Original Research Article

Correlation between platelet counts and subcon junctival hemorrhage in patients with malaria

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Abstract

Objective: To correlate the subconjunctival hemorrhage (SCH) with platelet counts in patients diagnosed with malaria **Materials and Methods:** All the inpatients who were diagnosed with malaria and referred to the department of ophthalmology were included in the study. Patients underwent a thorough ocular examination. Platelet counts, hemoglobin and type of malaria parasite isolated were collected. **Results:** Total of 72 patients with malaria infection were included in the study. 56 (77.77%) had P. Vivax, 8 (11.11%) had P. Falciparum and 8 (11.11%) had mixed infection. On ocular examination 7(9.7%) patients had subconjunctival hemorrhage, 1 (1.3%) patient had retinal hemorrhage. Platelet count of <69000/dl was associated with SCH in our study. **Conclusion:** Occurrence of subconjunctival hemorrhage in malaria can herald the onset of thrombocytopenia. It can be a marker for the early identification and management of complications of malaria.

Key Words: malaria, subconjunctival haemorrhage, thrombocytopenia.

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INTRODUCTION

Subconjunctival hemorrhage (SCH) also known as hyposphagma refers to bleeding under the conjunctiva. Spontaneous SCH is an admonishing clinical condition for systemic diseases such as hypertension, diabetes cardiovascular and bleeding abnormalities.[1] Malaria being a true hematological infectious disease, is known to cause anemia and thrombocytopenia.[2] These hematological changes in malaria have received more attention in the scientific literature due to the associated mortality.[3] Ocular involvement in malaria has been reported in10 to 20% of patients.[4] Eye being one of the accessible sites for diagnosing changes has been screened in this study to aid in identifying the early complications of malaria. This study attempts to correlate the ocular manifestation like subconjunctival hemorrhage with platelet counts in patients with malaria, to ensure early, prompt and effective management in developing countries.

MATERIAL AND METHODS

A prospective observational study was conducted on 72 malaria diagnosed inpatients in our hospital between June 2016 and Dec 2016. The study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional ethical committee board. Informed written consent was obtained from all patients prior to their enrollment in this study. All the other causes of subconjunctival hemorrhage like trauma, hypertension, bleeding disorders were looked for. All the patients were evaluated for any other co-existing systemic disease. All patients underwent a thorough ocular examination that included visual acuity, slit lamp examination, direct and indirect ophthalmoscopy. As platelet counts were done repeatedly in these patients, platelet count done on the day of eye examination was

documented. Serum hemoglobin and the type of malaria parasite isolated were recorded. Exclusion criteria included patients with co-existing causes for anemia, thrombocytopaenia and subconjunctival hemorrhage.

Statistics: The data was checked for its distribution by Anderson Darling test. Statistical analysis was performed using SPSS 21.0 software (SPSS Inc., Chicago, IL, USA) and Minitab® 17.1.0 © 2013 Minitab Inc. statistical software. Sample size was calculated based on previous incidences claimed by different authors and confirmed using 'area under ROC curve sampling' method and this would calculate the required sample size for the comparison of the area under a ROC curve with a null hypothesis value. A minimum total of 70 patients were required when the ratio of detected positive incidences of disease (SCH) to the negative incidences as 0.1, with minimum area under ROC curve as 0.8 (null hypothesis value 0.5, Type I error, 0.05 and Type II error, 0.2). A P-value of <0.05 was considered as statistically significant.

RESULTS

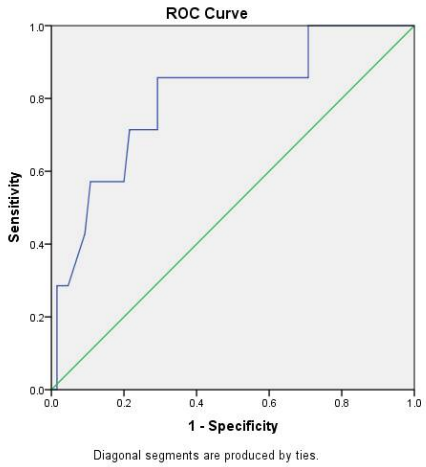

Figure 1: Receiver Operating Characteristic curve (ROC curve) for subconjunctival haemorrhage

Table 1: Multivariable regression analysis of SCH the possible predictors

Predictor	OR	VIF	P(adjusted P)
Platelet count	1.0010	1.08	0.017
Age	1.0172	1.08	0.593
Hemoglobin	0.9054	1.08	0.586
P.Falciparum	1.2805	1.1	0.811

Goodness of Fit, Pearsons P=0.452, Deviance P= 0.998, R^2=18.6, Adjusted R^2=8.7 AIC- 47.6

Data collected from 72 malaria diagnosed patients were analysed. Mean (SD) age of presentation was 33.4(13.3) years. There were 13 (18.1%) females and 59(81.9%) males. Mean (SD) hemoglobin was 12.5(2.4). Median Platelet count was 82000 (60000-119500, interquartile range, IQR, 59500). Among subjects, 56(77.8%) had P.Vivax, 8(11.1%) had P. Falciparum and 8(11.1%) had mixed malarial infections. Incidence of subconjunctival hemorrhage was 9.7%. Retinal hemorrhage was observed in 1(1.4%) patient. We defined thrombocytopenia as platelet count equal or less than 1, 00,000/dl. Thrombocytopenia was observed in 50(69.44%) patients. Binary logistic regression was used (yes or no) depending on presence or absence of subconjunctival hemorrhage to assess the predictors of subconjunctival hemorrhage in evaluation of malaria patients. The logit link function, the calculated odds ratio and 95% CI for odds ratio was considered to determine whether the association between the response events and predictors is statistically significant with α(alpha) of 0.05 (adjusted Pvalue=P/no. of predictor). Predictors included in the final model are age, hemoglobin, presence of falciparum type of malaria. The model fit was checked using AIC, VIF, Pearsons deviance "P" value of Goodness of Fit tests. The positive coefficient and an odds ratio that is greater than one would indicate that a higher chance of subconjunctival hemorrhage with respective predictors. (Table1) Multiple logistic regression was performed using multiple variables described for the factors that may affect the subconjunctival hemorrhage incidences. The response variable was subconjunctival hemorrhage and the platelet count, age, type of malarial parasite were included in the final model. Binary logistic regression analysis (P = 0.049) revealed platelet count as a significant predictor for sub-conjunctival hemorrhage (P = 0.008) and others were not (P >0.05). The variance inflation factors were near 1. The models Goodness of Fit tests observed Hosner-Lemeshow P values as 0.461(P >0.05) signifying the reliability on model as appropriate one. The ROC analysis described the cut off value of platelet count for occurrence of thrombocytopenia associated subconjunctival hemorrhage. At or below 69000 platelet count, the patients are likely to develop subconjunctival hemorrhage (sensitivity of 86% with false positive rate of 29%, ROC curve Pvalue=0.009 Area under curve, AUC=0.799 (Figure 1). Thrombocytopenia has been defined as platelet count of less than 100000 per deciliter in our study and causation of subconjunctival hemorrhage for the definition of thrombocytopenia was evaluated. When cross-tabulation was attempted, it revealed the sensitivity as 85.7% and specificity as 32.3%, positive predictive value (PPV) of 11.97% and Negative predictive value of 95.46%. This suggests that the true negatives (TN), i.e. the absence of subconjunctival hemorrhage was associated with absence of thrombocytopenia in malaria affected patients

DISCUSSION

Malaria is deemed to be preventable and curable, yet a major public health problem. Of the 2.14 million confirmed P.Vivax cases occurring globally, 18% are seen in India.[5] A systematic review and meta-analysis conducted by Cho Naing identified P.Vivax as a major cause of severe malaria.[6] Hay and colleagues also found non Falciparum malaria, predominantly P.Vivax accounts for 25-40% of global malaria burden with 132-34 million cases per year. In our study population predominancy of P.Vivax 56(77.8%) was observed.[7] Clinical symptoms of malaria are nonspecific and cannot be distinguished from other febrile illness. Only recently P.Vivax has been shown to cause anemia, respiratory distress and coma. Eye has always been considered to be the window to human body. Significant intraocular abnormalities are not seen in most patients with otherwise uncomplicated malaria, although lid oedema, conjunctival chemosis and haemorrhage, anterior uveitis and scleral icterus secondary to hyperbilirubinaemia due to liver function abnormalities are known to occur. [8]However changes in the eye secondary to anemia, thrombocytopenia can occur. SCH though considered a benign condition of eye may need a further evaluation of hematogical profile of a malarial patient. A study by Kochar DK *et al* [9] on eye changes in cerebral malaria with P. Falciparum showed an incidence of SCH in 2.8% patients. Kaimbo *et al* reported a case of bilateral subconjunctival haemorrhage in a patient who had no abnormality other than malaria. They reported an incidence of SCH as 0.9%. [10] However in these studies SCH has been reported in P.Falciparum cases. In comparison to this our study revealed an incidence of SCH in 9.72%, two patients having mixed (Falciparum and Vivax) infection and five having P.Vivax infection. The occurence of SCH could be due to the emerging strains of P.Vivax Incidence of thrombocytopenia in patients with malaria range from 40.5-85%. In our study low platelet count (<1,00,000/dl) was seen in 51(70.83%), with majority(86.27%) occurring in P.Vivax infection similar to other studies.[11,12] Thrombocytopenia in malaria is thought to be caused by increased splenic sequestration, immune mediated destruction, shortened platelet survival, oxidation stress, direct interaction between plasmodium and platelets.[12] Marked thrombocytopenia < 50,000/µl emerged to be significantly associated with ocular hemorrhage among all the parameters evaluated by Kapoor *et al* [13] in dengue related SCH. Howevever in a study by Coelho HCC *et al* [12] and Sharma A and Khanduri U [14]on malaria patients, thrombocytopenia was not associated with bleeding complications. Dan Ning Hu *et al* in a nationwide study in Taiwan found thrombocytopenia and purpura to be significantly associated with non traumatic subconjunctival hemorrhage, with an adjusted OR at 1.34 (95% CI 1.19–1.50).[15] Kochar D K *et al*[16] in their prospective study of 303 malaria proven children found 150(49.5%) patients had severe malaria of which abnormal bleeding was present in 22(21.6%). All children with abnormal bleeding had thrombocytopenia (mean platelet count 58142.85 cells/ cmm). Malaria patients with platelet count equal to or less than 69000/dl were likely to develop subconjunctival hemorrhage in our study. Retinal hemorrhages in severe and non severe forms of malaria have been documented earlier with no statistical correlation with thrombocytopenia. [17,18] In our study fundus examination revealed retinal hemorrhage in 1 (1.4%) mixed malarial parasite infection patient with a platelet count of 34000/dl. Severe anaemia, sequestration of erythrocytes, cytoadhearance of erythrocytes to capillary endothelial cells and rosetting of erythrocytes have been described in the pathogenesis of intraocular hemorrhages. The majority of retinal hemorrhages appear to be caused by metabolic steal by the parasites resulting in cellular hypoxia and local nutritional deficiency of the retina. [18]

CONCLUSION

Platelet count was a significant predictor for SCH in our study. Cut off value of platelet count for occurrence of thrombocytopenia associated SCH in malaria was 69000/dl, above which subconjunctival hemorrhage was unlikely to happen.

REFERENCES

1. Sahinoglu-Keskek N, Cevher S, Ergin A. Analysis of subconjunctival hemorrhage. Pak J Med Sci. 2013 Jan-Mar; 29(1): 132–134.
2. Wickramasinghe SN, Abdalla SH. Blood and bone marrow changes in malaria. Baillieres Best Pract Res ClinHaematol.2000; 13(2): 277-299.
3. Lacerda MV, Mourão MP, Coelho HC, Santos JB. Thrombocytopenia in malaria: who cares? Mem Inst Oswaldo Cruz. 2011; 106(1):52-63.
4. Hidayat AA, Nalbandian RM, Sammons DW, Fleischman JA, Johnson TE. The diagnostic histopathologic features of ocular malaria. Ophthalmology.1993; 100:1183–6.
5. World Health Organization World Malaria Report 2014. 2015. http://www.who.int/malaria/publications/world-malaria-report-2015/en/ Available at. Accessed July 23, 2016
6. Naing C, Whittaker MA, Nyunt Wai V, Mak JW 2014. Is Plasmodium vivax malaria a severe malaria? : a systematic review and meta-analysis. PLoS Negl Trop Dis 8:e3071. doi:.10.1371/journal.pntd.0003071

7. Hay SI, Guerra CA, Tatem AJ, Noor AM, Snow RW. The global distribution and population at risk of malaria: past, present, and future. Lancet Infect Dis 2004; 4(6): 327-336
8. Wayne T Cornblath. Protozoa and protozoal diseases. In : Neil R Miller, Nancy J Newman eds. Walsh and Hoyts clinical neuro-ophthalmology Vol 3 6th ed, Baltimore: Lippincott Williams and Wilkins ;2005.p.2957-3048
9. Kochar DK, Shubhakaran, Kumawat BL, Vyas SP. Prognostic significance of eye changes in cerebral malaria. J Assoc Physicians India. 2000; 48(5):473-7.
10. Kaimbo Wa Kaimbo D, Missotten L Severe subconjunctival haemorrhage associated with malaria. Bull Soc Belge Ophtalmol. 1999; 271:51-3.
11. Kochar DK, Das A, Kochar A, Middha S, Acharya J, Tanwar GS, Gupta A, Pakalapati D, Garg S, Saxena V, Subudhi AK, Boopathi PA, Sirohi P, Kochar SK. Thrombocytopenia in Plasmodium falciparum, Plasmodium vivax and mixed infection malaria: A study from Bikaner (Northwestern India) Platelets. 2010;21(8):623–7
12. Coelho HCC, Lopes SCP, Pimentel JPD, Nogueira PA, Costa FTM, Siqueira AM, Melo GC, Monteiro WM, Malheiro A, Lacerda MVG et al. (2013) Thrombocytopenia in Plasmodium vivax Malaria is Related to Platelets Phagocytosis. PLoS ONE 8(5): e63410. doi:10.1371/journal.pone.0063410
13. Kapoor HK, Bhai S, John M, Xavier J Ocular manifestations of dengue fever in an East Indian epidemic. Can J Ophthalmol. 2006 Dec; 41(6):741-6.
14. Sharma A and Khanduri U. How Benign is Benign Tertian Malaria?. Journal of Vector Borne Diseases 2009:46; 141-144.
15. Hu D-N, Mou C-H, Chao S-C, Lin C-Y, Nien C-W, Kuan P-T, Jost B. Jonas JB, Sung FC (2015) Incidence of Non-Traumatic Subconjunctival Hemorrhage in a Nationwide Study in Taiwan from 2000 to 2011. PLoS ONE 10(7): e0132762.
16. Kochar DK, Tanwar GS, Khatri PC, Kochar SK, Sengar, G. S., Gupta, A Kochar A, Middha S, Acharya J, Saxena V, Pakalapati D, Garg S, Das, A. (2010). Clinical features of children hospitalized with malaria—a study from Bikaner, northwest India. Am J Trop Med Hyg. 2010; 83:981–989.
17. Kochar A, Kalra P, Sb V, Ukirade V, Chahar A, Kochar DK, Kochar SK. Retinopathy of vivax malaria in adults and its relation with severity parameters. Pathog Glob Health. 2016; 110:185–93.
18. Lakhotia M, Singh J, Pahadiya HR, Kumar H, Choudhary PK et al. Retinal Hemorrhages in Severe Non-cerebral Plasmodium vivax Malaria in an Adult.JClinDiagnRes.2015Jun;9(6):OD01-3. doi:10.7860/JCDR/2015/11930.6003.

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