RESEARCH ARTICLE

Red Cell Distribution Width and High Sensitivity C-Reactive Protein as Risk Markers in Hypertension

Jithesh TK[1], Riju Mathew[2], Jayapal V[3], Vijayakumar T[4]
[1] Department of Biochemistry MES Medical College, Perinthalmanna
[2] Research Fellow, Yenapoya University, Mangalore
[3] Hrithyalaya Institute of Preventive Cardiology, Trivandrum
[4] Basic Medical Sciences, Educare Institute of Dental Sciences, Kottakkal
Correspondence to: Jithesh TK (jitheshtk@gmail.com)

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ABSTRACT

Background: Even though red cell distribution width (RDW) and C reactive protein (CRP) are considered as markers of inflammation and cardiac injury studies on the diagnostic and/or prognostic applications of these parameters as renal markers in hypertension (HT) are scanty.

Objective: To evaluate the association, if any, between RDW and high sensitive CRP (hs-CRP) with renal complication in HT.

Materials and Methods: One hundred and twenty patients with clinically proved hypertension under treatment formed the test group and 60 age and sex matched healthy adults formed the control group. . Blood collected in EDTA was used for complete blood cell count (CBC). Serum was separated immediately after clotting and is used for the estimation of hs-CRP by particle enhanced immunonephelometry.

Results: A significant elevation in hs-CRP was observed in both the male and female patients with HT compared to the control group. In the case of RDW even though the values were higher in the test group than control, the elevation was significant only in the male test subjects indicating they are at a higher risk than the females.

Conclusion: The elevation of hs-CRP and RDW in the test group suggest that inflammation may be one of the cause or effect of hypertension. Long term inflammation may lead to chronic kidney disease and cardiovascular disease hence monitoring of these markers may be of use in predicting the outcome of hypertension.

Key Words: Hypertension; Chronic Kidney Disease; End Stage Renal Disease; Red Cell Distribution Width; C - Reactive Protein

INTRODUCTION

Hypertension (HT) has been identified as the leading risk factor for morbidity and mortality, and is ranked third as a cause of disability-adjusted life-years. The risks of chronic kidney diseases (CKD) and concomitant cardiovascular diseases (CVD) make HT a serious health problem. The damage to the blood vessels due to damage of vascular endothelium in HT can lead to complications in other parts of the body.[1,2] Apart from kidneys and heart, brain, peripheral circulation and eyes are the major target organs affected by HT.[3] Renal hypertension puts stress and increased pressure on the kidney, and is a major cause of end-stage renal disease in the elderly. Hypertensive nephropathy is a medical condition referring to damage to the kidney due to chronic high blood pressure. Additional complications often associated with hypertensive nephropathy

include glomerular damage resulting in proteinuria and haematuria.[4]

As a cause of CKD and as a significant cardiovascular disease risk factor, HT presents a unique problem in patients with CKD. HT increases the risk of several important adverse outcomes, including the progressive loss of kidney function leading to kidney failure, early development and acceralated progression of CVD and premature death. HT plays a significant role in the high CVD morbidity and mortality in CKD patients and CVD remains leading cause of death in all patients with any form of CKD, particularly in those with ESRD.[5] An elevation in blood pressure is a strong independent risk factor for ESRD. Preventing progression of CKD to ESRD may improve quality of life and help save health care expenses. A concerted approach to manage CKD patients effectively starts with early detection and integrated management by multiple specialties.[6] CKD is a complex disease that often affects multiple organ systems and often coexists with numerous associated conditions, such as cardiovascular disease, diabetes mellitus, hypertension, lupus, chronic inflammation etc. CKD prevalence studies in India are scanty and inconclusive.[7]

The rapid increase in the prevalence of CKD and its major role in increasing the risk of cardiovascular disease make HT one of the most important public health problems. The relationship between systemic arterial pressure and morbidity appear to be quantitative rather than qualitative. CKD frequently leads to end stage kidney disease requiring dialysis or transplantation, and is a “disease multiplier” that increases the risk of death from cardiovascular causes.[8] One of the most important goals of HT therapy is the control of blood pressure.

High sensitive C - reactive protein (hsCRP) is a nonspecific serum marker of inflammatory response and is emerging as an independent risk marker for CVD. It normally circulates at low levels but acute inflammatory process can cause a several fold increase in serum levels. An association between CVD and hs-CRP has been reported.[9] It is also reported to be a predictive marker for inflammatory process leading to HT and CVD.[10]

Red cell distribution width (RDW) is a measure of the variation in the size of circulating erythrocytes. It is routinely measured by automated haematology analysers and is elevated in conditions of ineffective red cell production, haemolysis and after blood transfusion. RDW is reported to be elevated in inflammatory stress and renal dysfunction. It is associated with increased morbidity and mortality in CVD and its role in chronic inflammation are equivocal.[11] Recently Cetin et al[12] had shown that RDW is associated with coronary atherosclerosis in patients with stable angina pectoris.

Even though RDW and hsCRP are considered to be markers of inflammation, studies on their diagnostic and/ or prognostic applications as markers for renal complication in HT have not been assessed previously. The aim of the present study was to evaluate the association, if any between RDW and hsCRP with renal complication in HT.

METHODS

The study was conducted at Educare Institute of Dental Sciences, Kottakkal, MES Academy of Medical Science, Perinthalmanna and Hrithayalaya institute for preventive cardiolgy, Trivandrum, Kerala. One hundred and twenty clinically proved patients below the age of 65 years formed the test group. The control group consisted of 60 subjects selected from the siblings, teaching and nonteaching staff of the institutes. Detailed clinical, epidemiological and anthropometric characteristics were recorded using proforma. Five ml of fasting venous blood (2 ml in K_3 EDTA vacuitainer and the remaining 3 ml in vacuitainer containing clot activators) from all the subjects after getting the informed consent, as per the criteria laid down by the Institutional Ethics Committee. Blood collected in EDTA was mixed by inversion several times and used for complete blood cell count (CBC) in in BC 5800

Auto Haematology Analyser of Mindray and for the estimation of erythrocyte sedimentation rate (ESR) by Wintrobe method. Serum was separated immediately after clotting and is used for the estimation of hsCRP by particle enhanced immunonephelometry on the BNA nephelometer (Dade Behring, Liederbach Germany). The reagents, calibrators and quality controls were supplied by the respective companies.

RESULTS

There were 180 subjects in the present study out of which 120 formed the test group and the remaining were age and sex matched control. The male to female ratio of both the test and control group were the same i.e. 57:43. The mean age of the study population was 57.41 ± 10.12 years while that of the control population were 48.6. The haematological data of the test and control groups are given in table 1 and Figure 1.

For the present study only three parameters namely, RDW, Haemoglobin (Hb) and ESR were taken for analysis. ESR were found to be significantly elevated whereas Hb was found to be significantly decreased both in male and female test group compared to the corresponding controls. In the case of RDW even though the values are elevated in both the male and female test group, a significant elevation was observed only in the male subjects.

The serum hsCRP levels of the test and control groups of the present study are given in table 2 and figure 2.

Table-1: Hematological Parameters of Control and Test

	Male (control –n =34 , test – n =68)			Female (control - n= 26, test, n= 52)	
	Group	Mean ± SD	p value	Mean ± SD	p value
RDW	Control	13 ± 1.1	<0.05	12.77 ± 1.1	0.39
	Test	14.16 ± 2.46		13.04 ± 2.35	
Hb, gm/dl	Control	15.87 ± 0.68	<0.05	12.93 ± 0.65	<0.05
	Test	12.84 ± 2.14		11.48 ± 1.52	
ESR , mm/hr	Control	11 ± 3.95	<0.05	11.46 ± 3.97	<0.05
	Test	37.13 ± 24.18		36.23 ± 18.7	

Figure-1: Histogram of Hematological Parameters

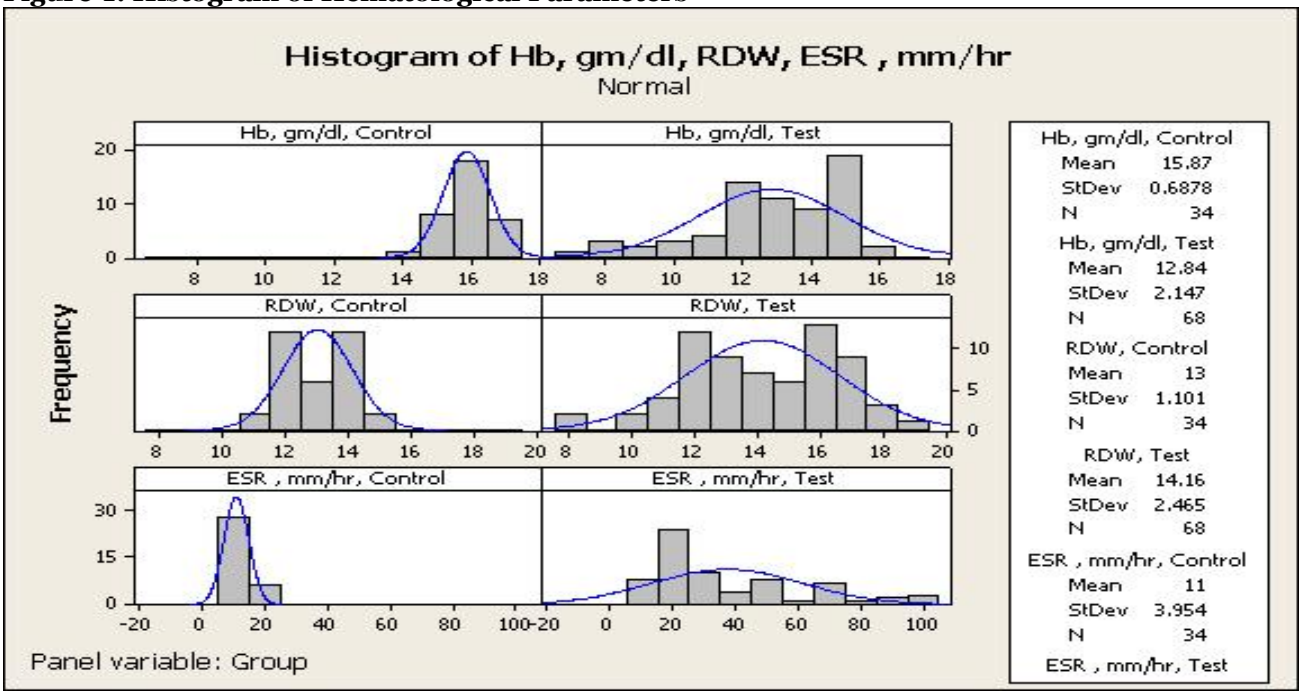
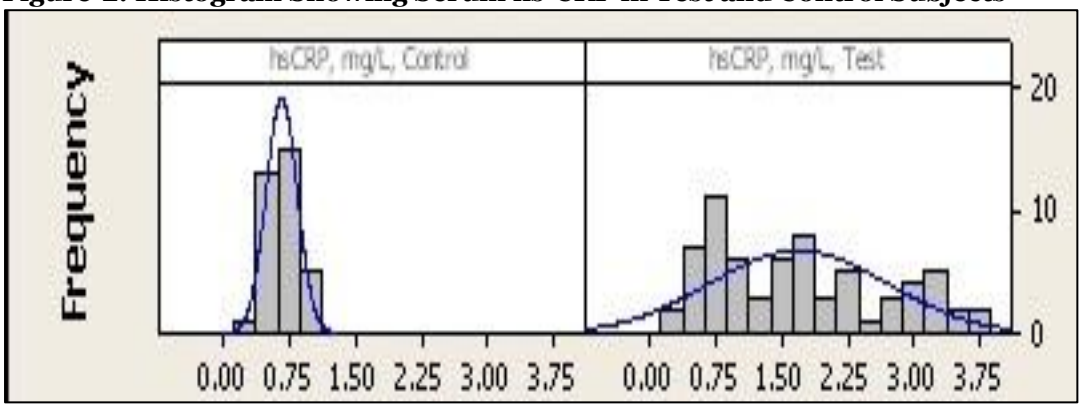


Table-2: Serum hs-CRP in Test and Control Subjects

Group	Male (control –n =34 , test – n =68)		Female (control - n= 26, test, n= 52)	
	Mean ± SD	p value	Mean ± SD	p value
Control	0.66 ± 0.17	<0.05	0.58 ± 0.32	<0.05
Test	1.68 ± 1.01		1.3 ± 1.01	

Figure-2: Histogram Showing Serum hs-CRP in Test and Control Subjects



Serum hs-CRP levels were significantly elevated both in male and female subjects of test group compared to their normal counterparts. This demonstrates that there is some level of inflammation in HT which results in elevated levels of hs-CRP and RDW.

DISCUSSION

Hypertension makes the heart and can damage blood vessels throughout the body resulting in endothelial dysfunction and vascular damage. Damage, if any, of the blood vessels in the kidney will result in the filtration process of the kidney and may lead to microalbuminuria and CKD. Inflammatory markers such as hs-CRP may serve as a screening test for the development of CVD.[13] In the present study none of the patients were having CVD but their hs-CRP values were significantly elevated indicating that these patients may be at high risk of developing CVD. Our work is well in agreement with that of Veeranna et al[14], who observed that hs-CRP along with RDW can be used as predictive markers of CVD outcome.

Red cell distribution width is automatically recorded in any automated haematology analysers and studies have shown a strong association of RDW and long term mortality risk in patients with CKD, CVD and chronic heart failure.[15-17] It was also reported by Arhan et al[11] that RDW can also be used as a marker for inflammatory diseases. In the present study it was observed that RDW is elevated in patients with HT, elevation being more pronounced in males rather than in females. This finding is well in agreement with that of Wen et al who observed an elevated level of RDW in patients with HT.[18] Red cell distribution width was reported to be of clinical use in predicting the outcome of acute myocardial infarction.[19] The aim of the present study was to evaluate the usefulness of RDW along with hs-CRP as risk markers of HT. We have observed that both the above markers are elevated in patients with HT since these parameters are concerned as inflammatory markers as reported by Cetin et al[12] indicating that inflammation may be one of the causes for HT and may predispose an individual into CKD and CVD. Further studies are needed to correlate RDW and hs-CRP with renal function test to assess to usefulness of these markers in predicting the renal involvement in HT.

CONCLUSION

The elevation of hs-CRP and RDW in the test group suggest that inflammation may be one of the cause or effect of hypertension. Long term inflammation may lead to chronic kidney disease and cardiovascular disease hence monitoring of these markers may be of use in predicting the outcome of hypertension.

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