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ORIGINAL ARTICLE

Role of von Willebrand Factor, Fibrinogen, C Reactive Protein, Complete Blood Count and ABO type in monitoring Cardiovascular Disease patients attending University of Calabar Teaching Hospital, Nigeria

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Abstract

Introduction: Cardiovascular disease is known to be the leading cause of death globally and it is responsible for one third of all global deaths. The research was conducted to assess some complete blood count, von Willebrand factor, fibrinogen, C reactive protein and ABO blood group that could serve as a biomarker for the diagnosis and management of cardiovascular disease.

Materials and Methods: Three hundred and sixty persons were studied, comprising 200 CVD subjects and 160 apparently healthy persons as controls, between 35-82 years of age. Fifty-nine percent of the CVD subjects were male while female constituted 41%. Questionnaires and folders were used to obtain information. Data was analyzed by SPSS version 22. ABO blood group was determined by standard tube method. Complete Blood Count was carried out with Sysmex counter, von Willebrand factor, Fibrinogen levels and C reactive protein were determined by Enzyme-Link Immunosorbent Assay methods, while plasma glucose and lipid profile were determined by colorimetric method. Systolic Blood Pressure and Diastolic Blood Pressure of the participants were determined.

Results: Significantly higher value were observed for SBP, DBP, vWf, WBC, RDW-CV, FPG, CRP and MPV among CVD subjects, when compared to control group, While significant lower level of platelet count were recorded among CVD subjects (200.43±70.45/l) compared to control group (234.91±48.85). CVD subjects on treatment recorded significant lower value of vWf (p=0.000) and FPG (p=0.000), compared with untreated subjects. Classification of subjects based on ABO blood type revealed that group O had significantly lower vwf (p=0.000), Group A had significant higher value of plasma glucose compared to other groups. Group A also recorded significant higher value of LDL than other blood groups. CVD subjects who smoke cigarettes had significant raised glucose

levels (p=0.005) than non-smokers. Significantly lower level of CRP (4.63±3.77mg/L) was seen in female subjects compared to the male (6.41±4.35mg/L).
Conclusion: It concludes that CBC, vWf, SBP, and DBP showed mild significant increase in their plasma level in CVD subjects and their assay should form part of the markers for routine diagnosis of CVD in UCTH and can be useful for monitoring of treatment.
Keyword: Cardiovascular disease, Haemoglobin, von Williebrand factor, Fibrinogen, ABO blood group, C Reactive Protein.

Introduction

The cardiovascular system (CVS) is a system that functions in the transportation of substances around the body. It is made up of three components which include the heart, blood vessels and the blood (1). Diseases that come under CVD include; Coronary artery disease (CAD), cerebrovascular disease, Rheumatic heart disease, congenital heart disease and Deep vein thrombosis (DVT). Cause of CVD include building up of plaque in the blood vessels which result in thickening and narrowing of the vessels. This can block arterial walls and obstruct the flow of blood to vital organs. Atherosclerosis, a term used to describe deposition of plaques in blood vessels occurs as a result of unhealthy diet, lack of exercise, overweight and smoking (2). There are many manifestations of CVD and these include cardiac arrhythmias which is an abnormal heart rhythm and can be caused by either congenital heart defect, coronary artery disease, high blood pressure, diabetes, smoking, excessive use of alcohol, drug abuse and stress (3).

According to WHO report CVD stands out as number one cause of global death. It is responsible for an estimated 17.9 million deaths annually(4). The disease is the cause of 31 % of all global deaths. Of the deaths over 80 % occur in low and middle income countries (4). High blood pressure is the most important risk factor for CVD. It is known to affect about 20 million people in Africa (5). Complete Blood count (CBC) is a laboratory test that is used to assess the number and functions of cellular components of the blood. The test evaluates RBC, WBC and platelets. It is used to detect wide range of disorders like anaemia, leukaemia and infections. Recent studies have linked CBC results with incidences of CVD. Elevated WBC and their subtypes is strong predictor of coronary artery disease. The elevated WBC is also associated with peripheral artery disease and stroke. Red cell distribution width, a measure of variability in the sizes of circulating RBCs is also used to predict adverse outcome in CVD patients (6).

Fibrinogen is a soluble glycoprotein synthesized in the liver and plays a central role in blood coagulation. First, it is a substrate for fibrin formation and also acts as a ligand for platelet α11b/β111 receptor which promotes platelet aggregation (7). During vascular injury fibrinogen is converted enzymatically to fibrin by thrombin. Fibrinogen functions primarily to occlude blood vessels and thereby stop excessive bleeding. However fibrinogen products also have anti-thrombin activity (8). Fibrinogen is a major determinant of blood viscosity and flow. Fibrinogen is an acute phase protein and level rises in response to

inflammation or injury. The level is known to rise in various forms of cancer (9). Studies have shown that high level of the protein is a risk factor for cardiovascular disorder which includes ischaemic heart disease, stroke and thrombo-embolism(10).

C-reactive protein (CRP), an acute phase protein synthesized in the liver has its highest level during inflammation. CRP test is used to detect inflammation and to monitor disease severity and chronic conditions. High levels have also been linked to CVD risk. As a marker of inflammation, the protein plays role in vessel damage and clinical cardiovascular event. CRP levels greater than 10mg/L strongly correlate with CVD risk (11). Von Willebrand factor (vWf) is a large adhesive glycoprotein produced in endothelial cells, megakaryocyte and platelets. The protein was named after a paediatrician from Finland, Erik von Willebrand who first described it in 1924 after attending to a young girl with bleeding diathesis. The gene controlling the production of vWf is located on the short arm of chromosome 9. von Willebrand factor has two functions in haemostasis; it aid in platelet sub-endothelial adhesion and platelet to platelet aggregation. It also serves as a carrier protein to factor VIII and prolongs its half-life in circulation and mobilizes it to the site of vascular damage. Deficiency of von Willebrand factor is the cause of von Willebrand disease while higher than normal level is a risk factor for thrombosis (12). von Willebrand factor levels are affected by many factors such as ABO blood group, oestrogen level, smoking, age, diabetes mellitus, stress and high blood pressure. Most of these factors are well known risk factors for cardiovascular disease. A study has associated high level of the protein to coronary heart disease (13).

ABO blood group system was first described by an Austrian scientist Karl Landsteiner in 1901. The blood group is classified based on the type of antigen expressed on it cell surface. ABO blood group is the most important blood group in transfusion science. The occurrence and severity of disease like gastric cancer, pancreatic cancer, peptic ulcer and infection with plasmodium falciparum, helicobacter pylori is influenced by ABO blood type (14). ABO blood group is also a risk factor for CVD with group AB, A and B being more affected while group O records the least number of cases. ABO blood group is known to influence CVD through its influence on the plasma level of von Willebrand factor. von Willebrand factor is higher in non-group O than in blood group O individuals (15). So far, some Complete Blood Count (CBC), C-reactive protein (CRP), von Willebrand factor and fibrinogen are yet to be used routinely for the diagnosis and assessment of CVD patients in UCTH, hence the need for the study. The study will assess the impact of these parameters in CVD patients when compared with the control group so as to possible use them as newer parameters alongside the older ones for routine diagnosis and management of CVD patients in UCTH.

Materials and Methods

The setting of the study was University of Calabar Teaching Hospital (UCTH) located in Calabar town. The hospital is located along Unical Hotel road, close to University of Calabar and serves as reference hospital to residents of Cross River State and environs. University of Calabar Teaching Hospital has twelve clinical departments in which Internal Medicine where the CVD subjects attend is one. The Internal Medicine Department of UCTH has it clinic days on Tuesdays and Thursdays.

A cross sectional study design was used for the research. A total of three hundred and sixty persons were recruited for the study. Two hundred of these persons were male (118) and female (82) patients who presented with cardiovascular disease attending the outpatient clinics of University of Calabar Teaching Hospital (UCTH), while one hundred and sixty

were picked from apparently healthy population as age (35-82 years) and gender (male 87, female 73) matched controls. Ethical approval was obtained from Cross River State ministry of Health ethical committee (CRSMOH/RP/REC/2018/124). Informed consent was obtained from all the study participants.

A well-structured questionnaire was given to all the study participants to fill. The questionnaires captured information on bio-data and other demographic parameters, while other relevant information was retrieved from the patient's folders. Only male and female subjects who were clinically examined and diagnosed with cardiovascular disease were included in the study as test subjects while persons not diagnosed of CVD and do not smoke cigarette or consume alcohol were included as control. Pregnant women were excluded from being used as subjects while cigarette smokers and alcohol consumers were excluded from the control.

Sample collection

Blood samples were collected from the patients during their visits to the clinic, while for others a follow up samples were collected in their homes. A total of 8ml of blood was collected aseptically and randomly from each participant: 2ml was delivered into fluoride/oxalate container and used for the assay of plasma glucose; 4ml was placed in EDTA container and was used for the determination of complete blood count, fibrinogen and von Willebrand factor. Complete blood count and ABO blood group was carried out immediately after which the remaining sample was centrifuged at 2500 rpm and the plasma was separated and stored at -20 ^{o}C for the assay of vWf and fibrinogen. 2ml was delivered into plain bottles and was used to analyze lipid profile, troponin I and C-reactive protein. The samples in plain bottles were separated at 2500 rpm and the serum stored at -20 ^{o}C.

Procedures

Complete blood count **(**CBC) was carried out with automated machine, Sysmex Kx-21N. It is an automated multi-parameter blood cell counter for in vitro diagnostic use (Sysmex Corporation, Kobe, Japan).

Determination of ABO blood group**:** Standard tube method: standard tube method described (16) was used for the test. All the anti-sera used for the test were obtained from Smart Diagnostic laboratories, United Kingdom (Lot No. A1019-23B and B1119-28). Controls were carried out with standard ABO antisera and ABO cells.

Determination of von Willebrand factor (vWf)**:** Enzyme linked immune-sorbent assay (ELISA) kit was used for the test. The kit was obtained from Bioassay technology laboratory, Shangai, China.

Determination of fibrinogen**:** The ELISA kit used for the test was obtained from Bioassay Technology laboratory Shanghai China.

Estimation of C-reactive protein**:** ELISA method was used for the test. The kit was sourced from Calbiotech Inc, USA.

Statistical Analysis

Data generated from the study were analyzed with statistical package for social sciences (SPSS) software version 22.0 (California Inc.) for the determination of mean, standard deviation, student t-test, analysis of variance (ANOVA) chi square and Pearson's correlation. Statistical significance was drawn at $p \leq 0.05$.

Results

Table 1 compares the mean value of age, vWf, FIB, FPG, CRP and some CBC between CVD subjects and control groups. From the findings VWF (173.19±58.60 iu/L), WBC (5.80±1.35x10^{9}/L), RDW-CV (15.70±2.16), MPV (11.58±1.78), revealed significantly higher mean value when com-

pared with the respective parameters in the control group, (122.99±5.41 iu/L, 4.84±1.84 x10^9/L, 12.99±0.94, 9.43±0.67). However it was observed that total platelet count (200.43±70.45x10^9/L) was significantly lower in the CVD subjects when compared with the control group (234.91±48.85x10^9/L), (p=0.00). However no significant difference was observed between FIB and Hb levels of CVD subjects and the control group. CVD subjects presented with significant higher fasting plasma glucose (6.32±0.92 mmol/L) and CRP (5.68±4.19 mg/L) when compared with the control, (4.63±0.51 mmol/L and 2.90±2.24 mg/L). Table 2 compares the vital signs, vWf, FIB, FPG, CRP and some CBC among CVD subjects based on the duration of the disease. According to findings CVD subjects who had suffered from the disease for less than a year had vWf of (209.89±43.08 iu/L). This is followed by those who had suffered from the condition for 1-5 years (175.35±59.11 iu/L) while those who suffered it for over 5 years had the mean level of 155.08±56.77 iu/L. Post Hoc analysis revealed that the value for the third group is significantly different from that of the first group. However there was no significant change in vWf level between those who suffered from the disease for <1 year and those who suffered the disease for 1-5 years.

Table 3 compares vital signs, vWf, FIB and some CBC among CVD subjects based on treatment status. The table shows that vWf (199.23±48.71 iu/L) was significantly higher among the CVD subjects who were not on treatment when compared to those who were on treatment (155.83±58.55 iu/L). It also result revealed that fasting plasma glucose (7.38±2.36 mmol/L), were significantly higher among the CVD subjects who were not on treatment when compared to those who were on treatment; fasting plasma glucose (5.62±1.10 mmol/L). The vital signs, vWf, FIB, CRP and some CBC of CVD subjects based on their ABO blood group are shown in Table 4. The result revealed that group O subjects had significantly lower value of vWf (131.87±45.67 iu/L) when compared to group AB, A and group B, (197.29±68.28 iu/L, 191.75±44.45 iu/L, 208.69±51.51 iu/L). Group A subjects presented with significantly higher mean value of plasma glucose (7.15±2.78 mmol/L) when compared with other ABO blood groups. CRP also showed significantly lower value in group O (4.19±3.60 mg/L) when compared with group AB, B and A (8.11±4.04 mg/L, 6.31±4.32 mg/L, 6.57±4.31 mg/L) respectively.

Table 5 examines the level of the vital signs, vWf, FIB, CRP and some CBC in subjects who were cigarette smokers and compared them with those of non-smokers. There was no significant difference in some CBC parameters between the two groups. CVD subjects who also smoke had significantly higher plasma glucose level, (9.33±2.75 mmol/L) when compared with that of non-smokers, (6.23±1.83 mmol/L), while CRP parameter appear to be similar among the two groups.

Discussion

In this study, majority of the subjects were in the age bracket of 51-66 years. This agrees with earlier findings that CVD is disease of the elderly(17). It revealed that 59 % of the CVD subjects were male while the female constituted only 41 %. This finding is in line with reports from other studies that concluded that the incidences of the disease are more among male than female(18,19). In Table 1, a comparison of vWf level between CVD subjects and control group shows that the subjects had significantly higher vWf levels than the control, (p=0.000). The finding is in line with that of Van Schie et al (20). Von Willebrand factor perform a major function in haemostasis by facilitating platelet adhesion and aggregation. It also acts as a carrier protein for factor VIII. High level of vWf can cause thrombosis.

Though still within the normal range for healthy population, total WBC was found to be significantly higher among subjects when

compared with control. Kim et al.(21) reported a high leukocyte count in CVD subjects than in control group and concluded that it could result in future heart attack, because according to them increased total WBC causes inflammation and oxidative damage to endothelial cells. This explains the level of inflammation experienced by most CVD patients, and if not tackled early enough it could lead to further complication. The migration of monocytes and its differentiation into macrophages result in excessive endocytosis of LDL cholesterol and formation of foam cells(22). WBC and endothelial cells also produce cytokines involved in inflammation and apoptosis. The study also revealed a significant higher Red cell Distribution Width in the test subjects than control group, (p=0.000). RDW is a component of CBC and describes the degree of variation in the sizes of red blood cells. This finding is in agreement with that of Wen (23). The decreased perfusion of the tissues as a result of CVD may lead to increased stimulation of erythropoietin production. This could results in the production of new and bigger RBC that coexists with older and smaller ones. This creates sizes and volume gap between circulating red cells. It is also possible that inflammation caused by the disease tends to reduce the production of new RBCs and this makes the older but smaller RBCs to persist longer in circulation and this can also cause increased RDW observed among the CVD subjects. This test is cheap and simple to perform and should be included in routine test for CVD management.

A lower platelet count was found among CVD subjects than control group, (p=0.000) while the test subjects had a significantly higher MPV than the control, (p=0.000). Similar findings were reported by Khode et al.(24). Bigger platelets have higher enzymatic and metabolic activities(25). These excessive activities can result in thrombus formation. Larger platelets also release more pro-coagulant substances like thromboxane A_2, thrombomodulin and adhesion molecules (26). All these tend to increase the rate of blood coagulation and that increase the chances of venous thrombosis. The fact that most of the CBC parameters tested for in this study showed significant change in the subjects compared to control is an indication that it could be relied upon for routine use in the screening and management of CVD in UCTH. The test is simple to perform and is currently automated which has reduced the turnaround time. Its inclusion in the panel of test for CVD will expand the scope for diagnosis and management of the disease.

Fasting plasma glucose was significantly higher in CVD subjects than control. This is in line with previous findings that high glucose level is risk factor for cardiovascular disease. Hyperglycemia causes inflammation and damage to vascular endothelium. The damage leads to the release of pro-inflammatory and pro-coagulant substances. Excessive activities of these substances can cause heart disease. C-reactive protein, an acute phase protein synthesized in the liver is significantly higher in the test subjects than control group, (p=0.000). Though CRP levels tend to rise in inflammation and infection, recent findings also indicate that high CRP level causes increased macrophages absorption of LDL cholesterol, reduced endothelial function, inhibition of nitric oxide production and increased production of pro-inflammatory cytokines .These activities of CRP tend to worsen CVD. This justifies the level of inflammation reported in CVD patients, (27). The inclusion of CRP into routine screening test for CVD will help to expand the scope of the diagnosis of the disease.

When the levels of the vWf, FIB, FPG, CRP and some CBC parameters were compared among the subjects based on the duration of the disease, it was observed that only vWf showed significant difference among the three groups. VWf showed a progressive decline in the concentration between subjects who suffered from the disease for less than one year and those who suffered it for greater

than five years period, (p=0.046). Comparison of the level of the vWF, FIB and some CBC parameters among subjects based on their treatment status revealed a significant reduction in the plasma concentration of vWf, This is an indication that effective treatment could improve the condition of CVD patients by assessing vWF test. When the haematological parameters of the CVD subjects were compared on the basis of their blood groups, vWf was significantly lower in group O subjects. A significant increase in fasting plasma glucose was seen in group A subjects than other blood groups. von Willebrand factor is one the proteins that carries ABO blood group antigens and ABO blood group affects plasma level of von Willebrand factor. The lower concentration of the factor in group O is attributed to increased rate of clearance by ADAMTS 13 enzyme in group O subjects. This also partly explains why CVD is more common in non-group O subjects than group O. A significant higher glucose concentration in blood A observed in this study also agrees with findings of other studies (28). The mechanism behind this is not very clear, but ABO blood group has been linked with changes in the level of intracellular adhesion molecule 1 and tumour necrotic factor receptor 2. The two factors have been found to be elevated in patients with type 2 diabetes mellitus. The effect could have been mediated through these two factors. ABO blood group also modulate the composition of intestinal microbiota, the organism participates in metabolism by affecting energy balance, glucose metabolism and inflammation. Since the presence and composition of the organism affects glucose metabolism, then it is possible that blood group A individuals have higher level and varied composition of these organisms. C-reactive protein was significantly lower in group O (p=0.025). These also support other study reports that group O have reduced risk of CVD.

Smokers had higher levels of both SBP and DBP . The effect of smoking on BP is mediated by nicotine. Nicotine increase BP and heart rate. It narrows and hardens the wall of the artery and also causes thrombus formation. This makes a smoker prone to heart attack. The research showed higher plasma glucose level in smokers when compared to non-smokers. This is in agreement with the conclusion of Sari et al.(29). As a result of oxidative stress imposed by adrenalin and noradrenalin produced by cigarette smoking, this can lead to hyperglycemia by causing hepatic breakdown of other substances like protein and lipids to form glucose. Male subjects also recorded higher level of CRP than the female. Since CRP level increases proportionately with decline in cardiac function, the study has further affirmed earlier findings that CVD is more common among male than female.

Conclusion

The present study has revealed that CVD can lead to significant increases in plasma levels of vWf, WBC count, RDW and MPV There appear to be inverse relationship between MPV and total platelet count and this is likely to be a protective mechanism to ensure that CVD subjects do not experience bleeding. These parameters can therefore be added as routine test for CVD subjects. Parameters like VWf, which level improves after treatment can be used for monitoring the effectiveness of CVD treatment. ABO blood group affects the incidences of CVD in the study with group A presenting with the highest cases and group O with the least. When the subjects were considered on gender basis, more males than females presented with higher level CRP. Our findings also revealed that CVD is a disease of the elderly as 77 % of the subjects were between 51 and 82 years of age.

Table 1: Age, vWF, FIB, FPG, CRP and some CBC among CVD subjects and control

Parameter/Group	CVD subjects n = 200	Control n = 160	p-value
Age (years)	58.44±9.95	57.59±10.37	0.578
VWF (IU/L)	173.19±58.60	122.99±45.41	0.000*
FIB (g/l)	4.11±1.03	3.13±0.62	0.271
WBC (L/L)	5.80±1.35	4.84±1.29	0.000*
Hb (g/dl)	14.85±10.27	13.01±1.01	0.113
RDW (%)	15.70±2.16	12.99±0.94	0.000*
PLT (×10⁹/ L)	200.43±70.45	234.91±48.85	0.000*
MPV (fl)	11.58±1.78	9.43±0.67	0.000*
FPG (mmol/l)	4.63±0.51	6.32±1.92	0.000*
CRP (mg/l)	2.90±2.43	5.68±4.19	0.000*

Values are expressed as mean ± SD. Where VWF=von willebrand factor, FIB=fibrinogen, WBC=white cell count, Hb=haemoglobin, RDW=red cell distribution width, PLT=total platelet count, MPV=mean platelet volume, CBC = Complete Blood Count, FPG = fasting plasma glucose and CRP = C-reactive protein.

*= significant at $p < 0.05$

Table 2: Vital signs, vWF, FIB, FPG, CRP and some CBC among CVD subjects based on duration of the disease

Parameter/Group	6 - 12months n = 18	13 – 60months n = 130	>60months n = 52	f-ratio	p-value
BMI (Kg/m²)	25.96±5.35	2726±5.21	28.38±5.36	0.821	0.443
SBP (mmHg)	153.67±15.56	153.26±15.85	159.81±19.05	1.456	0.238
DBP (mmHg)	88.33±7.50	88.95±13.05	92.46±8.61	0.919	0.403
VWF (IU/L)	209.89±43.08	175.35±59.11	155.08±56.77[a]	3.186	0.046*
FIB (g/l)	4.26±1.49	4.27±1.47	4.07±15.52	1.305	0.276
WBC (L/L)	5.80±1.34	5.66±1.37	6.14±1.28	1.189	0.309
Hb (g/dl)	13.20±0.66	13.95±0.22	17.68±3.91	1.364	0.261
RDW (%)	15.98±1.56	15.55±2.35	15.96±1.84	0.409	0.666
PLT (×10⁹/L)	191.44±67.14	200.73±77.26	202.81±5378	0.087	0.917
MPV (fl)	12.09±1.24	11.52±1.89	11.56±1.70	0.400	0.671
FPG (mmol/l)	7.14±2.23	6.41±2.08	5.83±1.15	1.788	0.173
CRP (mg/l)	5.47±3.54	5.86±4.63	5.31±3.25	0.172	0.842

Values are expressed as mean ± SD. Where VWF=von willebrand factor, FIB=fibrinogen, WBC=white cell count, Hb=haemoglobin, RDW=red cell distribution width, PLT=total platelet count, MPV=mean platelet volume, CBC = Complete Blood Count, FPG = fasting plasma glucose and CRP = C-reactive protein.

*= significant at $p < 0.05$ a = significantly different from <1year

Table 3: Vital signs, vWF, FIB and some CBC among CVD subjects based on treatment status

Parameter/Group	On treatment n = 120	Not on treatment n = 80	p-value
BMI (Kg/m²)	28.36±5.58	26.03±4.41	0.029*
SBP (mmHg)	153.98±18.23	156.53±14.46	0.461
DBP (mmHg)	91.12±7.53	87.85±15.90	0.171
VWF (IU/L)	155.83±58.55	199.23±48.71	0.000*
FIB (g/l)	4.28±2.72	4.87±1.31	0.514
WBC (L/L)	5.80±1.33	5.80±1.38	0.993
Hb (g/dl)	15.59±13.18	13.75±1.78	0.383
RDW (%)	15.59±1.55	15.86±2.85	0.549
PLT (×10⁹/L)	200.27±59.87	200.68±84.71	0.978
MPV (fl)	11.47±1.52	11.75±2.13	0.438

Values are expressed as mean ± SD. Where VWF=von Willebrand factor, FIB=fibrinogen, WBC=white cell count, Hb=haemoglobin, RDW=red cell distribution width, PLT=total platelet count, MPV=mean platelet volume and CBC = Complete Blood Count,

*= significant at $p < 0.05$

Table 4: Vital signs, vWF, FIB, FPG, CRP and some CBC variation among CVD subjects based on ABO blood group system

Parameter/ Group	A n = 56	B n =32	AB n = 14	O n = 98	F-ratio	p-value
BMI (Kg/m²)	27.35±3.73	28.57±7.29	26.04±2.91	26.97±4.91	0.668	0.574
SBP (mmHg)	159.18±15.93	147.46±17.65	155.43±15.10	156.95±16.05	2.625	0.055
DBP (mmHg)	92.75±7.74	87.69±7.10	90.14±4.34	89.05±16.29	0.935	0.427
VWF (IU/L)	191.75±44.45	208.69±51.51	197.29±68.28	131.87±45.67[a]	15.945	0.000*
FIB (g/l)	4.56±1.38	4.19±1.51	3.90±1.18	4.04±1.36	0.882	0.453
WBC (L/L)	5.69±1.48	5.89±1.36	6.47±1.78	5.69±1.27	0.758	0.520
Hb (g/dl)	13.85±1.65	14.18±2.03	14.04±1.44	16.16±2.62	0.343	0.794
RDW (%)	16.25±2.42	14.95±2.50	15.74±1.34	15.79±1.73	1.723	0.167
PLT (×10⁹/L)	186.04±77.13	217.50±77.39	182.86±69.65	202.54±59.85	1.057	0.371
MPV (fl)	11.96±2.47	11.08±1.47	12.00±0.84	11.57±1.45	1.253	0.295
FPG (mmol/l)	7.15±2.78[b]	5.60±1.15	6.37±1.34	6.21±1.46	3.218	0.026*
CRP (mg/l)	6.57±4.31	6.31±4.32	8.11±4.04	4.19±3.68[a]	3.256	0.025*

Values are expressed as mean ± SD. Where VWF=von willebrand factor, FIB=fibrinogen, WBC=white cell count, Hb=haemoglobin, RDW=red cell distribution width, PLT=total platelet count, MPV=mean platelet volume, CBC = Complete Blood Count, FPG = fasting plasma glucose and CRP = C-reactive protein.

*= significant at $p < 0.05$

a = significantly different from A, B and AB

Table 5: Vital signs, vWF, FIB, FPG, CRP and some CBC among CVD subjects who are smokers and non-smokers

Parameter/Group	Smokers n = 50	Non-smokers n = 150	p-value
BMI (Kg/m²)	25.80±2.43	27.48±5.31	0.588
SBP (mmHg)	165.67±5.13	154.67±16.93	0.038*
DBP (mmHg)	90.55±7.73	66.00±54.62	0.000*
VWF (IU/L)	216.00±42.67	171.87±58.69	0.200
FIB (g/l)	4.85±1.10	4.20±2.16	0.901
WBC (L/L)	5.67±0.57	5.80±1.36	0.864
Hb (g/dl)	12.70±0.60	14.92±10.43	0.715
RDW (%)	16.00±1.32	15.67±2.18	0.807
PLT (×10⁹/L)	249.67±52.16	198.91±70.59	0.221
MPV (fl)	12.53±0.35	11.55±1.80	0.350
FPG (mmol/l)	9.33±2.75	6.23±1.83	0.005*
CRP (mg/l)	8.05±6.68	5.61±4.13	0.324

Values are expressed as mean ± SD. Where VWF=von willebrand factor, FIB=fibrinogen, WBC=white cell count, Hb=haemoglobin, RDW=red cell distribution width, PLT=total platelet count, MPV=mean platelet volume, CBC = Complete Blood Count, FPG = fasting plasma glucose and CRP = C-reactive protein.

*= significant at $p < 0.05$

Conflict of interest Statement

The authors declare no conflict of interest.

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