



Association Of Red Blood Cell Distribution Width and Carotid Intimal Media Thickness in Patients with Metabolic Syndrome

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Abstract

BACKGROUND: The present study aims to explore the association between red blood cell distribution width (RDW) and carotid intimal- media thickness (CIMT) in metabolic syndrome (MetS) patients.

METHODS: This cross-sectional study involves 200 patients with MetS who underwent carotid ultrasonography examination at Coimbatore Medical College and Hospital from January 2018 to January 2019. Demographic data were collected using a questionnaire. An automatic biochemistry analyzer measured RDW. Pearson correlation coefficient was used to evaluate the correlation between RDW and CIMT.

RESULTS: Cases with increased CIMT (> 1mm) have higher RDW level (P<0.001). CIMT was positively related to RDW (r=0.822, P<0.001). It also indicated that RDW was a predictor of CIMT \geq 1mm.

CONCLUSION: This present study suggested that high RDW is related to the increased CIMT in Metabolic Syndrome patients, which highlights the role of RDW in the progression of elevated CIMT in Metabolic Syndrome patients.

Keywords: Red blood cell distribution width, Metabolic Syndrome, Predictor.

INTRODUCTION

Metabolic Syndrome (MetS) can be defined as a group of conditions that involves obesity, glucose intolerance, insulin resistance, hypertension, hypertriglyceridemia. The most important pathophysiology of the syndrome has been the insulin resistance and the elevated blood pressure is the most prevalent component among them.^[1] Very early diagnosis and treatment of MetS is given the utmost importance, because of cerebrovascular and cardiovascular complications. According to The New International Diabetic Federation diagnostic criteria the diagnosis of MetS was made. Carotid artery atherosclerosis is a progressive disease, with increased carotid intima media thickness (CIMT) being the most

important complication. The incidence of ischemic stroke, chronic renal disease, coronary artery disease is associated with increased CIMT.^[2] The clinical features of increased CIMT was not that much significant in these group of patients. USG measurement of CIMT is used at present for identification of advanced subclinical atherosclerosis. There fore ever early identification of elevated CIMT is the most important step. The numerical measure of size variability of circulating red blood cells is called as red blood cell distribution width (RDW). It is a usual component of complete blood count. RDW is a strong and very independent predictor of cardiovascular sequelae and death.

Independently higher rates of Metabolic syndrome have been associated with increased RDW.

AIM OF THE STUDY

To identify the association between RDW and CIMT in the Metabolic Syndrome patients.

MATERIALS AND METHODS:

This cross-sectional study was undertaken in the Department of General Medicine, Coimbatore Medical College and Hospital, Coimbatore. A total of 200 age and sex matched patients who are fulfilling The New International Diabetes Federation (IDF) MetS diagnostic criteria included in the study based on inclusion and exclusion criteria. Patients age more than 18 years and less than 50 years and Patients Meeting the IDF diagnostic criteria for MetS were included, whereas minors, pregnant women mentally ill and non-volunteering patients were excluded from this study. The study is proposed to be conducted after obtaining informed signed consent from the patients. The duration of the study is one year from 2018 to 2019. The principal investigator after obtaining informed signed consent from the patients to participate in the study measures the height, weight, waist circumference, hip circumference of each patient. BMI is calculated using the formula weight in kilogram divided by square of height in meter. The waist to hip ratio to be calculated. SBP and DBP to be measured with patient sitting in a comfortable position twice at an interval of 15 mins. Blood for biochemical investigations to be taken and examined within four

hours. Routine complete blood count, Triglyceride, Total cholesterol, High density cholesterol (HDL), Low density cholesterol (LDL), fasting plasma glucose measured by automated analyzer. Radiologist perform the carotid ultrasonography (7.5MHz frequency) and CIMT measured. Elevated CIMT defined as > 1mm. All the datas that were obtained were entered in MS Excel and statistical analysis was done using SPSS Software. Numbers and percentages are used in reporting Categorical values. Mean and standard deviation are used while reporting Numerical values. Statistical analysis was done using chi-square test , unpaired T test and pearsons correlation coefficient. Statistical significance was considered if p value was less than 0.05.

RESULTS

The study consists of 200 cases consisting of 126 males and 74 females. They were divided into two groups of CIMT >1 and CIMT<1. 157 (78.5%) patients, males -100, females -57 have CIMT >1 and 43 males -26, females -17 (25.1%) have CIMT <1.

The mean age of cases in this study with CIMT >1 is 37.22±8.57 and with CIMT <1 is 35.62±9.11. 50 (25%) patients were in the age group of <30 years and 68 (34%) in the age group of 30-40 yrs and 82 (48%) in the age group of >40 yrs. Increased CIMT was more in the age group of >40 years.

Out of 200, 56 (28%) patients are smokers of which 44 have CIMT >1 and 12 have <1 which is found to be less significant. Totally 68 (34%) patients are alcoholic of which 52 have CIMT >1 and 16 have <1 which is found to be less significant.

Table1: BODY MASS INDEX

BMI	NO OF PATIENTS	PERCENTAGE
< 20	29	14.50%
21-25	75	37.50%
>25	96	48.00%

Table2: Body mass index Distribution

CIMT	BODY MASS INDEX			
	MEAN	SD	TEST	P Value
MORE THAN 1	25.25	4.75	UNPAIRED T TEST	0.021
LESS THAN 1	21.45	4.85		

Majority 96 (48%) persons were in BMI range of >25 and have increased CIMT which is significant . Increased BMI has increased risk of carotid artery atherosclerosis.

Table 3: Waist Circumference Distribution

CIMT	WAIST CIRCUMFERENCE			
	MEAN	SD	TEST	P Value
MORE THAN 1	94.68	2.1	UNPAIRED T TEST	0.001
LESS THAN 1	92.41	1.52		

The mean waist circumference with CIMT >1 was 94.68±2.1. Hence increased waist circumference is significantly associated with increased CIMT. The mean waist hip ratio with CIMT >1 was found to be 0.9±0.05 which is significant.

Table 4: Triglycerides Distribution

CIMT	TRIGLYCERIDES			
	MEAN	SD	TEST	P Value
MORE THAN 1	168.38	13.27	UNPAIRED T TEST	0.001
LESS THAN 1	154.95	5.08		

There was also significant association between increased triglycerides, reduced HDL, increased systolic BP, impaired fasting blood sugar.

Table 5: Red cell distribution width

CIMT	RED CELL DISTRIBUTION WIDTH			
	MEAN	SD	TEST	P Value
MORE THAN 1	15.19	0.78	UNPAIRED T TEST	0.001
LESS THAN 1	13.73	0.78		

Of the total, 116 (58%) have higher RDW. The mean RDW with CIMT >1 being 15.19±0.78 which is very much significant. RDW was on higher side in patients with increased CIMT. On Pearson correlation with CIMT significant association was found between increased CIMT and increased RDW. To summarise increased RDW is associated with increased CIMT, which is an indicator of early atherosclerosis.

Table 6: Hypertension Distribution

CIMT	HYPERTENSION			
	MEAN	SD	TEST	P Value
MORE THAN 1	73	84	CHI SQUARE	0.001
LESS THAN 1	5	38		

Hypertension also associated with RDW and statistically significant.

Table 7: Correlation test

PEARSON CORRELATION WITH CIMT			
PARAMETERS	R VALUE	P VALUE	SIGNIFICANCE
AGE	0.139	0.05	SIGNIFICANT
BODY MASS INDEX	0.123	0.083	NON SIGNIFICANT
WAIST CIRCUMFERENCE	0.607	0.001	SIGNIFICANT
WAIST HIP RATIO	0.446	0.001	SIGNIFICANT
SYSTOLIC BP	0.363	0.001	SIGNIFICANT
DIASTOLIC BP	0.155	0.02	SIGNIFICANT
FASTING BLOOD SUGAR	0.533	0.001	SIGNIFICANT
TRIGLYCERIDES	0.649	0.001	SIGNIFICANT
HDL	-0.358	0.001	SIGNIFICANT
TOTAL CHOLESTEROL	0.686	0.001	SIGNIFICANT

RED CELL DISTRIBUTION WIDTH	0.822	0.001	SIGNIFICANT
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DISCUSSION

Majority of the studies revealed that patients with raised CIMT had a greater risk of cardiovascular diseases than the patients who had normal CIMT [3,4] Wilansky et al (2011) & Kawase et al (2015). The raised RDW is a reliable predictor of carotid artery atherosclerosis in patients with cerebrovascular accident, Zhang et al. [5] The most important step is the early recognition because it is important for such a high risk progressing disease like carotid artery atherosclerosis, and the role of RDW would vary among different setting of patients.

Our study found that patients with CIMT more than 1 mm have higher RDW than those with CIMT less than or equal to 1 mm. The increased RDW is significantly associated with raised CIMT, which is not dependent of a variety of important confounding factors. Our findings more strongly document the role of RDW role in the progression of carotid artery atherosclerosis. The relationship between RDW and increased CIMT may be ascribed to two reasons. Cytokine-mediated inflammatory response being the most reliable factor. Several efforts have been attempted to reveal the mechanism of atherosclerosis in the past so many years, it clearly denotes that inflammation could be the important reliable reason. As told already, majority of inflammatory cytokines play important roles in the evolution of increased CIMT, that could cause carotid artery atherosclerosis. As reported, Patients with increased CIMT have higher level of Hs-CRP than the participants who are unaffected, and interleukin-6 and tumor necrosis factor- α levels was also increased. [6,7] The increased CIMT is often associated with subclinical atherosclerosis. It is stated that inflammatory arthropathies of inflammatory origin could be augmented by anti-tumor necrosis factor- α therapy in the advancement of CIMT. [8] These findings clearly states inflammation largely occurs in patients with increased CIMT. Most significantly, a large cohort study reveals a very strong, and positive relationship among RDW and hs-CRP. [9] Furthermore, concentration of erythropoietin is adhered to exaggerated inflammation in adults who are not anemic, and is inversely associated in anemic

population. [10] The above finding suggests that RDW could anticipate CIMT in MetS patients. Furthermore, RDW in its highest quartile is strongly correlated with increased incidence of total CVA and cerebral infarction, and an intimate relationship between high RDW and IMT, as well as the incidence of carotid plaque, is described in SHT patients. [11, 12]

LIMITATIONS OF THE STUDY

It is a cross-sectional design, that curbs the innovative relationship between CIMT and RDW. Despite, after the summarization of previous findings the relationship is probably reasonable. Only MetS patients were included, so the findings should be applied to other people settings with caution. Some persons might have been diagnosed with hypertension or diabetes mellitus, who might be receiving treatment. The drug history was not included in the final analysis, which could have certain influences on the final results. Finally, the most probable relationship between elevated CIMT and RDW was made, but could not illustrate the accurate mechanism. Hence, further investigations are needed.

CONCLUSION

Variations in size of circulating RBCs increases as CIMT increases and correlation was found between RDW and CIMT which enlightens the role of RDW in advancement of increased CIMT. Hence RDW combined with other clinical examination could be used as a proinflammatory biomarker to estimate early carotid artery atherosclerosis in Metabolic syndrome patients because it is less expensive and easily available and convenient

REFERENCES:

1. Miller JM, Kaylor MB, Johannsson M, Bay C, Churilla JR. Prevalence of metabolic syndrome and individual criterion in US adolescents: 2001–2010 national Health and Nutrition Examination Survey. *Metab Syndr Relat Disord.* 2014;12(10):527–32.
2. Peer N, Lombard C, Steyn K, Levitt N. High prevalence of metabolic syndrome in the Black

- population of CapeTown: The Cardiovascular Risk in Black SouthAfricans (CRIBSA)study. *EurJPrevCardiol*.2015;22(8): 1036–42.
- MookadamF, TanasunontW, JalalU, MookadamM, WilanskyS. Carotid intima-media thickness and cardiovascular risk. *Future Cardiol*.2011;7(2):173–82.
 - VercozaAM, BaldisserottoM, deLosSC, Polide-FigueiredoCE, D’AvilaDO. Cardiovascular risk factors and carotid intima-media thickness in asymptomatic children. *Pediatr Cardiol*.2009;30(8):1055–60.
 - JiaH, LiH, ZhangY, LiC, HuY, XiaC. Association between red blood cell distribution width (RDW) and carotid artery atherosclerosis (CAS) in patients with primary ischemic stroke. *Arch Gerontol Geriatr*.2015;61(1):72–5.
 - KawaseIK, KokuboY, YokotaC, HidaE, MiyataT, ToyodaK, MatsumotoM, MinematsuK, MiyamotoY. Effect of plasma fibrinogen, high-sensitive C- reactive protein, and cigarette smoking on carotid atherosclerosis: the Suita study. *J Stroke Cerebrovasc Dis*.2015;24(10):2385–9.
 - Vazquez-Del MM, Nunez-Atahualpa L, Figueroa-Sanchez M, Gomez-Banuelos E, Rocha-MunozAD, Martin-MarquezBT, Corona-SanchezEG, Martinez-GarciaEA, Macias-ReyesH, Gonzalez-LopezL, et al. Serum levels of anticycliticitrullinated peptide antibodies, interleukin-6, tumor necrosis factor- alpha, and C-reactive protein are associated with increased carotid intima-media thickness: a cross-sectional analysis of a cohort of rheumatoid arthritis patients without cardiovascular risk factors. *Biomed Res Int*.2015;2015:342649.
 - HanQF, WuL, LiT, MengXY, YaoHC. There is a link between carotid intima media thickness and coronary artery disease: It might be inflammation. *IntJ Cardiol*.2016;203:1144–5.
 - LippiG, TargherG, MontagnanaM, SalvagnoGL, ZoppiniG, GuidiGC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected out patients. *Arch Pathol Lab Med*.2009;133(4):628–32.
 - FerrucciL, GuralnikJM, WoodmanRC, BandinelliS, LauretaniF, CorsiAM, Chaves PH, Ershler WB, Longo DL. Proinflammatory state and circulating erythropoietin in persons with and without anemia. *AmJMed*.2005;118(11):1288.
 - Soderholm M, Borne Y, Hedblad B, Persson M, Engstrom G. Red cell distribution width in relation incidence of stroke and carotid atherosclerosis: a population-based cohort study. *PLoSOne*.2015;10(5):e124957.
 - WenY. High red blood cell distribution width is closely associated with risk of carotid artery atherosclerosis in patients with hypertension. *Exp Clin Cardiol*.2010;15(3):37–40.