ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Hyperglycemic induced variations in Hematological Indices in Type 2 Diabetics

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Manuscript Info

Manuscript History:

Received: 14 September 2013
Final Accepted: 23 September 2013
Published Online: October 2013

Key words:
Diabetes Mellitus, HbA1c, Erythrocyte indices, Leukocyte indices, Platelet indices,

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Abstract

Elevated blood glucose level is a major factor in development of diabetic complications due to unfavorable hyperglycemic induced biochemical as well as hematological indices changes.
The objective of present study was to determine the relationship of Glycemic control on Hematological Indices (Erythrocyte indices, Leukocyte indices and Platelet indices) in type 2 Diabetic patients. This study was conducted on 92 Control and 170 Diabetic subjects. Blood sample of diabetic subject were collected from Baqai Institute of Diabetology and Endocrinology (BIDE) and were analyzed for fasting blood glucose, HbA1c, and for 18 Hematological indices (RBCs, HGB,HCT, MCV, MCH, MCHC, RDW, WBCs, %LYM, %MON, %GRA, #LYM, #MON, #GRA, PLT, PCT, PDW, MPV). Result show that the blood glucose, HbA1c, were significantly increased in diabetic patient which is the sign of insulin deficiency, glycation of hemoglobin also observed in diabetics which is a risk factor of developing vascular complications. Among Platelet Indices MPV and PDW were found to be significantly increased in diabetic patients as compared to control group. It is considered that alteration in platelet morphology and functions are associated with pathological processes and increased risk of vascular complications in patients with diabetes.

Introduction

Diabetes mellitus (DM) is a group of metabolic disorder characterized by abnormal carbohydrate metabolism resulting chronic hyperglycemia (high blood glucose levels) caused by defective insulin production or appropriate and efficient utilization of insulin by cells. This disease is spreading like epidemic all over the world. Inappropriately managed diabetes cause severe complications The chronic, long term complications are related to blood vessel diseases and are generally classified into micro vascular disease (small vessel disease) such as those concerning the eyes(retinopathy), kidneys(nephropathy) and nerves (neuropathy) and; macro vascular disease concerning the heart and blood vessels (large vessel disease) (Jawa et al, 2004). Recent studies have indicated that the unfavorable biochemical changes associated with hyperglycemia include increased flux of glucose.

Blood, a carrier of metabolic products from and to the various regions of the cardiovascular system, is affected by the clinical status of the tissue environment. Due to the addition of altered biochemical and tissue products in the blood and their interactions with the blood constituents, the functional properties of erythrocytes are changed (Jones and Peterson, 1981) Erythrocytes stay in hyperglycemic environment during their life span, which provokes the changes in erythrocyte deformability and the aggregation. The impairment of erythrocyte deformability is attributed to the alterations in the membrane structure. These changes may include: Altered concentration ratio of cholesterol / phospholipid in the membrane core, amplified membrane lipid peroxidation i.e. (Srour et al, 2000). Erythrocytes aggregation depends on the composition of membrane and the plasma proteins fibrinogen and globulin. The aggregation is amplified with increased fibrinogen plasma concentration, in type 2 diabetes and is likely to be a main alteration, contributing to the cardiovascular risk factor (Ceriello, 1997).Variable or persistent hyperglycemia

induces various changes in the erythrocyte membrane and its cytoplasm, leading to modification in the deformability. With prolonged diabetic conditions the deformability of erythrocytes is further decreased, whereas its aggregation increases, hence they make whole blood more viscous that may obscure the flow of these cells in micro vessels (Shin et al, 2007 and Young et al, 1995). In diabetes mellitus hemorheological parameters distressed which include: hematocrit, plasma proteins, erythrocyte aggregation, and erythrocyte deformability, are linked with marked raise in both plasma and whole blood viscosity (Watala et al, 1985). Independently, high values of glycosylated hemoglobin have been found to be associated with decreased deformability of erythrocytes (Bauersachs et al, 1989). Alteration in leukocyte indices has also been reported in diabetes. Peripheral blood leukocytes are made up of polymorphonuclear cells (PMNCs), including monocytes and lymphocytes. In diabetic states, Polymorpho- and mononuclear leukocytes can be stimulated by advanced glycation end products, oxidative stress, angiotensin II, and cytokines. Activated leukocytes discharge many kinds of cytokines and transcription factors including TNF-α, interleukin-1β, NF-κB, , and transforming growth factor β, that have a fundamental role in inflammation Furthermore, activated leukocytes can also liberate superoxide radicals and proteases, all of which promote oxidative stress. It is expected that low-grade chronic inflammatory responses, together with other risk factors can lead to extensive vascular damage, endothelial dysfunction, and increased oxidative stress, ultimately participating in the pathogenesis of diabetic micro- and macro vascular complications (Chung et al, 2005). Numerous studies have shown that in diabetes, many alterations in neutrophil function might contribute to the high prevalence of infections in diabetic patients. Further the extreme production of cytokines may lead to inappropriate activation and tissue damage and even to increase vulnerability to invasive microorganisms. Therefore, the increased neutrophils responsiveness in diabetes may be considered as a part of diabetic physiopathology (Hatanaka et al, 2006).

Platelet hyperactivity may play a role in the expansion of vascular complications of this metabolic disorder. Platelets play a vital role in the integrity of normal homeostasis and mean platelet volume (MPV) is the marker for its function. Platelets are varied in size, density, and reactivity, these changes arising at or before thrombopoiesis. Large platelets are younger and reveal more activity (Kodiatte et al, 2012).Changes in these variables may be concerned in the natural history of vascular disease. Larger and functionally more reactive platelets have been found following myocardial infarction and in diabetics (Wincour et al, 1985). The large platelets hold more dense granules, are more persuasive than the smaller platelets, and are hence more thrombogenic. Increase in MPV has been recognized in patients with metabolic syndrome, stroke and diabetes mellitus (Tavil et al, 2007).There is strong link of platelet dysfunction with platelet hyperactivity in both type 1 and type 2 DM (Ferroni et al, 2004). Distorted platelet morphology and function have been reported in patients with Diabetes and MPV was found to be extensively higher in diabetic patients who are likely to be linked with the pathological processes and increased risk of vascular disease (Papanas et al, 2004). Increased MPV has also been predictable in gestational diabetes mellitus (Bozkurt, 2006), congestive cardiac failure (Chung et al, 2007) and coronary artery ectasia (Bitigen, 2007). Increased platelet reactivity has been suggested as a potential mechanism of the accelerated atherosclerosis and enhanced rate of arterial thrombosis in diabetics (Tschoepe et al, 1989 and Winocour, 1985). Hyper-reactivity of platelets from T2DM patients is indicated by increased aggregation, greater fibrinogen binding, and thromboxane production (Davı` et al, 1990).

MATERIALS AND METHODS:

The study was conducted on 170 diabetic patients (Type-2), both males (n=93) and females (n=77) between the age group 35-65 years who were registered at the diabetic clinic of Baqui Institute of Diabetology and Endocrinology Karachi, Pakistan. 92 age and sex matched control subjects (42 males and 50 females) were also selected from the general population at random for comparison. Ethical approval was obtained from the institutional ethical review board (IERB) before the commencement of the study. Informed consent of the patients was taken with the help of questionnaire. All patients who were diagnosed diabetes mellitus of type -2 using the ADA criteria of fasting blood glucose (FBG) of >126 mg/dl were included in the study. The patients with any recent critical illness were excluded from the study. The blood samples were collected in tubes with EDTA as anticoagulant and analyzed within 2 hours of venepuncture for Platelet indices and HbA1c. Plasma was also separated and analyzed for other Biochemical parameters. Fasting blood glucose was estimated by following glucose oxidase method on UV- visible spectrophotometer Jenway 6305.The HbA1c was measured by D10 Hemoglobin testing system (BIO RAD Laboratories).

EDTA whole blood was used for the estimation of hematological indices. The blood samples were analyzed by fully Automated Hematology Analyzer (18 parameters ABX Micros 60 (open tube) manufactured by HORIBA ABX

Diagnostics (France) (www.abx-horiba.com). The sample (10 µl) was automatically sucked by the auto-sampler of the equipment and analyzed. The results of the following 18 parameters were recorded. RBCs, WBC, HGB, HCT, MCV, MCH, MCHC, PLT, PCT, MPV, PDW, RDW, LYM (% and #), MON (% and #), GRA (% and #).

Statistics:

Data were statistically analyzed using Statistical Package for Social Sciences version 20.0 (SPSS Inc, Chicago, IL, USA). Means and standard errors of means were calculated in independent samples by descriptive statistics, while paired two tailed student's t test was performed to calculate the level of significance between the means at 95% confidence intervals (CI). The strength of association between the pairs of variables was assessed by Pearson Correlation Coefficient (r).The p value < 0.05 was considered significant.

RESULT:

Total 170 Diabetic patients (Type-2) (93 male & 77 females) and 92 healthy control (42 male & 50 females) subjects fulfilling the selection criteria were allocated to male and female groups. Mean age of control is 45.5±0.77 years and 51.08±0.7 years for patients. Blood samples were collected and analyzed for fasting blood glucose, HbA1c, Erythrocyte indices (RBCs, HGB, HCT, MCV, MCH, MCHC and RDW), Leukocyte indices (WBCs, %LYM, %MON, %GRA, #LYM, #MON, #GRA) and Platelet indices (PLT, PCT, PDW, MPV). The results of biochemical parameters, and hematological indices were compared in diabetic patients and control subjects. Significant increase in FBG was found in diabetic patients 157.68±4.14as compare to control group 100.1±2.28.The level of HbA1c was also greater in diabetic patients 9.15±0.17as compare to control group 4.87±0.047. **(Table -I)**.
In Erythrocyte indices significant increase in RBCs, HGB, HCT, MCH, MCHC and RDW was found in diabetic patients as compared to control group **(Table-I).** When the comparison was made on the basis of sex; male patients exhibits significant elevation in all erythrocyte indices with the exception of MCH whereas female patients showed significant increase in all erythrocyte indices with the exception of MCV when compare to their respective controls. **(Table –II)**.

In Leukocyte indices significant increase in %MON, %GRA and #MON was found in diabetic patients as compared to control group ($P < 0.0001$,$P= 0.0013$, $P < 0.0001$ respectively) **(Table-I).** When the comparison was made on the basis of sex; male patients exhibits significant elevation in %MON ($P < 0.0001$), %GRA ($P < 0.05$) and #MON ($P < 0.0001$) in comparison of respective controls. Whereas female patients showed significant increase in %MON ($P < 0.0001$), %GRA ($P = 0.0131$) and #MON ($P < 0.0001$) when compare to their respective controls. **(Table –II)**.
Among Platelet indices significant increase in MPV ($P < 0.0001$) and PDW ($P < 0.0033$), was found in diabetic patients as compared to control group **(Table-I).** When the comparison was made on the basis of sex; male patients exhibits significant elevation in MPV ($P < 0.0001$) when compare to their respective controls. Whereas female patients showed significant increase in MPV and PDW (($P < 0.0001$ and $P= 0.0121$ respectively) when compare to their respective controls. **(Table –II)**.

Table – I
Biochemical Parameters and
Hematological Indices (18 Parameters) in Controls and Diabetic Subjects.

Variables	Control Subjects (n = 92)	Diabetic Patients (n = 170)	P-Value
Biochemical Parameters			
FBG (mg/dl)	100.10±2.28	157.68±4.14	P < 0.0001
HbA1c (%)	4.87±0.047	9.15±0.17	P < 0.0001
Erythrocyte (R.B.Cs) Indices			
RBCs (10^6/mm^3)	4.62±0.08	5.93±0.13	P < 0.0001
HGB (g/dl)	12.98 ±0.23	17.79±0.40	P < 0.0001
HCT (%)	36.39±0.75	48.20 ±1.15	P < 0.0001
MCV (µm^3)	78.72±0.92	81.28±0.65	P = 0.0214
MCH (pg)	28.34±0.46	30.77±0.37	P = 0.0001
MCHC (g/dl)	35.90 ±0.50	37.89±0.34	P = 0.0008
RDW (%)	13.69±0.16	14.41±0.14	P = 0.001
Leukocyte (W.B.Cs) Indices			
WBCs (10^3/mm^3)	7.28±0.19	7.47 ±0.25	P = 0.9004
LYM (%)	32.59±0.70	35.63±1.22	P = 0.0805
MON (%)	5.99±0.20	10.44±0.43	P < 0.0001
GRA (%)	61.68±0.76	54.63±1.55	P = 0.0013
#LYM (10^3/mm^3)	3.46±1.09	3.01±0.59	P = 0.6970
#MON (10^3/mm^3)	0.37±0.02	0.70±0.04	P < 0.0001
#GRA (10^3/mm^3)	4.59±0.13	4.45±0.20	P = 0.6083
Thrombocytes (Platelet) Indices			
PLT (10^3/mm^3)	234.93±6.87	237.40±6.33	P = 0.8047
PCT (%)	0.21±0.01	0.23±0.02	P = 0.4858
MPV (µm^3)	8.60±0.12	9.48±0.10	P < 0.0001
PDW (%)	14.12±0.22	15.02±0.19	P = 0.0033

n = No of observations, Values are represented as mean ± S.E.M (Standard error of mean).Student's t -test was used to compare the means between the control & Diabetic groups. P value < 0.05 was considered significant.

Table – II
Hematological Indices (18 Parameters) in Control and Diabetic Subjects on Gender Basis

Variables	MALE		P-Value	FEMALE		P-Value
	Control (n= 42)	Diabetic (n=93)		Control (n= 50)	Diabetic (n=77)	
Erythrocyte (RBC) Indices						
RBCs (10^6/mm^3)	4.80±0.13	6.17±0.16	P < 0.0001	4.47± 0.08	5.65±0.22	P < 0.0001
HGB (g/dl)	13.78±0.39	18.38±0.49	P < 0.0001	12.30±0.23	17.07±0.64	P < 0.0001
HCT (%)	38.66±1.27	51.03±1.44	P < 0.0001	34.48±0.78	44.78±1.78	P < 0.0001
MCV (µm^3)	79.67±1.35	82.92±0.80	P = 0.0313	77.92±1.25	79.29±1.02	P = 0.3973
MCH (pg)	32.63±2.48	31.13±0.47	P = 0.4100	27.80±0.58	30.33±0.58	P = 0.0038
MCHC (g/dl)	35.78±0.76	37.78±0.45	P = 0.0184	36.01±0.66	38.03±0.51	P = 0.0153
RDW (%)	13.55±0.24	14.38±0.20	P = 0.0157	13.80±0.21	14.45±0.19	P = 0.0249
Leukocyte (WBC) Indices						
WBCs (10^3/mm^3)	7.12±0.27	7.38±0.39	P = 0.6658	7.42±0.27	7.57±0.30	P = 0.7306
% LYM	33.54±1.02	36.70±1.73	P = 0.2409	31.78±0.96	34.36±1.69	P = 0.2532
% MON	6.15± 0.28	10.45±0.56	P < 0.0001	5.87±0.27	10.42±0.67	P < 0.0001
% GRA	60.33±1.11	53.89±2.14	P = 0.0517	62.82±1.03	55.53±2.23	P = 0.0131
#LYM (10^3/mm^3)	2.37±0.13	2.47±0.21	P = 0.7643	4.32±1.96	2.37±0.10	P = 0.2188
#MON (10^3/mm^3)	0.38±0.03	0.68±0.06	P = 0.0014	0.37±0.02	0.72±0.06	P = 0.0001
#GRAN (10^3/mm^3)	4.38±0.16	4.53±0.30	P = 0.7419	4.77±0.18	4.34±0.26	P = 0.228
Thrombocyte (Platelet) Indices						
PLT (10^3/mm^3)	226.83±11.06	231.89±7.99	P = 0.7188	241.74±8.54	244.05±10.12	P = 0.8722
PCT (%)	0.19±0.01	0.24±0.04	P = 0.4211	0.22± 0.01	0.21±0.01	P = 0.6615
MPV (µm^3)	8.50±0.17	9.39±0.13	P < 0.0001	8.68±0.15	9.58±0.14	P < 0.0001
PDW (%)	14.00±0.30	14.78±0.26	P = 0.0771	14.21±0.31	15.30±0.28	P = 0.0121

n = No of observations, Values are represented as mean ± S.E.M (Standard error of mean). Student's t -test was used to compare the means between the control & Diabetic groups. P value < 0.05 was considered significant.

DISCUSSION:

Hyperglycemic induced variation in hematological parameters has been reported by several studies. Elevation in glucose concentration is one of the major factor that effects the erythrocyte morphology i.e., the severity in the change of erythrocyte shape depend upon the plasma glucose level. This in turn, affects their flow properties through alteration and deformation at individual level and aggregation at collective level (Singh and Shin, 2009). There is frequently a reduction or change in blood viscosity which predisposes a person's system in reacting inadequately to insulin. The present study shows a significant increase in all erythrocyte indices in diabetic patients as compared to control group. Significant increase was also observed in RBCs, HGB, HCT, MCHC and RDW in both males and females patients when compared to controls. However the increase in MCV was significant in diabetic males and insignificant in diabetic females, while reverse was true with MCH when compared with respective controls (Table-II). Significant decrease in RBCs, HCT and MCV were found in diabetic females as compared with diabetic males ($P < 0.01$), while no significant difference was observed in HGB, MCH, MCHC and RDW between male and female diabetics. Elevated level of erythrocyte indices can be used as potential indicators in finding the risk of developing micro and macro vascular complications in diabetic patients (Jabeen et al, 2012). High RBC values may be due to smoking, exposure to carbon monoxide, chronic kidney disease, liver disease, certain forms of heart disease, lung disease, some cancers, alcoholism, polycythemia vera (a rare disorder of the bone marrow) or a rare disorder of hemoglobin. Conditions that influence water content of the body may also cause elevated RBC values. These conditions including diarrhea or vomiting, excessive sweating, dehydration, use of diuretics and the severe burns. The HCT level in blood is the measurement of RBCs and body's capability to produce the cells. In patients having type-2 diabetes, HCT levels are found to be higher than normal. It is also known that HCT is a determining factor of blood thickness if it is increased it could develop insulin resistance. Low MCV is consistent with iron deficiency anemia or thalassemia. Considerable elevations in hematocrit (HCT) and mean corpuscular volume (MCV) might be due to the fact that erythrocytes are continuously subjected to a variety of morphological changes due to the compositional changes in plasma, associated with some deviation in type 1 and type 2 diabetes (Marcinkowska-Gapinska and Kowal, 2006). MCH is increased in macrocytic anemias and MCHC is increased in hereditary spherocytosis (Waggiallah and Alzohairy, 2011).Correlation studies revealed that no significant correlation existed between fasting blood glucose and erythrocytes indices in diabetic patients except MCH which was found negatively correlated with FBG ($r = -0.163^{*}$). MCHC was found to be positively correlated with HbA_{1c} ($r = 0.243^{**}$). RBCs was found to be positively correlated with HGB, HCT and negatively correlated with MCH & MCHC **(Table-III).**Our results indicate that any change in biochemical parameters particularly glycemic control is reflected by erythrocyte indices which can be used as indicator for diabetic complications. In Present study Correlation analysis revealed significant positive correlation between FBG and HbA1c ($r=0.282^{*}$,$P = 0.048$),(**Table III)**.

Oxidative stress and inflammation are supposed to play roles in the pathogenesis of diabetes. Monocytes (MON) are crucial cells in the genesis of atherosclerotic lesions, as they stick to endothelium, which results in cardiovascular disease. Possible mechanism of increase in oxidative stress in PMNs and MON in relation to diabetes, hypertension and CRP remains to be elucidated. High blood Pressure and high glucose are reported to trigger protein kinase C activation, which may play a role in increasing PMN oxidative stress induced by hypertension and diabetes (Yasunari et al, 2002). In the present study the leukocyte indices were evaluated and significant increase was observed in percentage and number of monocytes and decrease in the percentage of granulocyte in both male and female diabetic patients in comparison with respective controls (Table I and II). Correlation studies indicated that number of granulocyte was positively correlated with FBG. WBCs was found to be positively correlated with %GRA, #LYM, #MON, #GRAN and negatively correlated with %LYM & %MON **(Table-IV).** Previous studies have indicated that WBC count is elevated in the diabetic patients and may contribute to the micro- and macro-vascular complication. The white blood cells are activated by the AGE products in response to the hyperglycemic states. It is also possible that immune system activation caused by inflammation, might increase WBC and therefore cytokine production such as cytokines (e.g. IL-6), are produced by activated white blood cells, which may decrease insulin sensitivity (Vozarova et al, 2002). Type 2 diabetes is accompanied by a priming of PMNs, resulting in Oxidative stress and increased self-necrosis, which starts a chain of inflammatory reactions that result in cell recruitment and in the long run, with Oxidative stress, may result in endothelial dysfunction (Shurtz-Swirski, 2001).

The study also included the comparison in the platelet indices between the control and the diabetic patients. Highly significant elevation of MPV and PDW were observed in both diabetic males and females in comparison with the control subjects(Table-I). Our results are in accordance with several clinical studies that have shown an altered (increased) population of circulating platelets compared with non-diabetics. This is because of the fact that, in addition to thrombopoietin (a chief hormonal regulator of platelet production) nitric oxide which is generated during

oxidative stress in diabetes, can also stimulate platelet production (Battinelli et al, 2001). Distorted platelet morphology and function have also been reported in patients with Diabetes Mellitus. An early finding showed that diabetic platelets exhibit enhanced arachidonic acid- thromboxane production. Thromboxane (TXA_2), an effective platelet activating and vasoconstriction agent, is produced from the arachidonic acid and has a positive correlation with glucose level. Therefore, elevated glucose level in diabetes may encourage the platelet activation (Davi et al, 1990). Upon activation, platelets change from a discoid to a sphere-shaped with long, spiky pseudopods. Consequently, the platelets are larger and more activated, expressing higher levels of the adhesion receptors like GPIIb /IIIa. Activated platelets show an increased adhesiveness and aggregation, and are a threat factor for developing coronary thrombosis, leading to myocardial infarction (Tschoepe et al, 1989). Moreover, efficient platelet abnormalities in DM have been linked with various 'intracellular' platelet alterations, hence diabetic platelets have increased Ca^{2+} ATPase activity resulting in high intracellular Ca^{2+} concentrations and platelet hyperactivity (Li and Woo, 2001). We observed no significant difference in PLT and PCT level between diabetic and control groups where as MPV and PDW was increased significantly in diabetic patients as compared to control subjects (P = 0.0001 and P = 0.003 respectively) (Table I). This is because Platelet hyperactivity results in increase in MPV due to increase number of platelet glycoprotein receptors on the platelet membrane, the thromboxane synthesizing capability and the platelet granule secretions (Tschoepe et al, 1989). Platelets are produced in bone marrow and thus can be decreased in bone marrow disease and after excessive chemotherapy or anemias caused by B12 deficiency. Decreased values can result in spontaneous bleeding. Low platelets values can occur in pregnancy or idiopathic thrombocytopenic purpura (ITP) and other situations that destroy platelets. Large spleen can lower the platelet count (Papanas et al, 2004). Age, sex, obesity and duration of diabetes have no effect in platelet indices but PCT was significantly reduced in patients with poor glycemic control (P = 0.004).As we have earlier reported (Jabeen et al, 2013) it can be concluded that variation in platelet morphology and functions are linked with pathological processes and greater risk of vascular complications in patients with diabetes. In this study elevated HbA1c level in diabetics shows that higher the blood concentration greater will be chance of glucose molecules that bound to hemoglobin which may affects the proper functioning of hemoglobin and concern with diabetic complications.

Correlation analysis for Platelet indices revealed that significant positive correlations were found between PLT and PCT (r=0.245**, P = 0.001), MPV and PDW (r = 0.364**,P= 0.000) **(Table-V).** As we have prior reported that variation in morphology of platelets and roles are linked with pathological processes and high risk of developing vascular complications in diabetic patients (Jabeen et al, 2013). Outsized platelets are more thrombogenic and thus putting the patient at a privileged risk status. Furthermore increased MPV is linked with greater risk for stroke, myocardial infarction and transient ischemic attacks. Scatter plots for hematological indices showed that FBG level positively correlated with HbA1c, #GRAN, PDW and negatively correlated with MCH and MPV whereas HbA1c was found to be positively correlated with MCHC **(Figure-1)**. There is a need to develop risk factor modification to reduce the impact of long-term complications (Khuwaja et al, 2004). Oral antiplatelet therapy such as Aspirin and other antiplatelet drugs is an effective strategy to attenuate ischemic event occurrence in patients with coronary artery disease with or without diabetes (Patrono, 2005)

Table – III

Correlations between glycemic index and Erythrocyte indices

		FBG	HbA1c	RBCs	HGB	HCT	MCV	MCH	MCHC	RDW
FBG	Pearson Correlation	1	.183*	.082	.001	.038	-.129	-.163*	-.028	-.030
	Sig. (2-tailed)		.017	.289	.989	.623	.094	.034	.715	.694
	N	170	170	170	170	170	170	170	170	170
HbA1c	Pearson Correlation	.183*	1	.002	.149	.032	.114	.149	.243**	-.112
	Sig. (2-tailed)	.017		.977	.052	.675	.140	.052	.001	.145
	N	170	170	170	170	170	170	170	170	170
RBCs	Pearson Correlation	.082	.002	1	.764**	.903**	.066	-.246**	-.332**	.095
	Sig. (2-tailed)	.289	.977		.000	.000	.393	.001	.000	.216
	N	170	170	170	170	170	170	170	170	170
HGB	Pearson Correlation	.001	.149	.764**	1	.862**	.452**	.283**	-.001	-.046
	Sig. (2-tailed)	.989	.052	.000		.000	.000	.000	.987	.549
	N	170	170	170	170	170	170	170	170	170
HCT	Pearson Correlation	.038	.032	.903**	.862**	1	.398**	.051	-.279**	-.001
	Sig. (2-tailed)	.623	.675	.000	.000		.000	.506	.000	.990
	N	170	170	170	170	170	170	170	170	170
MCV	Pearson Correlation	-.129	.114	.066	.452**	.398**	1	.590**	.054	-.242**
	Sig. (2-tailed)	.094	.140	.393	.000	.000		.000	.487	.002
	N	170	170	170	170	170	170	170	170	170
MCH	Pearson Correlation	-.163*	.149	-.246**	.283**	.051	.590**	1	.689**	-.240**
	Sig. (2-tailed)	.034	.052	.001	.000	.506	.000		.000	.002
	N	170	170	170	170	170	170	170	170	170
MCHC	Pearson Correlation	-.028	.243**	-.332**	-.001	-.279**	.054	.689**	1	-.030
	Sig. (2-tailed)	.715	.001	.000	.987	.000	.487	.000		.700
	N	170	170	170	170	170	170	170	170	170
RDW	Pearson Correlation	-.030	-.112	.095	-.046	-.001	-.242**	-.240**	-.030	1
	Sig. (2-tailed)	.694	.145	.216	.549	.990	.002	.002	.700	
	N	170	170	170	170	170	170	170	170	170

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table – IV

Correlations between glycemic index and Leucocyte indices

		FBG	HbA1c	WBCs	%LYM	%MON	%GRA	#LYM	#MON	#GRA
	Pearson Correlation	1	.183*	.075	-.100	-.106	.146	-.039	-.066	.182*
FBG	Sig. (2-tailed)		.017	.332	.194	.168	.058	.617	.393	.017
	N	170	170	170	170	170	170	170	170	170
	Pearson Correlation	.183*	1	-.047	-.014	.042	-.010	-.106	-.034	.012
HbA1c	Sig. (2-tailed)	.017		.541	.856	.590	.894	.167	.663	.879
	N	170	170	170	170	170	170	170	170	170
	Pearson Correlation	.075	-.047	1	-.296**	-.168*	.303**	.703**	.405**	.730**
WBCs	Sig. (2-tailed)	.332	.541		.000	.029	.000	.000	.000	.000
	N	170	170	170	170	170	170	170	170	170
	Pearson Correlation	-.100	-.014	-.296**	1	.480**	-.852**	.203**	.099	-.608**
%LYM	Sig. (2-tailed)	.194	.856	.000		.000	.000	.008	.198	.000
	N	170	170	170	170	170	170	170	170	170
	Pearson Correlation	-.106	.042	-.168*	.480**	1	-.603**	.153*	.601**	-.435**
%MON	Sig. (2-tailed)	.168	.590	.029	.000		.000	.047	.000	.000
	N	170	170	170	170	170	170	170	170	170
	Pearson Correlation	.146	-.010	.303**	-.852**	-.603**	1	-.200**	-.277**	.694**
%GRA	Sig. (2-tailed)	.058	.894	.000	.000	.000		.009	.000	.000
	N	170	170	170	170	170	170	170	170	170
	Pearson Correlation	-.039	-.106	.703**	.203**	.153*	-.200**	1	.579**	.235**
#LYM	Sig. (2-tailed)	.617	.167	.000	.008	.047	.009		.000	.002
	N	170	170	170	170	170	170	170	170	170
	Pearson Correlation	-.066	-.034	.405**	.099	.601**	-.277**	.579**	1	.016
#MON	Sig. (2-tailed)	.393	.663	.000	.198	.000	.000	.000		.841
	N	170	170	170	170	170	170	170	170	170
	Pearson Correlation	.182*	.012	.730**	-.608**	-.435**	.694**	.235**	.016	1
#GRA	Sig. (2-tailed)	.017	.879	.000	.000	.000	.000	.002	.841	
	N	170	170	170	170	170	170	170	170	170

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

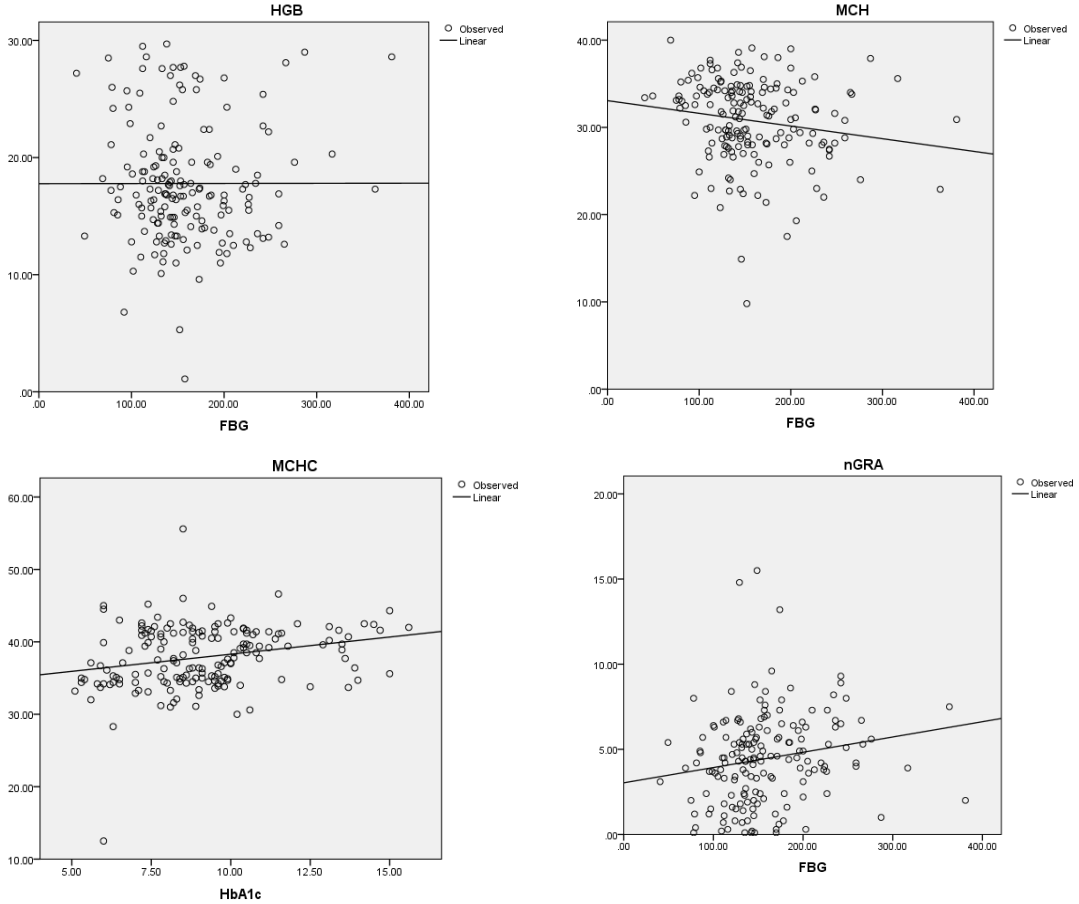
Table –V

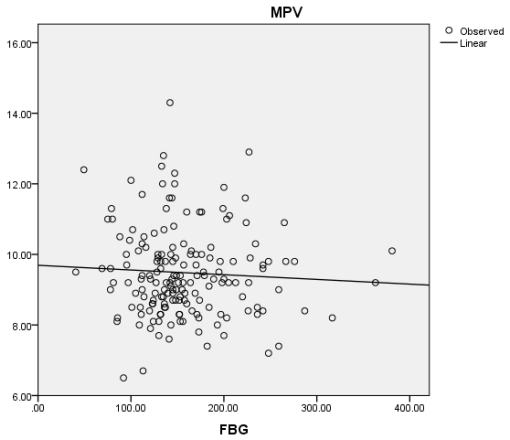
Correlations between glycemic index and Platelet indices

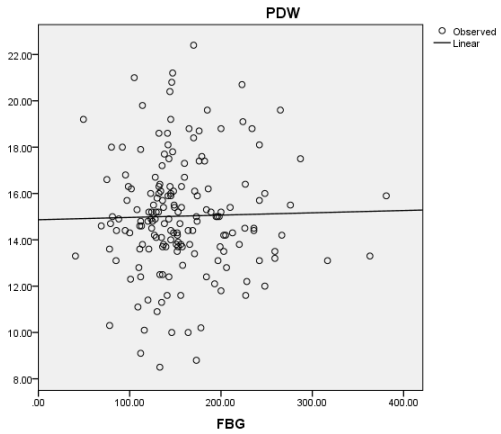
		FBG	HbA1c	PLT	PCT	MPV	PDW
FBG	Pearson Correlation	1	.183*	.143	-.005	-.057	.021
	Sig. (2-tailed)		.017	.064	.947	.460	.782
	N	170	170	170	170	170	170
HbA1c	Pearson Correlation	.183*	1	.010	-.093	.023	.003
	Sig. (2-tailed)	.017		.899	.226	.765	.970
	N	170	170	170	170	170	170
PLT	Pearson Correlation	.143	.010	1	.245**	-.082	.039
	Sig. (2-tailed)	.064	.899		.001	.288	.612
	N	170	170	170	170	170	170
PCT	Pearson Correlation	-.005	-.093	.245**	1	-.043	-.012
	Sig. (2-tailed)	.947	.226	.001		.577	.873
	N	170	170	170	170	170	170
MPV	Pearson Correlation	-.057	.023	-.082	-.043	1	.364**
	Sig. (2-tailed)	.460	.765	.288	.577		.000
	N	170	170	170	170	170	170
PDW	Pearson Correlation	.021	.003	.039	-.012	.364**	1
	Sig. (2-tailed)	.782	.970	.612	.873	.000	
	N	170	170	170	170	170	170

*. Correlation is significant at the 0.05 level (2-tailed).

Figure 1- Scatter plot showing correlation between glycemic index and hematological indices







Conclusion

Poor Glycemic control causes alteration in various biochemical parameters as well as hematological indices. Hyperglycemia induces the production of ROS causing oxidative stress as well as lipid peroxidation which may accelerate vascular complication in diabetics. The study indicates the clinical usefulness of HbA1c level; Erythrocyte indices, leukocyte indices and platelet indices chiefly MPV and PDW and as surrogate markers for diagnostic point of view. furthermore complete hematological indices is cost effective & possibly benefit for subjects at increased risk of developing micro / macro vascular complication and can help in preventive treatment. It will also point out patients on increased risk of developing complications in countries with poor socioeconomic status like Pakistan. Good glycemic control (either by diet or oral hypoglycemic drugs) could be supportive and beneficial in reducing harmful effects in diabetics.

Acknowledgement:

The Author desire to acknowledge Baqai Institute of Diabetology & Endocrinology (BIDE) for their assistance in providing blood samples as well as patient's data for analysis.

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