Metabolic syndrome is a complex disorder and an emerging clinical challenge which is associated with 2 folds increase in CVD risk and 5 folds increase in T2DM. In a view to gain better insight into the interplay of obesity, IR and inflammation in the pathophysiology of MetS, diabetes mellitus and CVD, this study was done so that the information will help the physician to develop better treatment strategies for managing patients of MetS, screening T2DM risk and CVD risk, and thus improving the prognosis. Our study was undertaken in the Deptt. of Biochemistry jointly with Deptt. of Medicine, MM Institute of Medical Sciences and Research, Mullana, Ambala. One hundred clinically diagnosed patients with metabolic syndrome as stated in NCEP-ATP III criteria with age range of more than thirty years of either sex, were selected to serve as subjects for the study. Fifty healthy subjects who did not meet the NCEP-ATP III criteria for MetS were included to serve as controls.

Anthropometric measurements like height, weight, BMI, waist circumference, hip circumference, WHR and BP were measured. For biochemical investigations, fasting levels of plasma glucose, plasma insulin, serum lipid profile, serum hs-CRP and HOMA-IR were estimated in all the subjects. The results thus obtained were statistically compared between healthy control and patients with MetS.

In the present study, the healthy controls were younger in age as compared to subjects with MetS, but were statistically insignificant. The height of the healthy control was almost comparable to the subjects with MetS which was not significant statistically and do not show any role of height in progression of MetS.

The difference in body weight was statistically significant between two groups; subjects with MetS having more body weight as compared to healthy controls. It shows that subjects with increase in weight are more prone to MetS. Cariappa KB,38 Bennet et al.,39 and Alissa EM et al.284 are also in support that the weight in patients with MetS is found to be increased as compared to healthy control. The reason behind increased weight in patients with MetS is due to obesity.
One of the major disorders leading to development of metabolic syndrome is abdominal obesity. BMI is non-invasive, inexpensive and easy-to-use system of indexing body weight. The mean BMI of subjects with MetS was higher as compared to healthy control which was highly significant. Our result is in agreement with a huge number of publications that shows the significant increase in BMI in patients with MetS as compared to healthy control. The increased weight due to obesity leads to higher BMI in patients with MetS. The data revealed that around 70% of cases had abnormal BMI which consist 34% obese (≥30 Kg/m²) and 36% overweight (25-25.9 Kg/m²). It was also observed that 25% cases had basal metabolic rate (18.5-24.9 Kg/m²) within normal range and around 5% cases were underweight (<18.5 Kg/m²). These observations from the present study demonstrate that although obesity is the major cause of MetS, patients with normal weight and underweight also are diagnosed with metabolic syndrome. Other reasons like insulin resistance caused due to genetic predisposition, sedentary life styles, high carbohydrate or sugar intake, chronic stress etc. other than obesity-induced insulin resistance also perform significant part in the genesis of MetS. Asian Indian are physically nonobese but are metabolically obese. Even with modified BMI cut-off values for South Asians/Asians, 1/3rd of subjects still had metabolic syndrome but did not have general obesity. Asian Indians had been known to have more prevalence of cardiometabolic abnormalities than other ethnic groups, for any given level of BMI. Decades ago, it was revealed existence of individuals who are not obese on the basis of height and weight, but are hyperinsulinemic, IR, and predisposed to T2DM, hypertriglyceridemia, and premature coronary heart disease just like those overt obese people. Eversince then, there has been strong opinion developed that MONW (metabolically obese, normal weight) people are said to be reported among common people and these MONW people are said to be sub-clinically suffering from the syndrome of insulin resistance. Very low percentage i.e. 5% of patients including 2% of male and 3% of female diagnosed with metabolic syndrome were found to be underweight according to their BMI measurement. Similarly, a hospital based study in rural Kerala done by Srinivasan et al. found 2.3% of patients with metabolic syndrome were underweight, 24.7% had normal weight, 27% were overweight and 46% were obese. Zonana-Nacach et al. have found the distribution of patients with MetS on the basis of BMI as 2% were
underweight, 35% had a normal weight, 37% were overweight, and 25% were obese.\textsuperscript{291} Another study of Kumar et al. done in Andhra Pradesh of India also have shown the BMI distribution of MetS patients as 5.45% underweight, 43.6% normal weight, 40% overweight and 10.9% obese.\textsuperscript{292}

The data provided by BMI to explain the spreading of fat tissues in the body is limited which decreases the importance of BMI. The biological variances in the magnitudes among the muscular, osseous and fat cells are excluded when scientists present their research data. These presented data can further be influenced by various factors like age of the population, gender of the population, composition of the body and physical activities done by the population. One of the vital causes for the initiation and progress of metabolic illnesses, revealed by many researches from their studies, is thought to be obesity the abdomen which is also called abdominal obesity. This type of obesity is also said to play its role for calculating risks responsible for developing cardiovascular disorders.\textsuperscript{293} It was observed in our study that the mean waist circumference of subjects with MetS was higher (96.88 ± 7.59 Cm) as compared to healthy control (85.48 ± 5.89 Cm) which was statistically highly significant (p<0.001). Similar observations were reported by Haddad N.,\textsuperscript{46} Naik et al.,\textsuperscript{224} Alissa et al.,\textsuperscript{284} Guha et al.,\textsuperscript{287} Aye and Sazali\textsuperscript{294} who suggested that when compared with BMI, waist circumference is preferred biological indicator to detect the initiation of metabolic syndrome. They put forward their suggestion that individual having waist circumference greater than 80 centimeters (without any role of BMI) will be at higher risk to getting metabolic syndrome independent of the individuals’ sex. Calculation of the abdominal fat tissues becomes much easier when the measurement is done via waist circumference and this measurement was suggested by Bouguerra et al. It is well understood fact that abdominal obesity is related to development of diabetes mellitus and is also related to the development of other heart disorders.\textsuperscript{295}

In the present study, the mean hip circumference of patients with metabolic syndrome (100.69± 7.679 Cm) was higher as compared to healthy controls (89.04± 6.104 Cm) which was statistically highly significant (p<0.001). It was also observed that mean waist hip ratio (WHR) of patients with metabolic syndrome (0.9616± 0.00982) was higher as compared to healthy controls (0.9606± 0.00867) which was
statistically highly significant \((p<0.001)\). The observations were in support of Haddad N,\(^{46}\) Sigdel et al.,\(^{286}\) whereas Alissa et al.\(^{284}\) have not shown any significant association of hip circumference and WHR between patients with MetS and healthy control.

The mean SBP of patients with metabolic syndrome \((143.77\pm 17.865\) mmHg) was observed to be higher as compared to healthy control \((126.08\pm 6.203\) mmHg) in the present study, which was statistically highly significant. Similarly, mean DBP of patients with metabolic syndrome \((89.57\pm 11.46\) mmHg) was also higher as compared to healthy control \((80.76\pm 2.63\) mmHg) which was statistically highly significant. The results observed are in support of study done by Naik et al.,\(^{224}\) Guha et al.\(^{287}\) Sigdel et al.\(^{286}\) Colantonio et al.,\(^{296}\) and Gomez-Sanchez et al.\(^{297}\) Pre and/or Hypertension is also an important constituent of MetS. It is believed be multifaceted and multifactorial causes of high blood pressure in the metabolic syndrome. The essentials involved in metabolic syndrome causation like obesity, insulin resistance, and the characteristic dyslipidemia are also said to be tangled in facilitating changes causing hypertension and altering its evolution. Obesity may play the most significant role in creating the conditions that lead to hypertension in the MetS.\(^{298}\) Obesity leads to increase in FFA, insulin, leptin and aldosterone and decrease in NO (Nitric Oxide) levels, and has also been demonstrated with activation of RAAS (Renin Angiotensin aldosterone System). On one hand increased level of FFA, insulin, leptin, aldosterone and activated RAAS further activates the sympathetic nervous system. Activated sympathetic nervous system along with increased level of leptin, aldosterone and activated RAAS acts on kidney which leads to sodium and water retention followed by hypertension. On another hand, decreased NO, increased aldosterone and activated RAAS helps in vasoconstriction and lead to hypertension.\(^{254, 299}\)

In the present study it was observed that Fasting Plasma Glucose of patients with metabolic syndrome \((166.072\pm 85.42\) mg/dl) were higher as compared to healthy control \((86.58\pm 7.84\) mg/dl) which was significant at 0.01 level. The results are in agreement with Haddad N.,\(^{46}\) Naik et al.,\(^{224}\) Sigdel et al.,\(^{286}\) Guha et al.\(^{287}\) and Siu PM.\(^{300}\) Pre-diabetes (Hyperglycaemia but below that of clinical Diabetes) is commonly associated with the metabolic syndrome whereas, diabetes mellitus is the
morbidity of metabolic syndrome. IR is a common factor for hyperglycaemia in MetS. Majority of the persons with both conditions (pre-diabetes and metabolic syndrome) are obese. Elevated free fatty acids (FFAs) in circulation and other “adipokines” are the result of increased adipocytes, whereas, the latter appear to underlie both a pro-inflammatory as well as prothrombotic state. An increase in FFAs induces IR in muscle, which contributes to an elevation of glucose level in circulation. Nearly 80 Percent of glucose taken by skeletal muscle cells (which is chief glucose utilizing cells) when we talk about healthy individual having normal blood glucose level. The glucose in the skeletal muscle is used for break-down by glycolysis as well as glycogenesis (formation of glycogen). Insulin resistance can be declined by insulin signalling via IRS-1 PI3K (phosphatidylinositol 3-kinase)/Akt and this process finally lowers the GLUT4 (the glucose transporter) translocation to the membrane of plasma causing high blood glucose level due to reduced glucose uptake by the cells because of compromised insulin-activated glucose transportation.

It was observed that Fasting Plasma Insulin of patients with metabolic syndrome (20.268±11.479 μIU/ml) were higher as compared to healthy controls (5.624±1.719 μIU/ml) which was significant at 0.01 level. This is in accordance with studies of Allam-Ndoul et al., Ghamarchehreh et al., Kurl et al., which observed significantly increased insulin readings among the subjects suffering from metabolic syndrome. Hyperinsulinemia is the consequence of IR. The pancreas compensates by increasing the insulin secretion into the blood circulation to overcome defects in peripheral insulin action in the early stages of insulin resistance. There may be increased blood insulin level due to hypertrophy of beta cells because of amplified insulin production demand in case of early insulin resistance stages. The method to assess insulin resistance used was HOMA-IR.

The present study demonstrated suggestively (p<0.001) higher HOMA-IR in patients with metabolic syndrome (8.747±7.968) as compared to healthy controls (1.202 ± 0.389). This is in agreement with the findings of Barseem NF, Shekhar et al., and Gowdaiah et al. In some cases, it is seen that insulin resistance and type 2 diabetes mellitus can be caused due to mutation in the genes or molecular abnormalities involved in insulin signalling process. Long-lasting tissue
inflammation has its role in causing peripheral insulin resistance and this type of inflammation can be due to obesity (oversupply of lipid) and changes metabolism of substrate because of lack of physical activities. The above-mentioned obesity or fat deposition in the surrounding cells accelerate pathways of proinflammatory signalling and this deposition also accelerate protein kinase C. These all processes and factors weaken insulin signal transduction via tempering chief biological events of phosphorylation and vital interactions between proteins. Most of the impairments in muscle insulin action are caused by post receptor defects. The biological role of insulin can be diminished at IRS-1 level when stress kinases (JNK (c-Jun N-terminal kinase) and nuclear factor-κB kinase-beta and phosphorylation of IRS-1 can also be decreased.

According to HOMA–IR Score, it was observed in the present study that 61% of patients with metabolic syndrome were with severe insulin resistance (>5) consisting 38% of male and 23% of female. 18% cases were found to be with moderate insulin resistance (3-5) including 11% male and 7% female whereas 21% of the patients with MetS were with normal insulin resistance (<3). The observation from the present study demonstrates that though majority of patients with MetS were with severe insulin resistance and moderate insulin resistance there were also MetS patients who had normal insulin resistance. It concludes that only insulin resistance is not the merely cause of MetS. A number of publication supports that the majority of insulin resistance seen in MetS is obesity induced.

Dyslipidemia is another important constituent of MetS. Upraise readings of total blood cholesterol, low-density-lipoprotein-cholesterol (LDL-C) and lower value of cholesterol attached to high density lipoprotein alone or in combination with high blood triglyceride level define dyslipidemia. Lower HDL-cholesterol readings and hypertriglyceridemia are thought to be biochemically inter-connected and their collaboration has been defined as “atherogenic dyslipidaemia”, which is also considered by amplified concentrations of small-dense LDL particles with comparatively normal total LDL-cholesterol, and insulin resistance. In the present study, it was observed that Triglycerides of patients with metabolic syndrome were higher as compared to healthy control which was statistically highly significant; which is in accordance with the previous studies of Haddad N., Naik et al., Alissa
et al.,\textsuperscript{284} Janghorbani M.\textsuperscript{318} and Udgire P.\textsuperscript{319} It is observed that visceral fatness and up-scaled intra-abdominal fat are causative factors leading to progression of insulin resistance. Increased flux of free fatty acids to the liver from the periphery in obesity and the synthesis of triglyceride in the liver are stimulated by state of insulin resistance and this hepatic synthesis promotes the gathering and secretion of triglyceride consisting VLDL and hepatic apo B synthesis as well.

It was observed that mean values of total-Cholesterol, LDL-Cholesterol and VLDL-Cholesterol of subjects suffering from metabolic syndrome scored higher compared to healthy individuals which were statistically significant, and it was in support of work done by Naik et al.,\textsuperscript{224} Sigdel et al.,\textsuperscript{286} Guha et al.\textsuperscript{287} whereas Alisa et al.\textsuperscript{284} do not show significant increased TC and LDL in patients with MetS as compared to healthy control. Increased FFA levels due to increased lipolysis caused by impaired insulin signalling assist as a substrate for TG formation in the liver. Free fatty acids also cause stabilization of apoB synthesis, resulting in more VLDL production as apoB is the key lipoprotein of very-low-density lipoprotein (VLDL) units. Second, PI3K-dependent pathway is involved in degradation of apoB by insulin and consequently insulin resistance straight forward enhances VLDL formation. Third, insulin controls the action of lipoprotein lipase; the rate-limiting and major moderator of VLDL clearance.\textsuperscript{63} From the available literature, it is understood that high triglyceride (TG) level in blood stimulates conversion to TG from very low-density lipoprotein and also the conversion to IDL for cholesterol-ester from high density lipoprotein with the help of CETP with the determined action of hepatic lipase. This lipase causes the creation of little dense low-density lipoproteins. These little dense low-density lipoproteins are gradually digested with 5-day residence time and thus encouraging to cause atherogenicity.\textsuperscript{321,322} Thus, increased triglyceride level in blood during obesity along with or without insulin resistance causes uprise in values of VLDL and LDL-cholesterol which finally causing increase in total blood cholesterol levels.

It was observed that mean HDL-Cholesterol levels of patients with metabolic syndrome were lower as compared to healthy control which was statistically highly significant. The result of the present study is in agreement with the studies done by Cariappa KB,\textsuperscript{38} Haddad N,\textsuperscript{46} Alissa et al.,\textsuperscript{284} Sigdel et al.,\textsuperscript{286} Guha et al.\textsuperscript{287} whereas
Naik et al.\textsuperscript{224} who also did not find any significant decrease in HDL levels in MetS patients as compared to healthy control. Due to high number of fragments of chylomicrons and VLDL in conjunction with impaired break down of lipids, HDL metabolism is highly affected by obesity. CETP activity is said to exchange cholesterylesters from high density lipoproteins for triglycerides from very low-density lipoproteins and low-density lipoproteins and this CETP activity is thought to be increased due to uprise in the number of TG-rich lipoproteins.\textsuperscript{323} Hepatic lipase causes break-down of these TG-rich HDL and this break-down forms small HDL with diminished attraction form apo A-1, forming separation of apo A-1 from high density lipoproteins. This process at last causes to lower down the concentrations of HDL-C and thus lowering the circulating HDL subunits which interferes the reserve cholesterol transportation process.\textsuperscript{324}

Metabolic syndrome is a low grade chronic inflammation state. Obesity and insulin resistance leads to inflammation and hence development of MetS. In our study hs-CRP was estimated to find out the association between inflammation and MetS and to find out the CVD risk in patients with MetS. We observed that mean hs-CRP level (4.93±1.45 μg/ml) of patients with metabolic syndrome was higher as compared to healthy control (1.70±0.61 μg/ml). The increase was highly significant (p<0.001). Previous studies performed by Cariappa B,\textsuperscript{38} Chopra et al.,\textsuperscript{43} Huffman et al.,\textsuperscript{325} Canoza- Gomez et al.,\textsuperscript{326} Kang et al.,\textsuperscript{327} Majid et al.,\textsuperscript{328} and Taki et al.\textsuperscript{329} have also demonstrated high hs-CRP level in MetS patients as compared to groups without MetS. C-reactive protein is an inflammatory sign synthesized and released by the liver under the influence of cytokines such as TNF-α, IL-1 and IL-6.\textsuperscript{330} In the obese condition, adipocytes have an integral role in the growth of obesity-induced inflammation. They induce increased secretion of various pro-inflammatory chemokines and cytokines such as MCP-1, TNF-α, IL-1, IL-6 and IL-8. These cytokines further stimulate liver for synthesis of CRP.\textsuperscript{19} In obesity, adipocytes also activates JNK and NF-κB signalling pathways and increases the porduction of TNF-α, IL-1 and IL-6 and promote CRP synthesis.\textsuperscript{331} Besides being an inflammation marker, hs-CRP is also being estimated as a CVD risk predictor in patients by AHA/CDC on the basis of data obtained from population based studies. In our study
it was observed that 78% of the subjects with metabolic syndrome were under high risk (High risk: >3 μg/ml) of CVD where 50% were male and 38% were female, 12% of subjects were under medium risk (Medium risk: 1-3 μg/ml) of CVD whereas no patients were found under Low risk (<1 μg/ml) of CVD. Similarly a study done by Mahajan et al. in Delhi, India, reported 37.2% with high risk, 43.6% with intermediate risk and 19.2% with low risk out of 4066 patients with MetS. A study done by Gowdaiah PK in patients with MetS in Bangalore, India reported 72% with high risk, 22% with moderate risk and 6% with low risk of CVD. CRP plays a pivotal role in pathogenesis of atherogenesis and CVD. It helps in increased uptake of LDL into macrophages and enhances conversion into foam cells. It inhibits an enzyme Nitric-oxide synthase expression in endothelial cells. Due to decrease in synthesis of NO there are diminished anti-atherogenic activities like platelet aggregation, vasoconstriction, and smooth muscle cell proliferation. This protein also activates macrophages to tissue factor secretion which may cause disseminated intravascular coagulation and thrombosis.

Obesity is claimed to be the main culprit for pathogenesis of MetS and its morbidities. Major tools like BMI, WC and WHR etc. are used widely for the measure of obesity. In the present study, to find out the association between obesity and other parameters of MetS, the Pearson’s correlation of BMI as well as WC with other parameters of MetS was done. First, the correlation between both the tools of obesity measurement i.e. BMI and WC was calculated which shows the significant positive association. The result is in accordance with the studies of Gierach et al., Raghavan et al., and Aras et al. This is probably due to both the parameters being the marker of obesity.

In our study, there was no strong noteworthy association of BMI and WC with glucose level whereas a significant positive correlation between BMI and glucose is reported by the number of studies like Raghavan et al., Aras et al., Vittal et al., Adamu et al., and Jhanghorbani et al. This is may be due to small sample size. The association between obesity and diabetes depends on ethnicity, and the different levels of association between obesity and blood glucose levels probably explained which are observed in various studies.
In the present study obesity shows a strong significant positive correlation with insulin resistance. Both the tools of obesity measurement i.e. BMI and WC show significant positive correlation with insulin as well as HOMA-IR. The result of our study is in support of various studies like Shekhar et al., Shah et al. Deepa et al. Warenberg et al. and Steele et al. Hyperinsulinemia is a pathological reason for both incipient obesity by over stimulating WAT and liver metabolic activity, and parallelly producing incipient muscle insulin resistance.

In order to find out the association between obesity and dyslipidemia, Pearson’s correlation of BMI and WC was done with lipid profile. BMI was found to be positively and significantly correlated with TG in present study which is in support with the study of Aras et al., Rezende et al., Faour et al. WC has also a significant positive correlation with TG in our study which is in agreement with the studies like Rezende et al. and Stanković V et al.

In the present study BMI as well WC do not show any significant correlation with TC and LDL-C which is in support of the study done by Rezende et al. and Premnathan M. This possibly indicates a lower interference of excess weight and central fat distribution, in cases of high blood levels of TC and LDL-C. Whereas; other results from Faouret al. and Ebron K et al. are in contrast with the present study which show positive correlation of BMI and WC with TC and LDL. In the present study BMI and WC both show negative correlation with HDL but not statistically significant. Even HDL is found significantly lower level in MetS patients than healthy control. The result is in agreement with the study of Premnathan M. Whereas; some of studies of Shen W et al., Aras et al. and Stanković et al. are in contrast with our findings. There was no consistent correlation between obesity and HDL level which probably would mean that obesity alone may not be responsible for the changes in HDL level. In the present study, BMI and WC both have a significant positive correlation with VLDL. VLDL increases along with increase in obesity. The result is in accordance with the studies of Weber et al. and Adiels et al. Obesity along with IR plays a major role to cause dyslipidemia in metabolic syndrome. Impaired lipase results in increased FFAs followed by increased TG synthesis. This results in increase VLDL and LDL.
but decrease in HDL. The decreased HDL is due to CETP activity and uptake by liver that characterize MetS.\textsuperscript{354}

Hypertension is also an important constituent of MetS. In the present study BP shows the significant positive correlation especially with obesity only. Pearson correlation between Diastolic Blood Pressure and measures of obesity (BMI and WC) are statistically significant which is in accordance with the studies of Stanković et al.,\textsuperscript{348} Ketherine et al.,\textsuperscript{350} Phan et al.,\textsuperscript{355} and Šutković et al.\textsuperscript{356} Activation of the SNS, activation of the RAS, and sodium retention are the major characteristics of obesity associated arterial hypertension.\textsuperscript{357}

In the present study, SBP and DBP both show non-significant correlation with glucose level. which is in contrast with the studies of Stanković et al.,\textsuperscript{348} Phan et al.,\textsuperscript{355} Šutković et al.,\textsuperscript{356} Chuang et al.,\textsuperscript{358} and Eftekhar et al.\textsuperscript{359} The reasons behind our result may be the small sample size or may be due to ethnicity. Even though researchers describe the notion that the hypertension and hyperglycaemia share mutual imprints such as inflammation, oxidative stress, SNS, adipokines RAAS, insulin resistance, and PPARs. These imprints interrelate and impact each other even causing a vicious cycle. Hypertension and hyperglycaemia/diabetes may develop one after the other in the same individual because both are end results of the metabolic syndrome.\textsuperscript{360}

Our study also shows the non-significant association of BP with total-cholesterol and LDL Cholesterol from the lipid profile which is in contrast with the study of Stanković et al.,\textsuperscript{348} and Šutković et al.,\textsuperscript{356} The mechanism by which dyslipidemia leads to BP elevation is not clearly understood till date. It is suggested that dyslipidemia causes endothelial dysfunction, the loss of vasomotor reactivity and arterial stiffness. Recently identified liver X receptor, are activated by lipid particles, which is a potential regulator of renin expression. The activation of RAAS increases BP.\textsuperscript{361}

The present study also shows the non-significant correlation of SBP and DBP, both with hsCRP an inflammation marker which is in contrast with the studies of Kanget al.\textsuperscript{327} Dar et al.,\textsuperscript{362} Sinha et al.,\textsuperscript{363} Yanchun et al.,\textsuperscript{364} Ravi et al.,\textsuperscript{365} and Chen et al.\textsuperscript{366}
They suggest that probable potential mechanism for the association is that increased BP; may promote inflammation of blood vessels from pulsatile blood flow due to inflection of mechanical stimuli.

Increased expression of sICAM-1 and VCAM-1 by endothelial cells and upregulation of MCP-1 by cyclic-strains leads to increased adhesion of monocyte to the endothelium.\textsuperscript{367, 368, 369} Several studies revealed that hypertension may lead to multiple inflammatory stimuli at the wall of blood vessels. It promote the production of numerous proinflammatory cytokines such as TNF, IL-6 and CRP as a defence against agents causing injury.\textsuperscript{362} Whereas our study is in accordance with some of the studies who also did not found any association between Blood Pressure and hsCRP.\textsuperscript{370, 371, 372}

In the present study, Pearson correlation of hsCRP was assessed with other anthropometric measurements and biochemical parameters. It was found that hsCRP was positively correlated with both the measures of obesity BMI as well as WC which were highly significant. Other research data done in different parts of the world by Guha et al.,\textsuperscript{287} Vikram N et al.,\textsuperscript{373} Aydinet al.,\textsuperscript{374} Dayalet al.,\textsuperscript{375} Brooks et al.,\textsuperscript{376} McDade et al.,\textsuperscript{377} and Moron et al.\textsuperscript{378} also suggests that there is a strong link between overweight/adiposity with elevated hsCRP or inflammation. Trayhurnet al.\textsuperscript{379} studied this obesity related inflammation and marked it as low grade inflammation. Obesity increases the expression of some proinflammatory agents like adiponectin, IL-6 and TNF-α from the adipose tissues which regulates synthesis of CRP from the liver introduced as an inflammatory marker.\textsuperscript{331}

In our study hsCRP had a significant positive correlation with insulin level or insulin resistance (HOMA-IR) which is in agreement with the studies of Guha et al.\textsuperscript{287} Farooq et al.,\textsuperscript{380} Pourfarzam et al.,\textsuperscript{381} Gelaye et al.\textsuperscript{382} and Sneha et al.\textsuperscript{383} emphasizing that IR is an inflammatory state and higher the hsCRP levels, higher the insulin resistance is. Obesity leads to inflammation by production of proinflammatory cytokines like TNF-α and IL-6 which regulates production of hsCRP on one side and stimulates signalling pathways like JNK pathway, IKKβ/NFκB pathway, JAK-STAT pathway on another side which leads to IR by serine/threonine
phosphorylation of IRS1, reducing expression of GLUT4 and IRS1 expression. Proinflammatory cytokine especially IL-6 has also been reported to cause IR in skeletal muscle. If STAT3 is activated the induction of TLR-4 gene expression consequences in skeletal muscle IR.\textsuperscript{331}

Correlation of hsCRP shows a significant association with TG, TC and VLDL among lipid profile which is in accordance with the studies of Naik et al.,\textsuperscript{224} Guha et al.,\textsuperscript{287} and Patel et al.\textsuperscript{384} The potential mechanism or the link between dyslipidemia and hsCRP is suggested that this unfavourable lipid profile may increase the inflammatory activity and high hsCRP level by facilitating the formation of foam cells in the arterial wall.\textsuperscript{385}

In accordance with other studies like, Barseem NF,\textsuperscript{84} Chaudhari SP et al.,\textsuperscript{386} Garg et al.,\textsuperscript{387} Jung et al.,\textsuperscript{388} and Gobato et al.\textsuperscript{389} our study also showed a substantial relationship of HOMA-IR with BMI and WC, emphasizing that insulin resistance is consequence of obesity and insulin resistances increases with increase in obesity. The potential mechanism that obesity leads to insulin resistance is through inflammation. Obesity induced proinflammatory cytokines synthesis have a major role to cause insulin resistance through phosphorylation of insulin signalling molecules.\textsuperscript{331} A significant correlation between HOMA-IR and glucose level was shown in our study which is in accordance with studies of Jung et al.,\textsuperscript{388} and Silva et al.,\textsuperscript{390} Impaired insulin signalling also results in increased release of glucose from liver resulting in impaired glucose homeostasis.\textsuperscript{391} There was not significant correlation between HOMA-IR and BP (SBP and DBP) in the present study which is in support of Jung et al.,\textsuperscript{388} Dowse et al.\textsuperscript{392} Zimmet et al.,\textsuperscript{393} and Chien et al.\textsuperscript{394} however, the result is in contrast with the study of Barseem et al.\textsuperscript{84} who found that blood pressure may vary, even in the same ethnicities. The association between HOMA-IR and hsCRP is also highly significant which has already been discussed. HOMA-IR has been significantly correlated with TG which is in accord with the study of Jung et al.,\textsuperscript{388} and Singh et al.\textsuperscript{83} whereas; the study is not in support of the studies like Barseem et al.,\textsuperscript{84} and Shekhar S. et al.\textsuperscript{307} HOMA-IR is not significantly correlated with TC, HDL and LDL in the present study which is in support of the study done by Barseem et al.\textsuperscript{84} Jung et al.\textsuperscript{388} and Shekhar et al.\textsuperscript{307}
In the present study, HOMA-IR is significantly correlated with VLDL, which is in agreement with the study of Faria et al.\textsuperscript{395} and Shalaurova et al.\textsuperscript{396} In insulin resistant states, enhanced lipolysis and increased fatty acid flux from the adipose tissues ultimately leads to increased level of TG and VLDL in circulation.\textsuperscript{397} Triacylglycerols are precursors for the VLDL synthesis; therefore, increase in blood TGs level is followed by increase in this lipoprotein. TGs and VLDL show significant correlations with HOMA-IR and insulin as compared to total cholesterol presenting a higher association with insulin resistance.\textsuperscript{395}

Receiver Operating Characteristic (ROC) Curve was analysed for hs-CRP in the present study for prediction of metabolic syndrome. From the ROC curve analysis AUC (Area Under Cover) was found 0.995 which was highly significant (p<0.001). From the criterion values and coordinates values of the ROC curve, when hsCRP level 2.55μg/ml was selected as a cut-off point for predicting metabolic syndrome, it was found to have a sensitivity of 97% and specificity of 96%. As compared, Chopra et al.\textsuperscript{43} have adopted 2.83 cut-off value of hs-CRP in predicting MetS with sensitivity of 94% and specificity of 78%.

ROC was analysed for HOMA-IR in the present study for prediction of metabolic syndrome. From the ROC curve analysis AUC (Area Under Cover) was found 0.945 which was highly significant (p<0.001). From the criterion and coordinates values of the ROC curve, when HOMA-IR level 2.50 was selected as a cut-off point for predicting metabolic syndrome, it was found to have a sensitivity of 87% and specificity of 100%. As compared, in study of Gayoso-Diz et al.\textsuperscript{82} HOMA-IR cut-off values for MetS ranged from 2.07 at 50 years to 2.47 at 70 years.

Overall, our results demonstrated that the anthropometric measurements, plasma level of glucose and insulin, blood pressure and serum levels of lipid profile, hsCRP and HOMA-IR are altered in MetS cases clearly suggesting the presence of insulin resistance, inflammation, hypertension and atherogenicity which may be related to diabetes and CVD. However, the interplay of various hormones of adipocytes and proinflammatory cytokines in the pathophysiology of MetS and leading to morbidities like diabetes and CVD is rather complex and needs further elucidation. The inflammation or the inflammatory marker like hs-CRP may serve as an important
orchestration between obesity, IR, dyslipidemia, glucose metabolism and endothelial
dysfunction especially in MetS patients. Further studies of adipose tissue hormones
and inflammatory cytokines like adiponectin, leptin, resistin, vaspin, IL-6, TNF-α
etc. along with their intracellular signalling and gene regulation in a larger sample
size may shed new light on their function, molecular targets and potential clinical
relevance in the prevention and treatment of obesity, insulin resistance, MetS and
morbidities like T2DM and CVD.