5. DISCUSSION

Majority of the south Asian countries are in developing phase with low human development index (HDI). Illness puts a high burden on families in developing countries. Globalization has brought different countries of the world close to each other in many ways. A number of deadly diseases have spread beyond their traditional boundaries due to globalization. Developing nations are striving to attain a better economic status. The side effect of upswing in economy is a switch to sedentary habits, with India being no exception. Physical inactivity and high calorie food increase obesity, diabetes mellitus, hypertension, dyslipidemia and all-cause mortality. High prevalence of metabolic syndrome (MS) seen earlier in the affluent countries is now affecting developing countries also due to economic growth and change in lifestyle.

5.1 Prevalence of MS: The prevalence of MS in developed counties is more than in developing countries. Mishra et al. observed that MS is increasing exponentially in India, in both the urban and rural areas showing the prevalence range from 11% to 41%. The prevalence of MS in men and women shows a wide variation around the world. Deepa et al. found the prevalence of MS in south Indian population to be 18.3%. Another study from Bangalore by Kanjilal et al. concluded that prevalence of MS was 40.3%. A study conducted in rural area of district Wardha, Maharashtra found the overall prevalence of MS as 9.3%. The prevalence of MS was found to be 9.2% in rural part of district Ambala of Haryana. The prevalence of MS is rising throughout India. Initially it was seen in urban areas only. According to a study, the prevalence of MS is increasingly getting affected because of transformation in life style of the rural people. Selvaraj et al. reported 36% prevalence of MS in a south Indian study on rural women. Prasad et al. observed a prevalence rate of 33.5% in urban Eastern India. Punith et al. found that the prevalence of MS is rising in the rural areas of the country. This is likely to be due to the impact of changing life style and change in nutritionalstatus.

5.2 Age and Sex ratio: In the present study, 51.25% patients were male and 48.75% were female, constituting male to female ratio of 1.05:1.00. Majority of patients were in the age group of 41-50 years (N=75, 26.89%) followed by the age group of 51-60 (N=68, 24.37%). Mean age of all patients was 50.37±13.99 years (Males 49.77±13.77 years and Females 50.98±14.25 years). A study from Bangalore has reported maximum prevalence of MS in the age group of 50-59 years. An Indian multi-centric study on industrial population has found the highest prevalence of MS was seen in the age group of 60 years. In a study on 21-94 years-old subjects, the highest prevalence of MS was seen in the age group of 65-74 years and lowest was seen in the age group of 21-34 years in an African-American population. The differential distribution in different age
groups is reportedly due to differences in life style, work habits and food types. The prevalence of metabolic syndrome was found to be higher among females as compared to males in a number of studies.\textsuperscript{210,211,212,213} It has been reported that males and females between 40 and 59 years were three times more likely to have MS as compared with those ranging in age from 20–39 years.\textsuperscript{214} Shasha et al. also observed that the females had higher prevalence of MS while males had increasing trend in rural northeast China.\textsuperscript{215} However, Gisela et al. observed that the prevalence of MS in females was 22.7\% and in males 23.3\%; thus, in their study the female/male ratio was 0.98.\textsuperscript{216} Our results are similar because in our study, female and male ratio was 0.95. Park et al. observed the association of MS with advanced age for both men and women with greater prevalence of MS in middle-aged men than in women; these patterns were reversed in people 60 years or older.\textsuperscript{217} It is clear that prevalence of MS changes with age.

\textbf{5.3 Life style and socio-demographic classes:} The patients were divided into sedentary work, moderate work, and hard work group\textsuperscript{218}. There was only one patient in the hard work group, 183 patients fell in the moderate work group and 95 in the sedentary work group. Thus maximum number of MS cases belonged to the moderate work group.

According to socio-demographic classification, the patients were divided into lower class, middle class, and upper class. There was no patient in the upper class, 105 patients in the middle class and 174 patients in the lower class. Thus, maximum patients were in the lower class.

Metabolic syndrome is usually believed to afflict high-income sedentary persons. But in the present rural sample of MS patients, lower income and moderately active persons outnumber the middle income and sedentary persons. As shown later, obesity was not a common component of MS in the present sample. Thus, majority of patients are non-obese, low-income and moderately active. This is in contrast to urban MS patients. A comparison with other studies is not possible as similar studies in rural areas are scanty.

\textbf{5.4 BMI:} The World Health Organization has described BMI as the most useful epidemiological measures of obesity and it is most commonly used to track obesity and related diseases although BMI does not account for the distribution of body fat.\textsuperscript{219,220} Obesity is a curse of modern and sedentary life style. When the prevalence of obesity was determined in our MS patients according to BMI, 46.95\% patients were normal-weight, 29.39\% were overweight and 23.66\% were obese. 20.98\% and 32.87\% of males were found respectively in obesity and overweight group. Female MS patients having obesity and overweight were respectively 26.47\% and 25.74\% of the total. BMI range from 18.5 to 24.9 kg/m\textsuperscript{2} was taken as normal. For overweight and obesity, we have used the cut-off given by WHOi.e. 25 and 30 kg/m\textsuperscript{2} respectively have been used in this study. International task
force for Asia-Pacific suggested lower cut-off values of 23 and 25 kg/m² for overweight and obesity respectively.\textsuperscript{221} In a study from rural Wardha, it was found that BMI above 21.7 kg/m² in males and 21.2 kg/m² in females and WC above 72.5 cm in males and 65.5 cm in females increased the risk of hypertension.\textsuperscript{222} Abdominal obesity was the most common MS component in women in one study.\textsuperscript{103} Meng proposed the term of Metabolically Obese, Non-Obese (MONO) individuals to emphasize the presence of metabolism-associated disorders in individuals who were not obese.\textsuperscript{223} This term was helpful to identify the patients who were having MS but were non-obese.

**5.5 MS criteria:** Regarding the number of MS criteria in a given patient, 75.63\% patients in this study were found to have three MS criteria followed by 20.79\% with four and 3.58\% with five MS criteria. Gisela et al found that 57.7\% MS patients had three criteria, 30.2\% had four criteria and 11.1\% five criteria in an urban population.\textsuperscript{216}

Zhang et al. found that the most common MS criteria were increased fasting plasma glucose followed by abdominal obesity.\textsuperscript{224} As reported previously, abdominal obesity is the most common MS criterion in women.\textsuperscript{103} In the present rural study, 25.45\% subjects were found outside the normal range of WC. More women (27.94\%) were found outside the normal range of WC than men (23.07\%). In fact, all combinations that were more common in women than men contained waist circumference, whereas the metabolic syndrome combinations in men were more heterogeneous in their make-up. This finding may suggest that abdominal obesity has more importance in developing MS in females than males. Kuk et al. observed that the anthropometric measures of obesity are more strongly associated with mortality risk in females than in males.\textsuperscript{225} In our study, increased WC was found to be the least common criterion in MS patients. On the contrary, several studies in America and Canada found that abdominal obesity (indicated by WC) was the most common criterion of MS.\textsuperscript{226,227,214} It may be due to taking high caloric food in developed countries. The prevalence of high blood pressure (hypertension) has decreased or remained stable,\textsuperscript{228,229,230} while the prevalence of obesity has increased and remained at a high level\textsuperscript{231,332,233} in the developed countries over the past decades. An Indian study has shown that high waist circumference and hypertriglyceridaemia are more prevalent in urban population than in rural population.\textsuperscript{234} High WC and hypertension were found to be the most prevalent determinants in patients with MS in a Swedish population,\textsuperscript{235} while the most prevalent criteria were high WC and high TG in a Hungarian study.\textsuperscript{236}

Hypertension has been increasing in India, both in rural and urban regions. In our study, 59.85\% of the MS patients were hypertensive. High blood pressure (Hypertension) was found to be the fourth leading criterion of MS in this study. Maximum hypertensive subjects were found in the age group 41-60 years. In contrast, 25.2\% of the MS patients were hypertensive in a study of rural population.
Discussion

in Tamil Nadu. Prevalence of hypertension in rural areas of Tamil Nadu in the age group of 45-60 years was 33%. In the present study, hypertension was more common in females than in males.

Edris et al. observed that hypertension, hyperglycemia, and low HDLc were the most frequently occurring components of MS in their study population. In our study, low HDLc was the most common criterion of MS, found in 85.3% cases. The most prominent age group having this HDLc criterion was 41-50 years. HDLc was found to be significantly lower (P<0.001) when it was compared with controls. Low HDLc (63.4%) in men and hypertriglyceridemia (73.2%) in women were most prevalent components of MS found by Park et al. In our study, low HDLc was the commonest component in both the sexes. It was more prevalent in females (91.18%) than in males (79.72%) followed by hyperglycemia and then hypertriglyceridemia.

Pokharel et al. found that the prevalence of high BMI, central obesity and low HDLc was significantly higher in females. In U.S.A., Butler et al. found low HDLc to be the fourth commonest metabolic syndrome criterion in younger and older women. Thus, prevalence of different components of MS differs in different parts of the world.

In MS patients in eastern India, low HDLc level was found to be more prevalent in females as compared to males. In a study on MS in Pakistan, low HDLc (68-81%) was found to be the most common abnormality followed by hypertension. In a rural population of Karnataka, low HDLc was seen as the most common component of MS followed by hypertension, hyperglycaemia and hypertriglyceridaemia. It was also found that low HDLc level was more common in women (93.2%) than in men (76.97%). A report from Ghana showed low HDLc, high BP, and central obesity as the predominant criteria of MS in a rural population.

The numbers of MS components have a relationship with mortality. In younger adults having all five MS criteria, there was higher mortality risk whereas in older men, none of the MS combinations were associated with mortality. In older women, elevated glucose or low HDLc as one of the MS components was most strongly associated with mortality risk. In a study from Himachal Pradesh, the most common component of MS was found to be lowered serum HDLc. Thus, it may be concluded that low HDLc is the commonest component of MS in our country and obesity is the least common component. This is in sharp contrast to developed countries.

5.6 CKD and eGFR: In a community based study, hypertension and hyperglycemia came out to be the most effective predictors of chronic renal failure (CRF) and the prevalence of CRF in general population in India makes it a serious problem in need of urgent efforts to contain it. Anupama and Uma found that the prevalence of proteinuria was 2.8% in a survey on south Indian rural population for
CKD evaluation. They found CKD in 6.3% subjects when eGFR was estimated by MDRD equation. Developing countries are becoming major reservoirs of renal dysfunction. The incidence of renal dysfunction is rising rapidly in India. Emem-Chioma et al. showed that CKD was more common in subjects with MS as compared to those without MS. In another study, 25% to 40% MS patients were found to be at risk to face CKD. CKD has been recognized as a risk factor for end stage renal disease which is among the leading causes of death in developing countries. Kurella et al. conducted a prospective study and found that 7% MS patients developed CKD during a 9-year follow up. They concluded that MS is independently associated with an increased risk for CKD in non diabetic adults.

In this study, increasing number of MS criteria was found inversely associated with decreasing eGFR. Nand et al. compared the prevalence of CKD (eGFR<60ml/min) in patients with MS and controls. The prevalence was three fold higher in MS patients but curiously, their control subjects were not completely healthy. A progressive increase in CKD was observed with increasing number of components of MS (3, 4 and 5 components respectively). Boronat et al. investigated the prevalence of MS in CKD patients in a Spanish study, and found that 68.9% of the CKD patients had MS, thus, showing an association between CKD and MS. In a study from Taiwan, it was found that presence of MS accelerated the progression of early-stage CKD. In an Iranian population, prevalence of CKD was found to be higher in patients with MS than in those without MS. Moreover, the risk of CKD increased with increasing number of MS components. In a meta-analysis covering USA, Europe and Asia, Thomas et al. observed that the risk for eGFR<60ml/min increased as the number of components of MS increased.

The present study was conducted on patients residing in rural area of Jaipur. A few studies have been done in urban Indian subjects on the prevalence of CKD. The prevalence in general population has been found to be 17.2% in one study and 1.39% in another study.

In the present study, five tests were used to detect renal dysfunction—eGFR, serum urea, serum creatinine, creatinine clearance and proteinuria (by dipsticks). eGFR was found to be below normal in a sizeable proportion of MS patients. It was below 60ml/min/1.73sq metres in 41.22% of the patients. This proportion is much lower than that found in a western hospital—based study in which eGFR was found to be below 60ml/min/1.73sq metres in 71.81% of MS patients. No similar Indian report based on modified MDRD equation is available for comparison. However, a study was done by Singh et al. using the same equation to find out renal dysfunction in North Indian normal population. In this study, 16.6% women and 11.1% men were found to have eGFR below 60ml/min/1.73sq metre. In our north Indian MS population, 49.26% women and 33.56 % men had eGFR below 60ml/min/1.73sq metre. Thus, prevalence of low eGFR was three fold higher in our MS population as
compared to that in normal population studied by Singh et al. This difference could only be due to the presence of MS.

When renal function was assessed by serum urea and serum creatinine, 32.26% of our MS patients had values above the upper limit of normal. When renal function was evaluated by creatinine clearance, only 23.62% of our MS patients had values below the lower limit of normal. When renal function was assessed by detection of proteins in urine (by dipsticks), 19% of the MS patients had proteinuria but half of them had only trace amount of proteins in urine.

Thus, the prevalence of renal dysfunction was found to varied widely depending upon the method used to detect renal dysfunction. MDRD equation is being used widely as a measure of GFR. Recently, it has been reported that MDRD equation was found to overestimate GFR by up to 29% (Rule et al, 2004). In MDRD equation, different factors are used for different ethnicities. Original equation was for American population in which different factors were used for blacks and non-blacks. Later on factors developed for Chinese and Japanese population but no factor has been developed for Indian population. A recent report from Chandigarh concludes that existing creatinine-based equations (e.g. MDRD) are not suitable for Indians, and hence a correction factor or a new equation is required for Indian Population (Kumar et al). Therefore, the high prevalence of renal dysfunction found in this study by MDRD equation may be due to limitations of the equation. Nevertheless, significant number of MS patients were found to have renal dysfunction by other methods also. This is in concordance with earlier reports, but at the same time it has been reported that the cause-and-effect relationship between MS and renal dysfunction is not yet proven.

It has also been reported that, instead of MS as a whole, various components of MS have individual associations with incidence and progression of chronic kidney disease. In our study, a significant association was found between MS and hypertension (P<0.006), MS and high FPG (P<0.019) and MS and high TG (P<0.025). This is in tune with earlier reports. Hypertension and diabetes mellitus are well known causes of renal dysfunction. In our study, 63% of the patients were diabetics and 60% were hypertensive. These two components of MS might have contributed to renal dysfunction.

Low HDLc was the commonest component of MS in our study but it was not found to have an association with renal dysfunction. This is in agreement with an earlier report in which all the components of MS except low HDLc were found to have an association with kidney disease.

When the effect of life style and socio-demographic factors was considered, it was found that prevalence of low eGFR was higher in sedentary persons as compared to those who were moderately active. The difference was significant. The prevalence
of low eGFR in lower socio-demographic class was significantly higher as compared to that in middle class.