A STUDY OF METABOLIC SYNDROME IN PATIENTS UNDERGOING CORONARY ANGIOGRAPHY AT KIMS HOSPITAL, HUBBALLI, KARNATAKA, INDIA

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ABSTRACT

BACKGROUND

Coronary heart disease has become an epidemic since 20th century. Deaths due to the same are increasing of around 17.5 million deaths in year 2012. The deaths are increasing more in developing countries and metabolic syndrome is a cluster of disorders, which are promoting the development of coronary artery diseases. The disorders include central obesity, insulin resistance, dyslipidaemia and hypertension. Increasing prevalence, changing lifestyle and progression of the disease without obvious symptoms had led to increasing morbidity and mortality. The non-infectious epidemic of the century is posing great challenges to healthcare and research in development of more infrastructure and funds to prevent and treat the disease.

MATERIALS AND METHODS

A total of 100 patients diagnosed with CAD and posted for Coronary Angiogram (CAG) in ICCU at KIMS Hospital, Hubballi, were studied over a period of one and a half year. Cases were categorised according to ATPIII and new IDF criteria for metabolic syndrome and compared. Clinical evaluation, ECG, lipid profile and 2D-echo was done. Statistical analysis done using unpaired t-test, Mann-Whitney tests, Chi-square test and Kappa statistics.

RESULTS

Of the total 100, 57 had metabolic syndrome by either ATP criteria or IDF criteria. Kappa=0.859 (p-value <0.001) indicating there was a statistical significant agreement between two criteria and women were more at risk for metabolic syndrome. FBS (63%) was the most prevalent independent component of metabolic syndrome followed by hypertension (57%). All the components in metabolic syndrome were more common in patients with metabolic syndrome group than patients without metabolic syndrome group and were highly significant. High BP was the most common component of metabolic syndrome followed by TGs >150 mg/dL and DM or FBS >100 mg/dL (p value <0.001). The mean values of SBP (144.0 vs. 120.8), DBP (85.6 vs. 73.8) and waist circumference (95.4 vs. 87.7) was statistically significant (p value <0.01) between patients with metabolic syndrome and without metabolic syndrome with IDF criteria (p value <0.001). It was observed LAD (28.1%) was the most common vessel involved individually. There was no much significance related to metabolic syndrome. Incidence of CAD was more common in patients with metabolic syndrome than other group.

CONCLUSION

The prevalence of metabolic syndrome was high in patients with CAD. Both metabolic syndrome definitions identify subset of patients who are at high risk for CAD and are cost effective, easily practicable tools.

KEYWORDS

Metabolic Syndrome, ATPIII, IDF, Coronary Angiogram.

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BACKGROUND

Coronary artery disease has become an epidemic since 20th century. Deaths due to the same are rapidly increasing and there was around 17.5 million deaths in the year 2012.[1] Deaths are rapidly increasing in the developing country and accounting to about 75%. Industrialisation, urbanisation, lifestyle changes and changing food habits play an important role in the pathogenesis.[2] Epidemiological transition has spread to developing countries beginning late 20th century and in the 21st century, which has increased the incidence of coronary heart disease.

Metabolic syndrome, also known as syndrome X is another cluster of features promoting the development of coronary artery disease. It includes central obesity, insulin resistance, dyslipidaemia and hypertension.[3] It is important to recognise the syndrome, its clinical features and prognostication of the disease to reduce the morbidity and mortality. Healthcare, research programmes and government are in need to allocate more infrastructure and funds to prevent the disease complications and to manage the existing burden in the society.

South Asians and Indians are particularly prone for development of the metabolic syndrome and there is increase in number of cases in recent years at an alarming rate. The Indian phenotype is characterised by low BMI and high visceral fat mass. The visceral fat mass secrete the adipokines for metabolic derangements. Dyslipidaemia is an important cause for the atherosclerosis associated with the coronary artery disease. Dyslipidaemia is felt to be an important cause of atherosclerosis in Asian Indians, which could majorly be associated with diet and eating habits.

Many novel markers are being discovered for early detection of metabolic syndrome and coronary artery disease. Chemerin is one of the same, which is gaining importance now a days. The Endothelial Progenitor Cells (EPC's), which are released from bone marrow, which replenish the endothelial lining and their circulating levels are used as biomarker. The exhaustion of the EPC's and their cell count is a new promising independent marker of population with cardiovascular risk.[4]

In case of western countries, the exact prevalence of metabolic syndrome is available. But, the developing countries lack the same, and in case of the Indian population, scant data is available with angiography and angiographically-proven coronary artery disease.[5]

MATERIALS AND METHODS

Among patients posted for coronary angiography in ICCU, KIMS Hospital, Hubballi, over a period of one and a half years, 100 patients were scrutinised for presence of metabolic syndrome according to ATPIII guidelines and IDF guidelines. Patients with suspected coronary artery disease with an age >30 years of either sex were included. Patients with myocardial infarction, CVA, angina pectoris, valvular heart diseases, conduction defects, aged <30 years and existence of asthma or COPD were excluded from the study.

The study was observational and cross sectional in type. The blood sample was drawn at admission and the fasting lipid profile and FBS were done on the day posting patient for coronary angiogram. A 12-lead ECG, coronary angiogram and 2D echocardiogram was also done.

Statistical analysis was done and results were expressed as mean ± SD and median for continuous data and were compared by unpaired t-test/Mann-Whitney test between 2 groups. Categorical data was analysed by Chi-square test. Kappa statistics was used to find agreement between the two data. Waist circumference was measured by the WHO STEPwise Approach to Surveillance (STEPS)[6] protocol for measuring waist circumference, which instructs that the measurement be made at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest.

RESULTS

Results were expressed as mean ± SD and median for continuous data and were compared by unpaired t-test/Mann-Whitney test between two groups. Categorical data were analysed by Chi-square test. A p value of 0.05 or less was considered for statistical significance. Kappa statistics was used for finding the agreement between two definitions.

Out of the 100 cases in the study group, age incidence was more in the younger age mainly between the age group 51-60 followed by 41-50 years. 75 cases among 100 were males and they predominated the subjects of study.

Age Group (in Years)	Frequency	Percentage
<=40	16	16
41-50	31	31
51-60	34	34
≥61	19	19

Table 1. Age Distribution of Patients Admitted for Coronary Angiography with Suspected CAD

Most common mode of presentation was chest pain (94%), followed by sweating (45%). Breathlessness (31.6% vs. 11.6%) was more common in metabolic syndrome compared to those without metabolic syndrome.

Presenting Complaint	Frequency	Percentage
Chest pain	94	94
Sweating	45	45
Breathlessness	23	23
Vomiting	18	18
Palpitation	7	7
Cough/sputum	5	5
Syncope	5	5

Table 2. Distribution of Presenting Symptoms among Patients Admitted for Coronary Angiography with Suspected CAD

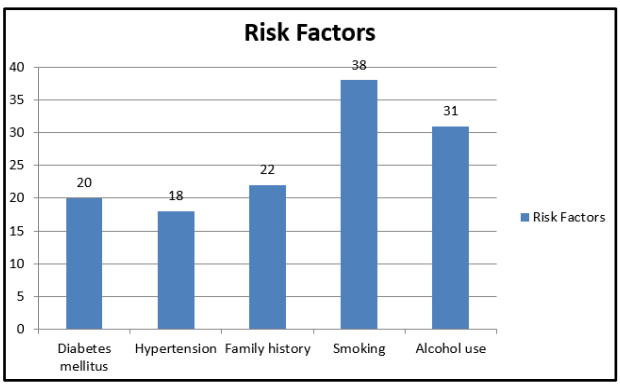
Smoking (38%) followed by alcohol abuse (31%) were most common risk factors for CAD. Maximum number of patients were overweight (48% vs. 52%), but there was no significant gender difference in BMI and metabolic syndrome.

Risk Factors	Frequency	Percentage
Diabetes mellitus	20	20
Hypertension	18	18
Family history	22	22
Smoking	38	38
Alcohol use	31	31

Table 3. Distribution of Risk Factors among Patients Admitted for Coronary Angiography with Suspected CAD

BMI Categories	Male N (%)	Female N (%)	p-value
Less than 18.5	4 (5.3)	0	0.354
18.5 to 23	25 (33.3)	6 (24.0)	
23 to 27.5	36 (48.0)	13 (52.0)	
More than 27.5	10 (13.3)	6 (24.0)	
Total	**75**	**25**	

Table 4. BMI and Gender



Graph 1. Risk Factors

FBS of >100 mg/dL (63%) was the most prevalent independent component of metabolic syndrome followed by hypertension, i.e. SBP >130 mmHg and DBP >85 mmHg (57%).

Of the total 100 study cases, 57 had metabolic syndrome by either ATP criteria or IDF criteria. The age incidence was more between the age group 51-60 years in patients who had metabolic syndrome and 41-50 years in those who did satisfy criteria. However, there was no statistical difference in age between 2 groups (p value 0.447).

Among males, only 49.3% had metabolic syndrome, whereas among females, nearly 80% had metabolic syndrome (p-value=0.007).

The past history of DM, HTN and alcohol abuse was more common in the metabolic syndrome group compared to those without metabolic syndrome.

All the components in metabolic syndrome group were more common in metabolic syndrome group than patients without metabolic syndrome group and were highly significant. High BP was the most common component of MS followed by TGs >150 mg/dL and DM or FBS >100 mg/dL.

Risk Factors	Metabolic Syndrome Present - n=57 (%)	Metabolic Syndrome Absent - n=43 (%)	p-value
FBS >100 mg/dL	42 (73.7)	21 (48.8)	<0.001
SBP >130 or DBP >85 mmHg	44 (77.2)	13 (30.2)	<0.001
Triglyceride >150 mg/dL	42 (73.7)	12 (27.9)	<0.001
Low HDL (<40 in male and <50 in female)	33 (57.9)	17 (39.5)	0.069
Waist circumference (ATP)	22 (38.6)	5 (11.6)	0.002
Waist circumference (IDF)	42 (73.7)	12 (27.9)	<0.001

Table 5. Distribution of Components of Metabolic Syndrome among Patients Admitted for Coronary Angiography with Suspected CAD

It was observed LAD (28.1%) was the most common vessel involved individually. There was no much significance related to metabolic syndrome.

Coronary Artery	Metabolic Syndrome Present - n=57 (%)	Metabolic Syndrome Absent - n=43 (%)	p-value
No coronary involvement	11 (19.3)	8 (18.6)	0.6639
Only LAD	16 (28.1)	14 (32.6)	
Only RCA	7 (12.3)	3 (7.0)	
Only LCX	5 (8.8)	1 (2.3)	
Double vessel	13 (22.8)	11 (25.6)	
Triple vessel	5 (8.8)	6 (14.0)	

Table 6. Association between Presenting Symptom and Metabolic Syndrome among Patients Admitted for Coronary Angiography with Suspected CAD

Symptoms	Metabolic Syndrome Present - n=57 (%)	Metabolic Syndrome Absent - n=43 (%)	p-value
Chest pain	53 (93)	41 (95.3)	0.621
Breathlessness	18 (31.6)	5 (11.6)	0.019
Cough	1 (1.8)	4 (9.3)	0.086
Palpitation	4 (7.0)	3 (7.0)	0.994
Syncope	3 (5.3)	2 (4.7)	0.889
Sweating	26 (45.6)	19 (45.2)	0.970
Vomiting	10 (17.5)	8 (18.6)	0.891

Table 7. Association between Presenting Symptom and Metabolic Syndrome Among Patients Admitted for Coronary Angiography with Suspected CAD

Risk Factors	Metabolic Syndrome Present - n=57 (%)	Metabolic Syndrome Absent - n=43 (%)	p-value
Diabetes	13 (22.8)	7 (16.3)	0.419
Hypertension	13 (22.8)	5 (11.6)	0.149
Family history	11 (19.3)	11 (25.6)	0.452
Smoking	17 (29.8)	21 (48.8)	0.052
Alcohol use	19 (33.3)	12 (27.9)	0.561

Table 8. Risk Factors

DISCUSSION

Metabolic syndrome is also known as Reaven's syndrome and syndrome X. It is a combination of elevated blood pressure, altered glucose metabolism and dyslipidaemia. There are multiple definitions given by many different institutes and agencies. But, as per Reaven, the metabolic syndrome comprises of glucose intolerance, hypertension, increased very low-density lipoprotein, increased triglycerides and decreased high-density lipoprotein cholesterol and presence of insulin resistance.[7]

In our study, 52% and 55% of patients' satisfied criteria for metabolic syndrome by ATPIII and IDF criteria, 57% satisfied criteria for both. Our study was comparable with Rajendra et al[8] (2016) study where 45.9% and 37.4% of subjects satisfied criteria for metabolic syndrome by ATPIII and IDF. Antonio et al[9] (2004) study had 50% prevalence of

metabolic syndrome by ATPIII. These findings suggest that metabolic syndrome defined by NCEP-ATPIII and IDF criteria is very common in patients with CAD almost in 1:2 ratio.

In the present study, mean age incidence was 51.96 ± 10.31 years and study correlates with Wasir et al,[10] which had mean age of 40 ± 18 years. There is early incidence of metabolic syndrome in present study compared to other Antonio et al and Todd et al[11] studies. In general, myocardial infarction develops 5-10 years earlier in Asian Indian than in other population.

In present study, out of 100 patients undergoing coronary angiogram, 46% had single-vessel disease, 24% had double-vessel disease, 11% had triple-vessel disease and 19% had normal coronaries. Study by Namita et al[12] and Faria et al showed 25.3% and 23.8% prevalence of double-vessel disease, respectively. Single-vessel disease prevalence was 24.05%, 30.7% and 22.3% with Hassanin et al,[13] Faria et al[14] and Namita et al studies, respectively.

WHO Definition of Metabolic Syndrome-[15]

Glucose intolerance, Impaired Glucose Tolerance (IGT) or Diabetes Mellitus (DM) and/or insulin resistance together with two or more of the components listed below-

1. Raised arterial pressure, i.e. ≥140/90 mm of Hg.
2. Raised plasma triglyceride (≥150 mg/dL) and/or low HDL-C (<35 mg/dL in men and <39 mg/dL in women).
3. Central obesity, i.e. Waist-Hip Ratio (WHR) >0.9 in men and >0.85 in women and/or Body Mass Index (BMI) >30 kg/m^2.
4. Microalbuminuria, i.e. urinary albumin excretion rate ≥20 µg/minute or albumin/creatinine ratio ≥30 µg/mg.

Many other definition are available for defining metabolic syndrome, namely European Group for Study of Insulin Resistance (EGIR), NCEP-ATPIII definition, International Diabetes Federation Global Consensus Definition, Updated NCEP/American Heart Association definition.

NCEP-III defines metabolic syndrome, if the person satisfies 3/5 following criteria-

1. Abdominal obesity- WC ≥102 cm in men and ≥88 cm in women.
2. Hypertriglyceridaemia- ≥150 mg/dL (1.695 mmol/L).
3. Low HDL-C- <40 mg/dL in men and <50 mg/dL in women.
4. High Blood Pressure (BP)- >130/85 mmHg.
5. High fasting glucose- >110 mg/dL.

Researchers prefer using NCEP-ATPIII definition as it is simple and clinically applicable. Waist circumference is different as per different definitions, but for Asians generally accepted definition is 90 cm in male and 80 cm in female.[16]

Indian Diabetes Risk Score-[17,18] it includes many other simple clinical parameters to define metabolic syndrome. The score of >60 is useful to predict the metabolic syndrome and cardiovascular diseases. It includes the age, abdominal obesity, physical activity and family history. The scoring system is as follows-

Particulars	
Age (Years)	**Score**
<35 (reference)	0
35-49	20
>50	30
Abdominal Obesity	
Waist 80-89 cm (female); >90-99 cm (male)	10
Waist >90 cm (female); >100 cm (male)	20
Physical Activity	
Vigorous exercise or strenuous (manual) labour at home/work	0
Mild-to-moderate exercise or mild-to-moderate physical activity at home/work	20
No exercise and sedentary activities at home/work	30
Family history	
No family history (reference)	0
Either parent	10
Both parents	20
Minimum score	0
Maximum score	100
Interpretation	
Score <30 low risk, score 30-50 medium risk and score >60 high risk for type 2 diabetes and cardiovascular diseases	

Table 9. The Scoring System is as Follows

Other markers like hs-CRP (high-sensitivity C-reactive protein) are also used as a predictor of metabolic syndrome.

The prevalence of the metabolic syndrome is increasing day by day in western countries.[19,20] As per NHANES 2003-2006 (National Health and Nutrition Examination Survey), 34% of population meet the criteria for metabolic syndrome, ATPIII 2001 guidelines 27% meet the criteria and ATPIII revised guidelines 32.3% meet the criteria.[21]

According to Snehalata and Ramachandra[22] in Indian population centers have estimated a prevalence of the metabolic syndrome to encompass approximately one-third of individuals residing in large cities. Kanjilal et al[23] have shown in their study that Asian Indians have a high predisposition to metabolic syndrome and coronary artery disease. Roopali Khanna[24] et al in their study, it was seen that metabolic syndrome was common in Indian patients with angiographically documented coronary artery disease.

A complex array of factors lead to the metabolic syndrome in Asian-Indians.[25]

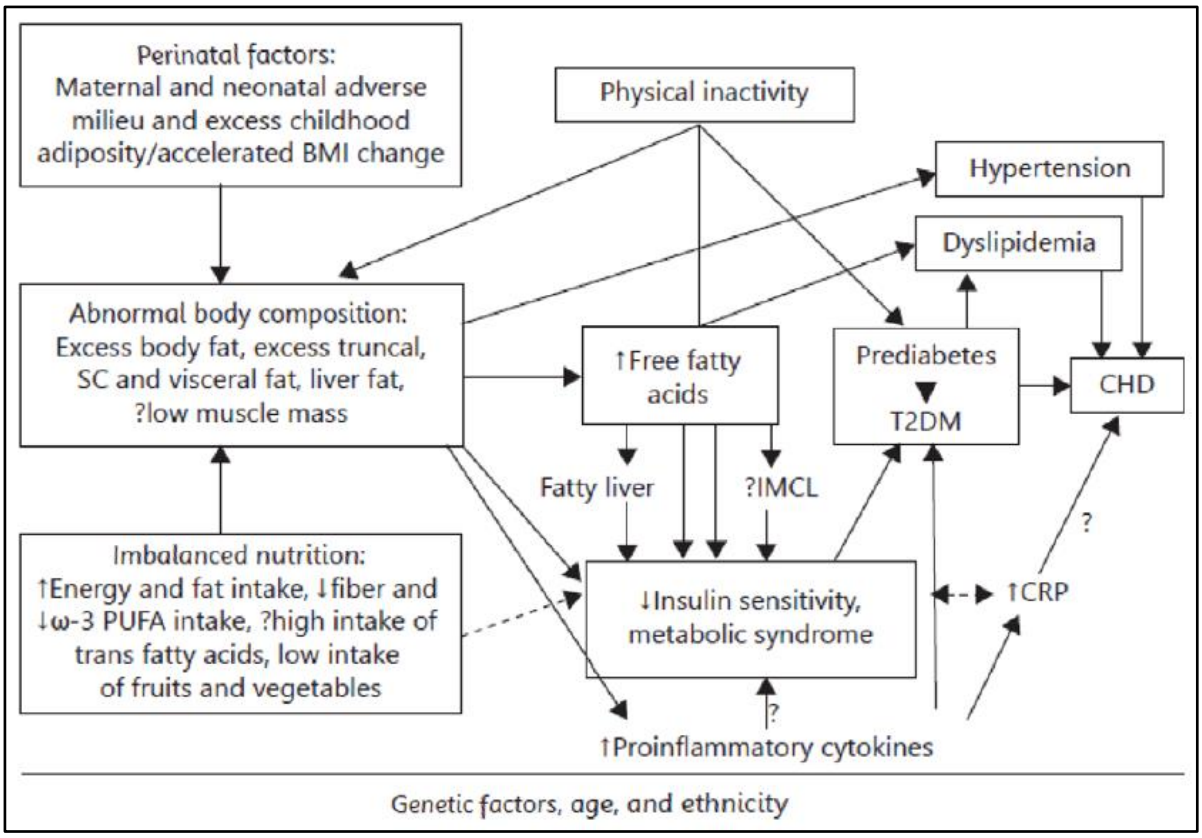


Figure 1. Genetic Factors, Age and Ethnicity

National Obesity and Metabolic Syndrome Summit revised diagnostic cut-offs for BMI and waist circumference for South Asians. The normal values for BMI were established to be 18-22, 9 kg/m^2. Abnormal waist circumference was considered to be more than 90 cm for men and 80 cm for women.

The metabolic risk factors that make up the syndrome include atherogenic dyslipidaemia, elevated blood pressure, dysglycemia, a prothrombotic state and a proinflammatory state. The three main contributing factors of metabolic syndrome are- Obesity, adipose tissue disorders and insulin resistance. Multiple independent factors like ageing, hormones and molecules of vascular, immunologic and hepatic origin also have significant role.

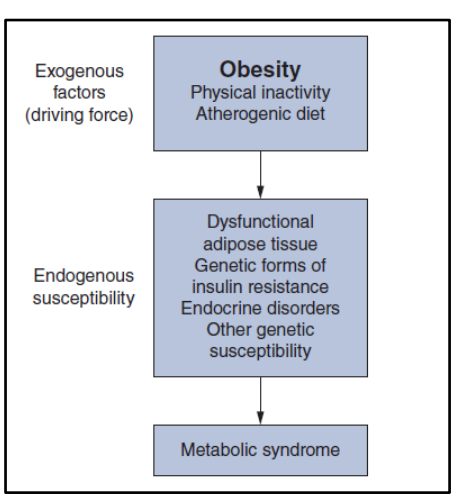


Figure 2. Pathogenic Scheme for Development of Metabolic Syndrome which is a Result of Interaction of Exogenous and Endogenous Factors

The syndrome develops as a result of the interaction of exogenous and endogenous factors.26 Central adiposity is a key feature of the syndrome. Sedentary lifestyle is an emerging risk factor. Compared with individuals who watch television or videos or use the computer <1 hour daily, those who do so for >4 hours daily have a twofold increased risk of the metabolic syndrome. Individuals with the metabolic syndrome are twice as likely to die of cardiovascular disease as those who do not, and their risk of an acute myocardial infarction or stroke is threefold higher.27,28 The approximate prevalence of the metabolic syndrome among patients with Coronary Heart Disease (CHD) is 50%.

Obesity is defined as driving force of metabolic syndrome. A pattern of abdominal obesity (or upper body) obesity correlates with insulin resistance than more strongly with insulin resistance and metabolic syndrome than does lower body obesity.[29] Adipose tissue also release several molecules, which worsen the metabolic syndrome, among them the most important is Non-Esterified Fatty Acids (NEFA). During fasting time, more of NEFA is released and its serum level further rises.

Hormone sensitive lipase is the main lipolytic enzyme. Its activity is increased by catecholamines and reduced by insulin. If excess of NEFA is released by lipolysis, the excess of the NEFA accumulates in fat and liver called as ectopic fat. This ectopic fat leads to increased insulin resistance. The factors like Tumour Necrosis Factor-alpha (TNF-α), interleukin-6 (IL-6) fuel up the pathological process of atherosclerosis. Adipose tissue also releases plasminogen activator inhibitor - 1 and also leptin. Leptin causes satiety. But, in obese individuals, there is leptin resistance in many cases.

It is also to be noted that waist circumference fails to differentiate between the subcutaneous adipose tissue from visceral fat. This is also a major drawback of waist circumference measurement. For the estimation of visceral fat either CT/MRI is required.

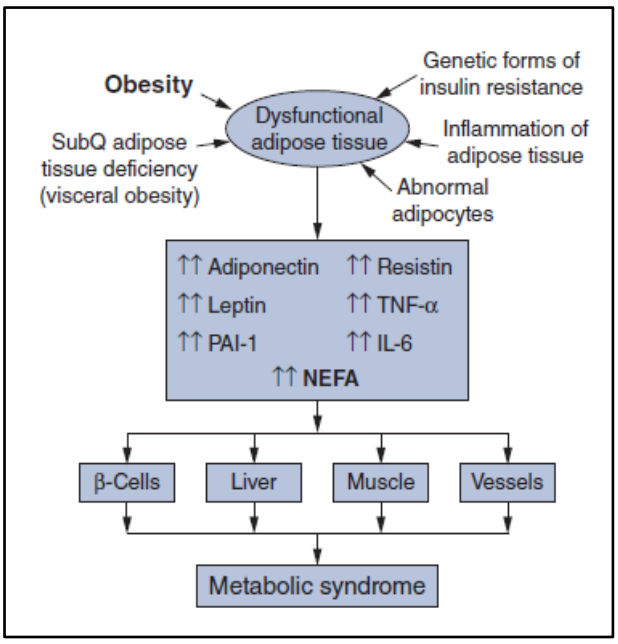


Figure 3. The Role of Obesity and Dysfunctional Adipose Tissue in Causation of the Metabolic Syndrome

Dyslipidaemia, insulin resistance and hypertension are other important factors, which have their individual own role to play in the development of metabolic syndrome.

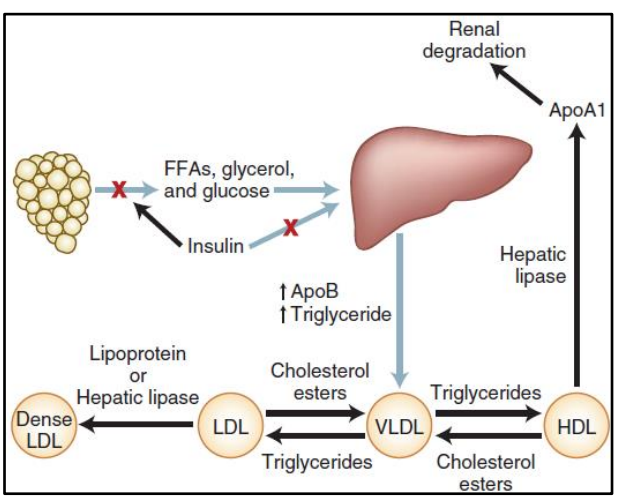


Figure 4. Pathogenesis of Insulin Resistance and Dyslipidaemia

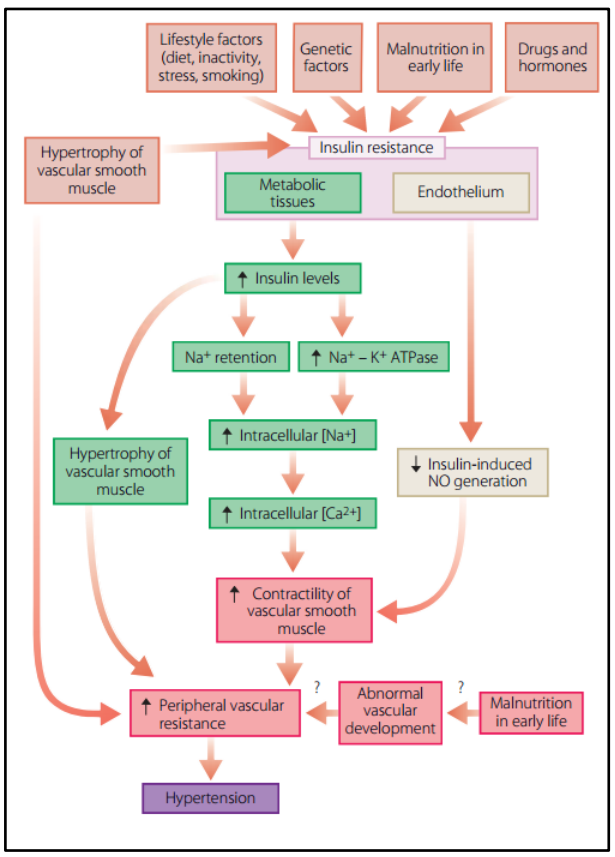


Figure 5. Possible Mechanisms of Hypertension in Insulin Resistance

Clinical features of the metabolic syndrome are not associated with much symptoms. On examination, there may be increased waist circumference and hypertension. Biochemical analysis of the blood may reveal abnormalities. Lipodystrophy and acanthosis nigricans are also seen rarely.

Presence of excess dorsocervical fat (buffalo hump) and excess fat deposit under the chin (double chin) may be used as novel phenotypic markers for insulin resistance and metabolic syndrome among Asian Indians (ref number 64).

Coronary artery disease is 1.5 to 3 times more common in people with metabolic syndrome. The role of Non-Alcoholic Fatty Liver Disease (NAFLD) is unclear in this context. It is unclear that whether it is a manifestation of syndrome or has an active role in the natural history of the disease.[30,31,32] Polycystic Ovarian Disease (PCOD) is increasing with insulin resistance and metabolic syndrome. The prevalence of PCOD is about 40-50%.[33] Obstructive sleep apnoea is also frequently found associated with metabolic syndrome.

The management of metabolic syndrome is by proper screening programme at the right time. It was reported by Vural et al that adolescence maybe the appropriate time to start the interventions. Lifestyle changes and other goals like reducing abdominal obesity, increased physical activity and less atherogenic diet having low-sodium diet will all contribute in preventing the occurrence and also prevent in progression of the disease.

CONCLUSION

The present study was carried out to describe the prevalence of metabolic syndrome in coronary artery disease and to know the concordance of various definitions. There was a statistically significant agreement between two criteria in terms of prevalence.

Metabolic syndrome is rapidly increasing strong risk factor for diabetes mellitus and coronary artery disease. The impact of rapid urbanisation, socioeconomic factors, sedentary lifestyle and alterations in traditional diet pattern are all found to play a major role in increasing prevalence in South Asian populations. Further studies in younger populations without CAD with more variables in the categorisation of study population needs to elucidate whether either definition is a better predictor of CAD.

As association of MS with the severity of CAD was not assessed. This is one of the limitation of this study.

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