

Original article

## Study of association between Qrisk2 score, components of metabolic syndrome and oxidative stress in subjects with metabolic risk factors

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### Abstract

**Introduction:** The most fearful outcome of metabolic syndrome is cardiovascular events leading to morbidity and mortality. Q risk2 score was developed by physicians working in UK National Health Service to estimates the risk of cardiovascular disease incidence over the next 10 years. Qrisk2 score <10% indicates mild risk, 10-20-% moderate risk, >20% high risk of CVD. MRF are progressive inflammatory processes leading to rise in serum hsCRP and depletion of GSH, indicating increased oxidative stress which has been associated with higher risk of CVD. Therefore, this study has been designed to study the association of QRISK2 score with oxidative stress in apparently healthy adults at metabolic risk.

**Material and Methodology:** Subjects of both genders, age between 25 to 45 years were enrolled as per inclusion & exclusion criteria and detailed clinical history was taken. All candidates were subjected to Anthropometry (height, weight, BMI, Waist Circumference), BP measurements, lipid profile, GSH, hsCRP and fasting blood sugar. Qrisk2 score was calculated by online calculator (<https://qrisk.org/2017/>)

All subjects were screened for metabolic risk factors (MRF). Subjects without any MRF were put into Group A and those with any MRF were kept in Group B. All recruited subjects were divided into low-risk group (Qrisk2 score <10%) & high-risk group (Qrisk2 score >10%). Then, various components of metabolic syndrome and oxidative stress will be compared in both groups.

**Results:** In this study, weight, BMI, BP, TG, LDL, total cholesterol, fasting blood sugar, GSH and hsCRP was statistically significantly higher in subjects with MRF. Smoking, diabetes, HTN and obesity was more common in high Qrisk2 score group (Qrisk2 score >10). Systolic BP was statistically significantly higher in high Qrisk2 score group but difference in diastolic BP was not statistically significant. TG, LDL, total cholesterol, fasting blood sugar, serum GSH and hsCRP was statistically higher in high Qrisk2 score group whereas, HDL was statistically significantly lower.

**Conclusion:** Smoking, diabetes, HTN and obesity increases the future risk of CVD and systolic BP is more important than diastolic BP. We also observed high Qrisk 2 score is associated with increased oxidative stress

**Keywords:** Q Risk2 score, metabolic risk factors, Cardiovascular disorder, oxidative stress, GSH, hsCRP

### Introduction:

According to NCEP ATP III criteria<sup>[1]</sup>, Metabolic syndrome (MS) is a clinical condition consisting of at least three of the following conditions- Blood pressure  $\geq$  130/85 mmHg or treated for hypertension, fasting plasma glucose  $\geq$  110 mg/dl, Central obesity (waist circumference  $\geq$  90 cm in male &  $\geq$  80 cm in female (for Indian population)<sup>[2]</sup>, TG  $\geq$  150 mg/dl and HDL-C < 40 mg/dl in male, < 50 mg/dl in female. Thus, all five factors or components that may cause metabolic syndrome

are the risk factors for the development of MS. The most fearful outcome of metabolic syndrome is the cardiovascular events that may lead to both morbidity and mortality. Therefore, aim of treatment of all above mentioned risk factors is to reduce the future cardiovascular events. Many methods have been developed for estimation of future risk of cardiovascular disease. Q risk2<sup>[3]</sup> score was developed for the same purpose by physicians working in the UK National Health Service. Although QRISK2 score algorithm was

developed by collecting the data from population of UK but later it was further made suitable for several other ethnicity. This score considers ethnicity of the Indian population therefore, QRISK2 score prediction of future risk of cardiovascular accidents for Indians must be valid enough to consider it for research purposes.

QRISK2 score estimates the risk of developing cardiovascular disease (CVD) over the next 10 years in percentage. It also provides the relative risk for future cardiovascular disease. Higher the QRISK2 score, higher will be the chance of cardiovascular events in next 10 years. If Qrisk2 score is <10% it indicates mild risk, 10-20% moderate risk, >20% high risk of CVD in next 10 years. Subjects with >10 % score should be evaluated for future CVD risk and may be considered for statin therapy.<sup>[4]</sup> It has been concluded in many studies that Metabolic risk factors (MRF) are progressive inflammatory processes. This increased inflammation is indicated by increase in serum hsCRP<sup>[5]</sup>. Mohd Abu Farha et al<sup>[6]</sup> found a positive association between hsCRP, leptin, PAI-1 with increased MetS components and increase the odds of having MetS. Increased inflammation is responsible for exhaustion of antioxidant system of the body. Glutathione is an important intracellular antioxidant system of the human body which gets depleted in cases of chronic increased inflammation<sup>[7]</sup>. This increase in hsCRP levels and depletion of GSH indicates increased oxidative stress<sup>[8]</sup>. Thus, chronic inflammatory conditions increase the oxidative stress that is supposed to be the underlying pathology for the development of the complications<sup>[9]</sup> associated with MRF. It has been found that increased oxidative stress has been associated with higher risk of cardiovascular disease. We know that increased CVD risk is associated with higher

QRISK2 score also. Therefore, this study has been designed to study the association of QRISK2 score with oxidative stress in apparently healthy adults at metabolic risk.

#### **Material and Methodology:**

We carried out this study in the Department of Physiology at King Georges Medical University, Lucknow. Ethical clearance was taken from institutional ethical committee. Apparently healthy adults of age between 25-45 years from the urban area of Lucknow have been recruited after a written consent. Subjects with any known cardiovascular, respiratory, endocrine, metabolic, genetic, congenital disease, acute illness and females with pregnancy, lactation and any gynaecological disease were excluded from the study.

A detailed clinical, family and past history was taken in recruited subjects. anthropometric measurements (height weight, BMI, waist circumference) along with blood pressure, fasting blood sugar, lipid profile, serum GSH and hsCRP was measured in all subjects enrolled for the study. QRISK 2 score was calculated with the help of the online-calculator

(<https://www.qrisk.org/2017/index.php>).

#### **Study Design-**

All recruited subjects were screened for metabolic risk factors. Subjects without any metabolic risk factors were kept in Group A and all subject with any risk for Metabolic Syndrome were kept in group B. then we calculated Qrisk2 score with the help of online calculator and divided all the recruited subjects into two groups. Subjects with Qrisk2 score <10 % were kept in low risk group and subjects with >10 % score were kept in high risk group for future development of cardiovascular disease. Then, various components of metabolic syndrome and oxidative stress will be compared in both groups.

**Observations**

	Metabolic Risk factors Absent (n=43) Group A		Metabolic Risk factors Present (n=77) Group B		p-Value
	Mean	±SD	Mean	±SD	
Age (years)	34.05	5.49	35.68	5.76	0.134
Height (cm)	168.65	5.06	167.74	7.51	0.479
Weight (kg)	64.28	5.11	71.34	9.11	<0.001*
BMI	22.55	0.91	25.31	2.40	<0.001*
Systolic BP	118.05	7.55	134.78	13.33	<0.001*
Diastolic BP	78.23	4.96	86.13	13.50	<0.001*
TG	102.35	21.95	152.77	38.85	<0.001*
HDL	44.30	4.34	38.47	5.85	<0.001*
LDL	111.40	15.49	151.19	30.36	<0.001*
Total Cholesterol	176.02	18.55	219.53	31.16	<0.001*
FBS	89.44	5.91	104.13	23.35	<0.001*
GSH (ug/ml)	3.56	0.45	2.80	0.74	<0.001*
hsCRP (ng/ml)	2.95	0.42	2.36	0.66	<0.001*

**Table 2: Risk factors**

	Low Risk (Q risk 2 score ≤10) [n=106]		High Risk (Q risk 2 score >10) [n=14]		OR (95%CI)	p-Value
	n	%	n	%		
<b>Smoking</b>	35	33.02	13	92.86	0.04 (0.01-0.30)	<0.001*
<b>DM</b>	12	11.32	14	100.00	0.01 (0.01-0.80)	<0.001*
<b>HT</b>	32	30.19	12	85.71	0.07 (0.02-0.34)	<0.001*
<b>Obese</b>	38	35.85	12	85.71	0.09 (0.02-0.44)	0.001*

\*=Significant (p<0.001)

**Table 3: Physiological and biochemical parameters**

	Low Risk (Q risk 2 score ≤10) [n=106]		High Risk (Q risk 2 score >10) [n=14]		p-Value
	Mean	±SD	Mean	±SD	
Systolic BP	127.40	13.74	139.29	12.57	0.003*
Diastolic BP	82.57	11.78	88.86	10.89	0.061
TG	125.75	34.18	202.43	27.34	<0.001*
HDL	41.71	5.44	31.86	1.51	<0.001*
LDL	131.16	27.89	180.64	30.23	<0.001*
Total Cholesterol	197.66	29.61	251.5	31.06	<0.001*
FBS	93.66	13.54	138.29	19.53	<0.001*
GSH (ug/ml)	3.96	1.01	2.2	0.38	<0.001*
hsCRP (ng/ml)	3174.55	1615.24	7310	3066.26	<0.001*
RR	2.37	2.56	9.37	2.65	<0.001*

\*=Significant (p<0.001)

### Results-

In this study, 43 subjects were without any metabolic risk factors and 77 subjects were having at least one metabolic risk factors. Weight, BMI, blood pressure, TG, LDL, total cholesterol, fasting blood sugar, GSH and hsCRP was statistically significantly higher in subjects with metabolic risk factors. Table 2 shows that out of 120 subjects 106 subject were having low Qrisk2 score (<10) and 14 subjects were having high Qrisk2 score (>10). In low Qrisk group, 33% of subjects were smoker but in high Qrisk2 score group 92.86 % were smokers. 11.32% subjects were having diabetes in low Qrisk2 score group but in high Qrisk group all subjects had diabetes. Similarly, 30.19% and 35.85 % subjects were having hypertension and obesity respectively in low Qrisk2 score group whereas, in high Qrisk2 score group 85.71% subjects were having hypertension and obesity.

Table 3 shows that systolic blood pressure was statistically significantly higher in high Qrisk2 score group but diastolic blood pressure was higher in high risk group but the difference was not statistically significant. TG, LDL, total cholesterol, fasting blood sugar, serum GSH and hsCRP was statistically higher in high Qrisk2 score group whereas, HDL was statistically significantly lower in the same group

### Discussion-

Total 120 subjects were recruited for the study and 77 subjects were found to have one or more metabolic risk factors. Therefore, subjects with metabolic risk factors have statistically significantly higher weight, BMI, blood pressure, TG, LDL, total cholesterol, fasting blood sugar, GSH and hsCRP. Many studies have shown increased oxidative stress in subjects with metabolic risk factors.

In table 2, we have observed that 92.86% subjects of high Qrisk2 score group were smokers and only 33% of subjects in lower risk group were smokers. This indicates smoking is associated with increased risk of future cardiovascular disease and this increased risk is statistically significant. Robert H. Fagard et al<sup>[10]</sup> observed that in persons with DM and hypertension, smoking is a risk factor for mortality and Coronary Artery Disease. Kritz H et al<sup>[11]</sup> noted that even passive smoking is a risk factor for cardiac disease morbidity and mortality. Thus, smoking is an important culprit responsible for increased cardiovascular disease. We observed that diabetes mellitus was associated with only

11.32% (12) subjects in low Qrisk2 score group but it was associated with 100 % (14) subjects in high-risk group. We can easily conclude that diabetes mellitus is an important risk factor for cardiovascular disease. In an epidemiological study by Guptha LS et al<sup>[12]</sup> found a statistically significant difference in median QRISK2 scores between nondiabetic and diabetic subjects. In same study, the multivariate negative binomial regression revealed that T2DM significantly increased the QRISK2 10-year risk score by 77.7%.

We again observed in our study that only 30.19% and 35.85 % subjects were having hypertension and obesity respectively in low Qrisk2 score group in comparison to 85.71% subjects having hypertension and obesity in high-risk group. This indicates statistically significant association of hypertension and obesity with high Qrisk2 score. We also observed that mean systolic blood pressure in low-risk group was 127.40 and in high-risk group was 139.29mm of Hg and this difference was statistically significant. But diastolic blood pressure in low-risk group was 82.57 and in high-risk group was 88.86 mm of Hg and this difference was statistically non-significant. This observation indicates that systolic blood pressure is more important deciding factor for future cardiovascular events, this might be the reason why Qrisk2 score calculator takes only systolic blood pressure under consideration for future cardiovascular risk assessment.

Oxidative stress is a common hypothesized mechanisms linking several key risk factors to cardiovascular disease. Sharma P et al<sup>[13]</sup> found in their study that Subjects with metabolic syndrome ( $\geq 3$  risk factors) had poor antioxidants status & significantly increased oxidative stress in comparison to subjects without metabolic syndrome. In our study, we have observed higher hsCRP (7310ng/ml) in high Qrisk2 score group than in low risk2 group (3174.55 ng/ml). Johns I et al<sup>[14]</sup> also observed high hsCRP in high Qrisk2 score group. hsCRP is a protein synthesized by liver that activates the complement system of the body that further increases the inflammation. We also observed low serum GSH in high-risk group (2.2 ug/ml) and high GSH in low-risk group (3.96 ug/ml). This difference in hsCRP and serum GSH levels between both groups were statistically significant. Thus, our study suggests that subjects with high Qrisk2 score have high hsCRP and low GSH indicating higher oxidative stress.

### Conclusions-

- Smoking, diabetes and obesity increases future risk of CVD (higher Qrisk2 score)
  - High Qrisk 2 score is associated with increased oxidative stress
- and systolic blood pressure is more important in future CVD prediction

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