To Study of the Correlation between Vitamin B12 Level and Thrombocytopenia in Dengue Fever and Malaria

Yogesh Kumar Kansara1*, Eshan Sharma1

1*Department of General Medicine, National Institute of Medical Science and Research, NIMS University Rajasthan, Jaipur, India

Abstract: Introduction: Thrombocytopenia is a common symptom of malaria, and typically occurs more frequently in Falciparam malaria. It appears that P. vivax does trigger thrombocytopenia, contrary to popular belief. Therefore, patients with low platelets and fever ought to be considered for malaria, though B12 deficiency does not always accompany malaria cases. Methods: This study was conducted at indoor patients at the NIMS hospital to investigate the relationship between vitamin B12 with thrombocytopenia associated with dengue fever and malaria. Patients were investigated for routine investigations such as CBC, ESR, RFT, RBS, LFT, PBF, VIT B12 LEVEL, Dengue profile and MP card test. In out of 125 patients, 75 patients have dengue fever, and 50 patients have malaria fever. Result: In dengue fever out of 75 patients, 61 patients (81%) had thrombocytopenia with vitamin B12 deficiency (B12 level <100 pg/l). In malaria out of 50 patients, 28 patients (56%) have thrombocytopenia with vitamin B12 level (B12 level < 300 pg/l), 22 patients (44%) have thrombocytopenia with vitamin B12 level normal (B12 level 201-300). Vitamin B12 level < 190 pg/ml was found in 47(94%) patients with severe thrombocytopenia while 32 number (74%) patients with mild thrombocytopenia. In group with B12<190 pg/l need of SDP transfusion was significantly high i.e; (115.13±42.98) in comparison to other groups, as well as the recovery time of platelets to 20000/µl threshold, was found to be high in B12 <190 pg/l group (42.60±8.89 days) as compared to other groups. Conclusion: Using platelet analysis by PBF, the results of this study were obtained. There is no clumping of platelets, and the platelets show the normal size, color, and shape.

Keywords: Falciparam malaria, thrombocytopenia, vitamin B12.

INTRODUCTION

Thrombocytopenia, defined as a platelet count of less than 150*109/L, has numerous causes, can be broadly divided into two types i.e; congenital and acquired. A deficiency in folate or vitamin B12 may also be associated with low levels of platelets in some cases. Vitamin B12 is essential for erythropoiesis and thrombopoiesis. The incidence of thrombocytopenia in symptomatic B12 (cobalamin deficiency) is approximately 10%. B12 levels didn’t seem to be related to other dengue complications such as bleeding, septicemia, and shock. Apart from anaemia and leukopenia, severe vitamin B12 deficiency may also cause thrombocytopenia.

The goal of our study is
1. To assess the platelet morphology and counts in patients of dengue fever and malaria.
2. To correlate between vitamin B12 deficiency and severity of thrombocytopenia, platelets recovery and duration of hospital stay in dengue and malaria case.

MATERIALS AND METHODS

We carried out a prospective study over a period of 18 months, from January 2020 to Jun 2021; All the cases of dengue and malaria will be selected on the basis of selection criteria after detail history and clinical general and systemic examination of the patients. Patients will be investigated for routine investigations such as CBC, ESR, RFT, RBS, LFT, PBF, VIT B12 LEVEL, Dengue profile and MP card test. Clinical features, haematological and biochemical parameters and vitamin B12 levels will be measured. Data processing were performed using excel software.
125 patients were collected. In out of 125 patients, 75 patients have dengue fever and 50 patients have malaria fever.

**Fig 1: Age distribution of dengue patients**

**Fig 2: Age distribution of malaria patients**

**Fig 3: Diagram showing vitamin B12 level in the cases of dengue patients**
DISCUSSION

In this study showed that vitamin B12 level deficiency in patients with thrombocytopenia. There are 125 patients with dengue fever, and 50 patients with malaria, out of whom 75 are infected. In dengue fever out of 75 patients, 61 patients (81%) have thrombocytopenia with vitamin B12 deficiency (B12 level 300 pg/l), 22 patients (44%) have thrombocytopenia with vitamin B12 level normal (B12 level 201-300). Vitamin B12 level < 190 pg/ml was found in 47(94%) patients with severe thrombocytopenia while 32 number (74%) patients with mild thrombocytopenia. In group with B12<190 pg/ l
need of SDP transfusion was significantly high i.e; (115.13±42.08) in comparison to other groups, as well as the recovery time of platelets to 20000/µl threshold, was found to be high in B12<190 pg/l group (42.60±8.89days) as compared to other groups. In this study the finding were platelets analysis by PBF examination the platelets are normal in size, colour and shape as well as shown no presence of platelet clumping. Patients with dengue are often admitted because of thrombocytopenia and other symptoms relating to thrombocytopenia. In India, the duration of admission is often determined by the number of platelets recovered to a safe level (<20000/l). There is no direct correlation between thrombocytopenia severity and dengue complications in several studies. The recovery from thrombocytopenia in some dengue patients is swift, while in others it may take several days. The hypothesis presented in this study was that there may be other factors contributing to acute haematological / hematopoietic stress that lead to thrombocytopenia and slow recovery. By identifying and removing contributory factors, patients with severe thrombocytopenia and dengue fever may be able to decrease the duration of their hospital stay. The severe lack of vitamin B12 is often associated with thrombocytopenia, as well as anemia and leukopenia. The Indian population is prone to vitamin B12 deficiency; therefore, this study was designed to test the hypothesis that the level of vitamin B12 in some people, may lead to prolonged, severe thrombocytopenia. When vitamin B12 levels were under 100 pg/L. SDP requirements were the highest in comparison to those with B12 levels >300 pg/L, but it was not statistically significant. SDP was transfused only if platelets remained below 10000/l in current study, suggesting severe B12 deficiency prolongs severity of thrombocytopenia. An additional parameter measured, the platelets recovery time (time taken to reach >20000/l), confirmed this finding. It was selected as part of in-patient treatment since the platelets recover above 20000/l and if, in all other respects, the patient is considered fit to be discharged. Also, platelet recovery time was the fastest in B12300 pg/L (360±0days) baseline.

**CONCLUSION**

In dengue fever, there is a particularly high prevalence of thrombocytopenia, especially among Indians, which has been linked to vitamin B12 deficiency. B12 deficiency may require a prolonged hospital stay and increased healthcare costs as well as platelet transfusions. Thrombocytopenia is a common symptom of malaria, and typically occurs more frequently in F. malaria. It appears that P. vivax does trigger thrombocytopenia, contrary to popular belief. Therefore, patients with low platelets and fever ought to be considered for malaria, though B12 deficiency does not always accompany malaria cases.

**REFERENCES**

- Stover, P. J. (2004). Physiology of folate and vitamin B12 in health and disease. *Nutrition reviews*, 62(suppl_1), S3-S12.
- Nath, S. D., Koutoubi, S., & Huffman, F. G. (2006). Folate and vitamin B12 status of a multiethnic adult population. *Journal of the National Medical Association*, 98(1), 67-72.
- Oh, R. C., & Brown, D. L. (2003). Vitamin B12 deficiency. *American family physician*, 67(5), 979-986.
- Reynolds, E. (2006). Vitamin B12, folic acid, and the nervous system. *The lancet neurology*, 5(11), 949-960.
- Piyush, J., Manish, P. G., & Mandhuhingroni. (2017). Isolated thrombocytopenia in acute malaria associated with vitamin B12 and folic acid levels, 4(1), 125-127.
- Khan, S. J., Khan, F. R., Usman, M., & Zahid, S. (2008). Malaria can lead to thrombocytopenia. *Rawal Med J*, 33(2), 183-185.
- Faseela, T. S., Roche, R. A., Anita, K. B., Malli, C. S., & Rai, Y. (2011). Diagnostic value of platelet count in malaria. *Journal of Clinical and Diagnostic Research*, 5(3), 464-466.
- Leikin, S., & Vossough, P. (1967). 53 The Role of Folate and Vitamin B12 in the Etiology of the Thrombocytopenia of Iron Deficiency Anemia. *Pediatric Research*, 1(3), 214.
- Ryan, D. H., & Cohen, H. J. (2002). Bone marrow aspiration and morphology. In: Hoffman, R., Benz, Yogesh Kumar Kansara & Eshan Sharma., *East African Scholars J Med Sci*; Vol-5, Iss-2 (Feb, 2022): 29-34
• Keskin, E. Y., & Keskin, M. (2015). Severe vitamin B12 deficiency in a 15-year-old boy: presentation with haemolyisis and pancytopenia. *Case Reports, 2015*, bcr2015209718.

• Stabler, S. P. (2013). Vitamin B12 deficiency. *New England Journal of Medicine*, 368(2), 149-160.

• Scully, M., Cutaland, S., Copping, P., De La Rubia, J., Friedman, K. D., Kremer Hovinga, J., & Westwood, J. P. (2017). Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microangiopathies. *Journal of thrombosis and haemostasis*, 15(2), 312-322.

• Andrès, E., Affenberger, S., Zimmer, J., Vinzio, S., Grosu, D., Pistol, G., ... & Blickle, J. F. (2006). Current hematological findings in cobalamin deficiency. A study of 201 consecutive patients with documented cobalamin deficiency. *Clinical & Laboratory Haematology*, 28(1), 50-56.
- Garderet, L., Maury, E., Lagrange, M., Najman, A., Offenstadt, G., & Guidet, B. (2003). Schizocytes in pernicious anemia mimicking thrombotic thrombocytopenic purpura. *The American Journal of medicine*, 114(5), 423-425.

- Bakchoul, T., & Sachs, U. J. (2015). Platelet destruction in immune thrombocytopenia. Understanding the mechanisms. *Hamostaseologie*, 36(3), 187-194.

- Van Leeuwen, E. F., Van Der Ven, J. T., Engelfriet, C. P., & Von Dem Borne, A. E. (1982). Specificity of autoantibodies in autoimmune thrombocytopenia. *Blood*, 59(1), 23-26.

- He, R., Reid, D. M., Jones, C. E., & Shulman, N. R. (1994). Spectrum of Ig classes, specificities, and titers of serum antiglycoproteins in chronic idiopathic thrombocytopenic purpura. *Blood*, 83(4), 1024–1032.

- Audia, S., Santegoets, K., Laarhoven, A. G., Vidarsson, G., Facy, O., Ortega-Deballon, P., ... & Radstake, T. R. (2017). Fcy receptor expression on macrophages in adult immune thrombocytopenia. *Clinical & Experimental Immunology*, 188(2), 275-282.

- Roark, J. H., Bussel, J. B., Cines, D. B., & Siegel, D. L. (2002). Genetic analysis of autoantibodies in idiopathic thrombocytopenic purpura reveals evidence of clonal expansion and somatic mutation. *Blood, The Journal of the American Society of Hematology*, 100(4), 1388-1398.

- Kuwana, M., Okazaki, Y., Kaburaki, J., Kawakami, Y., & Ikeda, Y. (2002). Spleen is a primary site for activation of platelet-reactive T and B cells in patients with immune thrombocytopenic purpura. *The Journal of Immunology*, 168(7), 3675-3682.

- Kuwana, M., Kawakami, Y., & Ikeda, Y. (2003). Suppression of autoreactive T-cell response to glycoprotein Ib/IIia by blockade of CD40/CD154 interaction: implications for treatment of immune thrombocytopenic purpura. *Blood, The Journal of the American Society of Hematology*, 101(2), 621-623.

- McMillan, R., Wang, L., Tomer, A., Nichol, J., & Pistillo, J. (2004). Suppression of in vitro megakaryocyte production by antiplatelet autoantibodies from adult patients with chronic ITP. *Blood*, 103(4), 1364-1369.

- Chang, M., Nakagawa, P. A., Williams, S. A., Schwartz, M. R., Imfeld, K. L., Buzby, J. S., & Nugent, D. J. (2003). Immune thrombocytopenic purpura (ITP) plasma and purified ITP monoclonal autoantibodies inhibit megakaryocytepoiesis in vitro. *Blood*, 102(3), 887-895.

- Olsson, B., Andersson, P. O., Jernås, M., Jacobsson, S., Carlsson, B., Carlsson, L., & Wadenvik, H. (2003). T-cell-mediated cytotoxicity toward platelets in chronic idiopathic thrombocytopenic purpura. *Nature medicine*, 9(9), 1123-1124.

- Mert, A., Ozaras, R., Tabak, F., Bilir, M., Ozturk, R., & Aktugu, Y. (2003). Malaria in Turkey: a review of 33 cases. *European journal of epidemiology*, 18(6), 579-582.

- Mahmood, A., & Yasir, M. (2005). Thrombocytopenia: a predictor of malaria among febrile patients in Liberia. *Infect Dis J*, 14, 41-44.

- Memon, A. R., & Afsar, S. (2006). Thrombocytopenia in hospitalized malaria patients. *Pakistan Journal of Medical Sciences*, 22(2), 141-143.

- Akhtar, M. N., Jamil, S., Amjad, S. I., Butt, A. R., & Farooq, M. (2005). Association of malaria with thrombocytopenia. *Annals of King Edward Medical University*, 11(4), 536-537.

- Rehman, Z. U., Alam, M., Mubarak, A., Sattar, A., & Karamat, K. A. (1999). Thrombocytopenia in acute malarial infection. *Pakistan Journal of Pathology*, 10, 9-11.

- Jamal, A., Memon, I. A., & Lateef, F. (2007). The association of Plasmodium Vivax malaria with thrombocytopenia in febrile children. *Pak Paed J*, 31, 85-89.

- Kumar, A. (2006). Thrombocytopenia--an indicator of acute vivax malaria. *Indian journal of pathology & microbiology*, 49(4), 505-508.

- International Committee for Standardization in Haematology, (1971). Proposed recommendations for measurement of serum iron in human blood. *Br J Haematol*, 20.

- Scott, J. M., Ghanta, V., & Herbert, V. (1974). Trouble-free microbiologic serum and red cell folate assays. *The American journal of medical technology*, 40(3), 125-134.

- Anderson, B. B. (1964). Investigations into the Euglena method for the assay of the vitamin B12 in serum. *Journal of Clinical Pathology*, 17(1), 14-26.

- Wintrobe, M. M., Lee, G. R., & Boggs, D. R. (1981). In: Clinical Haematology, Philadelphia, Lea & Febiger. 8th ed. p. 1054 determination of platelet aggregation. *Am J Clin Pathol*, 125-134.

- Levine, P. H. The effect of thrombocytopenia on the, 65, 79-82.

- Smith, M. D., Smith, D. A., & Fletcher, M. (1962). Haemorrhage associated with thrombocytopenia in megaloblastic anaemia. *British Medical Journal*, 1(5283), 982.