Mean platelet volume and platelet counts in type 2 Diabetes: Mellitus on treatment and non-diabetic mellitus controls in Lagos, Nigeria

Akinbami Akinsegun1, Dada Akinola Olusola2, John-Olabode Sarah3, Oshinaike Olajumoke2, Adediran Adewumi6, Odesanya Majeed6, Ogbera Anthonia2, Uche Ebele1, Okunoye Olaitan6, Arogundade Olanrewaju, 1, Aile Kingsley7

1Department of Haematology and Blood Transfusion, Lagos State University, College of Medicine, Ikeja, Nigeria, 2Department of Medicine, Lagos State University, College of Medicine, Ikeja, Nigeria, 3Department of Haematology, Ben Carson School of Medicine, Babcock University, Ilisan-Remo, Ogun State, Nigeria, 4Department of Haematology, Faculty of Clinical Sciences, College of Medicine, University of Lagos, Idaaraba, Nigeria, 5Oak Hospitals, Ikorodu, Lagos, Nigeria, 6Department of Medicine, University of PortHarcourt, River State, Nigeria, 7Department of Haematology and Blood Transfusion, Lagos State University, Teaching Hospital, Ikeja, Nigeria

Corresponding author: Akinbami Akinsegun, Department of Haematology and Blood Transfusion, Lagos State University, College of Medicine, Ikeja, Nigeria

Key words: Mean platelet volume, platelet count, Type 2 diabetics on treatment, Controls

Received: 29/11/2013 - Accepted: 01/05/2014 - Published: 12/05/2014

Abstract

Introduction: The Mean platelet volume and platelet counts are indicators of thrombotic potentials, and risk factors for microvascular complications in diabetics. This study aimed to establish variations in platelet counts and mean platelet volume in type 2 diabetic patients on treatment and non-diabetic controls. Methods: This was an unmatched case-control study involving 200 participants consisting of 100 diabetics and 100 non-diabetic controls. Four and half milliliters of blood was collected from diabetics and non diabetic controls into EDTA anticoagulant tubes. Full blood count was performed using the Sysmex KN-21N, (manufactured by Sysmex corporation Kobe, Japan) a three- part auto analyzer able to run 19 parameters per sample including platelet counts and mean platelet volume. Results: The mean fasting blood sugar for the diabetics was 147.85±72.54 mg/dl and the controls 95.20±30.10 mg/dl. The mean platelet count for the diabetics was 235.29±76.81*10^9/L and controls, 211.32±66.44*10^9/L. The mean platelet volume, for the diabetics was 8.69±0.67 fl and the controls, 8.91±0.80 fl. There was a statistically significant difference in platelet counts of diabetics and healthy controls p =0.038 while none existed between the mean platelet volume in diabetics and healthy controls p=0.593. Conclusion: This study revealed a higher mean platelet count for diabetics on treatment than for non diabetic controls while mean platelet volume was lower in cases than controls. However, both parameters in diabetics on treatment were within the normal reference range for healthy individuals.

Pan African Medical Journal. 2014; 18:42 doi:10.11604/pamj.2014.18.42.3651

This article is available online at: http://www.panafrican-med-journal.com/content/article/18/42/full/

© Akinbami Akinsegun et al. The Pan African Medical Journal - ISSN 1937-8688. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
Introduction

Type 2 Diabetes mellitus (DM) accounts for 80% of all DM [1]. An interaction between environmental and genetic factors is responsible for the development of type 2 DM [1]. DM is characterized by enhanced platelets activation and coagulation proteins and reduced fibrinolytic activity [2]. This prothrombotic state precede the development of cardiovascular and atherosclerotic complications associated with DM [3]. Type 2 diabetes mellitus patients have two-four folds increase in risk of atherosclerosis [4]. Luscher et al [5] also documented an increased risk of coronary artery disease and cerebrovascular disease as a result of accelerated atherosclerosis in DM. In type 2 DM, platelet function is of pathophysiological importance in atherothrombosis [6]. Several authors have documented that increased morbidity and mortality in type 2 DM are associated with macro vascular (cardiovascular diseases, stroke, and peripheral arterial disease) and micro vascular (nephropathy, neuropathy and retinopathy) complications due to platelet dysfunction [7-9]. Also, an increased platelet counts and activity have been reported in diabetics as demonstrated by increases in GPs IIb/IIIa, 1b-IX, and 1a/IIa [10], CD62 and CD63 [11]. Mean Platelet Volume (MPV), the average volume of platelets, a parameter in full blood count measures platelet size distribution, and is not influenced by glycaemic control [12]. An increased MPV has been associated with high incidence of proliferative diabetic retinopathy [13] and myocardial infarction [14]. An activated megakaryocyte-platelet system in diabetes mellitus has been reported to be responsible for larger than normal platelets circulating in DM patients [15]. Platelet count and MPV are simple, effective and cheap tests that may be used to predict angiopathy in type 2 DM. Elevated MPV has been documented to predict bad outcome for acute ischaemic cerebrovascular events independent of other clinical parameters [16]. This study aimed to establish variations in platelet counts and mean platelet volume in type 2 diabetic patients on treatment and non-diabetic controls. To the best of our knowledge this study is novel in our environment and will serve as a foundation for other researchers in this field.

Methods

Study Population: This was a case-control study of 100 type 2 diabetic patients on treatment attending the diabetic clinic of Lagos State University Teaching Hospital (LASUTH) and 100 non diabetic controls consisting of medical students, nurses and doctors in the Institution. During the study period between June 2013 to September 2013 all patients who gave informed consent and satisfied the study inclusion criteria were recruited into the study. They were asked to fill structured questionnaires including demographic information, height, weight, last fasting blood sugar, blood pressure, drug history, and family history of diabetes. All the cases were on oral hypoglycaemic and antplatelet drugs like clopidogrel and vasoprin tablets, some were on antihypertensive and lipid lowering drugs. Information on family history of diabetes was also obtained from the controls and they were subjected to fasting blood sugar before enlistment.

Ethics: The research was approved by the Ethics Review Committee of LASUTH.

Inclusion Criteria for the cases: All non-insulin dependent diabetes mellitus patients on treatment attending the diabetes clinic.

Exclusion Criteria for the cases: Non-diabetic patients and insulin-dependent diabetes mellitus patients.

Inclusion Criteria for the controls: All consenting non-diabetics adults.

Exclusion Criteria for the controls: Diabetics adults on oral hypoglycaemic drugs.

Sample Collection: Blood specimen was withdrawn with minimal stasis from the ante-cubital vein using a dry sterile disposable syringe and needle. Four and half milliliters of blood was dispensed into EDTA anticoagulant tubes. The specimens were labeled with subject's age, sex and identification number. The EDTA samples were kept at room temperature until processed within 4 hours of collection.

Laboratory Analysis: Full blood count was performed using the Sysmex KN-21N, (manufactured by Sysmex corporation Kobe, Japan) a three- part auto analyzer able to run 19 parameters per sample including haemoglobin concentration, packed cell volume, red blood cell concentration, mean corpuscular haemoglobin, mean cell volume, mean corpuscular haemoglobin concentration, white blood cells and platelet count and mean platelet volume. Standardization, calibration of instrument and processing of samples were done according to manufacturer's instructions.

Procedure: Well mixed blood sample was aspirated, by letting the equipment sampling probe into the blood sample and then pressing the start button. Approx. 20 ul of blood was aspirated by the auto analyzer. Result of analysis is displayed after about 30 seconds. A printout copy of result is released on the thermal printing paper.

Statistical Analysis: Data were analyzed using SPSS version 16.0 (Statistical Package for Social Sciences, Inc., Chicago, III). The continuous variables were given as means ± standard deviation (SD). The Pearson chi squared test was used to test for association between discrete variables. P value was considered to be statistically significant when < 0.05.

Results

A total of 200 participants were enrolled into the study consisting of 100 diabetics and 100 non-diabetics controls. The mean age of the controls was 32.38±66.44 years with a minimum 17 years and a maximum of 70 years. The mean age of diabetics was 62.35±9.84 years, the minimum was 34 years and the maximum 90 years. The overall female: male ratio was 68%:32%, while the gender distribution in diabetics was 73%:27%, for the controls it was 63%:37% respectively (Table 1). The mean body mass index and fasting blood sugar of the diabetics were 32.10±4.85 kg/m² and 147.85±72.54 mg/dl respectively. For the controls they were 25±5.23 kg/m² and 95.20±30.10 mg/dl respectively. Amongst the diabetics, a total of 45 of 100 (45%) gave a positive family history of diabetes while 55% had no family history of diabetics. Only 5% of the controls gave a positive family history of diabetes. The mean duration of diabetes in the cases was 8.81±7.06 years. The overall mean platelet count was 223.49±72.71 *10⁹/L, for the diabetics 235.29±76.81 *10⁹/L and controls 211.32±66.44 *10⁹/L. The overall mean platelet volume was 8.8±0.74 fl, for the diabetics 8.69±0.67 fl and the non diabetic controls 8.91±0.80 fl (Table 2). There was a statistically significant difference in platelet count of diabetics and healthy controls platelet counts. p =0.038 while there was no statistically significant difference between the mean platelet volume in diabetics and healthy controls p=0.593.
groups t-test for platelet counts and mean platelet volume showed t-statistics of 2.36 and 2.108 while the two tail probabilities of 0.0192 and 0.0363 respectively were obtained. Among the diabetics, a positive correlation of Pearson's correlation was seen between MPV and fasting blood sugar ($r = 0.04, \ p < 0.001$), body mass index ($r = 0.142$) and duration of diabetics ($r = 0.045$). While a negative correlation was observed between platelet count and fasting blood sugar, $r = -0.059$, duration of diabetics ($r = -0.027$) but a positive correlation between platelet count and body mass index ($r = 0.002$) Correlating platelet count with mean platelet volume using Pearson's test in both the diabetic patients and non diabetic controls showed statistically significant levels of 0.000 in both groups $(r = -0.485, p < 0.05; and \ r = -0.403, \ p < 0.05$ respectively).

Discussion

The MPV and platelet counts are indicators of thrombotic potential, and risk factors for microvascular complications in diabetics [17-19]. MPV is an indicator of the average size and activity of platelets, with a higher MPV value indicating a larger average platelet size. Larger platelets synthesize more thromboxane A2, are able to aggregate better, and are able to secrete more serotonin and ß-thromboglobulin than smaller platelets [20-22]. Our study revealed a higher mean platelet count for diabetics than for the controls. This was in consonance with the findings by Thomas et al. [23], Zuberi et al [18], and Demirtunc et al. [24]. It is however in contrast with the findings of a study conducted by Hekimsoy et al. [17]. This suggests that the platelet count is the net result of the interplay of platelet survival and platelet production rate. The overall mean platelet volume was lower for the diabetics than for the non-diabetic controls. This was in contrast with the findings by Shah et al [25], Ates et al. [21], Hekimsoy et al [17], Demirtunc et.al [24], Zuberi et al. [18], Jindal et al. [26], Papanas et al. [27], and Thomas et al. [23]. However, this difference was not significant when subjected to statistical testing. ($p=0.593$). The discordant result in our study may be accounted for by the fact that the majority of diabetics utilized for this study had been on treatment and in particular antplatelet medications like clopidogrel and vasoprin for varying durations. This could impact the outcome of our result and a possible limitation of the study. Clopidogrel acts by irreversibly inhibiting the P2Y12 ADP receptor subtype on the platelet cell membrane, thereby preventing platelet activation and cross-linking by fibrin [28]. Activated platelets are larger, and prevention of platelet activation may prevent an increase in average platelet size and the mean MPV. This suggests that antplatelet medication may reduce the thrombotic potential without causing a reduction in the absolute platelet count. We however cannot postulate that clopidogrel alone accounts for this effect. More studies would be required to explicitly describe these characteristics and define a time and dose-response relationship.

The mean glycemic control of the diabetics utilized for our study was suboptimal (147.85±72.54 mg/dl). This may be accounted for by poor compliance to dietary modifications, lifestyle modifications and medications. We found a significant positive relationship between the MPV and glycemic control, as measured with the fasting blood sugar. A significant positive relationship was also seen in studies conducted by Shah et al. [25] who utilised HBA1c and fasting blood sugar levels, and Thomas et al and Demirtunc et al, who utilised the HBA1c levels of the patients [23, 24] This strongly indicates that achieving good glyemic control may limit platelet activation, and delay the onset or progression of microvascular complications in diabetics.

Our finding of a significant positive relationship between the MPV and the duration of diabetes gives credence to the fact that the risk of microvascular complications increases with the duration of diabetes. Discordant results were however found in studies conducted by Thomas et al and Hekimsoy et al. [23, 17]. This suggests that other factors may account for the thrombotic potential of diabetics with time [29]. More studies would be required to clarify this relationship. We also found a positive relationship between the MPV and BMI, unlike Thomas et al and Hekimsoy et al, who found no association [23, 17]. A falsely low platelet counts (pseudo-thrombocytopenia) may be due to misidentification of giant platelets as red cells by the automated platelet counts, other causes are EDTA-induced platelet clumping and satellitism [30]. A falsely high count may be due to markedly microcytic or fragmented red cells due to bacteria or fungi infection [31]. It is noteworthy that the mean platelet concentrations and mean platelet volume of both diabetics on treatment and controls were within the reference ranges in healthy individuals [32, 33]. The normal ranges obtained in diabetes patients could be a reflection of their adequate glycaemic control, although Sharpe et al. [12] reported glycaemic control is not related to mean platelet volume. More studies will elucidate this hypothesis. The results obtained in this study could be skewed in favor of the diabetics because of the unmatched age and gender in the diabetics and controls.

Conclusion

This study revealed a higher mean platelet count for diabetics on treatment than for non diabetics controls while mean platelet volume was lower in cases than controls. However, both parameters in diabetics on treatment were within normal reference ranges of healthy individuals.

Competing interests

The authors declare no competing interests.

Authors’ contributions

Akinbami Akinsegun conceptualized and designed the study; Dada Akinola Olusola drafted the literature review; John-Obadore Sarah reviewed the manuscript; Oshinaike Olajumoke reviewed the final manuscript; Adediran Adewumi general supervision; Odesanya Majeed developed the discussion; Ogbera Anthonia reviewed the final manuscript; Okunoye Olaitan recruited the patients; Arogundade Olarewaju recruited the controls; Aile Kingsley reviewed the manuscript. All the authors have read and approved the final version of the manuscript.

Acknowledgments

We appreciate the efforts of Mr. Isa Usman who assisted in bleeding the participants and Mr. Oluwamuhuru. Phillip.O. who carried out the full blood count on the samples.

Tables

Table 1: Sociodemographic data of participants

Table 2: Mean platelet counts, mean platelet volume, fasting blood sugar
References

1. Ostenson CG. The pathophysiology of type 2 diabetes mellitus: An overview. Acta Physiol Scand. 2001;171(3):241-247. doi:10.1111/j.0065-1325.2001.tb24290.x. PubMed | Google Scholar

2. Carr ME. Diabetes mellitus: A hypercoagulable State. J Diabetes complications. 2001; 15(1): 44-54. PubMed | Google Scholar

3. Mendel S, Sarode R, Dash S, Dash RJ. Hyper aggregation of platelets detected by whole blood platelet aggregometry in newly diagnosed non-insulin dependent diabetes mellitus. Am J Clin Pathol. 1993; 100(2): 103-107. PubMed | Google Scholar

4. Beckman JA, Creager M, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology and management. JAMA. 2002; 287(19): 2570-2581. PubMed | Google Scholar

5. Luscher TF, Creager MA, Beckman JA, Consentino F. Diabetes and vascular disease: pathophysiology, clinical consequences and medical therapy. Circulation. 2003;108(13):1655-1661. PubMed | Google Scholar

6. Colwell JA, Nesto RW. The platelets in diabetes: Focus on prevention of ischaemic events. Diabetes Care. 2003; 26(7): 2181-2188. PubMed | Google Scholar

7. Ferroni P, Basil S, Falco A, Davi G. Platelet activation in type 2 diabetes mellitus. J Thromb Haemost. 2004; 2(8):1282-1291. PubMed | Google Scholar

8. Ishii H, Umeda F, Nawata H. Platelet function in diabetes mellitus. Diabetes Metab Rev. 1992; 8:53-66. PubMed | Google Scholar

9. Vinik AI, Ebas T, Park TS, Nolan R, Pi Henger GL. Platelet dysfunction in type 2 diabetes. Diabetes Care. 2001;24(8):1476-1485. PubMed | Google Scholar

10. Tschoepe D, Roesen P, Kaufmann L, Schauseil S, Kehrel B, Ostermann H et al. Evidence of abnormal platelet expression in diabetics Mellitus. Eur J Clin Invest. 1990;20(2):166-170. PubMed | Google Scholar

11. Ebil N, Krugluger W, Strait G, Scerahbauer K, Hopmeier P, Schernthaner G. Improved metabolic control decreases platelet activation markers in patients with type 2 diabetes. Eur J Clin Invest. 2004; 34(3):205-209. PubMed | Google Scholar

12. Sharpe PC, Trinick T. Mean platelet volume in diabetes mellitus. Q J Med. 1993; 86(11):739-742. PubMed | Google Scholar

13. Tschoepe D. The active megakaryocyte-platelet system in vascular disease: Focus on diabetes. Semin Thromb Hemost. 1995; 21(2):152-160. PubMed | Google Scholar

14. Martin JF, Bath PM, Burr ML. Influence of platelet size on outcome after myocardial infarction. Lancet. 1991; 338(8780): 1409-1411. PubMed | Google Scholar

15. Sharpe PC, Trinick T. Mean platelet volume in diabetes mellitus. Q J Med. 1993; 86(11):739-742. PubMed | Google Scholar

16. Lalouschef W, Lang W, Mullner M. Vienna Stroke Study group; Current strategies of secondary prevention after a cerebrovascular event: the Vienna stroke registry. Stroke. 2001;32:2860-2866 doi:10.1161/hs1201.099891.. PubMed | Google Scholar

17. Hekimozy Z, Payzinz B, Ornek T, Kandogan G. Mean platelet volume in Type 2 diabetic patients. J Diabetes Complications. 2004; 18(3):173-176. PubMed | Google Scholar

18. Zuberi BF, Akhtar N, Afsar S. Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and non-diabetic subjects. Singapore Med J. 2009;49(2):114-116. PubMed | Google Scholar

19. Bae SH, Lee J, Roh KH, Kim J. Platelet activation in patients with diabetic retinopathy. Korean J Ophthalmol. 2003; 17(2):140-144. PubMed | Google Scholar

20. Colwell JA, Nesto RW. The platelet in diabetes-focus on prevention of ischemic events. Diabetes Care. 2003;26(7):2181-2188. PubMed | Google Scholar

21. Ates O, Kiki I, Bilen H, Keles M, Kocer I, Kulaoglugi DN, et al. Association of Mean Platelet Volume With The Degree of Retinopathy in Patients with Diabetes Mellitus. Eur J Gen Med. 2009;6(2):99-102. PubMed | Google Scholar

22. Chang HA, Hwang HS, Park HK, Chun MY, Sung JY. The Role of Mean Platelet Volume as a Predicting Factor of Asymptomatic Coronary Artery Disease. Korean J Fam Med. 2010;31(N68):606-666. PubMed | Google Scholar

23. Thomas AK, Udarya KM, Suraksha BR, Thej MJ, Madheri R, Harendra KML, Venkatasamy L. Mean platelet volume in type 2 diabetes mellitus. J lab physicians. 2012; 4(1):5-9. PubMed | Google Scholar

24. Demirtunc R, Duman D, Basar M, Bilgi M, Teomete M, Garip T. The relationship between glycemic control and platelet activity in type 2 diabetes mellitus. J Diabetes Complications. 2009; 23(2):89-94. PubMed | Google Scholar

25. Shah B, Sha D, Xie D, Emile R, Mohler ER, Berger JS. The Relationship between Diabetes, Metabolic Syndrome, and Platelet Activity As Measured by Mean Platelet Volume: The National Health and Nutrition Examination Survey, 1999-2004. Diabetes Care. 2012 May; 35(5): 1074-1078. PubMed | Google Scholar

26. Jindal S, Gupta S, Gupta R, Kakkar A, Singh HV, Gupta K, et al. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. Hematology. 2011;16(2):86-9. PubMed | Google Scholar

27. Papanas N, Symeonidis G, Maltezos E, Mavridis G, Karavageli E, Vosnakidis T, et al. Mean platelet volume in patients with type 2 diabetes mellitus. Platelets. 2004;15(8):475-478. PubMed | Google Scholar

28. Maegdefessel L, Azuma J, and Tsao PS. Modern role for clopidogrel in management of a trial fibrillation and stroke reduction. Vasc Health Risk Manag. 2010; 6: 95-103. PubMed | Google Scholar
29. Duerschmied D, Ahrens I, Mauler M, Brandt C, Weidner S, Bode C, Moser M. Serotonin Antagonism Improves Platelet Inhibition in Clopidogrel Low-Responders after Coronary Stent Placement: An In VitroPilot Study. PLoS One. 2012; 7(2): e32656. PubMed | Google Scholar

30. Gowland E, Kay HEM, Spillman JC, et al. Agglutination of platelets by a serum factor in the presence of EDTA. Journal of Clinical Pathology. 1969; 22(4):460-454. PubMed | Google Scholar

31. Van der Meer W, MacKenzie MA, Dinnisson JWB, et al. Pseudoplatelets: a retrospective study of their incidence and interference with platelet counting. Journal of Clinical Pathology. 2003;56(10):772-774. PubMed | Google Scholar

32. Demirin H, Ozhan H, Ucgun T, Celer A, Bular S. Normal range of mean platelet volume in healthy subjects: Insight from a large epidemiologic study. Thromb Res. 2011; 128(4):358-360. PubMed | Google Scholar

33. Lozano M, Narvaez J, Faundez A, Mazzaru R, Cld J. Platelet count and mean platelet volume in the Spanish population. Med Clin (Barc).1998;110(20):774-777. PubMed | Google Scholar

### Table 1: Sociodemographic data of participants

| Parameters                  | Diabetics (n=100) | Non diabetic Controls(n=100) |
|-----------------------------|-------------------|-----------------------------|
| **Mean Age**                |                   |                             |
| Gender                      | 62.35±9.84        | 32.38±66.44                 |
| Female                      | 73                | 63                          |
| Male                        |                   |                             |
| Educational Status          | 27                | 37                          |
| No Education                | 22                | Nil                         |
| Primary                     | 16                | Nil                         |
| Secondary                   | 24                | Nil                         |
| Tertiary                    | 38                | 100                         |
| Mean BMI                    | 32.10±4.85        | 25±5.23                     |

Abbreviations: BMI=Body mass index

### Table 2: Mean platelet counts, MPV and FBS

| Parameters                  | Diabetics     | Non diabetic Controls |
|-----------------------------|---------------|-----------------------|
| Mean Platelet counts        | 235.29±76.81  | 211.32±66.44 (p=0.038) |
| Mean MPV                    | 8.69±0.67     | 8.91±0.80 (p=0.593)    |
| Mean FBS                    | 147.85±72.54  | 95.20±30.10            |

Abbreviations: MPV= mean platelet volume, FBS= fasting blood sugar