

EVALUATING COMMON HEMATOLOGICAL AND BIOCHEMICAL BIOMARKERS AS PREDICTORS FOR ISCHEMIC HEART DISEASES AMONG ADULT SUDANESE PATIENTS

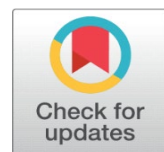


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ABSTRACT

Background: Ischemic heart diseases are the leading cause of death worldwide. It accounts for (20.07%) of total deaths with a death rate of 279.01 per 100.000 population. Being multifactorial in origin, the causes, diagnosis, prevention, control, and/or treatment of IHD remain active fields of biomedical research with considerable emphasis on the relativity of various risk factors and IHD.

Methods: This is a descriptive cross-sectional case-control prospective analytical study to evaluate the hematological and biochemical predictors in ischemic heart disease patients in Shendi locality, River Nile, State Sudan. The study excluded all patients with comorbidities that might affect the results of biomarkers.

Results: The mean values of Hb, PCV, RBCs, MCV, MCH, MCHC, RDW in case group were (12.3 g/dl), (37.7%), (4.2x10¹²/l), (87.9 fl), (28.9 pg), (32.9 g/dl) and (16.5) respectively and mean of TWBCs, Neutrophil, lymphocyte, monocyte, eosinophil, basophil, platelet count and MPV of (8.4 x 10⁹ /l), (66.6%), (25%), (5.9%), (2.5%), (0%), (301.9 x 10⁹ /l) and (8.4) respectively. The mean of hsCRP, D.dimer in case group were (5.896 mg/l), (1247.4 ng/ml), respectively. The case group had mean range of urea and creatinine (57.68 mg/dl) and (1.55 mg/dl) respectively, and mean of (Na⁺), (K⁺) and (Ca²⁺) of (136.1 mmol/l), (3.87 mmol/l) and (9.73 mg/dl) respectively.

Conclusion: When compared to healthy individuals in the control group, the case group had lower Hb, PCV, red cells indices, serum sodium (Na⁺), potassium (K⁺), and calcium (Ca²⁺) levels. And higher levels of TWBCs, Neutrophil, platelet, MPV, Serum hsC-reactive protein, plasma D.dimer, b.urea, and serum creatinine.

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Keywords: Ischemic Heart Diseases, Biomarkers, Inflammatory Markers, Atherosclerosis

1. INTRODUCTION

Ischemic heart diseases (IHD) are the number one cause of death, disability, and human suffering globally. It affects around 126 million individuals (1,655 per 100,000), which is approximately 1.72% of the world's population. Near nine million deaths are caused by IHD globally. With higher rates among men than women of a given age, CHD also carries a higher case-fatality rate among the male gender Khan et al. (2020). According to the latest WHO data published in 2018 IHD related deaths accounted for (20.07%) of total deaths with a death rate of 279.01 per 100.000 of the population Healthdata.org (2019). Numerous risk factors have been implicated in the disease process, morbidity and mortality, age,



gender, hypertension, diabetes, serum cholesterol levels, smoking, and excessive alcohol consumption [NPS Medicine wise \(2011\)](#), [Norhammar et al. \(2004\)](#), with a variable individual contribution of each risk factor between different communities or ethnic groups and remarkably strong consistency of the overall contribution of these risk factors to epidemiological studies. [Bertazzo et al. \(2013\)](#)

A biomarker is tool used in predicting, diagnosing, and staging diseases, thus help effectively manage patients by the provision of prompt and accurate treatment and/or prognosis [Biomarkers Definitions Working Group \(2001\)](#), [Yilmaz et al. \(2010\)](#). A biomarker may be measured on a bio-sample (as a blood, urine, or tissue test), recorded (blood pressure, electrocardiogram, or Holter), or it may be an imaging test (echocardiogram). A vast array of biomarkers maybe added to conventional cardiovascular risk factors in predicting the risk of future CVD; however, the clinical value of some biomarkers is still questionable [Threapleton et al. \(2013\)](#). Currently, biomarkers that may reflect a higher risk of CVD include coronary artery calcification, carotid intima-media thickness, higher fibrinogen, and PAI-1 blood concentrations. elevated homocysteine, elevated blood levels of asymmetric dimethylarginine, Inflammation as measured by CRP, elevated LDL levels, and elevated blood levels of (BNP). [Cihat et al. \(2012\)](#)

2. MATERIALS AND METHODS

Study design: This is a descriptive cross-sectional case-control prospective analytical study to evaluate the haematological and biochemical predictors in ischemic heart disease patients at Almak Nimir University Hospital; a Shendi University-affiliated tertiary hospital in Sudan. **Study population:** A total of (100) samples were collected from the Study group of ischaemic heart disease patients and (100) samples were collected from healthy individuals as a control group. **Inclusion criteria:** Patients of both sexes with ischaemic heart disease (who take drugs or not take), irrespective of treatment patients with no other medical conditions were included in the study.

Exclusion criteria: Patients with other comorbid diseases such as renal failure, liver disease, haematological diseases and other medical conditions or receiving certain treatment that affect the results were excluded from the study. Data was collected using a self-administrated pre-coded questionnaire which was specifically designed to obtain information that helped in the study then analysed using SPSS version 11.5. (Mean, standard deviation, standard error mean, P. value by using independent T.test).

CBC was done by using Mindray Hematology Analyzer (Mindray bc-3000); every film was first inspected at low power (x10) before the general examination was undertaken with the x 40 lenses. The x100 oil immersion lens is generally reserved for examining. B. urea, S.creatinine and S. Ca²⁺ using automated chemistry analyzer, Mindray BS 120). Estimation of serum electrolyte using an ion-selective electrode. hs C.reactive protein and D.dimer were measured via sandwich immunodetection.

3. RESULTS

A total of (100) blood sample collected from ischaemic heart disease patients and (100) samples collected as control from healthy individuals include frequency of sex was 32 males (32%) and 68 females (68%), frequency of age groups 40-80 years 95(95%). Frequency of weight (50-100) kg (97%) in the study group.

The average age of patients with ischaemic heart disease in the study was (61.44 ± 10.851), with a range of (40-80) years.

The majority of our patients (68) were of female gender (68%), and 32 (32%) were males. Regarding to weight, the average weight of patients with ischaemic heart disease in the study was (68.08 ± 11.912), with a range of (50-100 kg).

Characteristic		Frequency	Percent %
Study groups	Case	100	50%
	Control	100	50%
Sex	Male	32	32%
	Female	68	68%
Age/yrs	<40 yrs.	2	2%
	40-80 yrs.	95	95%
	>80 yrs.	3	3%
Weight/kg	Less than 50kg	2	2%
	50-100 kg	97	97%
	More than 100kg	1	1%

Participation to risk factors to ischaemic heart disease reflected that; 64 (64%) were HTN patients, while 36 (36%) were not. On the other hand, 32 (32%) were DM patients, while the remaining 68 (68%) were not.

Furthermore, 4 (4%) of the patients were smokers, while 96 (96%) of them were not. Concerning obesity, 24 (24%) of patients were obese, 76 (76%) with normal weight. Regarding family history, most of the patients 92 (92%) with no family history of ischemic heart disease and 8 (8%) were family history. [Table 2](#)

Characteristic		Frequency	Percent %
HTN	Yes	64	64%
	No	36	36%
DM	Yes	32	32%
	No	68	68%
Smoking	Yes	4	4%
	No	96	96%
Lipidaemia	Yes	24	24%
	No	76	76%
Family history	Yes	8	8%
	No	92	92%

The mean values of Hb, PCV, RBCs, MCV, MCH, MCHC, RDW in case group were (12.3 g/dl), (37.7%), (4.2x10¹²/l), (87.9 fl), (28.9 pg), (32.9 g/dl) and (16.5) respectively and in control group the mean values of Hb, PCV, RBCs, MCV, MCH, MCHC, RDW were (13.1 g/dl), (39.8%), (4.4x10¹²/l), (89.0 fl), (29.2 pg), (32.8 g/dl) and (15.6) respectively. [Table 3](#).

Table 3 Comparison between case and control in Hb, RBCs, RBCs indices and RDW

Groups		Number	Mean	SD	P. value
Hb g/dl	Case	100	12.3	1.59	0.003
	Control	100	13.1	1.88	
RBCsx10 ⁹	Case	100	4.23	0.519	0.001
	Control	100	4.48	0.55	
PCV %	Case	100	37.7	4.20	0.002
	Control	100	39.8	5.13	
MCV fl	Case	100	87.9	6.71	0.199
	Control	100	89.0	4.53	
MCH pg	Case	100	28.9	2.63	0.444
	Control	100	29.2	1.78	
MCHC g/dl	Case	100	32.9	1.86	0.707
	Control	100	32.8	0.76	
RDW	Case	100	16.5	2.53	0.000
	Control	100	15.6	0.68	

The mean of TWBCs, Neutrophil, lymphocyte, monocyte, eosinophil, basophil, platelet count and MPV in IHD were (8.4 x 10⁹ /l), (66.6%), (25%), (5.9%), (2.5%), (0%), (301.9 x 10⁹ /l) and (8.4) respectively. the mean of TWBCs, Neutrophil, lymphocyte, monocyte, eosinophil, basophil, platelet count and MPV in control were (5.7 x 10⁹ /l), (48.1%), (43.2%), (6.1%), (2.6%), (0%), (277.5 x 10⁹ /l) and (9.1) respectively. [Table 4](#)

Table 4 Relationship between case and control in WBCs count and their subtype, platelet and MPV

Group		Number	Mean	SD	P. value
WBCsx10 ⁹	case	100	8.44	6.53	0.000
	control	100	5.78	1.34	
Neutrophil %	case	100	66.60	11.26	0.000
	control	100	48.12	8.18	
Lymphocyte %	case	100	25.00	10.24	0.000
	control	100	43.28	7.55	
Monocyte %	case	100	5.92	1.72	0.377
	control	100	6.12	1.45	
Eosinophil%	case	100	2.54	1.10	0.541
	control	100	2.64	1.20	
Plateletx10 ⁹	case	100	301.92	117.52	0.070
	control	100	277.52	64.67	
MPV	case	100	8.412	.720	0.000
	control	100	9.136	.700	

The mean of hsCRP, D.dimer in case group were (5.896 mg/l), (1247.4 ng/ml), respectively. The mean of hsCRP, D.dimer in control group were (0.37 mg/l), (90.08 ng/ml), respectively. [Table 5](#)

Table 5 Comparison between case and control in hsC-reactive protein and D. dimer

Group		Number	Mean	SD	P. value
Hs-CRP mg/dl	case	100	5.89	3.77	0.000
	control	100	0.37	0.44	
D. dimer ng/dl	case	100	1247.44	2583.21	0.000
	control	100	90.08	25.60	

The mean of urea and Creatinine in case group were (57.68 mg/dl) and (1.55 mg/dl) respectively. The mean of urea and Creatinine in control were (30.00 mg/dl) and (1.18 mg/dl) respectively. [Table 6](#)

Table 6 Comparison between case and control in urea and creatinine

Group		Number	Mean	SD	P. value
Urea mg/dl	Case	100	57.68	42.742	0.000
	Control	100	30.00	12.358	
Creatinine mg/dl	Case	100	1.556	1.4612	0.020
	Control	100	1.184	0.6141	

The mean of (Na⁺), (K⁺) and (Ca²⁺) in case group were (136.1 mmol/l), (3.87 mmol/l) and (9.73 mg/dl) respectively. The mean of (Na⁺), (K⁺) and (Ca²⁺) in control group were (136.1 mmol/l), (3.87 mmol/l) and (9.73 mg/dl) respectively. [Table 7](#).

Table 7 Comparison between case and control in electrolyte

Group		Number	Mean	SD. Deviation	P.value
(Na ⁺) mmol/l	case	100	136.12	5.05	0.000
	control	100	138.44	2.98	
(K ⁺) mmol/l	case	100	3.876	0.5924	0.010
	control	100	4.048	0.3037	
(Ca ²⁺) mg/dl	case	100	9.736	0.5684	0.000
	control	100	10.656	0.5916	

4. DISCUSSION

It is now well comprehended that a complex matrix of genetic, environmental, biological, and social factors contributes to the development and progression of IHD influencing the disease at all levels of encounter from risk stratification and development, to complication anticipation and outcome prognosis. Thus, it is vital to denote any variations in demographic characteristics and the relations of biomarkers to known risk factors. [Batstone \(1997\)](#), [LaBaer \(2005\)](#)

While it's well acknowledged that among middle-aged people, coronary heart disease is (2) to (5) times more common in men than in women [Bridget \(2011\)](#). Our study results reveal the quite opposite, in which a total of 32 males (32%) and 68 females (68%) represented the study group. The world health organization estimated that (40%) of the variation in the sex ratios of coronary heart disease mortality was attributed to gender [Jackson et al. \(1999\)](#). One of the proposed explanations for the gender differences in CVD is hormonal difference. Studies have pointed out that Estrogen may have protective effects through glucose metabolism and the haemostatic system, and it may have a direct effect on improving endothelial cell function [Linden et al. \(1996\)](#). In terms of age distribution, (95%) of the study group aged (40-80 years). It is estimated that there is approximately a tripling of

risk of IHD with each decade of life [Sergio et al. \(2013\)](#), and that (82 %) of people who die of CHD are (65yrs) and older [Inaba et al. \(2012\)](#).

Multiple hypotheses linked aging with ischemic heart diseases, for example the marked increase in serum total cholesterol levels with age; (45to 50 years) in males and (60 to 65 year) in females [Jousilahti et al. \(1999\)](#). Additionally, studies have described that the coronary vascular walls showed considerable mechanical and structural changes, causing progressively diminishing elasticity and compliance; as major contributors to IHD. [Jousilahti et al. \(1999\)](#), [Toshio et al. \(2001\)](#)

The results of this study denoted that the hypertensive patients were at high risk to IHD and showed an increased prevalence as (64%) of the study group were found to be hypertensive, followed by diabetes as only (32%) were diabetic. Most of the patients were non-STEMI type, with predominantly inferior, anterior ECG changes.

Our study results demonstrated that there was a significant decrease in Hb, RBCs count, and PCV compared to control. (P-value >0.05). Results of this current study are different when compared to a study done by Toshio team in Japan which revealed that: high PCV and Hb were risk factors for IHD [Puddu et al. \(2002\)](#). Several factors related to RBCs are associated with IHD including Hb levels, PCV and ESR but there are not enough data to suggest a significant association between the RBCs count and cardiovascular disease. [Patel et al. \(2009\)](#)

The study findings prevailed a decrease in the mean of RBCs indices (MCV, MCH & MCHC) and there was no association when compared to the control group (p-value <0.05).

With the significant increase in the mean of RDW compared to the control group, there was a strong significant statistical value depicted among the study population; (P. value 0.000). These findings are in line with the study conducted by Patel VK et al, in which RDW was significantly associated with an increased risk of death secondary to CVD in cross-sectional studies of the population of the U.S [Madjid and Fatemi \(2013\)](#). In addition, the RDW is an independent predictor of death in patients who have had previous MI or stroke and in men referred for coronary angiography. [Madjid and Fatemi \(2013\)](#)

The results of this study also confirmed an increase in the mean of WBCs & neutrophils and a decrease in lymphocytes, eosinophils & monocytes means with a significant statistical relationship found among the study population; (P. value 0.000). Results of the present study were in agreement with a previous study done by Mohammad Madjid, and Omid Fatemi suggesting that: leucocytosis can be considered as a marker of inflammatory changes in atherosclerotic lesions. [Korean \(2016\)](#)

While our data implied an increase in the mean of platelet compared to the control group -with no significant statistical difference observed among the study population; (P = 0.070)-

There was a considerable decrease in MPV mean compared to control, with strong significant statistical value demonstrated among study population; (P. value 0.000). It thus, appears that the role of platelets in the pathogenesis of IHD is due mainly to their functional properties and their interaction with plasma and tissue factors.

This is coherent with the findings of various similar studies such as one conducted by Dong-Hyun Choi, Seong-Ho Kang and Heesang Song showing a significant correlation between MPV, the risk of ischemic stroke in AF patients, and poor clinical outcomes after PCI in patients with coronary artery disease. [Volanakis \(2001\)](#)

The results of the tests conducted showed an increase in the mean of hs-CRP compared to the control group. There was a strong significant statistical difference appeared among the study population; ($P = 0.000$). The recent study showed a strong association between hs-CRP and IHD. The results were in agreement with multiple other studies that presented an increase in CRP of IHD patients. One study denoted that: an increase in hs-CRP was associated with increased incidence of recurrent angina, coronary revascularization, and cardiovascular death. It has recently been suggested that hs-CRP is a marker of inflammation, along with serum cholesterol, which may be a critical component in the development and progression of atherosclerosis [John et al. \(2001\)](#). Our study also shows an increase in the mean of D.dimer compared to the control group with significant statistical differences estimated among the study population. This current study found that an increased D.dimer was associated with IHD. A pathophysiological explanation is that D.dimer is hypothesized to be involved in the so-called inflammation-coagulation-axis. The results of the present study are relevant to the previous study done by [Ostfeld et al. \(2005\)](#)

The increased mean of urea & creatinine was observed in this study to be higher than the control group. This study indicated an association between increased urea, creatinine, and IHD, in coherence with the result adopted by [\(Kirtane et al, 2005\)](#), suggesting that renal dysfunction has been associated with adverse cardiovascular outcomes [Choudhury et al. \(2011\)](#).

Finally, a significant reduction in this study in serum sodium (Na^+), potassium (K^+), and calcium (Ca^{2+}) levels among the IHD patients were detected and compared to healthy individuals in the control group. This finding is in an accordance with the study carried out by [Choudhury et al. \(2011\)](#) which depicted an effect in (K^+) level in IHD patients [Yilmaz et al. \(2010\)](#).

5. CONCLUSION

Our study concluded that Hb, PCV, red cells indices were lower in IHD patients, and that TWBCs, Neutrophil, platelet, plasma D. dimer and serum hsC-reactive protein were higher when compared to healthy individuals. IHD patients also had abnormally increased renal function tests (urea and creatinine) and a lower level of sodium (Na^+), potassium (K^+), and calcium (Ca^{2+}) when compared to healthy individuals in the control group.

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