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Association of Oxidative Stress with Metabolic Risk Factors in Apparently Healthy Adults A Correlative Analysis

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ABSTRACT

Diabetes, hypertension, obesity and dyslipidemia are all recognized as contributing factors to metabolic syndrome (MS). Previous research has demonstrated a connection between each of these risk factors and heightened levels of inflammation. The present study aims to explore the relationship between oxidative stress and metabolic risk factors in ostensibly healthy adults. A cohort of ostensibly healthy adults (n = 165) was enlisted, with measurements taken for waist circumference, blood pressure, lipid profile, fasting blood sugar, serum glutathione (GSH) and hsCRP levels. Of these participants, 106 were identified with one or more metabolic risk factors (Group M), with a waist circumference exceeding 90 cm for males and 80 cm for females, while 59 individuals exhibited no metabolic risk factors (Group N). Subsequently, comparisons were made between serum hsCRP and GSH levels among the groups. Individuals with metabolic risk factors displayed heightened oxidative stress, as evidenced by elevated hsCRP levels and diminished serum GSH levels. These differences in hsCRP and GSH levels between the case and control groups were statistically significant. Additionally, our study identified elevated baseline hsCRP levels among the control group, consistent with findings from the AHA/CDC study. Our study suggests that Indians lacking metabolic risk factors for MS exhibit comparatively higher CRP levels and face an intermediate risk of cardiovascular disease. Furthermore, as the number of metabolic risk factors increases, hsCRP levels rise while serum GSH levels decline, indicating a positive association between the accumulation of risk factors and heightened oxidative stress.

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Key Words
Glutathione, high-sensitivity C-reactive protein, inflammation, metabolic syndrome

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INTRODUCTION

The rise in the prevalence of diabetes, hypertension, obesity and dyslipidemia, attributed to sedentary and stressful lifestyles, underscores the growing burden of metabolic syndrome (MS). Notably, India exhibits substantial rates of overweight and obesity (12.1-16%), with diabetes prevalence at 8.63%. Hypertension rates vary between rural (27.6%) and urban (33.8%) areas, with an overall prevalence of 29.8%. Dyslipidemia, notably prevalent in India[1], adds to the constellation of metabolic risk factors, each manifesting over prolonged periods[1-4]. MS, characterized by central obesity, dyslipidemia, hypertension and hyperglycemia, heralds a spectrum of diseases. Criteria, such as modified waist circumference for the Indian population, underscore the multifaceted nature of MS. Inflammatory processes underlie its progression, with oxidative stress implicated in ensuing complications[5-7].

Glutathione (GSH), a vital antioxidant, mitigates reactive oxygen species (ROS) in clinical settings. Elevated high-sensitivity C-reactive protein (hsCRP), a nonspecific inflammatory marker, signifies inflammation associated with MS. Imbalances in ROS and antioxidants precipitate endothelial dysfunction and cellular damage[8,7,6,5], potentially exacerbating MS-associated inflammation. Antioxidant depletion and altered hsCRP levels, reflective of increased inflammation, accompany hypertension, diabetes and obesity[7]. Elevated hsCRP precedes cardiovascular events[9,10,11], prognosticating future risks[9,10,11,12,13]. Thus, oxidative stress escalates with each MS risk factor, though discerning its status amidst multiple factors and at disease onset remains elusive his study aims to elucidate the interplay between oxidative stress and metabolic risk factors at diagnosis, particularly in individuals with multiple MS risk factors.

MATERIALS AND METHODS

This study was conducted in an Indian tertiary level medical institute. Subjects of both genders, aged between 21 and 45 years, were enrolled after providing written informed consent. Pregnant or lactating females, those with known gynecological issues and those experiencing premenstrual symptoms were excluded. Additionally, individuals with diagnosed cardiac disorders, endocrine diseases, inflammatory conditions, infectious diseases (bacterial or viral), or other metabolic or oncological issues were excluded. Comprehensive personal, family and medical histories were obtained from all recruited subjects. Measurements of waist circumference and blood pressure were taken for all enrolled subjects. Serum levels of high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), total cholesterol, and fasting blood sugar were assessed. Subjects without any risk factors for metabolic syndrome (obesity, elevated blood pressure or blood sugar, increased TG and low HDL) were assigned to the control group, while those with one or more risk factors (according to NCEP ATP III criteria[6], with a modified waist circumference criterion of >90cm in males and 80cm in females for the Indian population) were placed in the case group. Subsequently, serum glutathione (GSH) and hsCRP levels were measured in all subjects (both cases and controls) and the levels of both markers were compared between the groups. The sample size for this study comprised 165 subjects.

RESULTS AND DISCUSSIONS

The age, gender and height of subjects in both the control and case groups exhibited statistically non significant differences. However, body weight and waist circumference were significantly higher in the case group, comprising individuals at metabolic risk (Table 1). Additionally, systolic blood pressure (SBP), diastolic blood pressure (DBP), triglycerides (TG), low-density lipoprotein (LDL) and fasting blood sugar (FBS) were significantly elevated, while high-density lipoprotein (HDL) was significantly lower in the case group with metabolic risks (Table 2). Our analysis revealed that individuals with metabolic risk factors exhibited higher hsCRP levels compared to those without risk factors, with this difference being statistically significant. Furthermore, individuals with metabolic risk factors (cases) demonstrated lower GSH levels compared to those without risk factors and this disparity was statistically significant (Table 3). Notably, (Table 4) illustrates a progressive increase in hsCRP levels and a corresponding decrease in GSH levels as the number of metabolic risk factors rises.

In the current study, a total of 165 subjects were recruited, among whom 59 subjects did not exhibit any risk factors for MS, while 106 subjects presented with one or more risk factors for MS. The levels of high-sensitivity C-reactive protein (hsCRP) in the control group suggest that normal individuals in the Indian population, devoid of apparent risk factors, exhibit an intermediate risk for cardiovascular disease, as per the AHA/CDC study[13]. This observation aligns with the tendency for the onset of type 2 diabetes and hypertension to occur at a younger age compared to Western populations, as evidenced by Kamath *et al*[14]. who reported a mean hsCRP value of 1.88 mg/l in their case-control study, higher than that of Western populations. The predisposition to metabolic risk factors may stem from various factors such as genetic predisposition, sedentary lifestyle, heightened stress levels, or environmental influences. It is imperative to conduct a larger prospective study encompassing diverse age groups, employing standardized hsCRP measurements and prolonged follow-up periods, to ascertain baseline hsCRP levels in the local population and establish precise hsCRP cutoff values for predicting

Table 1: Anthropo-demographic variables in study participants

Variables	Cases (n = 106)	Control (n = 59)	p-value
Age (years)	36.12±5.52	33.72±5.79	0.219
Male	90	47	0.056
Female	16	12	
Height (cm)	166.89±6.92	169.12±5.43	0.372
Weight (Kg)	70.67±8.77	63.93±4.96	<0.05
Waist Circumference(cm)	90.15±17.48	78.58±7.33	<0.05

Table 2: Metabolic risk factors among cases and controls

Parameters	Cases (n = 106)	Control (n = 59)	p-value
SBP (mmHg)	136.42±12.87	116.20±7.10	<0.05
DBP (mmHg)	87.65±13.02	79.07±5.22	<0.05
FBS (mg/dl)	102.78±24.74	90.93±6.31	<0.05
HDL (mg/dl)	37.94±6.32	45.12±4.77	<0.05
LDL (mg/dl)	148.26±28.91	113.85±14.73	<0.05
TG (mg/dl)	155.63±36.92	100.87±20.14	<0.05

Table 3: Serum GSH and hs-CRP among cases and controls

Parameters	Cases (n = 106)	Control (n = 59)	p-value
GSH (ug/ml)	3.12±0.79	4.92±0.73	<0.05
hs-CRP (ng/ml)	4779.6±2089.37	1636.8±555.82	<0.05

Table 4: Effect of no. of risk factors on GSH and hsCRP

	Numbers of metabolic risk factors			
Variables	1 (n = 39)	2 (n = 38)	3 (n = 18)	4 (n = 11)
GSH (ug/ml)	3.74±0.68	3.31±0.55	2.39±0.39	1.93±0.18
hs-CRP (ng/ml)	3703.2±118.45	4486.5±876.72	6495.6±2405.84	6838.5±359.72

future cardiovascular disease development. Our study revealed that individuals with any metabolic risk factors exhibited hsCRP levels exceeding 3000 ng/ml, indicating a high risk of future cardiovascular events according to AHA/CDC criteria. Thus, the presence of even a single risk factor hastens the countdown to a potential cardiovascular event. Additionally, our findings demonstrated that hsCRP levels were significantly higher in the case group compared to controls, with a positive correlation between hsCRP levels and the number of metabolic risk factors. This association suggests that each metabolic risk factor represents a state of subtle oxidative stress and inflammation[7,15], which intensifies with an increasing number of metabolic risk factors.

Furthermore, our study identified lower serum glutathione (GSH) levels in the case group compared to controls. Previous research by Vaziri *et al*[16]. illustrated that drug-induced glutathione depletion induces oxidative stress in previously healthy rats. Similarly, Pedro-Botet *et al*[17]. observed significantly lower glutathione peroxidase (GPx) levels in newly diagnosed, normolipidemic mild hypertensive patients compared to controls. Additionally, Ghayour Mobarhan *et al*[18]. noted reduced serum GPx levels in obese individuals compared to non-obese individuals and those with metabolic syndrome. The diminished GSH levels in the case group of our study may be attributed to heightened inflammation leading to increased reactive oxygen species (ROS) production and subsequent glutathione depletion. Furthermore, our findings indicated an inverse relationship between serum GSH levels and the number of metabolic risk factors, suggesting that as inflammation escalates with accumulating metabolic risk factors, there is an increased demand for GSH to counteract elevated ROS production. In summary, heightened inflammation and oxidative stress, reflected by elevated hsCRP levels and reduced serum GSH levels, respectively, are associated with an increasing number of risk factors for metabolic syndrome. These factors contribute to tissue damage over time, thereby augmenting the risk of future cardiovascular events.

CONCLUSION

Baseline levels of hsCRP were observed to be higher in the Indian. Furthermore, individuals with metabolic risk factors exhibited a reduction in GSH, an antioxidant and an increase in hsCRP, an inflammatory marker. Our findings indicated a gradual decline in serum GSH and a gradual rise in hsCRP levels with an increase in metabolic risk factors, suggesting a corresponding escalation in oxidative stress.

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