Hematological Changes among Sudanese Patients with Acute Viral Hepatitis B

ABSTRACT:

Background: Viral hepatitis bB is a common cause of liver disease with considerable morbidity and mortality throughout the world. As the liver is responsible for producing many haemopoietic factors and performs many critical functions that affect metabolism throughout the body, haematological alterations are commonly detected in the setting of acute hepatitis. The aimof this study is to determine the haematological complications in patient with acute viral hepatitis B, a thing that can help in treatment and follow up of such patients.

Material and Method: The current studywas a descriptive cross-sectional one. It included forty nine subjects of diagnosed with acute hepatitis B recruited from the out-patienthepatology clinics of Ibnsina ,Dr Fatima Farah private clinic and the out-patient clinics of the military hospital. The cases were defined as acute hepatitis B based on elevated liver function tests, HBsAg and HBeAg positivity determined by Enzyme-linked Immune Sorbent Assay (ELISA).The hematology analyzer (Sysmex)in addition to thin blood film were used to asses there full blood count.

Results: Anaemia was detected in 57% of patients (80% of female and 47% of male),macrocytosis in2.04% ,microcytosis in22.45% , leucopenia in12.24% ,leucocytosis in8.16%., neutrophilia in 10.20%, lymphocytosis in 40.72%,and thrombocytopeniain10.20%).

Conclusion: Haematological alteration were encountered as extrahepatic complications following acute hepatitis B. Anaemia was seen in more than half of cases with acute hepatitis B along with abnormalities inother blood lineages. It is recommended that haematological tests are to be included as part of the diagnostic and follow up packages for acute hepatitis B infection, in order to avoid fatal haematologic extrahepatic complications.

Key words: Acute hepatitis B, extrahepatic abnormalities, anemia, thrombocytopenia, leukopenia,neutropenia,leucocytosis,neutrophilia,macrocytosis,microcytosis,lymphoc--ytosis,pancytopenia,hepatocellular

Introduction

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Hepatitis is a term used to describe inflammation of one of the vital organs, the liver, which performs many critical functions pivotal tometabolism throughout the body in addition to synthesis of erythropoietin, thrombopoietin, plasma proteins and clotting factors. Liver disease is associated with a wide range of haematological alterations. Anemia arises through multiple mechanisms, where haem metabolism is disturbed, and liver disease causes alterations in red cell lipid metabolism. Defects in platelet number and function arise due to the effects of liver disease. (1)

There are different causes of hepatitis some of which are infectious while others are not. The infectious agents include virus, bacteria, fungi, and parasite. However, the foremost primary hepatic infections are the viral hepatitis. (2) Viruses (A, B, C, D, E, and G) are common causes of hepatitis, they affect many millions of people throughout the world with considerable morbidity and mortality.(3) The symptoms of hepatitis A usually appear suddenly, but are not followed by the chronic (long-lasting) problems that hepatitis B and C viruses can cause.(4) although HCV is the most common cause of cirrhosis and is responsible for >50% of liver transplants performed currently (3, 5, 6),Studies of hepatitis C virus showed a low seroprevalence of 2.2%–4.8% .Hepatitis B virus is the commonest cause of chronic liver disease and hepatocellular carcinoma and is the second commonest cause of acute liver failure in the Sudan.(7) Sudan is classified among countries with a high hepatitis B surface antigen (HBsAg) endemicity of more than 8%.(8) Primarily we have to distinguish between acute and chronic hepatitis, hepatitis is acute when it lasts less than six months and chronic when it persists longer with symptomatic, biochemical, or serologic evidence of continuing or relapsing hepatic disease. Acute hepatitis can be divided in to four phases: (A) an incubation period, (B) a symptomatic pr-eicteric phase (C) a symptomatic icteric phase (with jaundice and sclera icterus) and (D) convalescence. It heals on its own or can progress

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to chronic hepatitis. (2) Hepatitis B is mostly spread through blood and blood products (9, 10) and when hepatocytes are damaged by virus, a healthy liver cells begin to compensate and with fewer healthy cells, symptoms begin to appear. The most common symptoms include loss of Appetite, Nausea, Vomiting, Fever, Weakness, and Tiredness. These unspecific symptoms may mimic other infections that are common in the sub Saharan Africa like malaria and typhoid fever. Moreover it has been shown that, in cases with viral hepatitis, bone marrow hypoplasia and pancytopenia are frequently encountered in the setting of acute hepatitis B infectionensue, where they were attributed to immunological causes.(11) For the previous causes we wanted to determine the rates of hematological abnormalities (leukopenia, leukocytosis, neutropenia, anemia, thrombocytopenia, and pancytopenia) in cases diagnosed as acute hepatitis B. This will not only help in diagnosis of these patients, further more it can assist in there follow-up and treatment. So this article was focused on hepatitis B, particularly acute hepatitis B and its haematological complications.

Patient and method

The current study is a descriptive cross-sectional study. The limitation of this study was one month , During the period of 15th of January up to 16th of February 2016, Forty nine patients with clinical and laboratory evidence of acute hepatitis B viral infection seen at the medical out-patient hepatology clinics of Ibnsina, Dr Fatima Farah private clinic and military hospital, were recruited into the study. The diagnosis of acute hepatitis B was made by measuring elevated liver function tests(including elevated transaminases),, HBsAg and HBeAg positivity determined by Enzyme-Linked Immuno Sorbent Assay (ELISA). Cases with hepatitis B positivity (>6 months) were excluded from the study as well as patients with IFN-based treatment, renal disease, other liver disease.

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Acute hepatitis is defined as hepatitis lasting less than six months and while it is considered to be chronic when it persists longer with symptomatic, biochemical, or serologic evidence of continuing or relapsing hepatic disease.

Anemia is defined as values of hemoglobin, hematocrit or red cell counts that are less than two standard deviation of the norm.

Pancytopenia is defined as a decrease in at least two out of three blood lineages.

On the day of clinical attendance, 2ml of venous blood was collected from each patient into a bottle containing potassium Ethylene Diamine Tetra Acetate [K2-EDTA]. The blood samples were then mixed with their anticoagulant for immediate analysis.

Complete blood analyzer (Sysmex) in addition to thin blood film were used to determine the red cell count, packed cell volume (PCV), mean cell hemoglobin (MCH), mean cell volume (MCV), mean cell hemoglobin concentration (MCHC), white blood cells (WBCs) counts, differentials of WBC and absolute platelet count. Such parameters are not routinely checked in the setting of acute hepatitis B in the country.

Ethical Approval

Ethical approval was obtained from Alneelain University ethical committee. Each patient signed an informed written ethical consent. Statistical analysis was done using SPSS for proportions, frequency, means and standard deviations. Statistical significance was specified at (P>0.05).

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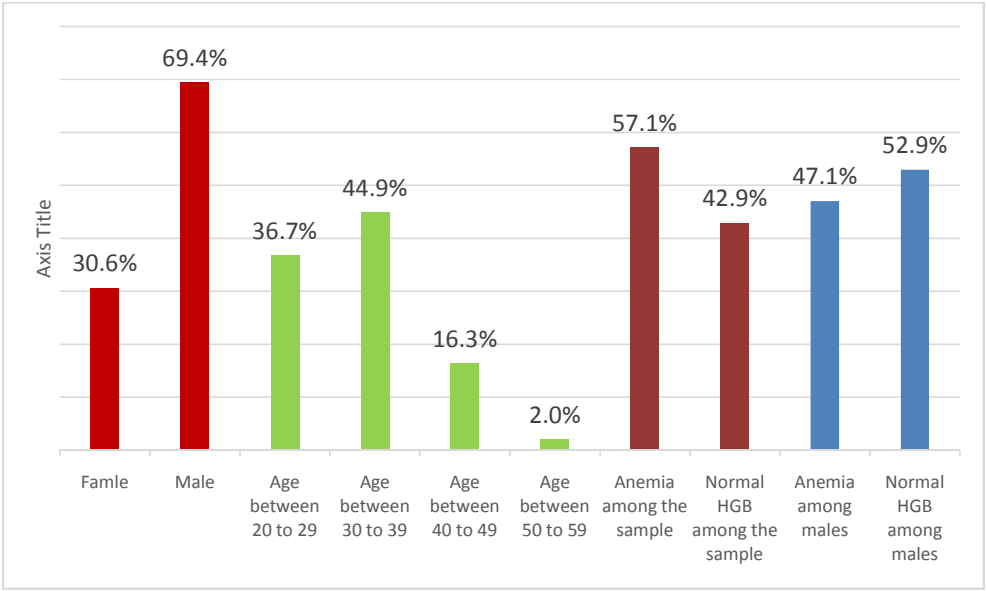
RESULTS:

figure 1 : MAIN FINDING OF THE STUDY 1



Our patient's population consisted of 49 patients, 34 male (69.4%), 15 female (31.6%) (Figure1), age of patients ranged between 22-55 with mean age 38.5 years old .Anemia was detected in (80%) of female (HBG<11.5g/dl) and (47.06%) in male (HBG<13.5g/dl). MCV normal in (75.51%), Microcytosis (MCV<80 fl) in (22.45%) and Macrocytosis (MCV>95 fl) in (2.04%). WBC counts were detected to be leucopenia (<4.000/mm3) in 12.24%, normal (4.000-11.000/mm3) in 79.59 % and leucocytosis (>11.000/mm3) in 8.16 % of the cases. The differential WBC showed Neutropenia (Neutrophils < 40%) was detected in 18.37% , Neutrophilia (Neutrophils >70%) in 10.20%, lymphocytosis in 40.72%. Table 1 shows haematological parameters comparing between male and female gender. Mean WBCs

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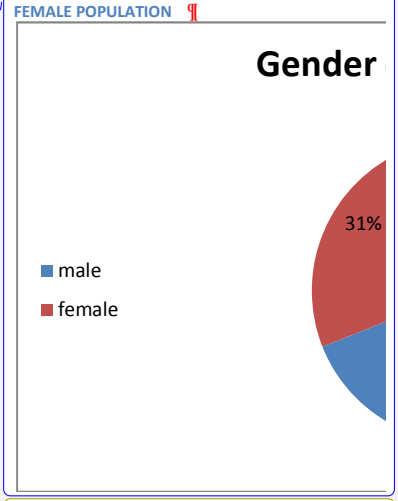

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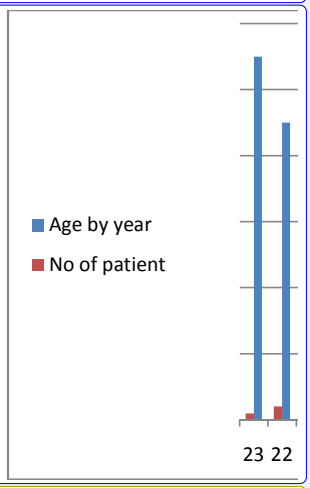
FIGURE 2: PATIENS NO IN RELATION TO AGE :Deleted



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count were 7.13±3.35×103/ mm3 and 6.55±2.53x103/mm3 for female and male respectively with no statistically significant (P > 0.05). Mean RBCs count were 4.23±.78×103/ mm3 and 4.93±.87x103/mm3 for female and male respectively with significant P value=.010. HBG was significantly loweramong females(mean 10.45±1.28 g/l) compared to males(mean 13.57±2.21g/l) with a significant P value =.000.Similarly, haematocrit wasalso lower among females(mean 34.62±4.4%) when compared to males(mean 39.87±7.72%)with P value 0.018.The duration of disease was divided in to twocategories, early (from first month up to third month of infection) and late (from forth month up to sixth month of infection), the higher frequency of patients' number was obtained in the second month (34.69%) but none the less the difference was not significant in terms of overall duration (P-value=.023) Thrombocytopenia was detected in 10.20% of cases and no case of pancytopenia was determined in our study.

TABLE 1: Difference between mean haemtological parameters in male and female groups

	Gender	Mean	Std. Deviation	P-value
Age	Female	31.67	4.81	.539
	Male	33.03	7.88	
WBCs	Female	7.13	3.35	.502
	Male	6.55	2.53	
RBC	Female	4.23	.78	.010
	Male	4.93	.87	
HBG	Female	10.45	1.28	.000
	Male	13.57	2.21	
HCT	Female	34.62	4.40	.018
	Male	39.87	7.72	
MCV	Female	83.69	12.13	.965
	Male	83.54	5.91	
MCH	Female	26.46	6.43	.368

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FIGURE 3: GROUP OF ANAEMIA AMONG FEMALE CASES WITH ACUTE HEPATITIS B **:Deleted**

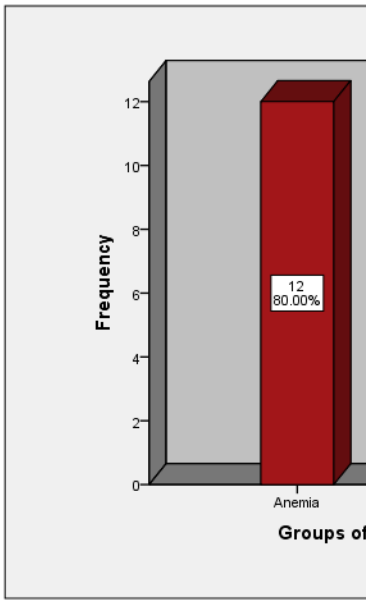

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FIGURE 4:GROUP OF ANAEMIA AMONG MALE CASES WITH ACUTE HEP **:Deleted** ... [3]

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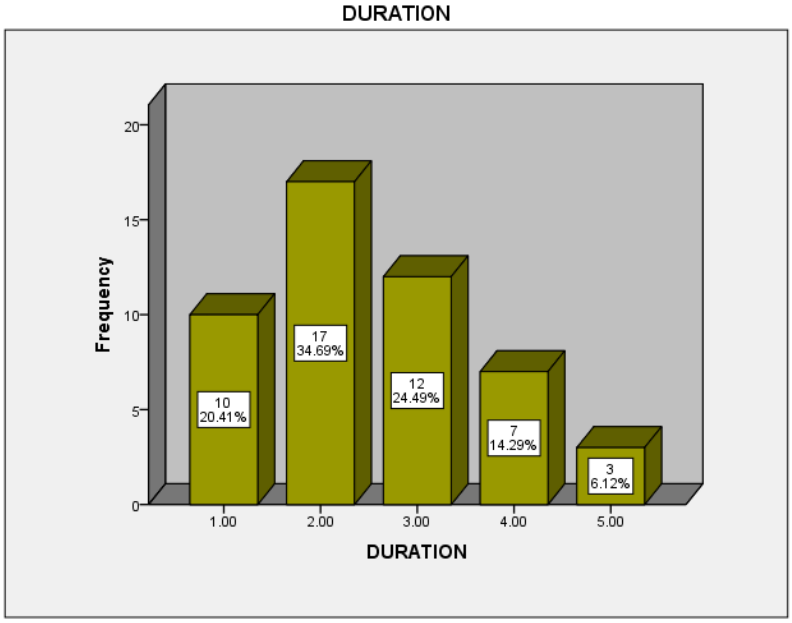
	Male	28.07	3.14	
MCHC	Female	30.89	3.79	.009
	Male	33.62	2.94	
PLT	Female	215.87	91.27	.300
	Male	241.79	74.49	
LYM	Female	14.43	14.43	.478
	Male	38.41	14.38	
EOS	Female	3.17	2.58	.833
	Male	3.04	1.70	
MONO	Female	3.73	2.49	.889
	Male	3.83	2.18	
NEUTRO	Female	51.44	13.94	.633

FIGURE 5: RELATION BETWEEN FREQUNCY OF CASES AND DURATION OF DISEASE IN MONTH



DISCUTION

Liver has many critical functions that affect general body metabolism, it forms and stores many of the elements and proteins needed in blood production, and therefore liver disease is associated with a broad spectrum of haematological abnormalities.

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This study aims to assess the haematological alterations accompanying acute hepatitis B viral infection.

In the current study, prominently higher (57.1%) rates of anemia was detected, this percentage is markedly increased when compared with other studies. (11-13) Not surprisingly as acute infections, either viral or bacterial, can cause anaemia through different mechanisms, such as mild idiopathic hemolysis and marrow inhibition(14). and more ever the burden of anemia remains highest in sub-Saharan Africa (15)In our cases, anaemia was detected in 80% of female of and (47.06%) in male. RBCs count; HBG and HCT were found to be decreased in female patients when compared to male groups with significant P values 0.010, 0.00 and 0.018respectively. Acute viral infection is not the unique cause of anaemia in our cases; it may also be due to nutritional or infectious reasons, in order to know the real cause further chemical and haematological investigations were needed. In mean corpuscular volume (MCV) Macrocytosis is detected in 2.04% while Microcytosis tended to be 22.45%, although there was no significant value between male and female (P value=.965), a significant haematological alteration in MCV overall (micro and macrocytosis) was detected with P-value =.000. In inflammation interleukin 6 and other cytokines increase hepcidin hormone the major hormonal regulator of iron homeostasis , lead to reduce iron absorption and iron release from macrophages and finally result in iron deficiency anemia(16), this may explain other mechanism causing anemia in our finding above ,since there was microcytosis had been observed. Furthermore dilution anemia is another possible explanation for this observation, as plasma volume is frequently increased in active hepatic disease (17).

Among WBCs group, Leucopenia was observed in 12.24% of cases it was relatively high when compared with previous studies (11-13) , while leukocytosis was detected in 8.16% and this percentage can comparable with Chinese study(12),but relatively high when compared with Nigerian one.(13) Leucopoenia rather than leucocytosis is a more frequent

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finding in acute viral hepatitis, though leucocytosis is often associated with fulminant viral hepatitis(18) , in recent years they discovered that HB virus directly invade the marrow interfering with leucopoiesis supports the more frequent finding of leucopaenia rather than leucocytosis(19),and this agrees with our finding in this study. Other alteration in WBCs was detected in neutrophil group, in which neutropenia was observed in 18.37% of cases, it was high percentage compared to that observed elsewhere(13) , neutrophilia also observed with high percent (10.20%). Lymphocytosis is another abnormality of WBCs differential, it is usually observes in viral infection, in our study, it was detected in 40.82% of all cases with P-value =.199. Acute and chronic hepatitis are characterized with marked infiltration of lymphocytes into the liver(20), this will result in liver injury in addition to elevated cytokine levels such as interleukin 6 (IL6) from such a response.

Liver disease is one of major causes of thrombocytopenia. Previous study conducted in London 2013 reported that liver disease is the cause of thrombocytopenia in 58% of outpatients(21).In our study thrombocytopenia was detected in 10.20% of cases, this finding is completely differ from Nigerian study(13), in which no case of thrombocytopenia had been observed, but agrees with other studies (11, 12) as thrombocytopenia had been reported. Agrees with previous studies (11, 13) no case of pancytopenia was detected in our study.

One of the limitations of the current study is the small sample size, another limitation is the reliance on the patients recall to the onset of symptoms a thing that might lead recall bias.

Conclusion

In summary, the present study suggested that Sudanese patients have more haematological abnormalities following acute hepatitis B viral infection, Such an observation reflectsan an important public health problems in our country. Haematology tests should be included in

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routine diagnostic investigations as well as follow up diagnosis, in order to avoid fatal complications.

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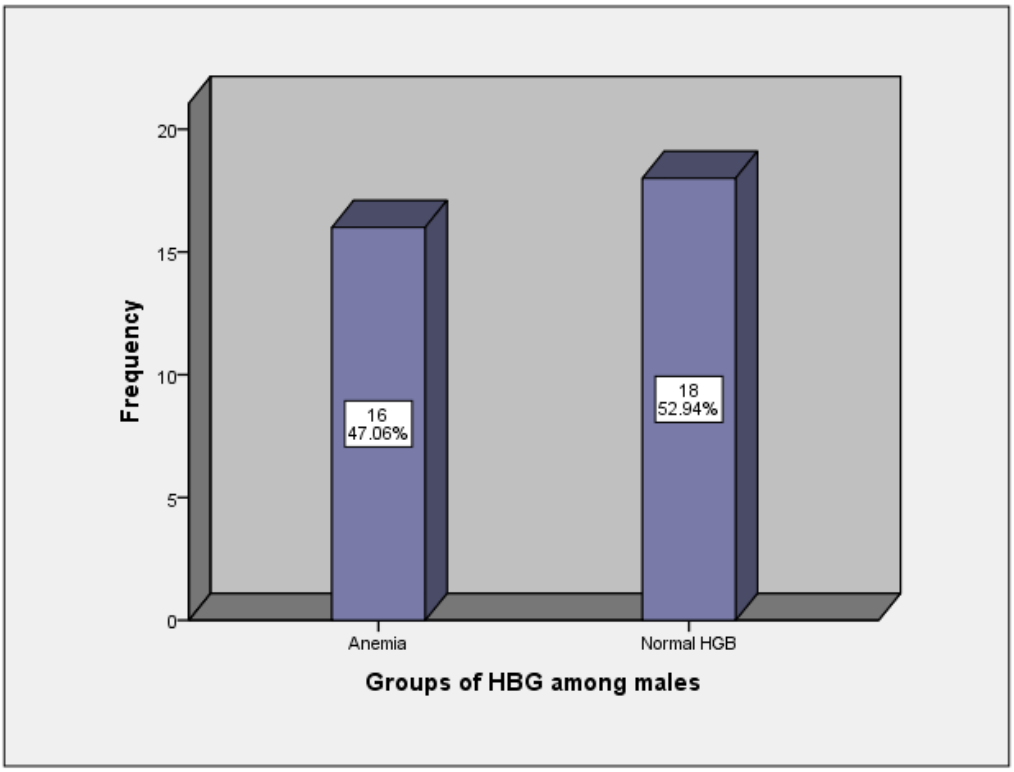

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