

Association between Glycosylated Hemoglobin, Complete Blood Count and Coagulation Parameters in Metabolic Syndrome

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Conflict of interest: Nil

Abstract

Complete blood count (CBC) & Coagulation parameters associate with multiple diseases. We investigated the relationship of metabolic syndrome in adolescences which imposes prolong risk causing micro-macro complication, which is leading global problems in 21st century. Therefore, the study aimed to determine the possible changes in CBC, Coagulation and glycosylated haemoglobin (HbA1c) in metabolic syndrome patients. The Adolescent subjects (students) who were visiting to the Medicine diabetic OPD and the subjects who were diagnosed with Metabolic syndrome in the emergency services department were grouped as group-A (patients) & group B (controls) in the study; both male /female patients who were also admitted. It was noticed to have a possible correlation between the CBC, Coagulation and HbA1c parameters in metabolic syndrome. In Both groups, Group A patients, HbA1c value is ($5.21 \pm 1.76\%$) Group B control HbA1c is ($3.21 \pm 0.82\%$). We analysed the CBC parameters, coagulation parameters. There was a statistical difference found in CBC parameters with increased (Hb, RBC, MCH, MCHC, RDW, PDW, MCV, Neutrophils, WBC, Hematocrit. Lymphocyte,) and statistically correlated with HbA1c. The results conclude that CBC & coagulation parameters associated with comparable change in HbA1c & blood cell indices. As they are the first to be exposed during hyperglycaemic conditions, with variable statistical changes implicated in the study. This study will be helpful tool for clinical correlation for the clinicians in the diagnosis, follow-up, prognosis of the of metabolic syndrome diseases.

Keywords: Metabolic syndrome, HbA1c, HB, RBC, MCH, MCHC, RDW, PDW, MCV,

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Background

Metabolic syndrome is one of risk factors for metabolic degeneration which has clusters of risk factors which increases the risk of hypertension, cardiovascular diseases and obesity. The characteristics that include in metabolic syndrome are obesity, atherogenic, dyslipidemia among which raise early in triglycerides (TG), then it followed by low density lipoprotein (LDL), low concentration of high-density lipoprotein cholesterol (HDL), High blood pressure and insulin resistance [1].

Prevalence of the metabolic syndrome has been studied in various population, mostly amongst adults in US, NHANES. Scientist in 1999-2000 reported an age-adjusted rate of 27% given the older National Cholesterol Education program (NCEP/ATPIII) [5,6]. Prevalence of world-wide varies considerably with some of the lowest rates being reported in France. About 10% in men and 7% in women aged between 30-65 [7]. In 1989 Kaplan *et al* renamed 'The Deadly Quartet' and then coined the term 'The Insulin Resistance Syndrome' [8,9,10]. It is now agreed that the well-established term 'metabolic syndrome' remains the most useful and widely accepted description of the clusters of metabolically related cardiovascular diseases.[11,12]. Recently the presences of metabolic syndrome have been used to identify individual at the high risk of (CVD) in the general population [13]. Abdominal obesity is a major characteristic of the (Mets). However, BMI measurements of the SCI individuals may not be sensitive indicators, in which an individual which has chronic SCI have a greater fat mass (FM) and a lower fat free mass per unit BMI that will be able to control the body fat. [14] Fat mass measured by the magnetic resonance in which it imaging (MRI) computed tomography (CT). It is more accurate compare then the measurement of the (BMI) The purpose of the current study is to

estimate the distribution of a metabolic syndrome in adolences by using a nationality representative sample of the Gujarat population. [15] According to the National Cholesterol Education Program (NCEP) adult treatment panel III (ATP III) persons meeting as having the metabolic syndrome elevated fasting plasma glucose (FPG) & Heart and blood vessel disease. [16] The explosions of the metabolic syndrome in aboriginal communities across north America has raised concerns about the metabolic syndrome in these populations [17]. In pima Indians there is higher diseases of metabolic syndrome it is partly explained by genetics, obesity, and lack of physical activity [18] The study Amongst the Oji-Cree of sandy lake first nation. Ontario showed a crude of 29.9% for adults and in another study oji-cree population in Manitoba and onaritio reevaluated an age standard of 37.5% for adults [19]. Several studies investigated by predisposing factors for metabolic syndrome in adolescence, but some specific risk has been identified yet .Although accumulating research suggests that birth the high and heavy new born having a higher probability of metabolic syndrome before there adulthood.[20] There is an association between the birth weight and metabolic syndrome in adolescence remains unclear [21]. Therefore, maternal obesity and gestational diabetes and the family history of diabetes having linked as offspring metabolic syndrome in adolescence in America. So, the prediction of the metabolic syndrome in adolescences study was conduct to construct the risk score for metabolic syndrome in adolescence using childhood, parental characteristics to test predictive accuracy score.

Methodology

Assessment of plan: This study was conduct

-ted with patients coming to medical diabetic OPD of Department of Medicine, Parul Sevashram Hospital; before the study, approval from IECHR was obtained, and Informed Consent was also obtained from the participants, thereafter once they are diagnosed for metabolic syndrome for treatment. The Blood sample for CBC test was collected in an EDTA tube for further diagnosis process.

Ethical consideration

The protocol for this study was approved by the Institutional Ethics and Research Committee (IERC) in accordance with the ethical standards of the committee on human institutional experimentation and with the Helsinki Declaration of 1975 that was revised in 2000.

Methods

Blood was collected in EDTA bulb for the CBC estimation. CBC values were analyzed with MINDRAY 600 BC the Reference values used were: HB (SLS) 13-17 g/dl, RBC 4.5 – 5.5 $10^{12}/L$; Hematocrit (ele.impedance) 40-54 %, Mean Corpuscular Volume MCV (calculated 83-101fl, MCH

(Calculated) 27-32pg, MCHC (calculated) 31.5 -34.5 g/dl, RDW (calculated) 11.5% - 14%; Total WBC count 4000-10000 come, Differential Count: Neutrophils (Flow cytometry) 50-62%, Lymphocytes (Flow Tyco) 20-40%, Monocytes (Flowcyto) 0-10%, Eosinophil (flowcyto)0-6%; Platelet Count (PLT) 150000 - 450000 /micro Liter; Mean Platelet Volume (MPV)FL; Platelet Distribution Width (PDW) %.

Blood was collected in Citrate bulb for the Coagulation Parameters, the coagulation parameters were analyzed by HEMOSTAR XF 1.0 Activated Partial Thromboplastin time (APTT) with 33.10 sec, Prothrombin Time (PT) with 12.10sec

Statistical Analysis

The results obtained were statistically analyzed by using SPSS, with version 20.0. The variables were presented as mean with standard deviations and then compared between different groups of the study by applying Independent's' test. Then values were taken as significant when the probability ($p < 0.001$) as percentage of the observing values of 't' at a particular degree of freedom.

Observation & Result

Table 1: CBC parameters of metabolic syndrome patients and control groups and significance value

Parameters	METABOLIC SYNDROME	Control	Significance P Value
Age (Years)	12-19	12-19	
Sex (M/F)	(12M - 6F)	(35M - 10F)	
Complete blood count (CBC) Mean/ SD			
Hemoglobin (13-17 g/dl)	9.85±2.96	13.7±1.06	0.000027 [#]
RBC (4.5 – 5.5 $10^{12}/L$)	3.87±1.21	5.080±0.36	0.000005 [#]
Blood indices Mean/ SD			
Haematocrit (40-54 %)	31.42±8.24	42.17±1.55	0.000008 [#]
MCV (83-101fl)	32.4±8.42	83.10±11.73	0.161871 [#]
MCH (27-32pg)	118.7±448.6	30.3±1.56	0.025902 [*]
MCHC (31.5 -34.5 g/dl)	30.65 ± 6.07	32.84 ± 1.17	0.025902 [*]

RDW (11.5% - 14%)	16.2±4.40	12.73±1.09	0.000027 [#]
Total WBC count Mean/SD			
WBC (4000-10000cmm)	15477.5±21488.3	8184.6±886.1	0.000185 [#]
Differential wbc count Mean/SD			
Neutrophils (50-62%)	75.91±11.4	55.9±3.94	0.000043 [#]
Lymphocyte (20-40%)	15.5±9.58	28.1±5.44	0.000170 [#]
Monocyte (0-10%)	6.30±2.71	6.03±2.72	0.001299 [#]
Eosinophil (0-6%)	2.6±1.88	3.46±1.52	0.000058 [#]
Basophils (0-2%)	0±0	0±0	0.000000
Platelets count			
Platelet (150000-450000/ μ L)	523868.5±1063327.5	319718.6±433	0.02416 [*]
MPV (fl)	9.82±2.15	13.06±19.86	0.037989 [*]
PDW (%)	16.40±0.56	16.02±0.414	0.06914 [#]
Three months average blood glucose			
HbA1c (%)	5.21 ± 1.76	3.21 ± 0.82	0.00011 [#]

Values are expressed as Mean \pm SD.

Student's t-test applied, $P < 0.05^*$, $P < 0.001^{\#}$ is statistically significant

RBC (red blood cell), MCV (mean corpuscular volume), MCHC (mean corpuscular hemoglobin concentration) RDW (red cell distribution width), WBC (white blood cell), MPV (mean platelets volume), PDW (platelets distribution width) HbA1c (Glycated hemoglobin)

Table 2: Coagulation parameters of metabolic syndrome patients and control groups

Parameters	Metabolic Syndrome	Control	Significance P Value
Activated Partial Thromboplastin Time (APTT) Seconds	39.4±8.83	32.1±0.431	0.000561 [#]
Prothrombin Time (Seconds)	27.92±10.19	12.48±0.0833	0.000001 [#]

Values are expressed as Mean \pm SD. Student's t-test applied, $P < 0.05^*$ statistically significant, $P < 0.001^{\#}$ is statistically highly significant

Table 3: Corelation coefficient between HBA1C and CBC parameters

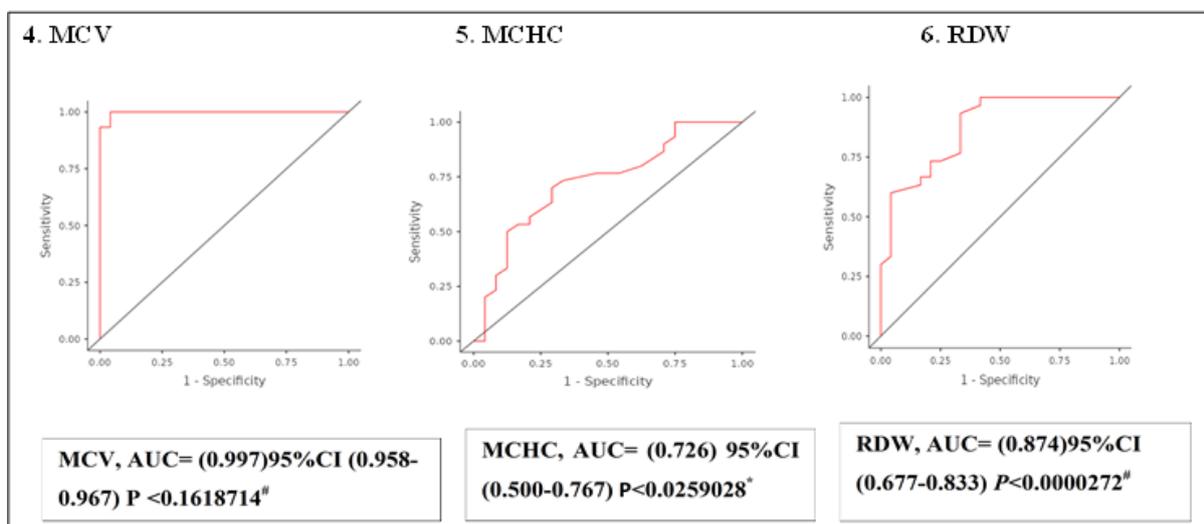
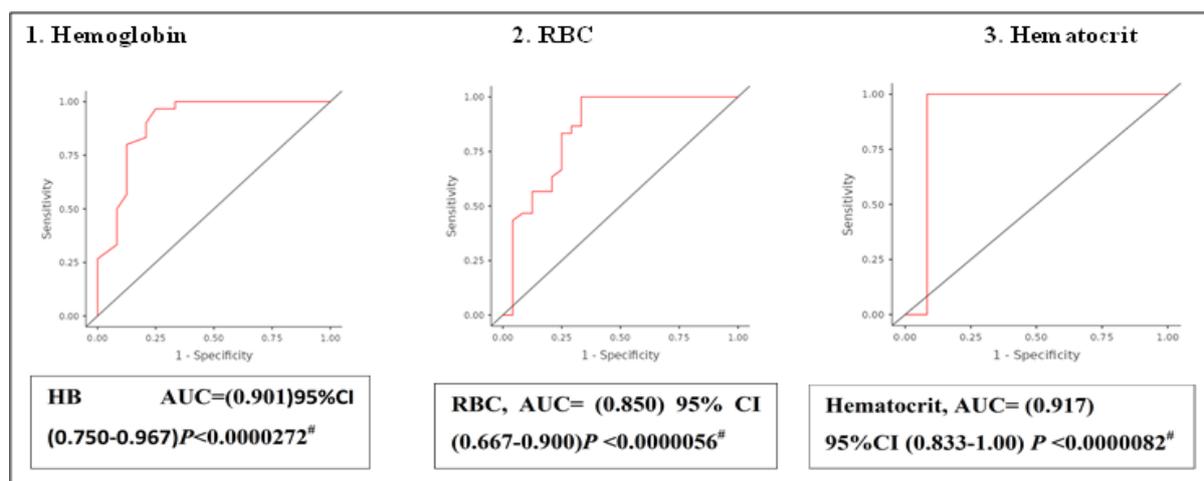
Neutrophil	WBC	RDW	MCHC	MCV	Haematocr	RBC	Hb	HbA1c	Variables
0.378	0.017	0.295	0.165	0.47	0.282	0.1	0.251	-	r*
0.005	0.905	0.032	0.2437	<0.001	0.863	0.471	0.067	-	P value
0.619	0.004	0.732	0.095	0.647	0.863	0.766	-	-	r*
<0.001	0.794	<0.001	0.5	<0.001	<0.001	<0.001	-	-	P value
0.651	0.004	0.732	0.095	0.647	0.897	-	-	-	r*
<0.001	0.978	<0.001	0.5	<0.001	<0.001	-	-	-	P value
0.651	0.042	0.622	0.043	0.67	-	-	-	-	r*
<0.001	0.761	<0.001	0.758	<0.001	-	-	-	-	P value
0.719	0.201	0.603	0.181	-	-	-	-	-	r*
<0.001	0.146	<0.001	0.194	-	-	-	-	-	P value
0.23	0.059	0.14	-	-	-	-	-	-	r*
0.098	0.674	<0.001	-	-	-	-	-	-	P value
0.491	0.051	-	-	-	-	-	-	-	r*
<0.001	0.715	-	-	-	-	-	-	-	P value
0.046	-	-	-	-	-	-	-	-	r*
0.739	-	-	-	-	-	-	-	-	P value
-	-	-	-	-	-	-	-	-	r*
-	-	-	-	-	-	-	-	-	P value
-	-	-	-	-	-	-	-	-	r*
-	-	-	-	-	-	-	-	-	P value
-	-	-	-	-	-	-	-	-	r*
-	-	-	-	-	-	-	-	-	P value
-	-	-	-	-	-	-	-	-	r*
-	-	-	-	-	-	-	-	-	P value
-	-	-	-	-	-	-	-	-	r*
-	-	-	-	-	-	-	-	-	P value
-	-	-	-	-	-	-	-	-	r*
-	-	-	-	-	-	-	-	-	P value

PDW	Eosinophil	Monocytes	Lymphocy
0.295	0.014	0.102	0.294
0.031	0.922	0.463	0.031
0.13	0.376	0.1	0.559
0.349	0.005	0.473	<0.001
0.309	0.417	0.13	0.54
0.003	0.002	0.351	<0.001
0.395	0.393	0.042	0.571
0.003	0.003	0.766	<0.001
0.065	0.215	0.11	0.596
0.643	0.119	0.43	<0.001
0.108	0.108	0.073	0.252
0.44	0.44	0.605	0.069
0.081	0.247	0.044	0.445
0.562	0.074	0.757	<0.001
0.254	0.135	0.063	0.179
0.004	0.33	0.651	<0.001
0.139	0.274	0.046	0.179
0.317	0.004	0.74	0.196
0.044	0.348	0.035	0.839
0.317	0.01	0.804	<0.001
0.069	0.133	-	-
0.666	0.399	-	-
-	-	-	-
-	-	-	-
-	-	-	-
-	-	-	-

r* = Pearson's Correlation coefficient value Pearson correlation analysis was done to determine the association of the parameters HB, RBC, Haematocrit, MCV, MCHC, RDW, WBC, Neutrophils, Lymphocytes, Monocytes, Eosinophils, PDW

**Correlation is significant at the 0.001 level (2-tailed)

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



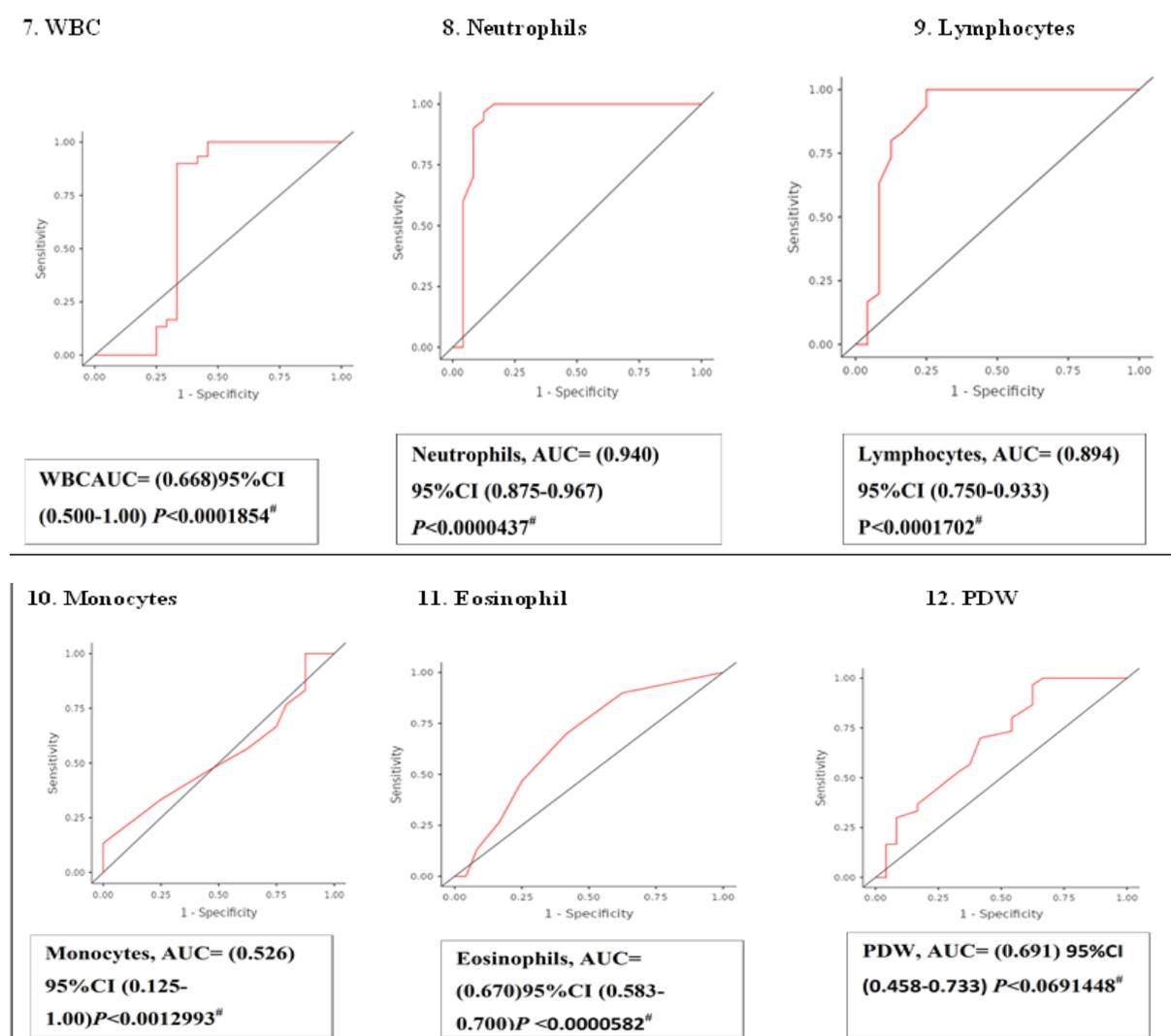


Figure 1: ROC Curves for individual parameters in metabolic syndrome

Results

According to the results the metabolic syndrome group A patients and Control Group B patients. There were no statistical differences by age and gender between the two groups (Table 1). Between the Metabolic syndrome group A and the control group B in that HB significance value was [P value 0.0000272*] RBC, significance value was [0.000056*], Haematocrit, significance value was [P value 0.0000082*] MCV, significance value was [P- 0.1618714*] MCHC, significance value was [P-0.0259028*] RDW, significance value was [P value 0.0000272*] WBC, significance value was [P value 0.001854*] Neutrophils, significance value was [P value 0.0000437*] Lymphocytes, significance value was [P value 0.001702*]

Monocytes, significance value was [P value 0.0012993*] Eosinophils, significance value was [P-0.0000502*] Platelets, significance value was [P value 0.024165*] MPV, significance value was [P value 0.037989*] PDW, significance value was [P value 0.0691448*] HbA1c, significance value was [P value 0.00011629*] In (Table 1) there is decreasing in Basophils, significance value was [P value 0.000000] This significance Values are expressed as Mean ±SD. Student’s t-test applied, $P < 0.05^*$, $P < 0.001^{\#}$ is statistically significant. In (Table no 2) Coagulation Parameters of Metabolic Syndrome Patients Group A and Control Groups B in that we find that both the Activated Partial Thromboplastin Time (APTT) Seconds significance value was

[P- 0.000561#] & Prothrombin Time (Seconds) significance value was [P value 0.000001#] This significance Values are expressed as Mean \pm SD. Student's t-test applied, ($P < 0.05^*$ statistically significant, $P < 0.001^{\#}$ is statistically highly significant).

In (Table no 3) we found the Correlation coefficient between HbA1c and CBC parameters there is a statistical analysis differences between the CBC and HbA1c parameters in which the 1st significance seen in between HB with RBC [P value is < 0.0001] then in between Hematocrit with HB, RBC [P value is < 0.0001] then in between HB, HbA1c, RBC, Hematocrit with MCV [P value is < 0.0001] then in between RDW with HB, RBC, Hematocrit, MCV, MCHC [P value is < 0.0001] then in between Neutrophils with HB, RBC, Hematocrit, MCV, RDW [P value is < 0.0001] then in between Lymphocytes & HB, RBC, Hematocrit, MCV, RDW, WBC [P value is < 0.0001] this values are expressed as correlation matrix of HbA1c and the CBC parameters.

Discussion

The chief purpose of this study is to evaluate the metabolic syndrome with HbA1C, CBC, & Coagulation parameters. Metabolic syndrome is a health problem which is associated with increased in risk of micro and macro vascular complication some of the parameters can easily be detected by various blood test or many test which are related to metabolic syndrome [22] The parameters like CBC parameters, Coagulation & HbA1c that can be used as a best biomarker through ROC for earlier detection changes for metabolic syndrome. A high fasting blood sugar is the common risk factors seen in the general metabolic syndrome patients. There is inter-dependence between insulin and the risk factors for a normal metabolism so that the metabolic syndrome and the various risk factors are associated and can mutually influence to each other [23].

We found that HB, RBC, Hematocrit,

MCV, MCHC, WBC, RDW, Neutrophils, Monocytes, Lymphocytes, Eosinophils, PDW with HbA1c having an increased significance value and the significance value of basophils has been decreases. Increases in HB causes hypertension, high TGs, abdominal obesity or elevated glucose were more likely to have higher hemoglobin levels. We evaluated the risk of developing in metabolic syndrome and its components according to serum hemoglobin concentration. Our significance value of HB was (P value 0.0000272*). Significance in RBC were found to be associated with *obesity*, hypertension and dyslipidemia factors having higher RBC level in metabolic syndrome patient's. Our significance value of RBC was [P 0.000056*]. The increasing in Hematocrit level can lead to reduced blood flow (via *increased* blood viscosity) in metabolic syndrome patients. Our significance value of Hematocrit was (P value 0.0000082*). The increasing in MCV value was common causes of macrocytic anemia, increased MCV causes folate deficiency anemia & Vitamin B12 deficiency anemia causes in metabolic syndrome. Our significance value in MCV was (P- 0.1618714*). Our results also show an increasing the significance value in MCHC, a high MCHC means that hemoglobin is more concentrated and may occur in a few ways. MCHC is often increased in the people who smoke. Our significance value for MCHC was (P- 0.0259028*) The increasing in RDW results could be an indication of a nutrient deficiency, as a deficiency of iron, folate, or vitamin B-12. The results could also indicate macrocytic anemia, when your body doesn't produce enough normal red blood cells, and the cells it does produce are larger than normal. Our significance value for RDW was [P value 0.0000272*].

Increasing in significance value of WBC (white blood cell) causes an infection, abnormalities in the bone marrow, smoking, chronic lung disease, immune disorders, inflammatory or allergic reactions or even physical and emotional

stress. Our significance value for WBC was [P value 0.001854*]. Increasing in significance value in Neutrophils cause abscess, boils, pneumonia, cough, and fevers can cause neutrophilia. Our significance for Neutrophils, (P value 0.0000437*). Increasing in Lymphocytes, Monocytes & Eosinophils is often associated with chronic infections. It can also be linked with some types of cancer, especially leukemia. Our significance value for Lymphocytes was [P value 0.001702*], Monocytes was [P value 0.0012993*], Eosinophils was [P-0.0000502*], Platelet count was [P value 0.024165*]. Increasing significance value of MPV associated with accelerated thrombopoiesis and an increased risk of cardiovascular diseases. Metabolic disorders as dyslipidemia, obesity, and elevated blood pressure & glucose are the risk factors for cardiovascular diseases. MPV [P value 0.037989*]. Increasing in PDW causes due to activation of platelet, resulting from platelet swelling and pseudopodia formation was hypothesized our significance value for PDW was [P value 0.0691448*].

Increasing in significance value of HbA1c cause much sugar in blood. This means more likely to develop diabetes complications, like serious problems with eyes and feet HbA1c significance value was (P value 0.00011629*) As per WBC count showed a significant relationship with diabetes, no significant association between platelet count and impaired glucose regulation, MPV was significantly associated with known diabetes only [24].

Kawamoto R et. al (2013) also found a significant relationship of HGB concentrations and diabetes and the association between HGB values and diabetes or prediabetes states are available. [25] Lin JD, Chiou WK et.al in (2006) & Lohsoonthorn V et al (2007), studies showed a relationship between HGB and metabolic syndrome. [26,27]. Jia L et.al in (1996) found that HGB is an important Nitric Oxide (NO) buffer and a modulator

of NO bioavailability and thus involved in the regulation of endothelial function [28]. Nakanishi N (2002) & Gokulakrishnan K (2009) *et al* found that WBC count was significantly associated which suggesting an association between WBC count and diabetes WBC count is a marker of systemic inflammation and may thus be involved in the pathophysiology of prediabetes states and subsequently in the manifestation of diabetes [29,30].

In table no 2 we discuss about the coagulation parameters in which the APTT and PT significance levels is increased. When the APTT significance levels increased it may result from an accumulation of circulating activated coagulation factors in plasma which is caused by enhanced coagulation activation. APTT significance value was in Seconds [P- 0.000561#] & when PT significance level is increased the arterial blood pressure, and abdominal obesity levels is increased in metabolic syndrome patients Prothrombin Time significance value was (Seconds) [P value 0.000001#]

At's per Coban *et al.* found in their study, that MPV levels is increased. [31] According to Kodiatte TA, *et al* MPV is an indicator for an increased platelet activity and thus thrombogenic activation, which may play a role in the development of vascular complications in persons with type 2 diabetes. A recent study found that MPV was significantly value is higher in the persons with diabetes than in non-diabetic persons. [32] Ferreiro JL et al in (2010) he found in his study that Platelet hypersensitivity is a well-known factor to the prothrombotic state in diabetics, causing increased coagulation, impaired fibrinolysis and endothelial dysfunction. Hyperactive platelet plays a critical role in the pathophysiology of the thrombotic events leading to diabetic complications [33].

Shah B *et al* in (1986) & Demirtunc R, *et al* in (2009) found in the study that Several research indicate positive correlation of RBS and HbA1c with MPV, PDW [34,35]

Coban E, *et al* in (2006) & Bavbek N, *et al* in (2007) It was proposed that increase in MPV could be because of raised blood sugar effect to osmotic swelling and shorter life span of platelets in diabetic patients. Alternatively, this may suggest that platelet activation is related to glycemic control [36,37].

According to Demirtunc R *et al* in (2009), Dindar S *et al* (2013) & Ozder A *et al* in (2014) Similarly his study results had shown significantly higher MPV in the group B compared to the group A. Those findings are mainly consistent with previous finding Besides Ozder *et al.* found that MPV was significantly higher in patients with HbA1c levels $\leq 7.0\%$ than in patients with HbA1c levels ≤ 6.9 . [38]

In table no 3 we discuss about Correlation coefficient between HbA1c and CBC parameters in which there is a statistical analysis differences between the CBC and HbA1c parameters. The significance that we found in the specific parameters are (HB with RBC), (Hematocrit with HB, RBC), (HB, HbA1c, RBC, Hematocrit with MCV), (RDW with HB, RBC, Hematocrit, MCV, MCHC) (Neutrophils with HB, RBC, Hematocrit, MCV, RDW) (Lymphocytes & HB, RBC, Hematocrit, MCV, RDW, WBC) in this the significance value for all parameters are in between [P value is < 0.0001]

According to Choi KM, *et al* in (2003) & Wang YY, *et al* in (2004) they found that hematological parameters play an

important role in insulin resistance [39] Papanas *et al* in (2004) & Shah B *et al* in (2012) found no association between PC and impaired glucose regulation, MPV was associated with known diabetes after multivariable adjustment in the present study. [40]

Conclusion

Our study demonstrated that CBC parameters, such as that Hb, RBC, MCH, MCHC, RDW, PDW Neutrophils, PT, APTT, WBC, Haematocrit, Lymphocyte, Eosinophils, Monocytes values were increased in metabolic syndrome. If confirmed in future follow – up studies this may provide a rationale to introduce the easy follow up studies in considering CBC, HbA1c and Coagulation Parameters results may be useful in the diagnosis of metabolic syndrome for prediction patients.

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Authors Contribution

Contribution	Author
Guidance and Exhortation to Study concept and design. Suggestions, Idea, Critical revision of results and interpretation of Research work.	Inampudi Sailaja ² , Ivvala Anand Shaker ⁵
Analysis and Interpretation of data, Statistical Analysis of Research data.	Neha D Sheth ³ , Tushar Pradhan ⁷
Collection of data and Analysis of Lab work, Collection of data, Technical suggestions research work.	Kean Shyamsundar Patil ¹ Shaik Basha ⁶ ,
Interaction with patients of every step of research work	Kean Shyamsundar Patil ¹ Shaik Basha ⁶

Critical revision of the manuscript for important intellectual content	Santosh Bidwe ⁴ , Ivvala Anand Shaker ⁵
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Reference

- Expert Panel on Detection E. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *Jama*. 2001 May 16;285(19):2486-97.
- World Health Organization. 2008-2013 action plan for the global strategy for the prevention and control of noncommunicable diseases: prevent and control cardiovascular diseases, cancers, chronic respiratory diseases and diabetes.
- Reaven GM. Role of insulin resistance in human disease. *Diabetes*. 1988 Dec 1;37(12):1595-607.
- Zimmet P, Alberti K, Shaw J. International Diabetes Federation: the IDF consensus worldwide definition of the metabolic syndrome. *Diabetes voice*. 2005; 50:31-3.
- Segura J, Ruilope LM. Obesity, essential hypertension and renin-angiotensin system. *Public health nutrition*. 2007 Oct;10(10A):1151-5.
- Ford ES. The metabolic syndrome and mortality from cardiovascular disease and all-causes: findings from the National Health and Nutrition Examination Survey II Mortality Study. *Atherosclerosis*. 2004 Apr 1;173(2):307-12.
- Cameron AJ, Shaw JE, Zimmet PZ. The metabolic syndrome: prevalence in worldwide populations. *Endocrinology and Metabolism Clinics*. 2004 Jun 1;33(2):351-75.
- Kaplan NM. The deadly quartet: upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. *Archives of internal medicine*. 1989 Jul 1;149(7):1514-20.
- Haffner SM, Valdez RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP. Prospective analysis of the insulin-resistance syndrome (syndrome X). *Diabetes*. 1992 Jun 1;41(6):715-22.
- World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus. World health organization; 1999.
- Pasternak RC. Report of the Adult Treatment Panel III: the 2001 National Cholesterol Education Program guidelines on the detection, evaluation and treatment of elevated cholesterol in adults. *Cardiology clinics*. 2003 Aug 1;21(3):393-8.
- Pasternak RC. Report of the Adult Treatment Panel III: the 2001 National Cholesterol Education Program guidelines on the detection, evaluation and treatment of elevated cholesterol in adults. *Cardiology clinics*. 2003 Aug 1;21(3):393-8.
- Garshick E, Kelley A, Cohen SA, Garrison A, Tun CG, Gagnon D, Brown R. A prospective assessment of mortality in chronic spinal cord injury. *Spinal cord*. 2005 Jul;43(7):408-16.
- Kenchiah S, Evans JC, Levy D, Wilson PW, Benjamin EJ, Larson MG *et al*. Obesity and the risk of heart failure. *N Engl J Med* 2002; 347: 305–313.
- Young TK, Reading J, Elias B. Type 2 diabetes mellitus in Canada ,s First Nations: status of an epidemic in progress. *Cmaj*. 2000 Sep 5;163(5):561-6.
- Ley SH, Harris SB, Mamakeesick M, Noon T, Fiddler E, Gittelsohn J, Wolever TM, Connelly PW, Hegele RA, Zinman B, Hanley AJ. Metabolic syndrome and its components as predictors of incident type 2 diabetes mellitus in an Aboriginal community. *CMAJ*. 2009 Mar 17;180(6):617-24.

17. Guerrero-Romero F, Aradillas-García C, Simental-Mendía LE, Monreal-Escalante E, de la Cruz Mendoza E, Rodríguez-Moran M. Birth weight, family history of diabetes, and metabolic syndrome in children and adolescents. *The Journal of Pediatrics*. 2010 May 1;156(5):719-23.
18. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics*. 2005 Mar 1;115(3):e2906.
19. Hirschler V, Roque MI, Calcagno ML, Gonzalez C, Aranda C. Maternal waist circumference and the prediction of children's metabolic syndrome. *Archives of pediatrics & adolescent medicine*. 2007 Dec 1;161(12):1205-10.
20. Goodman E, Daniels SR, Meigs JB, Dolan LM. Instability in the diagnosis of metabolic syndrome in adolescents. *Circulation*. 2007 May 1;115(17):2316-22.
21. Vickers NJ. Animal communication: when i'm calling you, will you answer too? *Current biology*. 2017 Jul 24;27(14):R713-5.
22. Sathish R, Mohan V. Diabetes and Thyroid diseases-a review. *International Journal of Diabetes in Developing Countries*. 2003; 23:120-3.
23. https://www.google.com/search?q=+increases+in+HB+metabolic+syndrome++causes+&rlz=1C1CHBF_enIN921IN921&ei=1EoTYvOxLJKTseMPgqG7kAM&ved=0ahUKEwjz69GerpD2AhWSSWwGHYLQDjIQ4dUDCA4&uact=5&oq=+increases+in+HB+metabolic+syndrome++causes+&gs_lcp=Cgdnd3Mtd2l6EAMyBQghEKABOgcIABBHELADOGUIABCiBDoECCEQFUoECEYYAEoECEYYAFCoBFjjhAFg5oYBaAJwAXgAgAH1AYgB0ySSAQYwLjIwLjeYAQCgAQHIAQjAAQE&client=gws-wiz
24. Kawamoto R, Tabara Y, Kohara K, Miki T, Kusunoki T, Abe M, Katoh T. Hematological parameters are associated with metabolic syndrome in Japanese community-dwelling persons. *Endocrine*. 2013 Apr;43(2):334-41.
25. Lohsoonthorn V, Jiamjarasrunsi W, Williams MA. Association of hematological parameters with clustered components of metabolic syndrome among professional and office workers in Bangkok, Thailand. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2007 Sep 1;1(3):143-9.
26. Un JD, Chiou WK, Chang HY, Liu FH, Weng HF, Liu TH. Association of hematological factors with components of the metabolic syndrome in older and younger adults. *Aging clinical and experimental research*. 2006 Dec;18(6):477-84.
27. Jia L, Bonaventura C, Bonaventura J, Stamler JS. S-nitrosohaemoglobin: a dynamic activity of blood involved in vascular control. *Nature*. 1996 Mar;380(6571):221-6.
28. Gokulakrishnan K, Deepa R, Sampathkumar R, Balasubramanyam M, Mohan V. Association of leukocyte count with varying degrees of glucose intolerance in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-26). *Metabolic syndrome and related disorders*. 2009 Jun 1;7(3):205-10.
29. Nakanishi N, Yoshida H, Matsuo Y, Suzuki K, Tatara K. White blood-cell count and the risk of impaired fasting glucose or Type II diabetes in middle-aged Japanese men. *Diabetologia*. 2002 Jan;45(1):42-8.
30. Coban E, Kucuktag S, Basyigit S. Platelet activation in subjects with impaired glucose tolerance. *Platelets*. 2007 Jan 1;18(8):591-4.
31. Kodiatté TA, Manikyam UK, Rao SB, Jagadish TM, Reddy M, Lingaiah HK, Lakshmaiah V. Mean platelet volume in type 2 diabetes mellitus. *Journal of laboratory physicians*. 2012 Jan;4(01):0059.
32. Ferreiro JL, Gomez-Hospital JA, Angiolillo DJ. Platelet abnormalities in

- diabetes mellitus. *Diab Vasc Dis Res*. 2010 Oct;7(4):251-9.
33. Nguyen AL, Green J, Enguidanos S. The relationship between depressive symptoms, diabetes symptoms, and self-management among an urban, low-income Latino population. *Journal of Diabetes and its Complications*. 2015 Nov 1;29(8):1003-8.
34. Shah B, Sha D, Xie D, Mohler III 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 1;35(5):1074-8.
35. Bavbek N, Kargili A, Kaftan O, Karakurt F, Kosar A, Akcay A. Elevated concentrations of soluble adhesion molecules and large platelets in diabetic patients: are they markers of vascular disease and diabetic nephropathy? *Clinical and Applied Thrombosis/Hemostasis*. 2007 Oct;13(4):391-7.
36. Coban E, Bostan F, Ozdogan M. The mean platelet volume in subjects with impaired fasting glucose. *Platelets*. 2006 Feb 1;17(1):67-9.
37. Nguyen AL, Green J, Enguidanos S. The relationship between depressive symptoms, diabetes symptoms, and self-management among an urban, low-income Latino population. *Journal of Diabetes and its Complications*. 2015 Nov 1;29(8):1003-8.
38. Ozder A, Eker HH. Investigation of mean platelet volume in patients with type 2 diabetes mellitus and in subjects with impaired fasting glucose: a cost-effective tool in primary health care? *Int J Clin Exp Med*. 2014;7(8):2292-2297
39. Choi KM, Lee J, Kim YH, Kim KB, Kim DL, *et al*. Relation between insulin resistance and hematological parameters in elderly Koreans-Southwest Seoul (SWS) Study. *Diabetes Res Clin Pract* 2003;60: 205-212.
40. Shah B, Sha D, Xie D, Mohler ER 3rd, 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;35: 1074-1078