DOI: 10.7860/JCDR/2021/45887.14459

Original Article

Biochemistry Section

High Sensitive C-reactive Protein Level in Relation to Increased Body Mass Index among Non-diabetic Non-hypertensive Women

GHADA A ELFADIL[1], ABDELGADIR ELMUGADAM[2], RASHEEDA A SAIED[3], SALAH OMAR HUSSEIN[4]

ABSTRACT

Introduction: An increased Body Mass Index (BMI) has an adverse effect on the socio-economic and healthcare sectors and may influence metabolic status. High sensitivity C-reactive Protein (hs-CRP) is an emerging biomarker. The association between dyslipidaemia and obesity is well established, and has been found to be the risk factors for CVD.

Aim: To study the relationship of hs-CRP with BMI, lipid profile and magnesium among obese and overweight non-diabetic non-hypertensive Sudanese women.

Materials and Methods: A cross-sectional study was conducted on 90 women in Khartoum state (Sudan), aged between 20 and 43 years, from June to November 2019. The study included three groups of women based on BMI. hs-CRP was measured by using latex immunoturbidimetric method, lipid profile was evaluated using Biosystems colourimetric methods and magnesium by a chemical method. Results were computed using Statistical Package for the Social Sciences (SPSS) version 20.

Results: There was significant increase in the mean values of hs-CRP, Total Cholesterol (TC), Triglyceride (TG), Low Density Lipoprotein Cholesterol (LDL-C), and a significant decrease in the mean values of High Density Lipoprotein Cholesterol (HDL-C) and magnesium in obese and overweight women, when compared to normal body weight women. Pearson's correlation coefficient revealed a positive correlation between hs-CRP, and BMI, Waist-To-Hip Ratio (WHR), TC, TG, and LDL-C (p-value <0.01).

Conclusion: Overweight and obese women have increased hs-CRP and atherogenic lipid profile, suggesting obesity to be a state of chronic inflammation. hs-CRP can be used to assess the risk of obesity-related disorders for early intervention.

Keywords: Lipid profile, Magnesium, Waist-to-hip ratio

INTRODUCTION

Obesity is a chronic disorder which is prevalent in both developed and developing countries. Obesity among women of reproductive age is increasing worldwide. The related co-morbidities are type 2 diabetes, chronic hypertension and CVD [1]. Obesity is an essential factor in the synthesis of hs-CRP which leads to induced adipose tissue inflammation in the liver and is considered as an independent risk factor for CVD [2,3]. hs-CRP is an acute-phase reactant protein, an indicator of systemic inflammation [4]. It may be related to chronic inflammatory conditions, such as atherosclerosis and after adjusting for risk factors for CVD, patients with high CRP levels are at a higher risk of acute myocardial infarction [5]. This biomarker has also been related to the increase of cardiovascular risk in patients with established disease and the occurrence of the first vascular event. From these facts, it can be concluded that hs-CRP is valuable in primary and secondary prevention and prophylaxis of CVD. Evaluation of this marker may help in knowing the severity of the disease, efficacy of the treatment and prognosis of CVD patients [6]. Magnesium is the second most abundant (after potassium) intracellular cation and is the fourth most abundant cation in the human body [7]. Hypomagnesemia is found to be associated with metabolically obese normal weight rather than metabolically healthy obese phenotypes [8].

Therefore, this study was conducted to evaluate the relationship of hs-CRP with BMI, fasting lipid profile and magnesium; and to compare these values between obese, overweight and normal weight adult Sudanese females.

MATERIALS AND METHODS

This cross-sectional community-based study was carried out at Body Master Centre in Khartoum State, Sudan from June 2019 to November 2019. Ethical approval was obtained from the concerned body before commencing the study. After verbal informed consent, a total of 90 blood samples were collected under aseptic conditions from non-diabetic non-hypertensive Sudanese women. They were then counselled and trained to reduce their weight in a gymnasium centre in Khartoum state.

Inclusion criteria: The study included three groups of normotensive, normoglycaemic adult women, aged between 20-43 years. The grouping was done based on BMI (normal: 18-24.9 kg/m^2, overweight: 25-29.9 kg/m^2 and obese: >29.9 kg/m^2), according to standards as per World Health Organisation (WHO) [9].

Exclusion criteria: Patients who had diabetes mellitus, malignancy, hypertension and CVD, endocrinal and metabolic disorders, bronchial asthma, chronic obstructive pulmonary disease, autoimmune disorders, inflammatory diseases, infectious diseases and also subjects who were smokers, who were on steroids, statins, anti-inflammatory drugs and who consumed alcohol were all excluded from this study.

Anthropometric measurements, including height and weight, were taken using standard protocols. BMI was calculated as weight (in kilograms) divided by height (in meters squared). Waist circumference was taken as the minimum circumference at the umbilicus level, and hip circumference as the maximum circumference around the buttocks. WHR was calculated as waist circumference divided by hip circumference [9]. All measurements were performed twice by the researchers and the mean was considered.

Estimation of hs-CRP

Serum levels of hs-CRP were measured by using auto-analyser called Cobas C-311. The principle of the reaction is based on the particle-enhanced immunoturbidimetric assay method (Cobas C-311®). Human CRP agglutinates with latex particles that are coated with monoclonal anti-CRP antibodies, and then, the precipitate is determined by turbidimetric assay [10].

Estimation of Lipid Profile and Magnesium

The quantitative determination of TC in serum was done by an enzymatic, colourimetric method with Cholesterol Oxidase-Peroxidase (CHOD-POD) [11]. Estimation of TG levels was done by colourimetric end point-Glycerol Phosphate Oxidase, Phenol+Aminophenazone (GPO-PAP) [12], while estimation of HDL-C was done by a direct homogenous enzymatic colourimetric method [13]. LDL-C was calculated using the formula: TC-(HDL-C-TG/5) [14]. Estimation of serum magnesium was done by Calmagite method, in which magnesium reacts with calmagite in alkaline medium forming a coloured complex proportional to the concentration of magnesium in the specimen [15-17].

STATISTICAL ANALYSIS

Descriptive statistics and one-way Analysis of Variance (ANOVA) was performed to compare the means of different groups based on BMI. Pearson's correlation was performed to find out the correlations between hs-CRP, lipid profile, and magnesium levels versus the anthropometric measurements. A p-value<0.05 was considered as statistically significant. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 20.

RESULTS

A total of 90 women with a mean age equal to 27.8±5.8 years were classified into three groups according to BMI as normal, overweight, and obese (30 subjects in each group).

[Table/Fig-1] shows study parameters which were classified based on BMI. Twenty-six (28.9%) out of 90 participants had >3.0 mg/L (High Risk) of hs-CRP; 22 participants (24.4%) were obese and four participants (4.5%) were overweight. Six (6.7%) participants out of total had high levels of TC; all of whom were obese subjects. Three (3.3%) participants out of total had high level of LDL-C, while nine (10%) participants out of total had moderate levels of HDL-C. A total of 66 (73.4%) participants had serum magnesium <1.8 mg/dL; 30 of them (33.3%) were obese.

Characteristic, parameter and reference range	Normal weight (n=30)	Overweight (n=30)	Obese (n=30)	Total (n=90)
hs-CRP (mg/L)				
<1.0 (Low risk)	27 (30%)	16 (17.8%)	03 (3.30%)	46 (51.1%)
1.0-2.9 (Intermediate risk)	03 (3.30%)	10 (11.1%)	05 (5.6%)	18 (20.0%)
>3.0 (High risk)	0	04 (4.5%)	22 (24.4%)	26 (28.9%)
Cholesterol (TC) (mg/dL)				
<200 (Optimal)	30 (33.3%)	29 (32.2%)	15 (16.7%)	74 (82.2%)
200-239 (Borderline)	0	1 (1.1%)	9 (10%)	10 (11.1%)
>240 (High)	0	0	6 (6.7%)	6 (6.7%)
HDL-C (mg/dL)				
>40 (Normal)	29 (32.2%)	29 (32.2%)	23 (25.6%)	81 (90.0%)
35-39 (Moderate risk)	01 (1.1%)	01 (1.1%)	07 (7.8%)	09 (10.0%)
LDL-C (mg/dL)				
Optimal (<100)	30 (33.3%)	28 (31.1%)	15 (16.7%)	73 (81.1%)
Near optimum (100-129)	0 (0%)	1 (1.1%)	8 (08.9%)	09 (10%)
Borderline high (130-159)	0 (0%)	1 (1.1%)	4 (4.4%)	05 (5.6%)
High (160-189)	0 (0%)	0 (0%)	3 (3.3%)	03 (3.3%)
Serum magnesium (mg/dL)				
≤1.8 (Hypomagnesaemia)	08 (8.9%)	28 (31.1%)	30 (33.3%)	66 (73.4%)
>1.8 (Normal)	22 (24.4%)	02 (2.2%)	0 (0%)	24 (26.6%)

[Table/Fig-1]: Frequency of study parameters classified based on BMI.
hs-CRP: Highly sensitive C reactive protein; TC: Total cholesterol; HDL-C: High-density lipoprotein-cholesterol; LDL-C: Low-density lipoprotein cholesterol

[Table/Fig-2] shows the comparison of three groups based on BMI (obese, overweight and normal BMI). The results reflect that there was a significant increase in Waist Circumferance (WC), WHR, hs-CRP, serum TC, TG and LDL-C levels; significant decrease in HDL-C and magnesium level in obese participants when compared to overweight and normal BMI participants.

Variables	Obese N=30	Overweight N=30	Normal weight N=30	p-value
Age/years	26.0±6.35	28.1±5.24	29.3±5.52	0.09
Body mass index (BMI) kg/m^2	38.2±5.0	27.0±1.5	22.6±1.3	<0.01
Waist circumference (WC) cm	106.1±11.3	89.0±6.0	79.2±4.6	<0.01
Hip circumference (HC) cm	27.27±3.99	28.03±5.33	29.33±5.4	0.289
Waist to hips ratio (WHR)	0.91±0.03	0.84±0.03	0.77±0.02	<0.01
hs-C-reactive protein (mg/L)	6.94±5.17	1.37±1.29	0.45±0.38	<0.01
Serum total cholesterol (mg/dL)	207±39.5	163±16.2	144±13.3	<0.01
Serum triglycerides (mg/dL)	119±23.9	92.6±20.2	73.6±18.7	<0.01
HDL-C (mg/dL)	40.0±2.65	45.1±5.22	53.0±9.74	<0.01
LDL-C (mg/dL)	104±38.3	78.7±15.5	60.0±14.9	<0.01
Serum magnesium (mg/dL)	1.54±0.12	1.67±0.20	1.97±0.23	<0.01

[Table/Fig-2]: Comparison between means of age, BMI, WC, HC, WHR, lipid profile, serum hs-CRP, and serum magnesium among obese and overweight versus normal body weight.
The results are in mean±SD.
**p-value <0.05 considered significant.
One-way ANOVA test was used for comparison

[Table/Fig-3] shows Pearson's correlation between hs-CRP, lipid profile, magnesium levels with anthropometric measurement. The results reflect statistically significant positive correlation between the hs-CRP, TC, TG, LDL-C with BMI, WC and WHR.

	BMI		WC		WHR	
Variable	R	p-value	R	p-value	R	p-value
hs-CRP	0.7	<0.01	0.74	<0.01	0.65	<0.01
Serum total cholesterol	0.59	<0.01	0.92	<0.01	0.84	<0.01
Serum triglycerides	0.68	<0.01	0.62	<0.01	0.60	<0.01
HDL-C	-0.52	<0.01	-0.53	<0.01	-0.52	<0.01
LDL-C	0.62	<0.01	0.59	<0.01	0.64	<0.01
Serum magnesium	-0.60	<0.01	-0.59	<0.01	-0.60	<0.01

[Table/Fig-3]: Pearson's correlations between anthropometric measurement and serum hs-C reactive protein (hs-CRP), lipid profile, and magnesium in the study group.

[Table/Fig-4] shows Pearson's correlation between hs-CRP with lipid profile and magnesium level. The results reflect statistically significant positive correlation between the hs-CRP with TC, TG, LDL-C; negative correlation with HDL-C and magnesium level.

	hs-CRP	
Parameters	R	p-value
Serum total cholesterol	0.55	<0.01
Serum triglycerides	0.57	<0.01
HDL-C	-0.47	<0.01
LDL-C	0.55	<0.01
Magnesium	-0.49	<0.01

[Table/Fig-4]: Pearson's correlations between hs-CRP and lipid profile, magnesium levels in the study group.

DISCUSSION

Obesity is one of the foremost public health crisis of our time. A chronic imbalance between energy intake and energy expenditure will ultimately lead to obesity. Excess adipose tissue, especially in intra-abdominal region, predisposes to type 2 diabetes, hypertension, dyslipidaemia and metabolic syndrome largely through increased lipolysis that raises the production of free fatty acids and adipokines [18]. The present study was conducted on a group of apparently healthy women with different BMI. It showed that 26 of participants were at high risk (hs-CRP>3 mg/L) for CVD; 22 of them were obese and four participants were overweight. These results are comparable with the findings of several studies [19,20].

The study reflects significant increase in means of hs-CRP, TC, TG, and LDL-C levels in obese and overweight females when compared to normal body weight females. Similar results were demonstrated by Klisic AN et al., [21]. The present study demonstrated positive correlation between hs-CRP with TC, TG, LDL-C, and inverse correlation with HDL-C with BMI, WC and WHR. These results were in line with that of a previous study by Rye KA and Barter PJ [22]. Similar positive relationship was established between WC and hs-CRP levels by Kao TW et al., and Lapice E et al., which demonstrated that abdominal adiposity is connected with higher CRP which was independent of BMI [23,24]. Festa A et al., showed that WHR was considerably correlated with hs-CRP [25].

Central obesity was found to have the strongest relationship with elevated hs-CRP levels by Florez H et al., [26]. Hence, signifying that abdomen adipose tissue is the chief source of cytokines like Tumour Necrosis Factor-α (TNF-α), Interleukin-6 (IL-6) which are the main determining factors of hepatic synthesis of hs-CRP. These inflammatory mediators lead to endothelial dysfunction and atherosclerosis, which play a major part in the pathogenesis of ischaemic heart disease and other obesity linked morbidities [18,25].

This study revealed that serum magnesium was significantly decreased in obese and overweight women when compared with normal BMI women. Similarly, a negative correlation between magnesium with anthropometric parameters and hs-CRP was established by Huang JH et al., and Randell EW et al., [27,28]. In obesity and adipocyte enlargement, the blood supply to the adipocyte may compromise with resultant hypoxia. Hypoxia may induce production of biologically active metabolites like adipocytokines which include CRP, plasminogen activator inhibitor-1, and pro-inflammatory mediators such as TNF-α and IL-6 [29].

Limitation(s)

The major drawback of this study was its small sample size and that it was conducted among females only. A single inflammatory marker, hs-CRP, was measured that possibly does not perfectly reveal long-term inflammatory status of the body.

CONCLUSION(S)

Study results revealed that increase in BMI is associated with substantial changes in hs-CRP, atherogenic lipid profile, and magnesium and it is considered that hs-CRP can be an early unique inflammatory indicator in apparently healthy overweight and obese women. Measures such as changes in lifestyle modification and increase in physical activity to lose weight can be advised at the earliest to prevent future morbidities.

REFERENCES

[1] Poston L, Caleyachetty R, Cnattingius S, Corvalán C, Uauy R, Herring S, et al. Preconceptional and maternal obesity: Epidemiology and health consequences. Lancet Diabetes Endocrinol. 2016;4(12):1025-36.
[2] Gruzdeva O, Uchasova E, Dyleva Y, Akbasheva O, Matveeva V, Karetnikova V, et al. Relationship key factor of inflammation and the development of complications in the late period of myocardial infarction in patients with visceral obesity. BMC Cardiovasc Disord. 2017;17(1):36.
[3] Rodríguez-Hernández H, Simental-Mendía LE, Rodríguez-Ramírez G, ReyesRomero MA. Obesity and inflammation: Epidemiology, risk factors, and markers of inflammation. Int J Endocrinol. 2013;2013:678159.
[4] Zakynthinos E, Pappa N. Inflammatory biomarkers in coronary artery disease. J Cardio. 2009;53:317-33.
[5] Adukauskiene D, Ciginskiene A, Adukauskaite A, Pentiokiniene D, Šlapikas R, Ceponiene I. Clinical relevance of high sensitivity C-reactive protein in cardiology. Medicina (Kaunas). 2016;52:1-10.
[6] Furuhashi M, Saitoh S, Shimamoto K, Miura T. Fatty Acid-Binding Protein 4 (FABP4): Pathophysiological insights and potent clinical biomarker of metabolic and cardiovascular diseases. Clin Med Insights Cardiol. 2015;8:23-33.
[7] Mohan LK, Escott-Stump S. Nutrition basis. Krause food and nutrition therapy. 12th ed. Philadelphia, PA: Imprint Saunders; 2012. page110-111.
[8] Guerrero-Romero F, Flores-García A, Saldaña-Guerrero S, Simental-Mendía LE, Rodríguez-Morán M. Obesity and hypomagnesemia. Eur J Intern Med. 2016;34:29-33.
[9] WHO. The Asia-Pacific perspective: Redefining obesity and treatment. Australia: Health communications Australia Pty Limited; Feb 2000.1-55. Available from: http://www.wpro.who.int/nutrition/documents/docs/Redefiningobesity.pdf
[10] Eda S, Kaufmann J, Roos W, Pohl S. Development of a new microparticle enhanced turbidimetric assay for C-reactive protein with superior features in analytical sensitivity and dynamic range. J Clin Lab Anal. 1998;12:137-44.
[11] Anderson CS, Cockayne S. Clinical chemistry concept and application. International ed. W.B Saunders. 1993.
[12] Fossati P, Prenciple L. Serum triglyceride determination colourimetrically with an enzyme that produce hydrogen peroxide. Clin Chem. 1982;28:2077-80.
[13] Arneson Wand Brickell J. Clinical Chemistry A Laboratory Perspective. 6th ed. Philadelphia. 2007.
[14] Burtis CA, Ashwood ER, Bruns DE. Tietz fundamentals of clinical chemistry. 6th ed. Saunders. 2008.
[15] Bishop ML, Fody EP, Schoeff LE. Clinical Chemistry Techniques Principles, Correlations. 6th ed, Philadelphia, 2010.
[16] Macy EM, Hayes TE, Tracy RP. Variability in the measurement of hs-CRP in healthy subjects: Implications reference intervals and epidemiological applications. Clin Chem. 2010;43:52-58.
[17] National Cholesterol Education Program Expert Panel. National Heart, Lung and Blood Institute. 2001;3:7-12.
[18] Lin CC, Kardia SLR, Li CI, Liu CS, Lai MM, Lin WY, et al. The relationship of high sensitivity C-reactive protein to percent body fat mass, body mass index, waist- to-hip ratio, and waist circumference in a Taiwanese population. BMC Public Health. 2010;10:579.
[19] Ortega FB, Lavie CJ, Blair SN. Obesity and cardiovascular disease. Circ Res. 2016;118(11):1752-70.
[20] Elagizi A, Kachur S, Lavie CJ, Carbone S, Pandey A, Ortega FB, et al. An overview and update on obesity and the obesity paradox in cardiovascular diseases. Prog Cardiovasc Dis. 2018;61(2):142-50.
[21] Klisic AN, Vasiljevic ND, Simic TP, Djukic TI, Maksimovic MZ, Matic MG. Association between C-reactive protein, anthropometric and lipid parameters among healthy normal weight and overweight postmenopausal women in Montenegro. Lab Med. 2014;45:12-16.
[22] Rye KA, Barter PJ. Anti-inflammatory actions of HDL: A new insight. Arterioscler Thromb Vasc Biol. 2008;28:1890-91
[23] Kao TW, Lu IS, Liao KC, Lai HY, Loh CH, Kuo HK. Associations between body mass index and serum levels of C-reactive protein. S Afr Med J. 2009;99:326-30.
[24] Lapice E, Maione S, Patti L, Cipriano P, Rivellese AA, Riccardi G, et al. Abdominal adiposity is associated with elevated C-reactive protein independent of BMI in healthy nonobese people. Diabetes Care. 2009;32:1734-36.
[25] Festa A, D'Agostino R Jr, Williams K, Karter AJ, Mayer-Davis EJ, Tracy RP, et al. The relation of body fat mass and distribution to markers of chronic inflammation. Int J Obes Relat Metab Disord. 2001;25:1407-15.
[26] Florez H, Castillo-Florez S, Mendez A, Casanova-Romero P, Larreal-Urdaneta C, Lee D, et al. C-reactive protein is elevated in obese patients with the metabolic syndrome. Diabetes Res Clin Pract. 2006;71:92-100.
[27] Huang JH, Lu YF, Cheng FC, Tsai LC. Correlation of magnesium intake with metabolic parameters, depression and physical activity in elderly Type 2 diabetes patients: A cross- sectional study. Nutrition Journal. 2012:11(41):1-10. https://doi.org/10.1186/1475-2891-11-41.
[28] Randell EW, Mathews M, Gadag V, Zhang H, Sun G. Relationship between serum magnesium values, lipids and anthropometric risk factors. Atherosclerosis. 2008;196:413-19.
[29] Kim DJ, Xun P, Liu K, Loria C, Okota KY, David R, et al. Magnesium intake in relation to systemic inflammation, insulin resistance, and the incidence of diabetes. Diabetes Care. 2010;33:2604-10.

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Clinical Chemistry, College of Medical Laboratory Science, University of Sciences and Technology, Khartoum, Sudan.
2. Associate Professor, Department of Clinical Chemistry, College of Medical Laboratory Science, University of Sciences and Technology, Khartoum, Sudan.
3. Laboratory Specialist, Department of Laboratory, Shan Al Hospital, Khartoum, Sudan.
4. Assistant Professor and Head, Department of Medical Laboratory Science; Clinical Laboratory Sciences, Almadina Almanwara, KSA, Saudi Arabia.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Salah Omar Hussein,
Assistant Professor and Head, Department of Medical Laboratory Science,
AL-Ghad International College for Applied Medical Sciences KSA: Al-Madinah Al-Monawarah, KSA, Saudi Arabia.
E-mail: salahomar2@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Aug 18, 2020
- Manual Googling: Oct 09, 2020
- iThenticate Software: Dec 17, 2020 (17%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 12, 2020**
Date of Peer Review: **Sep 08, 2020**
Date of Acceptance: **Oct 26, 2020**
Date of Publishing: **Jan 01, 2021**