

Platelet count can be used to determine the severity of oesophageal varices

Okonkwo K.C.¹, Olokoba A.B.², Bojuwoye O.M.², Aliyu, A.M.³

¹Department of Medicine, Federal Medical Centre, Owo, Nigeria

²Department of Internal Medicine, University of Ilorin, Ilorin, Nigeria

³Department of Internal Medicine, University of Ilorin Teaching Hospital, Ilorin, Nigeria

Article Info

Article type:

Original Article

Article history:

Received: March 15, 2024

Accepted: June 30, 2024

Published: December 15, 2024

Keywords:

Varices, endoscopy, platelet count

Corresponding author:

Okonkwo K.C.

ORCID-NO:<https://orcid.org/0000-0000-circumzided@yahoo.com>

circumzided@yahoo.com

The article can be accessed at:

www.rjhs.org

<http://dx.doi.org/10.4314/rjhs.v12i4.5>

Abstract

Introduction: Variceal haemorrhage is one of the most devastating consequences of portal hypertension. The risk of bleeding increases with severity of varices. It is important to see if there are parameters that can non-invasively predict severity of varices as endoscopy has some limitations.

Aims and Objectives: This study sought to determine if platelet count can be used to determine the severity of oesophageal varices in a low resource setting.

Methodology: This was a descriptive cross-sectional study, in which 79 patients with chronic liver disease and upper gastrointestinal endoscopy diagnosed varices were recruited consecutively to participate in the study. Blood sample for platelet count was taken from each patient. A proforma was used to document the demographic parameters as well as grade of varices and platelet count. The ability of platelet count to determine severity of oesophageal varices was assessed. Test of association between platelet count groups and grades of varices was carried out using the Chi-Square Test. Test of correlation between platelet count and grades of varices was carried out using the Spearman's coefficient.

Result: A total of 79 subjects were recruited into the study. Test of correlation between platelet count and grades of varices was statistically significant (ρ value: -0.783; p value: 0.001). There was a statistically significant difference in the median platelet count and grade of varices ($p < 0.0001$).

Conclusion: Platelet count, a simple, cheap and available investigation, can be used as a non-invasive predictor of severity of varices in resource poor settings with limited endoscopy services.

La numération plaquettaire peut être utilisée pour déterminer la gravité des varices œsophagiennes

Résumé

Introduction: L'hémorragie variqueuse est l'une des conséquences les plus dévastatrices de l'hypertension portale. Le risque de saignement augmente avec la gravité des varices. Il est important de voir s'il existe des paramètres permettant de prédire de manière non invasive la gravité des varices, car l'endoscopie présente certaines limites.

Buts et objectifs : Cette étude visait à déterminer si la numération plaquettaire pouvait être utilisée pour déterminer la gravité des varices œsophagiennes dans un contexte à faibles ressources.

Méthodologie: Il s'agissait d'une étude transversale descriptive, dans laquelle 79 patients atteints d'une maladie hépatique chronique et de varices diagnostiquées par endoscopie gastro-intestinale haute ont été recrutés consécutivement pour participer à l'étude. Un échantillon de sang pour la numération plaquettaire a été prélevé sur chaque patient. Un formulaire a été utilisé pour documenter les paramètres démographiques ainsi que le grade des varices et la numération plaquettaire. La capacité de la numération plaquettaire à déterminer la gravité des varices œsophagiennes a été évaluée. Le test d'association entre les groupes de numération plaquettaire et les grades de varices a été réalisé à l'aide du test du Chi carré. Le test de corrélation entre la numération plaquettaire et le grade des varices a été réalisé en utilisant le coefficient de Spearman.

Résultat: Au total, 79 sujets ont été recrutés dans l'étude. Le test de corrélation entre la numération plaquettaire et le grade des varices était statistiquement significatif (valeur ρ : -0,783 ; valeur p : 0,001). Il y avait une différence statistiquement significative dans la numération plaquettaire médiane et le grade des varices ($p < 0,0001$).

Conclusion: La numération plaquettaire, une enquête simple, peu coûteuse et disponible, peut être utilisée comme prédicteur non invasif de la gravité des varices dans les contextes aux ressources limitées et aux services d'endoscopie limités.

Mots clés: Varices, endoscopie, numération plaquettaire

INTRODUCTION

Variceal haemorrhage is one of the most devastating consequences of portal hypertension. It is an ominous event associated with a 15% to 20% 6-week mortality for each episode in spite of endoscopic and pharmacologic therapies,(1) with a 1-year mortality of 40%.(2) These therapies include variceal band ligation, injection sclerotherapy, somatostatin and vasopressin analogues, transjugular intrahepatic portosystemic shunt (TIPSS).(3) Variceal bleeding is the second commonest complication of chronic liver disease.(4–6) Varices can be formed in any part of the gut; however oesophageal varices is the major cause of variceal bleeding.(4) This is probably because varices become more superficial in the distal oesophagus predisposing to rupture and bleed.

The risk of bleeding from oesophageal varices is related to the severity of varices i.e large varices are more likely to bleed than small varices.(7)

Periodic endoscopic surveillance for oesophageal varices is currently recommended in every patient with cirrhosis for early detection of oesophageal varices and thus initiation of primary prophylaxis for variceal bleeding especially for high-risk patients. (8) Unfortunately, endoscopy is not readily accessible in most LMICs on account of cost.(9,10) It is also invasive, uncomfortable and fraught with complications.(11) In fact, inability to afford endoscopy is one of the reasons for mortality from upper gastrointestinal bleeding in this environment.(9)

Several non-invasive tests have emerged, aiming to facilitate access, reduce cost, and avoid unnecessary risks associated with endoscopic oesophageal variceal surveillance.(8) These include platelet count, spleen diameter, portal vein diameter, Child-Pugh classification, prothrombin activity, presence of telangiectasias, presence of ascites and transient elastography. Others include computed tomography scan and magnetic resonance imaging. (12,13)

Platelet count is one of the most amenable tools that have been evaluated for risk assessment of varices. Some studies in Sub-Saharan Africa has clearly shown that platelet count can be helpful in the delineation of large varices.(11)

The aim of this study is to add to the evidence and show that platelet count can indeed select high risk varices.

MATERIALS AND METHODS

The study was a cross-sectional, descriptive study carried out at the University of Ilorin Teaching Hospital (UIITH), Ilorin. The study population were patients with chronic liver disease presenting for gastroscopy at the endoscopy suite of the University of Ilorin Teaching Hospital over a 3-year period (January 2016 to December 2018). Each patient was adequately counselled on the need for upper GI endoscopy, and the procedure adequately described.

The patient was made to fast for 6-8 hours. On the morning of the procedure, a written consent was taken from the patient. Dentures if present were removed. They also had 10% plain xylocaine spray applied to the pharynx before undergoing upper GI endoscopy. The patient was placed in the left lateral position and with a mouth guard in place; the distal lubricated end of the endoscope was introduced into the mouth under direct vision. The patient was asked to swallow and the instrument advanced into the oesophageal lumen and presence and size of oesophageal varices were noted. The findings were recorded. They may also be classified into 3 sizes—small, medium, or large (Grade 1, 2 or 3)—as occurs in most centres by a semi-quantitative morphological assessment viz;

- Small varices are defined as minimally elevated veins above the oesophageal mucosal surface.
- Medium varices are defined as tortuous veins occupying less than one-third of the oesophageal lumen.
- Large varices are defined as those occupying more than one-third of the oesophageal lumen.

The procedure was carried out by the principal researcher. After the procedure, the patient was taken to the recovery room and monitored. Patients were also counselled on the findings on endoscopy, their implications and further care.

Ethical approval for the study was obtained from the University of Ilorin Teaching Hospital, Kwara State Research Ethics Committee with number ERC PAN/2016/06/1568. Individual informed consent was sought and documented, in accordance with the Helsinki Declaration.

The data was entered in SPSS Version 21.0 (Chicago, IL, USA). Test of association between platelet count groups and grades of varices was carried out using the Chi-Square Test. Test of correlation between platelet count and

grades of varices was carried out using the Spearman's co-efficient. Test of association between platelet count and grades of varices was carried out using the Chi-Square Test. All p values were two-tailed, with significance level of $p < 0.05$.

RESULTS

The mean age (SD) of the studied population was $47.5(\pm 9.9)$ years. There were 13 (16.5%) females and 86 (83.5%) males, with a male: female ratio of 6:1. Nineteen subjects (24.1%) had grade one varices; 32 (40.5%) had grade two varices and 28 (35.4%) had grade three varices.

The mean age (SD) of the studied population was $47.5(\pm 9.9)$ years. There were 13 (16.5%) females and 86 (83.5%) males, with a male: female ratio of 6:1 (Table 1).

Table 2 shows the frequency of varices based on grade. Nineteen subjects (24.1%) had grade one varices; 32 (40.5%) had grade two varices and 28 (35.4%) had grade three varices.

In Table 3, the platelet groups with larger numbers were significantly associated with lower grades of oesophageal varices ($p < 0.0001$).

Figure 1 showed that study subjects with small varices tended to have higher platelet count compared to those with medium or large varices.

Spearman's correlation also showed a significant negative correlation between platelet count and grades of esophageal varices

Median platelet count was also significantly lower in patients with grade varices as compared to patients with grade I varices ($p < 0.0001$).

DISCUSSION

The mean age of the patients recruited into this study was 47.5 ± 9.9 years (Table 1). The high frequency of patients with CLD found in the 5th decade of life as seen in this study is comparable with the mean age of patients in other low-and middle-income countries (LMIC) as ours.(14) This is in contrast to a study done in Sri Lanka where majority (28.6%) of the patients were in the over 60year age group(15) This difference is occasioned by the fact that the causative agent in the latter study was non-alcoholic fatty liver disease patients as compared to viral hepatitis which is the significant cause of morbidity and mortality in this environment. This peak age underscores the socio-economic impact of the disease as it targets the age group that constitutes the critical workforce in the country with its attendant effect on productivity.

One hundred and two subjects were recruited with 81 (79.4%) being males and 21 (20.6%) being females with a male: female ratio of 4:1. This is consistent with previous reports where males were the predominant gender.(16,17) This could be as a result of the fact that males are more involved in risky behaviour such as chronic alcohol ingestion which may predispose to chronic liver disease.(18) It is also known that the male gender is a risk factor for reactivation of HBV infection -after seroconversion of hepatitis B e antigen- and subsequent development of cirrhosis and hepatocellular carcinoma (HCC).(19)

Many of the participants had grade two varices (40.5%; Table 2). Of the remainder, 24.1% had grade one varices, and 35.4% had grade three varices. This is similar to the report by Mahassadi et al. and that by Kim et al.(20) where grade two varices were the commonest. The high risk varices were commoner in this study unlike studies done elsewhere Grade 1 varices predominate.(12,13)

In this study, increased platelet count greater than $150,000\mu\text{L}$ showed significant association with lower grades of varices ($p < 0.0001$) as seen in Table 3. It has been suggested that patients with chronic liver disease patients with normal platelet counts (above 150,000), especially in developing countries, can avoid screening endoscopy as they are at a low risk for variceal bleeding, and presence of large oesophageal varices (OVs) in these patients is much less common than in those with thrombocytopenia.(21) The Baverno VI consensus also proposes that patients with compensated cirrhosis with liver stiffness < 20 kPa (determined by transient elastography) and a platelet count $> 150,000/\text{mm}^3$ were very unlikely to have high-risk varices ($< 5\%$), and endoscopy could be safely avoided in them.(22) Another study also showed that high-risk varices in patients with hepatocellular carcinoma treated with levantinib were independently associated with platelets $< 150,000/\mu\text{L}$ (OR: 2.47; 95% CI: 1.35–4.50, $p = 0.003$).(23) This may be useful as about many as 84% of patients with cirrhosis have thrombocytopenia, and it is an independent variable indicative of advanced disease and poor prognosis.(24) One study showed that the mean percentage of small platelets were higher in patients who did not have OV compared with those with OV (40% versus 13% respectively, $P = 0.006$).(15)

Our study also showed that there is a significant negative correlation between the

platelet count and grades of esophageal varices ($\rho = -0.783$; $p < 0.0001$). This agrees with many studies done in Europe and Asia where there is similar significant correlation. (25,26) This was further confirmed by a meta-analysis that showed that pooled correlation coefficient between platelet count and grading of oesophageal varices in liver cirrhosis $r = -0.42$ (95%CI -0.65 to -0.13 ; $p = 0.005$; $I^2 = 96.06\%$). (27)

Median platelet count was also found to have significant relationship to grade of varices as seen in this study (Table 5). Many studies also show similar results. (25,28–30) The only study noted that seems to dispute the fact that platelet count can be used as a useful surrogate in the evaluation and treatment of patients with chronic liver disease was done in patients with compensated cirrhosis (15) The patients with chronic disease in this environment however are usually seen in the decompensated state.

There is no doubt that the mechanism of thrombocytopenia in chronic liver disease patients suggests that it has a role to play in the identification of patients with advanced disease which will benefit from primary prophylactic therapy against variceal haemorrhage.

It is hoped that more studies will be carried to establish the role of platelet as a surrogate marker for higher grades of oesophageal varices and possibly reduce the current need for endoscopy in patients with chronic liver disease. This will go a long way to reducing the morbidity and mortality of the condition in this environment.

Acknowledgments: We wish to thank the endoscopy nurses for their unalloyed support and professionalism throughout the course of the study.

Conflict of interest: The authors declare no conflict of interest.

Authors contribution: Okonkwo K.C. conducted the acquisition of data, analysis and interpretation of data. Okonkwo K.C. and Olokoba A.B. did the conception and design of the manuscript. Olokoba A.B. and Bojuwoye O.M. was involved in the drafting of the article and revision. Aliyu, A.M. did the article revision.

REFERENCES

- Villanueva C, Piqueras M, Aracil C, Gómez C, López-Balaguer JM, Gonzalez B, et al. A randomized controlled trial comparing ligation and sclerotherapy as emergency endoscopic treatment added to somatostatin in acute variceal bleeding. *J Hepatol.* 2006 Oct;45(4):560–7.
- Rajoriya N, Tripathi D. Historical overview and review of current day treatment in the management of acute variceal haemorrhage. *World J Gastroenterol.* 2014 Jun 7;20(21):6481–94.
- Jalan R. UK guidelines on the management of variceal haemorrhage in cirrhotic patients. *Gut.* 2000 Jun 1;46(90003):1iii–15.
- Liu YB, Chen MK. Epidemiology of liver cirrhosis and associated complications: Current knowledge and future directions. *World J Gastroenterol.* 2022 Nov 7;28(41):5910–30.
- Topdagi O, Okcu N, Bilen N. The Frequency of Complications and the Etiology of Disease in Patients with Liver Cirrhosis in Erzurum. *Eurasian J Med.* 2014 Jun 21;46(2):110–4.
- Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS. Liver cirrhosis. *The Lancet.* 2021 Oct;398(10308):1359–76.
- D'Amico G, Luca A. 3 Natural history. Clinical-haemodynamic correlations. Prediction of the risk of bleeding. *Baillieres Clin Gastroenterol.* 1997 Jun;11(2):243–56.
- D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies. *J Hepatol.* 2006 Jan;44(1):217–31.
- Alatise OI, Aderibigbe AS, Adisa AO, Adekanle O, Agbakwuru AE, Arigbabu AO. Management of overt upper gastrointestinal bleeding in a low resource setting: a real world report from Nigeria. *BMC Gastroenterol.* 2014 Dec 10;14(1):210.
- Perl D, Leddin D, Bizos D, Veitch A, N'Dow J, Bush-Goddard S, et al. Endoscopic capacity in West Africa. *Afr Health Sci.* 2016 May 9;16(1):329.
- Akande KO, Akere A, Otegbayo JA, Ola SO, Ousunmade D. Accuracy of non-endoscopic predictors of oesophageal varices in liver cirrhosis using platelet count, splenic size and portal vein diameter. *Afr J Med Med Sci.* 2016 Sep;45(3):243–51.
- Yu NC, Margolis D, Hsu M, Raman SS, Lu DSK. Detection and Grading of Esophageal Varices on Liver CT: Comparison of Standard and Thin-Section Multiplanar Reconstructions in Diagnostic Accuracy. *American Journal of Roentgenology.* 2011 Sep;197(3):643–9.
- Moftah SG, Kamal S, Hanna ATK. CT esophagography: Non invasive screening and grading of esophageal varices in cirrhosis. *The Egyptian Journal of Radiology and Nuclear Medicine.* 2014 Jun;45(2):263–70.
- Yang JD, Mohamed EA, Aziz AOA, Shousha HI, Hashem MB, Nabeel MM, et al. Characteristics, management, and outcomes of patients with hepatocellular carcinoma in Africa: a multicountry observational study from the Africa Liver Cancer Consortium. *Lancet Gastroenterol Hepatol.* 2017 Feb;2(2):103–11.

15. Perera K, Kodisinghe SK, Ediriweera DS, Moratuwagama D, Williams S, Pathmeswaran A, et al. Percentage of small platelets on peripheral blood smear and Child-Turcotte-Pugh class can predict the presence of oesophageal varices in newly diagnosed patients with cirrhosis: development of a prediction model for resource limited settings. *BMC Gastroenterol.* 2019 Dec 26;19(1):134.
16. Nwokediuko S, Osuala P, Uduma U, Alaneme A, Onwuka C, Mesigo C. Pattern of liver disease admissions in a Nigerian tertiary hospital. *Niger J Clin Pract.* 2013;16(3):339.
17. Ndububa DA, Ojo OS, Adetiloye VA, Aladegbaiye AO, Adebayo RA, Adekanle O. THE CONTRIBUTION OF ALCOHOL TO CHRONIC LIVER DISEASE IN PATIENTS FROM SOUTH-WEST NIGERIA. Vol. 13, *Nigerian Journal of Clinical Practice* Dec. 2010.
18. Jepsen P, Ott P, Andersen PK, Sørensen HT, Vilstrup H. Risk for Hepatocellular Carcinoma in Patients With Alcoholic Cirrhosis. *Ann Intern Med.* 2012 Jun 19;156(12):841.
19. Liaw YF, Brunetto MR, Hadziyannis S. The Natural History of Chronic HBV Infection and Geographical Differences. *Antivir Ther.* 2010 Apr 1;15(3_suppl):25–33.
20. Kim HY, Jin EH, Kim W, Lee JY, Woo H, Oh S, et al. The Role of Spleen Stiffness in Determining the Severity and Bleeding Risk of Esophageal Varices in Cirrhotic Patients. *Medicine.* 2015 Jun;94(24):e1031.
21. Abd-Elsalam S, Habba E, Elkhawany W, Tawfeek S, Elbatea H, El-kalla F, et al. Correlation of platelets count with endoscopic findings in a cohort of Egyptian patients with liver cirrhosis. *Medicine.* 2016 Jun;95(23):e3853.
22. Manatsathit W, Samant H, Kapur S, Ingviya T, Esmadi M, Wijarnpreecha K, et al. Accuracy of liver stiffness, spleen stiffness, and $\frac{LS}{PL}$ - spleen diameter to platelet ratio score in detection of esophageal varices: Systemic review and meta-analysis. *J Gastroenterol Hepatol.* 2018 Oct 30;33(10):1696–706.
23. Iavarone M, Alimenti E, Tada T, Shimose S, Suda G, Yoo C, et al. Incidence and Predictors of Esophagogastric Varices Bleeding in Patients with Hepatocellular Carcinoma in Lenvatinib. *Liver Cancer.* 2023 Sep 14;1–12.
24. Sigal SH, Sherman Z, Jesudian A. Clinical Implications of Thrombocytopenia for the Cirrhotic Patient. *Hepat Med.* 2020 Apr;Volume 12:49–60.
25. Javed M, Mohammad D, Masood Z, Sheikh GA, Iftikhar M, Hamed A. To determine the correlation between mean platelet count and frequency of grading of esophageal varices in patients of liver cirrhosis. *The Professional Medical Journal.* 2021 Jun 10;28(06):833–41.
26. Uong P, Chey V, Unn K, Nov N, Kang K, Un S, et al. Correlation of Platelet Count with Grading of Esophageal Varices in Cirrhotic Patients. *Open J Gastroenterol.* 2023;13(01):12–27.
27. Baihaqi FA, Delarosa DO. Correlation between Platelet Count and Grading of Esophageal Varices in Liver Cirrhosis Patients: A Meta-Analysis. *Open Access Maced J Med Sci.* 2022 Apr 10;10(F):513–21.
28. Afsar A, Nadeem M, Shah SAA, Hussain H, Rani A, Ghaffar S. Platelet count can predict the grade of esophageal varices in cirrhotic patients: a cross-sectional study. *F1000Res.* 2021 Nov 24;10:101.
29. Divya S, Nagarajan K, Thirumal. A Study of Correlation between Platelet Count and Severity of Esophageal Varices in Patients with Chronic Liver Disease. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* e-ISSN [Internet]. 2020;19:38–43. Available from: www.iosrjournals.org
30. Eloumou SAFB, Nga TWB, Ndam AN, Gouajio GGA, Djapa GRN, Shang CK, et al. Evaluation of Non-Invasive Markers of Liver Fibrosis in Chronic Hepatitis B Patients in a Sub-Saharan African Setting: Transient Elastography versus APRI, FIB4, GTT/Platelet Scores. *Open J Gastroenterol.* 2023;13(06):209–24

Table 1. Demographic characteristics of the study subjects

Variable	Frequency(n)	Percentage(%)
Age		
Mean ± SD	47.5 ± 9.9	
Range	30 – 69	
Gender		
Female	13	16.5
Male	86	83.5

Table 2. Frequency of varices based on grade

Variable	Frequency (n = 79)	Percentage (%)
Grade of varices		
Grade 1	19	24.1
Grade 2	32	40.5
Grade 3	28	35.4

Table 3. Association of platelet count group with grades of oesophageal varices.

Variable	Grades					Frequency	
Platelet count							
<50,000	Group 1	16	0	1	17		
50,000-99,999	Group 2	12	9	17	38		P value:
100,000-150,000	Group 3	0	3	10	13		<0.0001
>150,000	Group 4	0	7	4	11		

Table 4. Correlation of platelet count with grades of esophageal varices.

	Platelet count
Grade of varix	
ρ value	-0.783
p value	0.001

Table 5. Association of oesophageal varices grade with median platelet count

Grade of varix	Median platelet count	Frequency	
	58.74	19	
	47.80	32	P value:
	18.38	28	<0.0001

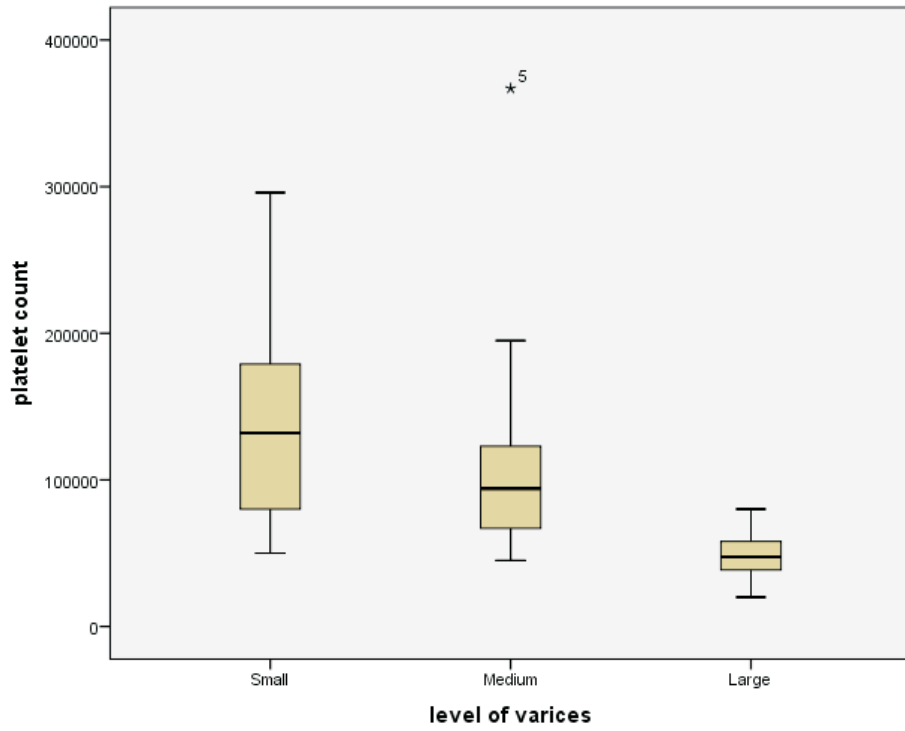


Figure 1 Platelet counts between small varices and medium to large varices