

A study of metabolic syndrome in newly diagnosed patients of type 2 diabetes mellitus in the tertiary care centre of Kumaun region

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Abstract

Introduction: Diabetes mellitus is the commonest metabolic abnormality in the world. Prevalence of type 2 diabetes is especially increasing in developing countries. The metabolic syndrome (Syndrome X) consists of a constellation of metabolic abnormalities that increase the risk of micro and macrovascular complications of type 2 diabetes mellitus. The major features of metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycaemia, and hypertension. The metabolic dysregulation associated with diabetes mellitus and metabolic syndrome cause secondary pathophysiologic changes in multiple organ system that impose a tremendous burden on the individual with diabetes and on the health care system. **Material and Methods:** - 100 Patients of age group 20-60 years with newly diagnosed type 2 diabetes mellitus were included in the study. Detailed physical and anthropometric examinations were done in all patients. Estimation of extended lipid profile including Apo B, KFT and microalbuminuria were done. **Results:** Of the 100 patients studied, 58 patients had metabolic syndrome according to the International Diabetes Federation criteria 2006. 85% of the patients with metabolic syndrome were either overweight or obese (calculated by their body mass index) as compared to 15% of patients without metabolic syndrome. Waist hip ratio was increased in 33% of males with metabolic syndrome and 100% of females with metabolic syndrome. Serum triglyceride ($p < 0.009$), VLDLc ($p < 0.007$) and microalbuminuria ($p < 0.01$) levels were significantly elevated in patients of metabolic syndrome as compared to those without metabolic syndrome. **Conclusion:** The present study shows that metabolic syndrome is increasingly present in patients with type 2 diabetes mellitus in the Kumaun region of Uttarakhand. Physicians treating type 2 diabetics should consider metabolic syndrome with greater emphasis in their patients and advice early intervention, to delay the development of micro and macrovascular complications of diabetes mellitus.

Keywords: Diabetes, Metabolic syndrome.

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INTRODUCTION

Diabetes Mellitus is the commonest metabolic abnormality in the world. Type 2 diabetes the commonest form of diabetes constitutes nearly 90% of diabetic population in any country. Prevalence of type 2 diabetes is increasing in most of the countries especially in developing countries.¹ Most people with type 2 diabetes are overweight and develop hyperglycemia as a result of

insulin resistance and insulin deficiency. Besides being overweight, some of the risk factors for developing type 2 diabetes include physical inactivity, first-degree relative with diabetes.² The metabolic dysregulation associated with diabetes mellitus cause secondary pathophysiologic changes in multiple organ system that impose a tremendous burden on the individual with diabetes and on the health care system. With an increasing incidence worldwide, diabetes mellitus will be a leading cause of morbidity and mortality for the foreseeable future. The Metabolic Syndrome (syndrome X, insulin resistance syndrome) consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease and diabetes mellitus. In 1988, Reaven introduced the term syndrome X, with insulin resistance as a common denominator for the syndrome.³ In addition to syndrome X, several other synonyms have been proposed such as deadly quartet, DROP syndrome (dyslipidemia, insulin resistance, obesity, and high blood pressure),

multiple metabolic syndrome, and insulin resistance syndrome.⁴ The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia, and hypertension. According to the new International Diabetes Federation (IDF) 2006 definition, for a person to be defined as having the metabolic syndrome they must have:

- Central Obesity (defined as waist circumference with ethnicity specific values).
- Plus any two of the following four factor:
- Raised Triglycerides > 150 mg/dl (1.7 mmol/L) or specific treatment for this lipid abnormality.
- Reduced HDL Cholesterol < 40 mg/dl (1.03 mmol/L) in males, < 50 mg/dl (1.29 mmol/L) in females or specific treatment for this lipid abnormality.
- Raised Blood pressure- Systolic Blood pressure >130 mmHg or Diastolic Blood pressure > 85 mmHg or treatment of previously diagnosed Hypertension.
- Raised Fasting Plasma Glucose >100 mg/dl (5.6 mmol/L) or previously diagnosed type 2 diabetes. If above 5.6 mmol/L or 100 mg/dl, oral glucose tolerance test (OGTT) is strongly recommended but is not necessary to define presence of the syndrome.

(If BMI is > 30 kg/m², central obesity can be assumed and waist circumference does not need to be measured.)

Insulin resistance describes the condition whereby there is a resistance to insulin mediated glucose uptake by cells and is central to the clustering of multiple metabolic abnormalities and clinical syndromes. The clustering phenomenon was first described by Kylin in 1923 when he described the clustering of three clinical syndromes: hypertension, hyperglycemia, and hyperuricemia.⁵ Obesity is a chronic health problem affecting increasing number of people worldwide and is now recognized as a global epidemic. In India, obesity is emerging as an important health problem particularly in urban areas, paradoxically co-existing with under nutrition. Simple measures of obesity are widely used in clinical practice; Body Mass Index (BMI), and waist-to-hip circumference ratio (WHR). The most widely used method to define thinness and fatness is BMI, a ratio of weight in kilograms divided by height in meters squared (kg/m²). Abdominal obesity is defined by easy-to-use parameters with WHR. Though BMI, WHR correlate well with each other, it is also believed that combined use of these parameters of generalized and abdominal obesity may be better in identifying people at risk of cardiovascular disease (CVD) than either of them alone.⁶ Hypertension is a very common condition which frequently remains undiagnosed until relatively late in its course, leading to a variety of

other life-threatening conditions like kidney damage and heart failure. It is a very prominent feature of the metabolic syndrome, present in up to 85% of patients. Hypertension is associated with the laboratory and anthropometric findings linked to the metabolic syndrome. One of the proposed mechanisms by which hypertension is linked with central obesity includes sympathetic nervous system over activation.⁷ C-reactive protein is an acute-phase protein of hepatic origin that increases following interleukin-6 secretion from macrophages and T cells. Inflammation, as assessed by C-reactive protein (CRP), is emerging as a predictor of cardiovascular disease (CVD), and it may be an important precursor of the metabolic syndrome.⁸ Microalbuminuria is also considered to be a predictor for cardiovascular disease both among diabetic and non-diabetic subjects.⁹ Hyperuricemia is associated with components of metabolic syndrome. A study has suggested fructose-induced hyperuricemia may play a pathogenic role in the metabolic syndrome.¹⁰ Considering the fact that the presence of metabolic syndrome in type 2 diabetes mellitus patients identifies those at increased risk of diabetic complication¹, and that metabolic syndrome is an independent clinical indicator of macrovascular and microvascular complication in diabetes mellitus¹, the objectives of the present study were to study the incidence of metabolic syndrome in newly diagnosed patients of type 2 diabetes mellitus, to evaluate the parameters of obesity, dyslipidemia, hypertension, inflammation and renal damage in the study subjects and to study the correlation between markers of obesity, dyslipidemia, hypertension, inflammation and renal damage in patients of diabetes mellitus with and without metabolic syndrome.

MATERIALS AND METHODS

The present study was carried out in the Department of Biochemistry, in association with the Department of Medicine, Government Medical College, Haldwani, during the period of 2014 to 2015 among 100 patients of newly diagnosed type 2 diabetes mellitus with age group 20-60 years. Patients with gestational diabetes mellitus were excluded from the study.

After a written informed consent, all patients were subjected to detailed history and thorough clinical examination.

Statistical Analysis

Results were expressed as mean ± SD. The data were analyzed with the help of SPSS software program using the relevant tests of significance such as Unpaired 't' test. A level of p < 0.05 was accepted as statistically significant.

OBSERVATIONS AND RESULTS

The present study was carried out in the Department of Biochemistry, in association with the Department of Medicine, Government Medical College Haldwani. The study subjects were newly diagnosed patients of type 2 diabetes mellitus attending the Medicine OPD of Government Medical College Haldwani. A total of 100

patients both male and female, were included in the study. **Fig.1** shows the age and sex distribution among the studied patients. All the patients studied were of the age group 25-60 years. 42% of the patients were in the age group 36-45 years followed by 38% within 46-55 years, 12% within 56-60 years and 8% within 25-35 years.

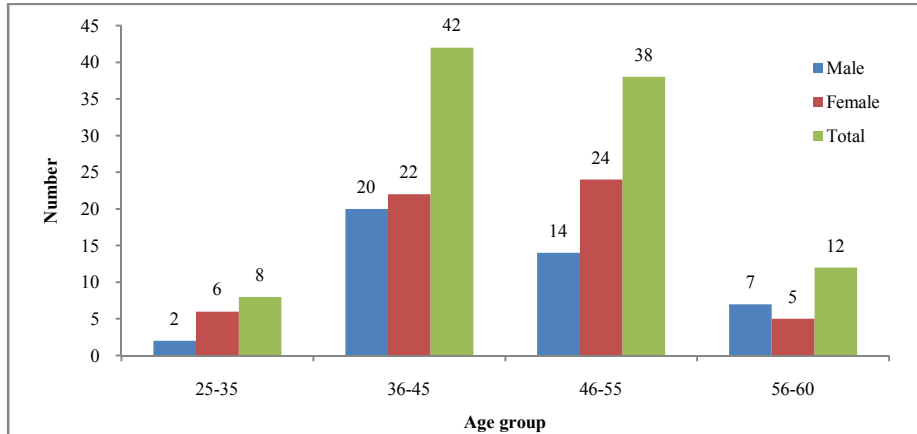


Figure 1: Age and Sex distribution of study subjects

Of the 100 patients studied, 58 patients has metabolic syndrome according to the International Diabetes Federation (IDF) criteria. Table 1 shows the age and sex distribution of patients with metabolic syndrome. 43 % of the patients with metabolic syndrome were in the age group 36-45 years followed by 38% within 46-55 years, 10% 25-35 years and 9% 56-60 years. Of all the patients with metabolic syndrome 60% were female. 24% of females with metabolic syndrome were in the age group 46-55 years, 22% within 36-45 years, 10% within 25-35 years and 4% within 56-60 years and 21% of males with metabolic syndrome were in the age group 36-45 years, 14% within 46-55 years and 5% within 56-60 years.

Table 1: Age and Sex distribution of patients with metabolic syndrome

Age group (years)	Male		Female		Total	
	No	%	No	%	No	%
25-35	0	0	6	10	6	10
36-45	12	21	13	22	25	43
46-55	8	14	14	24	22	38
56-60	3	5	2	4	5	9
Total	23	40	35	60	58	100

Table 2: Distribution of study subjects according to their Body Mass Index (According to WHO criteria)

Weight (based on BMI) kg/m ²	Male		Female		Total %
	No	%	No	%	
Under weight (≤ 18)	1	1	2	2	3
Normal (18-24)	17	17	24	24	41
Over weight (25-29)	16	16	21	21	37
Obese (>30)	9	9	10	10	19
Total	43	43	57	57	100

Table 2 shows the distribution of study subjects according to their BMI. Among male patients 17% were normal weight, 16% were overweight, 9% were obese and 1% was under weight. Among female patients 24% were normal weight, 21% were overweight, 10% were obese and 2% were underweight. Out of all patients 41% were normal weight, 37% were overweight, 19% were obese and 3% were underweight.

Table 3: Distribution of patients according to Waist Hip Ratio

WHR	Male (n=43)		Female (n=57)		Total No
	<0.90	>0.90	<0.85	>0.85	
NO	10	33	0	57	100

Table 3 shows the distribution of WHR in the studied subjects. The normal WHR ratio in male is <0.90 and female is <0.85. Among the studied subjects 33 males had increased WHR, whereas all the females had WHR > 0.85.

Table 4: Systolic blood pressure, Diastolic blood pressure and waist circumference in study subjects

Variables	Male with MS	Female with MS	Male without MS	Female without MS	Range (mmHg)
SBP (mmHg)(mean±SD)	140.26±2.08	133.25±1.46	129.1±1.24	128±1.22	120
DBP (mmHg) (mean±SD)	86.65±1.22	83.42±0.97	79.6±0.98	78.36±0.88	80
Waist circumference (cm) (mean±SD)	96.26±1.01	90.34±0.68	85.65±0.57	75.63±0.25	Male < 90 Female <80

Table 4 shows mean of systolic, diastolic blood pressure and mean of waist circumference in patients with and without metabolic syndrome. Among male subjects with metabolic syndrome mean SBP was 140.26±2.08 and mean DBP was 86.65±1.22 whereas in female subjects with metabolic syndrome mean SBP was 133.25±1.46 and mean DBP was 83.42±0.97. The mean waist circumference in males with metabolic syndrome was 96.26±1.01 and in females with metabolic syndrome was 90.34±0.68.

Table 5: HbA1c and serum uric acid levels in studied subjects (mean ± SD).

Variables	With MS (58)	Without MS (42)	Range	P value
HbA1c (%)	8.39±0.20	7.30±0.25	4.8-5.9	0.01
S. Uric acid (mg/dl)	4.85±0.14	4.57±0.22	Male 3.4 – 7.0 Female 2.4 – 5.7	NS

Estimation of HbA1c and serum uric acid was done in all patients with metabolic syndrome (n=58) and without metabolic syndrome (n=42). Table 5 shows the mean plasma HbA1c levels in patients with metabolic syndrome (8.39 ± 0.20) and without metabolic syndrome (7.30±0.25). The mean level was 1.09 times higher in patients with metabolic syndrome as compared to without metabolic syndrome. This difference in the mean level was found to be statistically significant (p<0.01). The mean serum uric acid levels in patients with metabolic syndrome (4.85 ± 0.14) and without metabolic syndrome (4.57 ± 0.22). No significant difference was found in uric acid levels in patients with metabolic syndrome as compared to without metabolic syndrome.

Table 6: Serum HDLc, LDLc, VLDLc and TG levels in the studied subjects (mean ± SD).

Variables	With MS (58)	Without MS (42)	Range (mg/dl)	P value
HDLc	40.03±1.12	42.51±1.51	Male > 55 Female > 65	NS
LDLc	114.60±5.01	108.10±6.75	90 – 130	NS
VLDLc	40.45±2.34	31.10±2.15	10 – 30	0.007
TG	256.52±24.92	166.74±13.59	< 150	0.009

Estimation of serum HDLc, LDLc, VLDLc and TG levels was done in all patients with metabolic syndrome (n=58) and without metabolic syndrome (N=42). The final result was expressed as mg/dl. **Table 6** shows the mean serum HDLc levels in patients with metabolic syndrome (40.03±1.12) and without metabolic syndrome (42.51±1.51). No significant difference was found in HDLc levels in patients with metabolic syndrome as compared to without metabolic syndrome. The mean serum LDLc levels in patients with metabolic syndrome (114.60±5.01) and without metabolic syndrome (108.10±6.75). No significant difference was found in LDLc levels in patients with metabolic syndrome as compared to without metabolic syndrome. The mean serum VLDLc levels in patients with metabolic syndrome (40.45±2.34) and without metabolic syndrome (31.10±2.15). The mean VLDLc level was markedly raised in patients of metabolic syndrome as compared to without metabolic syndrome. This difference was found to be significant (p <0.007). The mean serum triglyceride levels in patients with metabolic syndrome (256.52±24.92) and without metabolic syndrome (166.74±13.59). The mean triglyceride level was markedly raised in patients of metabolic syndrome as compared to without metabolic syndrome. This difference was found to be significant (p<0.009).

Table 7: Serum Apo B, hs-CRP and Microalbuminuria levels in the studied subjects (mean ± SD).

Variables	With MS (58)	Without MS (42)	Range	P value
Apo B	76.89±3.92	75.28±3.67	69 – 105 mg/dl	NS
hs-CRP	6.35±1.07	7.09±1.30	1 – 3 µg/ml	NS
Microalbuminuria	549.34±68.80	456.74±33.04	28 – 140 mg/24hrs	0.01

Estimation of serum Apo B, hs-CRP and Microalbuminuria levels was done in all patients with metabolic syndrome (n=58) and without metabolic syndrome (n=42). **Table 7** shows the mean serum Apo B levels in patients with metabolic syndrome (76.89±3.92) and without metabolic syndrome (75.28±3.67). No significant difference was found in Apo B levels in patients with metabolic syndrome as compared to without metabolic syndrome. The mean serum hs-CRP levels

in patients with metabolic syndrome (6.35 ± 1.07) and without metabolic syndrome (7.09 ± 1.30). There was no significant difference between the mean serum levels of hs-CRP in patients with and without metabolic syndrome. The mean microalbuminuria levels in patients with metabolic syndrome (549.34 ± 68.80) and without metabolic syndrome (456.74 ± 33.04). The mean microalbuminuria level was markedly raised in patients of metabolic syndrome as compared to without metabolic syndrome. This difference was found to be markedly significant ($p < 0.01$).

Table 8: Correlation between waist circumference with TG and microalbuminuria levels in patients of metabolic syndrome (n= 58)

	WC (cm)	TG (mg/dl)	Microalbuminuria (mg/24hrs)
Mean \pm SD	92.11 \pm 0.72	256.52 \pm 24.92	549.34 \pm 68.80
Correlation coefficient (r)		0.956	0.256
S.E.OF 'r'		0.363	0.256
Pvalue		<0.01	<0.05
Regression Coefficient(b)		0.885	0.311
'a' value		25.39	72.07

Table 8 shows the correlation of waist circumference with TG and microalbuminuria levels in patients of metabolic syndrome. Waist circumference had significant positive correlation with TG ($r=0.095$; $p<0.01$) and microalbuminuria ($r = 0.025$; $p < 0.05$). Our study shows that metabolic syndrome was increasingly present in patients with type 2 diabetes mellitus in the Kumaoun region. The population studied also showed high incidence of obesity and increase WHR. Our study also shows that significant dyslipidemia was present in patients with metabolic syndrome. Patients with metabolic syndrome also showed increased HbA1c and microalbuminuria levels. Our study showed significant correlation between waist circumference with TG and microalbuminuria levels in patients of metabolic syndrome.

DISCUSSION

Metabolic syndrome is a cluster of cardiovascular risk factors. The components of metabolic syndrome are obesity, hypertension, low glucose tolerance and dyslipidemia. Association of other components of metabolic syndrome with diabetes mellitus increases the risk of cardiovascular complications significantly. Insulin resistance and consequent diabetes mellitus are major component of metabolic syndrome. The metabolic syndrome accelerates both macrovascular and microvascular complications frequently observed in diabetes mellitus. The presence of metabolic syndrome in type 2 diabetes mellitus patients identifies those at increased risk of diabetic complication.¹ In the Kumaun region of Uttarakhand very few documented studies have been done on metabolic syndrome in diabetic patients. The present study was carried out in the Department of Biochemistry, in association with the Department of Medicine, Government Medical College Haldwani. The study was done over a period of one year. The objectives of the present study were to study the incidence of metabolic syndrome in newly diagnosed patients of type

2 diabetes mellitus, to evaluate the parameters of obesity, dyslipidemia, hypertension, inflammation and renal damage and to study the correlation between markers of obesity, dyslipidemia, inflammation and renal damage in patients of diabetes mellitus with and without metabolic syndrome. In the present study, according to the new International Diabetes Federation (IDF) 2006, out of 100 patients studied, 58 patients met the criteria of metabolic syndrome (**Table 1**). Alshkri and Elmehdawi found that prevalence of metabolic syndrome among type 2 diabetes mellitus patients in Libya was 92% according to NCEP-ATP III criteria and 80.8% according to IDF criteria.¹ Lin *et al*, found it to be 70% in USA, according to NCEP-ATP III criteria.¹ Monamiet *al*, found in Italy to be 68.4% according to NCEP-ATP III criteria and 73.7% according to IDF criteria.¹ Lu *et al*, found that prevalence of metabolic syndrome among type 2 diabetes mellitus patients in UK was 61% according to NCEP-ATP III criteria and 54% according to IDF criteria.¹ Our study showed that 60% of the patients of metabolic syndrome were female. There were overall female predominance with metabolic syndrome. In the study of Alshkri and Elmehdawi, out of 99 patients, 61 were female and 38 were males.¹ The results are comparable with the present study. Ford *et al*, found that prevalence of metabolic syndrome were more common in male which is in contrast with this study.¹¹ In conjunction with worldwide recognition of the metabolic syndrome, the size of waist circumference as an estimate of visceral obesity has been a matter of controversy. The International Diabetes Federation (IDF) has adopted different cut offs for waist circumference in different ethnicities;¹ the cut off points for Europids are 94 cm in men and 80 cm in women while those for Chinese, South Asians and Japanese are 90 in men and 80 in women.¹² In our study 67% of the diabetic patients had increased waist circumference, of which 58% met all the criteria for metabolic syndrome. In our study the mean waist circumference in patients of metabolic syndrome was (96.26 ± 1.01 cm) in males and

(90.34±0.68 cm) in females (**Table 4**). In a study by Oscar H *et al*, waist circumference in normal subjects was (89.016±13.056cm) and in diabetics (102.656± 11.52 cm), and incidence of metabolic syndrome was 40.6%.¹³ Abdominal obesity characterized by high waist circumference is a stronger predictor than generalized obesity defined by elevated Body Mass Index (BMI) of subsequent development of major coronary event, vascular mortality, diabetes and metabolic syndrome. BMI was calculated by the formula weight in kg/ (height in meter)². Overweight is defined as a BMI of 25-29 and obese as a BMI >30 (WHO, 1998). It is known that Indians are prone to developing diabetes at a lower BMI in comparison to the western population. Waist-hip ratio (i.e. the waist circumference divided by the hip circumference) was suggested as an additional measure of body fat distribution. The ratio can be measured more precisely than skin folds, and it provides an index of both subcutaneous and intraabdominal adipose tissue. The suggestion for the use of proxy anthropometric indicators arose from a 12-year follow-up of middle-aged men, which showed that abdominal obesity (measured as waist-hip ratio) was associated with an increased risk of myocardial infarction, stroke and premature death, whereas these diseases were not associated with measures of generalized obesity such as BMI.¹⁴ In our study WHR was increased in all the females studied (>0.85) while 33% of males had increased WHR (> 0.90) (**Table 3**). Results of the European Fat Distribution Study demonstrated importance of abdominal fat and greater WHR in cardiovascular and coronary heart disease mortality.¹⁵ Among Indians too, studies have shown that WHR is an important cardiovascular risk factor and greater levels are associated with multiple risk factors. Gupta R *et al*, reported that WHR >0.9 in men and >0.8 in women is associated with a significant increase in multiple risk factors. These cut-offs are similar to those suggested by earlier reports of US National Cholesterol Education program (ATP-II) (1994). Sanya *et al*, had lower prevalence rate than that of previous study for obesity utilizing WHR, it is noteworthy that it was a crude rate for both men and women.¹⁶ HbA1c is the most commonly measured parameter for long term monitoring of diabetes mellitus. The level of HbA1c has been widely accepted as an indicator of mean daily blood glucose concentration over the preceding 8-12 weeks. In our study HbA1c levels were significantly elevated (p < 0.01) in patients of metabolic syndrome as compared to without metabolic syndrome (**Table 5**). Osei *et al*, reported that in 219 non-diabetic, obese, first-degree relatives of African-American patients with Type 2 diabetes, the upper tertile of HbA1c reflected some components of metabolic syndrome. These results suggest that HbA1c may be a

surrogate marker not only of future diabetes, but also of CVD. Although there are many studies which report the utility of HbA1c in predicting CVD and diabetes, there are few which investigate the usefulness of HbA1c as a predictor of metabolic syndrome. Osei *et al*, observed that metabolic syndrome group showed significantly higher glucose, HbA1c levels and waist circumference.¹⁷ Elevated serum uric acid concentration is a common laboratory finding in subjects with metabolic syndrome/obesity, hypertension, kidney disease and cardiovascular events. Hyperuricemia has been attributed to hyperinsulinemia in metabolic syndrome and to decreased uric acid excretion in kidney dysfunction and is not acknowledged as a main mediator of metabolic syndrome, renal disease, and cardiovascular disorder development. Hyperuricemia is commonly observed in metabolic syndrome and numerous epidemiological investigations have confirmed the association of hyperuricemia with metabolic syndrome.¹⁸ While it has been suggested that uric acid may simply be a consequence of the increased uric acid absorption in the proximal tubule secondary to hyperinsulinemia,¹⁸ there is growing data that uric acid may predict the development of metabolic syndrome, obesity and diabetes.¹⁹ In the present study there was no significant difference between serum uric acid levels in patients of metabolic syndrome as compared to without metabolic syndrome (**Table 5**). Associations of high uric acid levels and the development of type 2 diabetes have been documented. A meta-analysis of 11 studies has revealed that every mg/dl increase in uric acid level is associated with 17% increased risk of diabetes. Serum uric acid being a risk factor is currently controversial, there is little controversy regarding its association as a risk marker associated with cardiovascular and renal disease.²⁰ LK Niskanen's *et al*, recently published article has demonstrated new information regarding this subject. They were able to demonstrate that elevation of serum uric acid level were independent of variables commonly associated with gout or the metabolic syndrome in association with CVD mortality in middle aged men.²¹ Kannelet *et al*, noted elevated serum uric acid was also associated with an increased risk of coronary heart disease for men aged 30-59.²² Chronic kidney disease (CKD) has become a worldwide public health problem and microalbuminuria an early marker of CKD. Many studies have shown that microalbuminuria is a strong and independent predictor of progressive CKD in diabetics and even in the general population. Microalbuminuria levels were found to be higher in patients with metabolic syndrome than without metabolic syndrome and were found to be significantly elevated (p<0.01) in the present study (**Table 7**). This finding is in agreement with several other finding. The

results from two Chinese studies demonstrated that all metabolic syndrome components were associated with microalbuminuria.²³ Study by Kundu D,²⁴ found microalbumin levels to be higher in cases and also found to be statistically significant in cases ($p < 0.01$). Klausen K.P,²⁵ also found strong association between microalbuminuria and metabolic syndrome. The increased microalbumin levels in diabetic subjects may be due to an altered glomerular filtration barrier, at the podocyte level. Damage to the podocyte may be explained by the fact that there is an increase in the extracellular release of reactive oxygen species. Dyslipidemia, the major constituent of the metabolic syndrome, is characterised as an increased free fatty acid, triglyceride, small dense LDLc and low HDLc levels. The hypertriglyceridemia seen with abdominal obesity and insulin resistance is related to the oversecretion of triglyceride-rich VLDL particles. An increased rate of hepatic FFA uptake stimulates the secretion of Apo B-100, leading to increased numbers of Apo B containing particles and possibly hypertriglyceridemia. HDL and VLDL metabolism are closely linked, which explains why increased plasma triglyceride is almost always associated with reduced HDLc levels. Cholesterol ester transfer protein mediates the exchange of triglyceride in VLDL for cholesterol ester in LDL and HDL, leading to the production of triglyceride-rich LDL and HDL particles. Subsequent hepatic lipase-mediated hydrolysis of these particles leads to the generation of small, dense LDL particles and a decrease in HDL cholesterol.²⁶ In our study serum VLDLc ($p < 0.007$) and serum triglyceride ($p < 0.009$) levels were significantly elevated in patients of metabolic syndrome as compared had without metabolic syndrome (**Table 6**). Whereas no significant difference was found between HDLc and LDLc (**Table 6**). Dyslipidemia is a widely accepted risk factor for coronary heart disease. Study by Prasad VS, observed high levels of serum triglyceride with metabolic syndrome than without metabolic syndrome and found to be extremely significant statistically according to NCEP-ATP III criteria. Prasad VS also showed that relative risk of Myocardial infarction correlates directly with increased triglyceride and inversely with HDL-c levels in both Caucasians and Asians Indians.²⁷ Apo B is one of the component found in chylomicron, VLDL, intermediate density lipoprotein and LDL. The association of Apo B with diabetes and metabolic syndrome has been shown, as it has potential role as a subclinical inflammatory agent. Apo B is a good surrogate measure of increased LDL particle numbers in people with metabolic syndrome and insulin resistance, and small LDL particle number was best correlated with Apo B (and triglycerides and HDL-cholesterol) in the Framingham Heart study.²⁸ The

present study shows Serum Apo B levels was not significantly elevated in patients of metabolic syndrome (**Table 7**), whereas Lim *et al*,²⁹ found serum Apo B to be higher in diabetic patients with metabolic syndrome than those without metabolic syndrome, and this difference was significant even after correcting with LDLc. Ryoo *et al*, conducted a cohort study which followed up 25,193 healthy Korean males without metabolic syndrome for 5 years, and reported that Apo B was a predictive factor for metabolic syndrome. During 5 years of follow up, 5,407 (21.5%) were diagnosed with metabolic syndrome, and there was a significant positive correlation between the occurrence of metabolic syndrome Apo B levels.³⁰ High sensitive C-reactive protein (hsCRP) is an acute phase reactant and a sensitive marker of systemic inflammation has been found to be raised in the conditions like diabetes mellitus, cardiovascular diseases, peripheral vascular disorders. Previous studies have proved that type 2 DM is frequently associated with chronic inflammatory state. Thus, chronic inflammation plays an important role in the development and progression of late complications of diabetes. It predicts the mortality in patients with type 2 diabetes mellitus. This emphasizes the utility of estimating hsCRP as cardiometabolic risk factor.³¹ Present study shows serum hs-CRP levels are not significantly elevated in patients of metabolic syndrome (**Table 7**). A number of studies show that both metabolic syndrome and elevated CRP are associated with increased incidence of cardiovascular events. In the epidemiological studies like West of Scotland Coronary Prevention Study, an 18-year follow up of 14,719 initially healthy American women, and in the Framingham Offspring Study it was shown that metabolic syndrome and CRP are associated with increased cardiovascular morbidity and mortality. CRP is released by the liver following stimulation by interleukin-6, and is also locally produced in atheromatous lesions. Although most studies relied on a single measurement of CRP, this is not expected to affect the results, as CRP levels have been shown to be stable with little or no diurnal variation, making CRP the most commonly used and best standardised inflammatory marker of cardiovascular and metabolic disorders.³²

Correlation between WC with TG, HDLc, hs-CRP, HbA1c and microalbuminuria levels in studied subjects

In present study positive correlation was found between waist circumference with triglyceride, hs-CRP, HbA1c and microalbuminuria levels except HDLc which showed negative correlation with waist circumference (**Table 8**). Fared F *et al*, found positive correlation between triglyceride, systolic and diastolic blood pressure except HDLc which showed a negative correlation with waist

circumference.³³ K. Tamakoshi *et al*, showed a significant positive correlation between obesity with triglyceride and hs-CRP levels, whereas negative correlation with HDLc.³⁴ Mendallet *et al*, reported that hs-CRP was associated with triglyceride and negative associated with HDLc.³⁵ Esteghamati *et al*, who found that there were positive correlation between waist circumference and blood pressure and dyslipidemia.³⁶ In a study by Sudha Vidyasagar *et al*, positive correlation was found between obesity and hs-CRP and diabetes mellitus.³⁷ previous studies³⁸ have shown a positive correlation between obesity and hs-CRP. Jasmine Sutkovie *et al*, reported positive correlation between waist circumference and HbA1c.³¹

CONCLUSION

The present study shows that metabolic syndrome is increasingly present in patients with type 2 diabetes mellitus in the Kumaun region of Uttarakhand. Physicians treating type 2 diabetics should consider metabolic syndrome with greater emphasis in their patients and advice early intervention like regular exercise, dietary modification, periodical checking of microalbuminuria and lipid lowering agents as needed to delay the development of micro and macrovascular complications of diabetes mellitus. Overall, metabolic syndrome can serve as a simple clinical approach to identify a person for intervention to reduce obesity and cardiovascular and renal complications. This can lead to decreased morbidity and mortality from microvascular and macrovascular complication in patients of type 2 diabetes mellitus and significantly enhance their life style. Identifying patients with metabolic syndrome and proper intervention in type 2 diabetes mellitus will also significantly reduce the burden on state health services.

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