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Association between High-Sensitivity C-Reactive Protein and Metabolic Syndrome and Its Components in Older Adults: Findings from Neyshabur Longitudinal Study on Ageing (NeLSA)

ABSTRACT

Objective: To evaluate the association between high-sensitivity C-reactive protein (hsCRP) and metabolic syndrome (MetS), components of the MetS as well as diabetes, and cardiovascular complications.

Materials and methods: In this cross-sectional analysis, the data were collected from the registration phase of Neyshabur Longitudinal Study on Ageing (NeLSA) comprising a total of 6034 people aged 50 and older. Association between hsCRP and MetS and its components was conducted by univariate and multivariate analyses in the presence of covariates and confounding factors.

Results: Baseline data including age, body fat mass, body mass index, waist-to-hip ratio, fasting plasma glucose, triglyceride, creatinine, albumin, and hsCRP also systolic blood pressure, and diastolic blood pressure were higher in the MetS group compared to the control group ($p < 0.001$ for all variables other than hsCRP, which was not significant ($p = 0.06$)). Also the univariate and multi variate analysis illustrated one-unit increase in the serum level of hsCRP was associated with 18% higher risk for diabetes [OR: 1.18; 95% confidence interval (CI), 1.06–1.30] and increased high-density lipoprotein cholesterol (HDL-C) by 15% (OR:1.15; (95% CI, 1.01–1.29). In subjects with MetS, one-unit (log of 1 mg/L) increase in the serum level of hsCRP was associated with 34% higher risk for atherosclerotic cardiovascular disease (ASCVD) (OR: 1.34; 95% CI, 1.11–1.63).

Conclusions: There is an association between serum level of hsCRP and the presence of the components of MetS including HDL-C and diabetes, especially in women. (Clin Diabetol 2024; 13, 1: 52–59)

Keywords: high-sensitivity C-reactive protein, metabolic syndrome, atherosclerotic cardiovascular disease, diabetes

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Introduction

Metabolic syndrome (MetS) is as a cluster of conditions characterized by insulin resistance/glucose intolerance, abdominal obesity, elevated serum triglycerides (TGs) and low high-density lipoprotein cholesterol (HDL-C) levels [1–3]. According to this definition, the MetS is characterized by the number of symptoms including insulin resistance, hyperinsulinemia, impaired glucose tolerance (IGT), dyslipidemia [decreased HDL-C and increased TGs], hypertension (HTN), and central obesity [4]. The presence of MetS in young people may predict the risk of developing type 2 diabetes (T2D) and atherosclerotic cardiovascular disease (ASCVD) in the future [5]. The association between MetS and ASCVD is especially important in the context of present COVID-19 pandemic since MetS is a significant factor for more severe forms of the disease [6].

The prevalence of the MetS is increasing dramatically worldwide. In some countries, the incidence of MetS is considerably higher in women than in men, However, it is more prevalent among men in some other countries [7]. MetS is a low-grade inflammatory condition which is associated with excessive visceral fat tissue. C-reactive protein (CRP) is one of the main inflammatory markers in different conditions, including MetS. High-sensitivity CRP is a pattern-recognition molecule produced by the liver in several inflammatory conditions and it is widely used to indicate inflammatory responses in the body. Evidence suggests that hsCRP could be considered as an independent predictor of ASCVD, but it is also associated with components of MetS [8]. The role of hsCRP as an independent risk factor for coronary artery disease can be explained by several mechanisms [9]. Nevertheless, until now no clear correlation was found between the simultaneous effect of MetS and hsCRP on ASCVD. But as it could be expected, several studies showed that the risk of developing ASCVD increases with more expressed components of the MetS [10]. However, there are few exceptions to these findings that could not associate MetS with the increased risk of ASCVD. Elevated hsCRP is associated with an increased risk of myocardial infarction, sudden cardiac death, and peripheral arterial disease and has been independently associated with the prevalence of ASCVD in several prospective studies [11]. It is also used in screening and predicting short-term and long-term cardiovascular outcomes not only in patients with ASCVD but also in seemingly healthy individuals [12]. In this study, we tried to investigate the correlation between hsCRP levels, and MetS and its components as well as with diabetes.

Methods

Study design and subjects

This is a cross-sectional study which is a part of the Neyshabur Longitudinal Study on Ageing (NeLSA). NeLSA is a part of the Prospective Epidemiological Research Studies in Iran (PERSIAN), a national follow-up study which was launched in 2016 [13]. This study was performed in Neyshabur city located in the northeast of Iran with a population of about half a million people. NeLSA is the first comprehensive longitudinal study on ageing among people aged 50 years and older in Iran aiming to assess the different aspects of ageing, monitoring changes in health and wellbeing of older adults using a wide range of data including a detailed questionnaire on demographic, socioeconomic, lifestyle, physical and psychological aspects, clinical checkup, as well as mobility assessment, biological samples (blood, urine, nail and hair) and anthropometric measures [14]. Since the data for the current study is based on the registration phase of NeLSA at one point in time, the design and analysis of data were performed as a cross-sectional study. After the registration phase, NeLSA includes longitudinal follow-up phases that will track participants' health and aging-related changes over time. It is important to note that while the current analysis is a cross-sectional study, it forms a part of the broader NeLSA study, which will allow for the examination of longitudinal trends and patterns in the future.

Written informed consent according to the Helsinki Declaration was obtained from all participants. The study was approved by the Research and Ethical Review Board of the Neyshabur University of Medical Sciences.

Data collection and measurements

Clinical study measurements were performed by a team of trained research staff. Height and weight were measured using a stadiometer and Seca scale, respectively. BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). For measuring waist circumference (WC), a non-elastic tape was placed horizontally around the participant's waist (just above the hipbones) in a standing position. Anthropometric measurements were obtained by bioelectrical impedance analysis (BIA) using the InBody 770, Biospace Korea connected to a BSM 370.

MetS was assessed by using the National Cholesterol Education Program Adult Treatment Panel (NCEP/ /ATP) III criteria (2005 revision). Participants with three or more of the following criteria were defined as having MetS: 1) WC $\geq$ 90 cm in men or $\geq$ 80 cm in women; 2) HDL-C $<$ 40 mg/dL in men or $<$ 50 mg/dL in women;

3) triglycerides (TG) ≥ 150 mg/dL; 4) blood pressure (BP) ≥ 130/85 mmHg; 5) fasting plasma glucose ≥ 100 mg/dL, and/or drug treatment to control hyperglycemia, dyslipidemia and hypertension. We used NCEP-ATP III criteria definition for WC in this study because it has more suitable WC cut-off points for Middle Eastern men and women which are 94 and 80 cm, respectively.

Venous blood samples were analyzed after at least 8 hours of fasting. Whole blood samples were collected in blood tubes and fractionated by centrifugation at 3000 rpm for 15 min to obtain serum. The collected serums were aliquoted into 1.5 mL tubes, and following parameters [normal range (NR)] were analyzed by an analyzer (BT1500, Italy; Pars Azmun kits, Iran): fasting plasma glucose (FPG) (< 100 mg/dL), urea (19–44 mg/dL), creatinine (0.7–1.4 mg/dL), total bilirubin (0.3–1 mg/dL), triglycerides (TG) (< 200 mg/dL), total cholesterol (TC) (< 200 mg/dL), thyroid stimulating hormone (TSH) (0.3–4.78 mU/L), free thyroxine (FT4) (0.8–1.8 ng/dL), aspartate aminotransferase (AST) (8–33 U/L), alanine aminotransferase (ALT) (7–55 U/L), and alkaline phosphatase (ALP) (44–147 U/L). Whole blood samples in EDTA-K3 were also obtained for measuring blood cell count. The tubes were immediately inverted several times to mix the anticoagulant additive with blood. The blood was processed within 2 hours after using the automated hematology analyzer (Celltac Alpha MEK-6510 K, Nihon Kohden, Tokyo, Japan). The following parameters (NR) were determined: red blood cell count (RBC) (4–5.4 M/μL), white blood cell count (WBC) (4.5–11.5 K/μL), platelet count (150–450 K/μL), hemoglobin (12–15 g/dL), hematocrit (35–49%), mean corpuscular volume (MCV) (80–94 fL), mean corpuscular hemoglobin concentration (MCHC) (31–36g/dL), mean corpuscular hemoglobin (MCH) (27–33 pg), and mean platelet volume (MPV) (7–12fL).

Potential biases

To minimize sample selection bias in the Neyshabur Longitudinal Study on Ageing (NeLSA), a systematic approach was employed. Random sampling was used to select households from different regions of Neyshabur city, aiming for representative population coverage. However, it is important to recognize that despite random sampling, selection bias can still exist due to non-response rates and potential underrepresentation of certain demographic groups. To mitigate this, efforts were made to encourage participation through community engagement, informed consent, and assuring data confidentiality. Multiple attempts were made to contact selected participants, and non-response analysis was conducted to assess systematic differences between participants and non-respondents. If needed, statistical techniques like weighting adjustments were considered. Measurement bias was minimized by standardized procedures, rigorous training, validated measurement tools, and regular quality control checks. Confounding variables were addressed through careful study design, statistical adjustments, and controlling for potential confounders during analysis. While it may not be possible to eliminate all biases entirely, recognizing and addressing potential biases enhances the validity and reliability of the study findings.

Statistical analysis

The statistical methods employed in this study aimed to provide a comprehensive analysis by investigating the associations between hsCRP, MetS and its components, diabetes, and ASCVD. Through the utilization of appropriate statistical techniques and the consideration of confounding variables, the researchers sought to obtain reliable and meaningful results to support their research objectives.

Data management and analysis were performed using the SPSS 20 statistics software program (IBM Corporation, Armonk, NY). Data were presented as mean and 95% confidence interval (CI) for normally distributed continuous variables, as well as median and inter-quartile range for skewed continuous variables. Frequency and percentage were used for categorical variables. The associations between categorical variables were examined using the chi-square test and Wilcoxon test. Logistic regression analysis was conducted to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between serum hsCRP levels and MetS components, as well as diabetes ASCVD. In the logistic regression models, covariates such as age, sex, cigarette consumption, education level, physical activity, and body mass index (BMI) were included. These covariates accounted for their potential influence on the relationships of interest. The logistic regression analysis yielded estimates of odds ratios, which quantified the relative likelihood of an event (e.g., having MetS or ASCVD) occurring based on changes in the predictor variable (e.g., hsCRP levels).

To account for potential confounding effects, adjustments were made for confounding variables when analyzing the associations between hsCRP, MetS, diabetes, and ASCVD. The study also explored potential interactions and differences between subgroups. Subgroup analysis allowed for the investigation of variations in associations based on participant characteristics or other factors. In this study, subgroup analyses were performed based on gender and the presence or absence of MetS or diabetes to evaluate whether the associations between hsCRP and ASCVD differed within these groups.

Table 1. Baseline Characteristics of Participants in Total and by Study Groups

	Categories	Total	Metabolic syndrome		
			Yes (N = 2903)	No (N= 3131)	P-value*
Gender, N (%)	Male		942 (16%)	1852 (31%)	< 0.001
	Female		1961 (32%)	1279 (21%)	
Smoking status, N (%)	Non-smoker		2733 (45%)	2663 (44%)	< 0.001
	Daily/sometimes		170 (3%)	468 (8%)	
Addiction status, N (%)	No addiction		2500 (42%)	2408 (40%)	< 0.001
	Occasional		140 (2%)	204 (3%)	
	Regular		263 (4%)	519 (9%)	
ASCVD, N (%)	No		2696 (44%)	3008 (50%)	< 0.001
	Yes		207 (4%)	123 (2%)	
Age [year]year		58.92 (54.58, 64.83)	59.42 (55.08, 65.54)	58.58 (54.42, 64.25)	< 0.001
BFM [kg]		26.30 (20.40, 32.80)	30.2 (25.8, 35.7)	21.6 (16.4, 28.1)	< 0.001
BMI [kg/m2]		27.70 (24.80, 30.70)	29.5 (27.3, 32.3)	25.4 (23.0, 28.5)	< 0.001
Physical activity, MET		64.57 (35.82, 146.14)	57.46 (35.25, 116.41)	76.32 (36.75, 160.35)	< 0.001
hsCRP [mg/L]		0.2 (0.1, 0.4)	0.2 (0.1, 0.4)	0.2 (0.1, 0.4)	0.06
Waist-to-hip ratio		0.94 (0.90, 0.98)	0.97 (0.93, 1.00)	0.92 (0.88, 0.96)	< 0.001
WC [cm]		94.20 (86.60, 101.80)	99.1 (93.6, 105.30)	89.2 (82.5, 95.95)	< 0.001
SBP [mmHg]		116 (104, 128)	120 (108, 132)	112 (101, 122)	< 0.001
DBP [mmHg]		70 (63, 79)	73 (65, 80)	69 (61, 77)	< 0.001
HDL-C [mg/dL]		57.25 (50.00, 65.50)	55.6 (48.20, 63.75)	59.0 (51.25, 67.20)	< 0.001
TG [mg/dL]		129.5 (96.5, 177.0)	160 (118, 210.15)	108.9 (84.8, 141.45)	< 0.001
FPG [mg/dL]		105 (95.00, 120.8)	113 (102, 136)	99 (92, 109)	< 0.001
Cr [mg/dL]		1.2 (1.1, 1.4)	1.2 (1.1, 1.39)	1.2 (1.1, 1.4)	< 0.001
Albumin [g/dL]		5 (4.7, 5.2)	5 (4.8, 5.25)	4.9 (4.7, 5.2)	< 0.001

*Wilcoxon and Chi-Square tests; Data was presented as number (%) and median (interquartile range) for categorical and continuous variables, respectively
ASCVD — atherosclerotic cardiovascular disease; BFM — body fat mass; BMI —body mass index; Cr — creatinine; DBP — diastolic blood pressure; FBG — fasting plasma glucose; HDL-C — high-density lipoprotein cholesterol; hsCRP — high sensitivity C-reactive protein; N — number; SBP — systolic blood pressure; TG — triglycerides; WC — waist circumference

Results

Baseline characteristics

Of 6034 participants, 47% were male and the mean age of participants was 58.9 years. The prevalence of MetS was 48%, 16% were males and 32% females, as shown in Table 1. According to this table, among those with MetS there were more women, less non-smokers, more non-smokers, non-addicted, older and more ASCVD. They had higher BMI, body fat mass (BFM), waist-to-hip ratio, WC, systolic blood pressure (SBP), diastolic blood pressure (DBP), TGs, FPG, albumin, and HDL-C ($p < 0.05$ for all these variables).

Association of metabolic syndrome and its components and diabetes with high sensitivity C-reactive protein

Table 2 shows the correlation between the serum hsCRP levels and the MetS components. Logistic regression models were performed to determine the effect of hsCRP serum levels on the odds of having MetS components. According to the results, serum hsCRP levels were only associated with HDL-C (OR: 1.15; 95% CI, 1.01–1.29) and diabetes (OR:1.18; 95% CI, 1.06–1.30) in the univariate model. Serum hsCRP levels were only associated with diabetes after adjusting for other variables including sex, cigarette consumption, education level, physical activity, and BMI. By increasing one mg/L of hsCRP, the odds of developing diabetes was increased by 14%. We also analyzed the effect of hsCRP on the MetS in both gender. No statically significant correlation was observed between serum level of hsCRP and the MetS in men. However, women showed a different result. There was an increasing trend in the odds of HDL-C, WC, and diabetes which was parallel with an increase in serum level of hsCRP. In addition, adjustment for other variables showed that with increasing serum level of hsCRP, the prevalence of diabetes also increased with an OR of 1.22 (95% CI, 1.05–1.41) for women. Therefore, increasing the serum hsCRP by one mg/L increased the odds of developing diabetes by 22%.

Table 2. Association between the Metabolic Syndrome and Its Components and High-Sensitivity C-Reactive Protein among Men and Women

MetS/Components+	hsCRP (continuous) OR (95% CI)					
	Totally (sex adjusted)		Men		Women	
	Univariate model$	Multivariable-adjusted model#	Univariate model$	Multivariable-adjusted model#	Univariate model$	Multivariable-adjusted model#
Metabolic Syndrome	1.03 (0.93, 1.13)	0.92 (0.82, 1.03)	1.02 (0.88, 1.17)	1.00 (0.82, 1.21)	1.02 (0.90, 1.18)	0.89 (0.77, 1.03)
HTN**	1.05 (0.95, 1.15)	0.96 (0.86, 1.06)	1.00 (0.86, 1.15)	0.96 (0.81, 1.12)	1.08 (0.95. 1.24)	0.97 (0.84, 1.12)
HDL-C [mg/dL]	1.15 (1.01, 1.29)*	1.10 (0.96, 1.24)	1.05 (0.77, 1.32)	1.00 (0.73, 1.27)	1.19 (1.03, 1.39)*	1.14 (0.97, 1.32)
TG [mg/dL]	0.96 (0.86, 1.05)	0.92 (0.83, 1.02)	0.90 (0.76, 1.04)	0.91 (0.76, 1.06)	1.01 (0.88, 1.15)	0.95 (0.82, 1.08)
WC [cm]	1.02 (0.92, 1.13)	0.95 (0.89, 1.12)	0.90 (0.78, 1.04)	0.93 (0.75, 1.16)	1.19 (1.01, 1.42)*	1.00 (0.77, 1.31)
Diabetes**	1.18 (1.06, 1.30)*	1.14 (1.03, 1.27)*	1.04 (0.89, 1.22)	1.07 (0.91, 1.25)	1.31 (1.14, 1.53)*	1.22 (1.05, 1.41)*
FPG [mg/dL]	1.06 (0.96, 1.18)	1.05 (0.95, 1.17)	1.00 (0.87, 1.16)	1.05 (0.91, 1.23)	1.12 (0.97, 1.32)	1.05 (0.91, 1.24)

+Metabolic syndrome outcomes and its components were analyzed as dichotomous variables with binary logistic regression; $The crude odds ratio; #Adjusted for age, sex, BMI, smoking, education level, and physical activity; *OR (95% CI) of model that were significant; **According to NCEP ATP III criteria
CI — confidence interval; FPG — fasting plasma glucose; HDL-C — high-density lipoprotein cholesterol; hsCRP — high-sensitivity C-reactive protein; HTN — hypertension; OR — odds ratio; TG — triglycerides; WC — waist circumference

Association between atherosclerotic cardiovascular disease and high sensitivity C-reactive protein depending upon the presence or absence of the metabolic syndrome and diabetes

The effect of hsCRP on ASCVD in two groups — with and without MetS — is shown in Table 3. As it can be seen, the association between hsCRP and ASCVD is statically significant in the group with MetS. In this group the odds of having ASCVD increased by 36% when serum hsCRP increased by one mg/L (OR: 1.36; 95% CI, 1.13–1.64). This association was still significant despite adjusting for the effect of other confounding variables (OR: 1.34; 95% CI, 1.11–1.63). Furthermore, men with MetS were more likely to have ASCVD than women after increasing the serum hsCRP by one mg/L of (OR: 1.46 vs. OR: 1.28).

According to the information provided in table 3, the effect of serum hsCRP on ASCVD is significant only in the non-diabetic group in the univariate model (OR: 1.27; 95% CI, 1.05–1.51). With an increase in the serum hsCRP by one mg/L, the odds of having ASCVD increased by 27%. This figure decreased by 10 % and lost its statistical significance after adjusting for the confounding variables (OR:1.17; 95% CI, 0.96–1.36). Non-diabetic men were more likely to have ASCVD by hsCRP elevated for one 1 mg/L (OR:1.25; 95% CI, 1.00–1.52). However, statistically insignificant relationship was seen after adjusting for other variables in non-diabetic men concerning ASCVD after an increase in hsCRP by 1 mg/L serum (OR:1.17; 95% CI, 0.96–1.46).

Discussion

Based on the findings of this study, with increasing serum hsCRP, the chance of developing ASCVD, especially in men with MetS, increased dramatically. Elevated serum hsCRP levels were observed only in those with low HDL-C, which had an effect on the single-factor model. Serum hsCRP levels were associated with diabetes only after adjusting for other variables such as gender, smoking, level of education, physical activity and BMI. With an increase of 1 mg/L in hsCRP, the risk of developing diabetes increases by 14%.

Insulin resistance, a significant characteristic of both type T2D and MetS, may serve as a plausible underlying mechanism that establishes a connection between diabetes and elevated levels of high-sensitivity C-reactive protein (hsCRP) [15]. The impaired response of tissues to insulin observed in insulin resistance leads to the elevation of plasma glucose. It is postulated that inflammation, as discerned by heightened hsCRP levels, potentially disrupts the intricate pathways involved in insulin signaling, consequently fostering insulin

Table 3. Association between Atherosclerotic Cardiovascular Disease and High-Sensitivity C-Reactive Protein According to the Presence or Absence of the Metabolic Syndrome and Diabetes among Men and Women

		hsCRP (Continuous) OR (95% CI)					
		Totally (Sex-adjusted)		Men		Women	
		Univariate model[$]	Multivariable-adjusted model[#]	Univariate model[$]	Multivariable-adjusted model[#]	Univariate model[$]	Multivariable-adjusted model[#]
ASCVD+	MetS Positive	1.36 (1.13, 1.64)*	1.34 (1.11, 1.63)*	1.52 (1.13, 2.08)*	1.46 (1.08, 2.03)*	1.29 (1.00, 1.64)*	1.28 (1.00, 1.64)*
	MetS Negative	1.11 (0.80, 1.38)	1.03 (0.72, 1.31)	1.10 (0.75, 1.44)	1.04 (0.67, 1.40)	1.12 (0.53, 1.61)	0.91 (0.43, 1.38)
ASCVD+	Diabetes Positive	1.18 (0.93, 1.45)	1.23 (0.96, 1.52)	1.37 (0.91, 1.96)	1.45 (0.95, 2.12)	1.15 (0.80, 1.48)	1.17 (0.82, 1.51)
	Diabetes Negative	1.27 (1.05, 1.51)*	1.17 (0.96, 1.36)	1.25 (1.00, 1.52)*	1.17 (0.90, 1.46)	1.30 (0.88, 1.72)	1.14 (0.75, 1.53)

[+]ASCVD was analyzed as dichotomous variable with binary logistic regression; [$]The crude odds ratio; [#]Adjusted for age, sex, BMI, smoking, education level, and physical activity; *OR (95% CI) of model that were significant
ASCVD — atherosclerotic cardiovascular disease; CI — confidence interval; hsCRP — high-sensitivity C-reactive protein; OR — odds ratio

resistance [16]. Consequently, it is hypothesized that heightened hsCRP levels may exert a direct inhibitory effect on insulin signaling, thereby aggravating glucose dysregulation and contributing to the development of diabetes [17]. Data analysis of the current study showed that there was no association between hsCRP and serum MetS in men. However, in women with elevated serum hsCRP the chances of having lower HDL-C, high WC and diabetes were increased. In addition, modulation of other variables showed that with increasing serum hsCRP, the prevalence of diabetes in women increased. This means that an increase of 1 mg/L in serum hsCRP increases the risk of diabetes by 22%. Those with increased hsCRP were more likely to be female, non-smoker, non-addicted, older, without ASCVD, with higher BMI, BFM, waist-to-hip ratio, waist circumference, SBP, DBP, TGs, FPG, albumin, and lower HDL-C. Findings from other studies show that an increase in hsCRP is directly related to an increased risk of T2D in patients with MetS [18]. The study of Mirhafez et al. showed that among the MetS components, increased FBG, WC, TGs, and hypertension were associated with hsCRP levels. Recent studies on the relationship between some components of MetS and hsCRP suggest that hsCRP can be used to identify patients with MetS [19].

The findings of this study showed that with increasing serum hsCRP by 1 mg/L, the chance of developing ASCVD increased by 36% are very important. In previous studies, the association of circulating levels of hsCRP with ASCVD and MetS has been confirmed separately. Men with MetS were more likely to develop ASCVD if they had elevated serum hsCRP [20]. According to previous researches, MetS, diabetes, and ASCVD are associated with alterations in lipid metabolism [17]. HsCRP can modulate lipoprotein metabolism, promoting the production of pro-atherogenic lipoproteins, such as very-low-density lipoprotein (VLDL) and low-density lipoprotein (LDL). Elevated hsCRP levels may contribute to dyslipidemia, thereby increasing the risk of ASCVD [21].

However, there are studies that have shown different results [22]. The vast majority of studies have shown that patients with MetS either are at higher risk for ASCVD or already have ASCVD [11]. According to the Framingham database, the age-adjusted relative risk for ASCVD in men with MetS was 2.88, which was higher than in women (1.54) [23]. The risk of ASCVD is doubled in people with a history of MetS who already have T2D or obesity [24]. McNeill et al. found that older people (mean age 72 years) with MetS were 20 to 30 percent more likely to have an ASCVD event than those without it [25]. Finally, as expected, an increase in number and intensity of MetS components increases the risk

of ASCVD [26]. Nevertheless, a study on non-diabetic Native Americans found no association between MetS and the incidence of ASCVD [27]. In a study of people with pre-existing ASCHD, MetS was associated with an increased ASCVD-induced mortality in women, while it had no effect on the risk of ASCVD-induced mortality in men [28]. However, the main limitation for comparing the results of different studies are the different criteria used to define MetS. A meta-analysis showed a clear association between MetS and risk of ASCVD even after adjusting for traditional cardiovascular risk factors [29]. Nevertheless, there are several studies that showed that the risk of ASCVD in subjects with MetS is not greater than the sum of its components [30]. In the study by Mirhafez et al. which used the definition of the International Diabetes Federation it was shown that most of the components of MetS were associated with an increase in serum hsCRP and the highest correlation was with serum hsCRP concentration and FBG [19]. Another study showed that changes of hsCRP in a multivariate model did not have a significant impact, while in a univariate model the level of hsCRP predicted the risk of T2D [31]. A number of epidemiological studies have indicated that high hsCRP is a significant risk factor for ASCVD in patients with hypertension and diabetes, and even in healthy individuals [32]. According to the results of a multivariate analysis by Velde M et al., including elevated hsCRP and the variables defining the MetS serum levels of hsCRP had added value to predicting new-onset ASCVD but not T2D [31]. There are a few exceptions to these findings. For example: a study on an Italian group of elderly people with T2D showed that MetS does not help predicting ASCVD further than the risks attributed to T2D. In this study, only in the non-diabetic subjects in univariate model, with increasing 1 mg/L hsCRP in serum, the risk of ASCVD increased for 27%. This study also showed that non-diabetic men were more likely to have ASCVD with an increase in hsCRP of 1 m/L. However, after adjusting for other variables in non-diabetic men, no association could be found between an increase of 1 mg/L of serum hsCRP and ASCVD [33].

Conclusions

This study provides evidence of a positive correlation between serum hsCRP levels and the presence of MetS components including HDL-C and diabetes, particularly in women. These findings suggest that individuals with high hsCRP levels should be monitored closely for the development of MetS and its components. However, further research is needed to deepen our understanding of the underlying biological mechanisms driving these associations. Additionally, healthcare professionals should consider incorporating hsCRP measurement into risk assessment and management strategies for MetS, diabetes and ASCVD. Continued investigation and prospective studies are warranted to determine the clinical utility of hsCRP as a predictive marker and to explore potential therapeutic interventions targeting inflammation in individuals at risk of MetS, diabetes, and ASCVD.

Article information

Data availability statement

Data will be made available on reasonable request.

Ethics statement

The study was approved by the Research and Ethical Review Board of the Neyshabur University of Medical Sciences.

Author contributions

Conceptualization: AS, SRM
Writing (original draft): AS, MAN
Writing (review) and editing: PH, SMH, NF, FST, ZR, SRM
Approval of the final version: all authors

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Conflict of interest

The authors declare no conflict of interest.

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