

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

الايه

((وَأَنْزَلَ اللَّهُ عَلَيْكَ الْكِتَابَ وَالْحِكْمَةَ وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ

عَلَيْكَ عَظِيمًا))

صدق الله العظيم

(سورة النساء. الآية رقم 113)

Dedication

To my

Mother and father

Sisters and brothers

Teachers and friends

Wife and Children

I dedicate this work with love

Omer

Acknowledgements

Firstly I would like Thanks to God for giving me health, mind and patience to study and do my research

I wish to express my thanks to all patients and volunteers who participated in this study and in particular to

Professor Babiker Ahmed Mohammad, my principle supervisor, for never-ending support in supervision and encouragement, for sharing his great scientific knowledge and for his patience in teaching me the research methods and scientific writing.

All staff of Hematology Department faculty of Medical Laboratory Sciences, SUST for their endless support

Last but not least, I would like to thank my family for their continuous support and encouragement

Abstract

This was prospective case control study conducted in Fidal specialized Hospital Khartoum State during the period from March - October 2015. The study aimed to investigate MPV and PDW in type II DM and its relation to cardiovascular complications (CVD), duration of diabetes and diabetic control status.

Platelet indices were determined in a total of 100 patients with DM type II (52 males and 48% female as cases) and 100 apparently healthy subjects 55 (55%) males and 45 (45%) females.

MPV and PDW values were significantly found elevated in diabetic patients compared to control subjects, ($P= 0.005$) ($P=0.009$) respectively. MPV and PDW values were significantly high in diabetic patients with CVD as compared to those without CVD, ($P= 0.002$) ($P= 0.020$) respectively. MPV and PDW were significantly increased with longer duration of type II DM, ($P=0.002$) ($P=0.020$) respectively. Platelet count MPV or PDW did not affected in control status of DM, ($P = 1.21$) ($P = 0.97$)($P =0.51$) respectively.

In conclusion, Type II diabetes mellitus is associated with high platelet indices (MPV and PDW) indicating platelet hyper-activation that contributes to CVD.

المستخلص

أجريت هذه الدراسة الوصفية في مستشفى فضيل التخصصي ولاية الخرطوم في خلال الفترة من مارس 2015 الي اكتوبر 2015. هدفت الدراسة لقياس مستشعرات نشاط الصفائح الدموية في مرضي السكر النوع الثاني وعلاقتهم بامراض الاوعيه الدمويه، وطول الاصابه بمرض السكر النوع الثاني وضبط سكر الدم التراكمي.

درست مشعرات نشاط الصفائح الدموية في مجموعة متطوعيين تتألف من 100 مريض بداء السكري النوع الثاني (52%) من الذكور و (48%) من الإناث و مجموعة تحكم تتكون من افراد اصحاء (55%) من الذكور و (45%) من الإناث).

كانت مستويات متوسط حجم الصفائح الدموية (MPV) ومتوسط الفرق بين احجام الصفائح الدموية (PDW) اعلى عند مرضى السكري مقارنة بمجموعة التحكم ($P = 0.005$) الفرق بين احجام الصفائح الدموية (PDW) اعلى التوالي. كانت مستويات متوسط حجم الصفائح الدموية (MPV) ومتوسط الفرق بين احجام الصفائح الدموية (PDW) اعلى في مرضى السكر الذين يعانون من مضاعفات في تصلب الشرايين من الذين لا يعانون معه ($P = 0.020$) ($P = 0.002$) علي التوالي. صاحب الزيادة في فترة مرض السكر ارتفاعا في مستويات متوسط حجم الصفائح الدموية (MPV) ومتوسط الفرق بين احجام الصفائح الدموية ($P = 0.020$) ($P = 0.002$) (PDW) علي التوالي. لم يتأثر متوسط حجم الصفائح الدموية (MPV) او متوسط الفرق بين احجام الصفائح الدموية (PDW) بالحالات المتحكم بمستوي السكر ($P = 0.51$) ($P = 1.21$) ($P = 0.79$).

خلصت الدراسة الى انه يرافق مرض السكري النوع الثاني نشاط مفرط للصفائح للدمويه بدلالة ارتفاع مستويات مشعرات نشاط الصفائح الدموية التي تساهم في حدوث مضاعفات تصلب الشرايين لدي مرضي السكري.

List of Contents

	Page No
Title	
الأية	I
Dedication	II
Acknowledgement	III
Abstract	IV
المستخلص	V
Contents	VI
List of tables	VIII
List of figures	IX
Abbreviations	X
1.1.1 Diabetes Mellitus	1
1.1.1.1 Definition	2
1.1.1.2 Incidence	2
1.1.1.3 Classifications	2
1.1.1.4 Complications of diabetes mellitus	4
1.1.1.5 Diabetes Mellitus and Vascular Diseases	4
1.1.2 Platelets	5
1.1.2.1 Definition	5
1.1.2.1 Platelet Production (Megakaryopoiesis and Thrombopoiesis)	5
1.1.2.2 Circulating platelets and their life span	5
1.1.2.3 Platelet structural and Functional Anatomy	5
1.1.2.4 Platelet Surface	6
1.1.2.5 Platelet Granules	6
1.1.2.6 Platelet structural	7
1.1.2.7 Platelet function	7
1.1.2.8 Platelet activation	8
1.1.2.9 Platelet shape change	9
1.1.2.10 Platelet Adhesion	9
1.1.2.11 Platelet release reaction	9
1.1.2.12 Platelet aggregation	10
1.1.2.13 Platelet procoagulant activity	11
1.1.3 Platelet Indices	11
1.1.3.1 Mean Platelet Volume (MPV)	12
1.1.3.1.1 Definition	12
1.1.3.1.2 Clinical Value of MPV	12
1.1.3.1.3 Causes of raised MPV	13
1.1.3.1.4 Causes of low MPV	13
1.1.3.1.5 Influences of drugs on MPV	14
1.1.3.2 Platelet distribution width (PDW)	14
1.1.3.3 Platelet indices measurement	14
1.1.3.3.1 Detection principle	15
1.1.3.3.2 Platelets discriminator	15
1.1.3.3.3 Platelet Histogram	15

1.1.4	Normal Values of platlet	17
1.1.5	Platelets as accelerators of Atherothrombosis	17
1.1.6	Endothelial dysfunction mediates CVD in type II DM	18
1.1.7	Platelet alterations in diabetes mellitus	18
1.1.7.1	Increased reactivity and adhesion	18
1.1.7.2	Amplified agonist-receptor coupling	19
1.1.7.3	Increased capacity for prostanoid generation	19
1.1.7.4	Decreased capacity for nitric oxide (NO-) generation	19
1.1.7.5	Enhanced generation of reactive oxygen species	20
1.1.7.6	Resistance to NO- and prostacyclin	20
1.1.7.7	Increased cytosolic calcium mobilization	20
1.1.7.8	Increased α -granule content with concomitantly increased release	21
1.1.7.9	Increased platelet volume	21
1.1.7.10	Increased numbers of glycoprotein receptors GPIb and GPIIb/IIIa	21
1.1.7.11	Increased membrane protein glycation	21
1.1.7.12	Altered membrane fluidity	21
1.1.7.13	Increased binding of adhesive RGD-protein ligands	22
1.1.7.14	Increased content and release of plasminogen activator inhibitor-1	22
1.2	Previous Studied	23
1.3	Rationale	26
1.4	Objectives	27
	Material and Method	28
2.1	Study design	29
2.2	Study area	29
2.3	Study population ,Included and Excluded Criteria	29
2.4	Sampling	30
2.5	Laboratory investigations	30
2.6	Ethical clearance	32
2.7	Statistical analysis	32
3	Result	33
4.1	Discussion	39
4.2	Conclusion	42
4.3	Recommendation	43
	References	44
	Appendices	53
	Annex I Questioner	55
	Annex II HbA1c Estimation	56

List of tables

Table number.	Contents	Page number
1.1	Content of Three different granule sub population of platelet	6
1.2	Normal population Reference Range platelet indices	17
3.1	Demographic data and platelet indices in case and control groups	34
3.2	Comparison between Platelet Indices in case and control groups	35
3.4	Associations of platelet indices with control status (judged by HbA1c) among the diabetic group.	36
3.5	Associations of platelet indices with duration of type II DM among the case group	36
3.6	Comparison of platelet indices between males and females	37

List of figures

Figure number.	Title	Page number
Fig. 1.1	Platelet structure	8
Figure 1.2	Histogram of platelet size distribution and the definition of platelet size deviation width (PDW), and platelet-large cell ratio (P-LCR).	16

Abbreviations

DAG	Diacylglycerol
DM	Diabetes mellitus
ICAM	Intercellular adhesion molecule
IDDM	Insulin dependent diabetes mellitus
IP ₃	Inositol Trisphosphate
LFA-1	Lymphocyte function-associated antigen-1
MPV	Mean Platelet Volume
NIDDM	Non-insulin dependent diabetes mellitus
NO	Nitric oxide
Pct	Platelet Crit
PKC	Protein kinase C
PLA ₂	Phospholipase A ₂
PLC-g	Phospholipase C-g
PDW	Platelet distribution width
PIP ₂	Phosphatidylinositol-4, 5-bisphosphate
PSGL-1	P-selectin glycoprotein ligand-1
SCCS	Surface-connected canalicular system
T2DM	Type II diabetes mellitus
TXA ₂	Thromboxane A ₂
vWF	von Willebrand factor