for sex. Out of 130 female patients, 117 female (90%) have GGT level more than normal for sex (i.e. >30 IU/L) and 13 patients (10%) have GGT normal for sex. In a study by A. Bhriguvanshi et al have found that aspartate transaminase (AST), ALT, alkaline phosphatase (ALP) and gamma glutamyl transferase (GGT) levels were elevated in 87%, 82%, 22%, and 26% respectively.^[28] In this study, out of 170 male patients, 165 males (97.06%) have serum bilirubin 20µmol/L or less and 5 patients (2.94%) have serum bilirubin > 20µmol/L. out of 130 females, 125 female patients (96.15%) have serum bilirubin 20µmol/L or less and 5 patients (3.85%) have serum bilirubin >20µmol/L. Denesh Narasimhan et al have also found that serum bilirubin is more than 2 mg/dl in 5% cases in their study.^[29] In this study, 111 males (65.29%) have total protein 64gm/L or less and 59 patients (34.71%) have total protein >64gm/L. Out of 130 females, 120 females (92.31%) have total protein 64gm/L or less and 10 (7.69%) have total protein >64 gm/L. From this, 94 male patients (55.29%) have serum albumin <35 gm/l and 76 males (44.71%) have serum albumin 35gm/l or more, whereas, 124 females (95.38%) have serum albumin <35 gm/l and 06 females (4.62%) have serum bilirubin >35 gm/l. A study by Anusha Mruthyunjaya Swamy et al, hypoalbuminemia was found in 9.1%, 21.4% and 50% patients of dengue without warning signs, with warning signs and severe dengue respectively.^[30] A study by Denesh Narasimhan et al, serum proteins were reduced in 19.6% of patients and serum albumin was reduced in 10.6% of patients.^[31]

CONCLUSION

Dengue, a mosquito borne viral fever, is a condition very commonly encountered in all over India. Along with haematological changes, some liver function tests are also found deranged in dengue patients. Liver involvement in the form of elevated transaminases, GGT, bilirubin, low protein, albumin were found in this study population. The spectrum of hepatic involvement in dengue can vary from asymptomatic biochemical changes to severe liver damage. The haematocrit level of dengue patients are increased significantly indicates the haemoconcentration of the patients. Platelet parameters give information about ongoing destruction of platelets in dengue patients. Limitation of this study is that no differentiation is examined between dengue fever and dengue haemorrhagic fever and coagulation profile is not assessed.

Acknowledgement

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