



## HAEMATOLOGICAL PARAMETERS IN NIGERIANS WITH ACUTE VIRAL HEPATITIS

F. A. Fasola\*, J. A. Otegbayo\*\*, U. M. A. Abjah\* and S.O. Ola\*\*

*Departments of Haematology\* and Medicine\*\*, University College Hospital /University of Ibadan, Departments of Haematology, Ibadan, Nigeria.*

Correspondence Address: Dr. EA Fasola, Departments of Haematology, University College Hospital / University of Ibadan, Ibadan, Nigeria. *E-mail:* folukefasola@yahoo.com

### ABSTRACT

**Background:** Alteration in hematological profile is a common finding in systemic and infectious diseases. The knowledge of the frequency of the haematological abnormalities in patients with acute viral hepatitis will support the need for this indispensable tool in the investigation of infectious diseases. The objective of this study is to describe the haematological profile of patients with acute viral hepatitis

**Methods:** Packed cell volume (PCV), white blood cell count (WBC), platelet count, prothrombin Time (PT) and partial thromboplastin time in kaolin (PTTK) were reviewed in 50 patients with acute viral hepatitis at the Gastroenterology and Haematology clinics of the University College Hospital Ibadan compared with controls. The patients were not followed up for outcome of disease.

**Result:** Among the patients, anaemia was detected in 12(24%) with mean WBC count of  $8.1 \pm 11.4 \times 10^9 / \text{mm}^3$ . The WBC count was abnormal in 8(16%) of the patients; 2(4%) of the patients were leucopenic. Neutrophilic and lymphocytic leucocytosis were observed in 6(12%) patients. Thrombocytopenia was not observed in any of the patients. One third of the patients had abnormal coagulation profile.

**Conclusion:** Haematological abnormalities in patients with acute viral hepatitis are non-specific. However, abnormal haematological profile found in one quarter of the patients underscores the need for routine blood count in acute viral hepatitis. Follow up of patients with leucopenia or bicytopenia even after recovery from acute viral hepatitis should constitute an essential part of these patients' management.

**Keywords:** Haematological Parameters, Nigerian, Acute Hepatitis.

### INTRODUCTION

Viral hepatitis continues to be a disease of major significance, in terms of both morbidity and mortality<sup>1</sup>. The incidence in sub-Saharan Africa ranges between 9% and 20%<sup>2</sup>. Various viral agents have been implicated in the aetiology of viral hepatitis. These viral agents range from specific hepatotropic viruses which include hepatitis A, B, C, D, E and G to systemic viral infections example of which are Epstein Barr virus and Herpes simplex. However, the most frequent aetiological agents of acute viral hepatitis (AVH) associated with high health burden in sub-Saharan

Africa are Hepatitis B and C viruses. In addition to the hepatic pathology, extrahepatic abnormalities are not unusual<sup>3</sup>. One of the most frequently identified extrahepatic abnormalities often seen at the time of diagnosis of AVH is the haematological abnormality. This is because every patient with acute viral hepatitis of necessity will require a full blood count to exclude bacterial sepsis as a cause of liver disease. The interpretation of the result will require an understanding of the frequency of detection of abnormal haematological results in these patients in relation to the disease. Patients with AVH unlike those with chronic



## Haematological parameters

hepatitis often present with non specific symptoms which may mimic other more common infections seen in sub-Saharan Africa. These other infections like malaria and typhoid fever sometimes present with some degree of hepatic involvement<sup>4</sup>. Alteration in the blood count may exclude to some reasonable extent the presence of these other infections. The knowledge of the frequency of haematological abnormalities will not only underscore the need for a blood count in all patients with acute viral hepatitis, it will also help to identify those patients that will need to be followed up or require additional treatment.

Viral hepatitis is a pan tropic disease with haematological manifestations<sup>5</sup>. Alteration in haematological profile may predict those likely to have haematological complications even after recovery from the acute viral hepatitis<sup>6</sup>. Therefore this study was carried out to describe the haematological abnormalities observed in Nigerian patients with acute viral hepatitis.

## PATIENTS AND METHODS

Fifty patients with clinical and laboratory evidence of acute uncomplicated viral hepatitis seen at the medical out-patient (MOP) gastroenterology clinic of the University College Hospital, Ibadan (UCH), were recruited into the study. Clinical features were jaundice, dark urine, anorexia, right upper quadrant abdominal pains, while laboratory parameters included alanine transaminase (ALT) rise greater than five times upper limit of normal (>200 IU/L) as well as Hepatitis B surface antigen (HB<sub>s</sub>Ag) and antibody to Hepatitis C virus (anti-HCV) determined by Enzyme-linked immunosorbent assay (ELISA). Fifty age and sex-matched control subjects were also recruited from apparently healthy individuals who were HB<sub>s</sub>Ag and anti-HCV negative.

On the day of hospital attendance, 2ml and 4.5ml of venous blood were collected from each patient into two bottles containing potassium ethylenediamine tetra-acetate [K<sub>2</sub>EDTA] and 0.5ml trisodium citrate respectively. The blood samples were then mixed with their respective anticoagulant for immediate analysis.

The blood samples in K<sub>2</sub>EDTA bottle were used to determine the packed cell volume (PCV), white blood cell (WBC) counts, differentials of WBC and absolute platelet count. The blood count parameters were assessed using the manual method as described by Dacie and Lewis<sup>7</sup>.

Blood samples were also similarly collected from controls for same tests that were conducted on the samples of patients. The coagulation profile was assessed using one stage prothrombin time to determine the prothrombin time and partial thromboplastin time in kaolin (k) by manual methods as described by Proctor and Rapaport<sup>8</sup>.

Statistical analysis was done using SPSS version 9.0 for proportions, frequency, means and standard deviations. Statistical significance was specified at (P>0.05).

## RESULTS

Patients' age ranged between 11-76 years with 30 males and 21 females. The male female sex ratio was 1.5:1. HB<sub>s</sub>Ag was positive in 47(94%) patients, while 18(36%) were seropositive for anti-HCV. Fifteen (30%) patients were seropositive for both viral markers.

Anaemia was detected in 12 (24%) patients. The mean PCV were 36.2L/L and 35.3L/L for males and female patients respectively. These were relatively lower than the 41.1L/L and 37.1L/L respectively obtained in controls. The statistical significance of this was only observed in the males (P = 0.00).

The mean WBC count among the patients was  $8.1 \pm 114 \times 10^9/L$  compared to  $5.2 \pm 1.6 \times 10^9/L$  in controls; the difference was, however, not statistically significant (P > 0.05). The changes in WBC tended to be more marked in male patients whose WBC range was 2.0-15.0x10<sup>9</sup>/L compared to 1.6-12.0x 10<sup>9</sup>/L in female patients(Table1). The WBC was abnormal in 8(16%) of the patients. Both leucocytosis and leucopenia were observed (Table-1).The patients with leucocytosis had both neutrophilic and lymphocytic leucocytosis. HB<sub>s</sub>Ag seropositivity was found in all patients with leucocytosis. Leucopaenia was observed in a patient with dual infection and one patient with hepatitis B virus infection only. The patient with dual infection also had anaemia with a PCV of 24L/L, though platelet count was normal. The platelet count was within the normal limit for all the patients.

Table 2 shows the WBC differentials of the patients and control. The eosinophil count ranged from 0.16-1.5x10<sup>9</sup>/L. Prothrombin time (PT) and Partial thromboplastin time in kaolin (PTTK) were as shown in Table 2. There was no significant correlation between the coagulation studies, white blood cell count and the hepatitis viral type.



F. A. Fasola, J. A. Otegbayo, U. M. A. Abjah and S.O. Ola

Table 1: Frequency of Haematological changes in patients with acute viral Hepatitis

Parameters	Number of patients(%)
PCV (mean+- SD:35.8±8.3L/L (range : 18-50L/L)	
Normal PCV	38(76)
Anaemia	12(24)
WBC count (mean+-SD: 8.1 ±11.4x10 <sup>9</sup> /L (range:1.6-15.0x10 <sup>9</sup> /L)	
Normal WBC count	42(84)
Leukocytosis	6(12)
Leukopenia	2(4)
Platelet count (mean+-SD:241,280 ±60,653x10 <sup>9</sup> /L (range: 135,000-399,000x10 <sup>9</sup> /L)	
Normal platelet count	50(100)
Thrombocytopenia	0(0)
PT(mean+-SD)15±4 s (range: 10-39s)	
Normal PT	31(62)
Prolonged PT	16(32)
Shortened PT	3(6)
PTR(mean+-SD) 1.2±0.35s	
PTTK (mean+-SD) 53±24s (range: 25-128 s)	
Normal PTTK	30(60)
Prolonged PTTK	18(36)
Shortened PTTK	2(4)

Control (mean+-SD) PCV-40±3.0L/L

WBC-5,2±1.6x10<sup>9</sup>/L

Platelet- 209,940±55.500 x 10<sup>9</sup>/L;

PT-12s

PTTK-40s

## DISCUSSION

The liver has incontrovertible influence on several essential functions of many organs in the body the haematopoietic system inclusive. Besides its role as an extravascular haemopoietic organ in early foetal life and bone marrow infiltrative disease, the liver forms and stores many of the elements and proteins necessary in blood production. It also plays an active role in the haemostasis.

Marked anaemia is an infrequent finding in patients with acute viral hepatitis<sup>7</sup>. The anaemia observed in 24% of our patients is not unusual in acute viral hepatitis<sup>9</sup>. Haematocrit in most patients with acute viral hepatitis decreases gradually during the first three weeks of illness<sup>10</sup>. This is attributed to a temporary bone marrow suppression and autoimmune haemolytic anaemia which may accompany viral hepatitis<sup>11</sup>. Shared epitopes of viral and human antigens presented by antigen presenting cells are known to be capable of causing an autoimmune trigger<sup>11,12</sup>. Increased haemolysis has also been observed in many patient with acute hepatitis due to extravascular defect in the red cells which leads to shortened red cell life span<sup>13,14</sup>. Dilutional anaemia is another possible explanation for this observation, as plasma volume is frequently increased in active hepatic disease<sup>5</sup>. Haemolytic disorder associated with viral hepatitis is often undetected because bilirubinaemia is usually attributed solely to liver disease and reticulocytosis does not occur until patient recovers from the acute symptom of hepatitis due to temporary bone marrow suppression<sup>10</sup>.

The leucocytosis observed in 12% of the patients is comparable to that observed elsewhere<sup>15</sup> but relatively lower than that observed in Turkey<sup>16</sup> in paediatric patients. Leucopaenia rather than leucocytosis is a more frequent finding in acute viral hepatitis, though leucocytosis is often associated with fulminant viral hepatitis<sup>18</sup>. Patients with anemia, thrombocytopenia or leukocytosis were observed to have significantly higher mean levels of serum bilirubin

Table 2. WBC differential count in patients and controls

Parameter(WBC)	Patients:mean+-SD	Controls:mean+-SD	P value
Neutrophils	4,446±1,466	2,451±131	0.0001
Lymphocytes	3,266±1,294	2,398±139	0.011
Monocyte	266±297	394±27	0.0001
Eosinophil	323±641	158±19	0.051
Basophil	0	0	



## Haematological parameters

and higher proportions of prolonged prothrombin time, suggesting that these haematological abnormalities were closely related to the severity of hepatocellular damage<sup>15</sup>. The discovery in recent years that leucocyte is another non-hepatic site for HBV replication and that the virus directly invade the marrow interfering with leucopoiesis supports the more frequent finding of leucopaenia rather than leucocytosis<sup>19</sup>.

Leucopaenia is less frequent in our patients when compared with other studies<sup>15,16</sup>. Leucopaenia develops, faster than anaemia because circulating red cells have a longer life span than white blood cells. Pancytopenia was not observed in any of our patients but it is worth noting that bicytopenia (anaemia and leucopenia) occurred in 4% of the patients. The consistent presence of hepatitis B infection in these patients suggests that hepatitis B virus is a culprit for serious haematological complication. Rarely patients with acute viral hepatitis proceed to develop a fatal aplastic anaemia,<sup>15</sup> therefore it will be necessary to follow up patients who develop leucopaenia or bicytopenia to exclude eventual aplastic anemia. Many authors suggest that virus infection provokes hypersecretion of IL-2, IFN-g and M-CSF from activated Th1 cells. Stimulated by these cytokines, macrophages proliferate, engage in hemophagocytosis and release IL-1, IL-6, TNF-a and ferritin. The resultant hypercytokinemia is assumed to be responsible for pancytopenia, bone marrow suppression and even disseminated intravascular coagulation.

It is interesting to observe that all our patients had normal platelet count though mild to moderate thrombocytopenia is not unusual in patients with acute viral hepatitis. HCV antibody positive individuals are 2.6 times more likely to have a low platelet count than those who are HCV antibody negative<sup>21</sup>.

Coagulation failure during the course of acute viral hepatitis is regarded as of prognostic importance. Bleeding in patients with acute viral hepatitis could be due to defect in vessel wall (Capillary fragility), Platelet, components of coagulation and in clot stability. Coagulation failure with prolonged prothrombin time and partial thromboplastin time in Kaolin usually indicate considerable parenchymal damage in contrast to purpuric haemorrhages with increased capillary fragility with or without thrombocytopenia which can occur in mild hepatic disease<sup>16</sup>.

A normal coagulation studies in two third of the patients suggests good prognosis with minimal hepatocellular damage in a significant proportion of the patients. Hypercoagulable state in some patients is

an unusual finding and may be due to traces of tissue factor from damaged hepatic cells resulting in low grade activation of extrinsic pathway. The use of herbal drugs which is common in our environment, may modify the coagulation profile of the patient.

## CONCLUSION

The haematological change in Nigerian patients with acute viral hepatitis is non-specific. Anaemia, leucocytosis and leucopaenia, are haematological abnormalities detected in these patients with uncomplicated viral hepatitis. Patients with leucopaenia should be followed for early detection of serious haematological complication even after recovery from the acute state. Thrombocytopenia is uncommon in our patients. There is need to further investigate those patients with hypercoagulable state and follow them up for eventual outcome.

## REFERENCES

1. Fakunle YM, Abdurrahman MB and Whittle H.B: Hepatitis B virus infection in children and adults in Northern Nigeria: A preliminary survey. *Trans. Roy. Soc. Trop. Med and Hyg.* 1981; 75: 626-629.
2. Kiire CF: The epidemiology and prophylaxis of hepatitis B in Sub-Saharan Africa: a view from tropical and subtropical Africa. *Gut* 1996; 38(Suppl. 2): 55 - 62.
3. Ikram N, Hassan K and Tufail F: Hepatitis-associated autoimmune haemolytic anaemia. *Int. J Pathol.* 2004; 2:44-46
4. Abro AH, Abdou AMS, Gangwani JL, Ustadi AM, Younis NJ and Hussaini HS: Hematological and biochemical changes in typhoid fever. *Pakistan J Med. Sci.* 2009; 25: 166-171
5. Conrad ME., Schwartz FD and Young AA: Infectious Hepatitis - a generalized disease. A study of renal, Gastrointestinal and Haematologic abnormalities. *Am J Med.* 1964; 37: 789-801.
6. Piccinini L, De Rienzo B, Bagnulo A, Curci G, Sacchi S and Di Marco G: Hematological complications of viral hepatitis. Case-list contribution. *Boll Ist Sieroter Milan.* 1984; 63: 319-324
7. Laffan MA and Bradshaw AE: Investigation of haemostasis: In Dacie JV, Lewis SM (ed).



*F. A. Fasola, J. A. Otegbayo, U. M. A. Abjah and S.O. Ola*

- Practical Haematology. Eight Edition. London Churchill Livingstone. 1999; 297-315.
8. Proctor RR and Rapaport SI. The partial thromboplastin time with kaolin. A simple screening test for first stage plasma clotting factor deficiencies. *American Journal of clinical Pathology* 1961; 36: 212-219.
  9. Perseghin P, Balduini CL., Piccolo G, Bertolino G, Bellusci M, Scelsi R *et al*. Guillain-Barre -a syndrome with autoimmune hemolytic anemia following acute viral hepatitis. *Italian J Neurol. Sci.* 1985; 6: 447-450
  10. Conrad ME, Schwartz FD and Young A.A. Viral hepatitis in Korea: clinical observation and studies performed during prospective studies to obtain specimens for virologic culture. *Progr. Liver Dis.*, 1965; 2: 395 – 415..
  11. Gumba SC and Chopra S. Hepatitis C: a multifactorial disease, review of extrahepatic manifestations. *Ann Intern Med.* 1995; 123: 615 – 620.
  12. Fellermann K and Stange EF Chronic hepatitis C, common variable immunodeficiency and autoimmune haemolytic anaemia - Coincidence by chance or common aetiology? *Hepatogastroenterology* 2000; 47: 1422- 1424.
  13. Conrad M.E. Persistent haemolysis after infectious hepatitis . *Gut.* 1969; 10: 516-521.
  14. Katz R, Velasco M, Guzman C and Alessandri H. Red cell survival estimated by Radioactive chromium in Hepatobiliary disease. *Gastroneterology.* 1964; 46: 399 – 404.
  15. Lin SM, Chu CM, Shih LY and Liaw YF Hematological abnormalities in acute viral hepatitis and acute hepatitis in HBsAg carrier *Changeng Yi Xue Za Zhi.*1991; 14: 253-258.
  16. Akarsu S, Erensoy A, Elkran O, Abdullah Kurt,A. Nefle Çatak Kurt and A. Denizmen Aygün. Haematological abnormalities in patients with acute viral hepatitis. *Ipediatr Inf* 2008; 3: 90 -95
  17. Seeff LB Diagnosis, therapy and prognosis of viral Hepatitis . In *Hepatology A text book of liver disease.* Zakim D, Boyer T.D (edi). Second edition vol. 2. WB. Saunders Co. London 1990; 958 – 1025.
  18. Pontissc O, Poon MC and Tiollais P, Brechot C. Detection of hepatitis B Virus DNA in mononuclear blood cells. *BMI.* 1984; 288: 1563 – 1566
  19. Jones GP and Evans EG. Idiopathic thrombocypaenic purpura in infective hepatitis *BMI* 1951; 2: 451 – 452.
  20. Ogha S, Matsuzaki A, Nishizaki M, Nagashima T, Kai T, Suda M and Ueda K. Inflammatory cytokines in virus-associated hemophagocytic syndrome. *Am J Ped Hem/Onc* 1993; 15: 291–298.