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Original Research Article

STUDY OF SERUM CYSTATIN C LEVEL IN METABOLIC SYNDROME SUBJECTS AND ITS CORRELATION WITH THE COMPONENTS OF METABOLIC SYNDROME

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ABSTRACT

BACKGROUND: Metabolic syndrome and Cystatin C consists independent and strong indicator of metabolic abnormalities that confer increased risk of cardiovascular, renal and diabetes mellitus and all cause of mortality and morbidity along with more sensitive parameter than creatinine clearance and creatinine level of renal function test. **AIMS AND OBJECTIVE:** To determine serum Cystatin C levels in healthy controls and metabolic syndrome subjects and its correlation with components of MetS. **MATERIAL AND METHODS:** The present study is a case control study, included 90 subjects of MetS and healthy controls (n=30). Total 120 Subjects were selected from Medical OPD of JLN Medical College and associated group of Hospitals, Ajmer, India. MetS subjects defined 5 components (NCEP-ATP III) and it was further subdivided into 3 groups of 30 patients each. Anthropometric components are BMI, Waist circumference and Fasting plasma glucose and Dyslipidemia and Blood Pressure which are divided into Group 2 (3 components) group 3(4 components) and group 4(5 components) of MetS Subjects of MetS were compared with 30 apparently healthy controls were included in group 1. All components were assessed by detailed history, clinical examination and biochemical methods. Sample collected under aseptic condition. **RESULT:** CysC was significantly increased in MetS subjects as compared to that in the healthy controls ($p<0.0001$). Level of CysC is positively correlated with BMI, waist circumference, fasting glucose level, triglycerides, Systolic and diastolic blood pressure and negatively correlated with HDL. No significant difference found in urea and creatinine. **CONCLUSION:** The present study shows that the level of Cystatin C is raised in metabolic syndrome subjects. The Present study has also revealed a positive correlation between the serum Cystatin C level with all 4 components except negative correlation with the HDL. Therefore CysC may be used as early marker of metabolic syndrome and renal dysfunction.

Keywords: Metabolic syndrome (MetS), Cystatin C (CysC), High Density Lipoprotein (HDL), Triglyceride (TG).

INTRODUCTION

Metabolic syndrome (MetS) comprises 20-25% of adult population of world. In India 29% of female and 23% of males are affected.**(1,3,5)**

MetS is characterized by central obesity, hypertension, dyslipidemia (elevated triglyceride and LDL with low HDL) and elevated plasma glucose. Each of these factors is associated with increased risk of cardiovascular events associated with abnormal renal function. **(1, 3, 5)** The most important underlying risk factors are abdominal obesity and insulin resistance. As a potential marker of renal function, Cystatin C may be closely related and an independent predictor of Metabolic Syndrome **(1, 3, 5)** and identify the renal dysfunction even when creatinine is normal **(6)** as creatinine

level is affected by inflammatory process, muscle mass, age and sex.**(7)**

Cystatin C consist 122 amino acid residues, an alkaline protein having low molecular weight. Cystatin C is an independent and strong indicator of diabetes, cardiovascular events and all cause of mortality and morbidity along with more sensitive parameter than creatinine clearance and creatinine level of renal function test. **(1-3)**

Cystatin C is generally considered to be constantly secreted and be freely filtered by the glomerulus but be neither secreted nor reabsorbed by renal tubule into circulation. **(8, 9)** Therefore, Cystatin C is useful for estimation of glomerular filtration rate (GFR) and known as a marker of renal function. **(10, 11)** Hypertension, dyslipidemia and diabetes were associated with increased Cystatin C level, which are the components of metabolic syndrome (MetS). **(17, 18, 19)** Cystatin C level increases in patients with MetS and may be used as a marker of MetS in general population.**(20,21,22)** Cystatin C as a prominent predictor of cardiovascular diseases(CVD) and acute coronary syndrome (ACS).(12,13)Cystatin C was not only a marker of GFR but also was correlated with inflammation and oxidative stress in CVD.**(14,15,16)** Cystatin C is closely related with various factors and process related with inflammation.**(1,4)**

Our study was aimed to assess and compare the status of serum Cystatin C level in healthy controls and metabolic syndrome subjects and its correlation with the waist circumference, BMI, blood pressure, fasting plasma glucose and lipid profile.

MATERIAL AND METHODS

This Case-Control study was carried out in Jawahar Lal Nehru Medical College and associated groups of Hospitals, Ajmer, Rajasthan, India. This study was conducted on total 90 subjects of MetS subjects and 30 healthy controls. Demographic profile of patients that includes Age, Height, weight, BMI (Body Mass Index) was measured along with waist circumference and Blood Pressure (Systolic and Diastolic). Metabolic syndrome subjects were selected from Medical OPD of Jawahar Lal Nehru Medical College and Associated Group of Hospitals, Ajmer, India. Age and sex matched Healthy controls (n=30). MetS subjects are defined as per modified National cholesterol education program (NCEP) adult treatment panel (ATP III) which include5 components: waist circumference, Serum Triglycerides, HDL, Plasma Glucose and Blood pressure. Metabolic syndrome subjects (90) in each group was not pre decided, depend upon the number of components of MetS present, these were further subdivided into 3 groups–

2. Group 2- BMI, Waist circumference, Fasting Bloodsugar.
3. Group 3- BMI, Waist circumference, Fasting sugar, BloodPressure.
4. Group4- BMI, Waist circumference, Fasting Sugar, Blood Pressure and Dyslipidemia components (Total Cholesterol, VLDL, LDL, and HDL).
1. Group 1- Healthy Controls.

The result of MetS subjects were compared with apparently healthy controls (n=30) included in group-1

INCLUSION CRITERIA-

1. Age (18-50years) and normal dietary habits.

EXCLUSION CRITERIA-

1. Any drug history especially drugs affecting lipidprofile.
2. Patients with chronic kidney disease, cardiovascular disease, hypothyroidism, chronic pain killer use, glucocorticoiduse.
3. Alcoholics and cigarette smokers.

Venous Blood sample were collected after an overnight fast (10hrs) under aseptic conditions from all the study participants. All samples were centrifuged and analysed for plasma glucose, urea, creatinine, Cystatin C, Lipid profile. The Fasting plasma glucose estimated by GOD-POD method, serum total cholesterol by cholesterol oxidase-peroxidase method (CHOD-POD), serum triglycerides by glycerophosphate oxidase (GPO) method, Serum HDL (high density lipoprotein) by modified polyvinyl sulfonic acid and polyethylene glycol methyl ether coupled classic precipitation method, urea by urease method, creatinine by Jaffe's method, and CysCby Latex enhanced immunoturbidimetric method. LDL (low density

lipoprotein), VLDL (very low density lipoprotein) by Friedwald'sformula.

STATISTICAL ANALYSIS

All data were analysed by ANOVA test. P<0.05 was considered as significant

RESULT

Total of 120 subjects were studied in this paper.

Table 1 represents the demographic characteristic of Group 1, Group 2, Group 3, and Group 4. There was a significant difference in weight, BMI and waist circumference in studied groups.

Table 2 represents CysC and biochemical parameters in all 4 studied groups. There was significant difference in SBP, DBP, fasting plasma glucose, CysC, total cholesterol, triglycerides, HDL, VLDL and LDL in studied groups.

The mean value of BMI, waist circumference and plasma glucose raised in group 2. Mean value of BMI, waist circumference, plasma glucose and Dyslipidemia components (Total Cholesterol, Triglyceride are raised and level of HDL is declined) in group 3, The mean value of all 5 components BMI, waist circumference, Systolic Blood pressure, plasma glucose and dyslipidemia components: TG, VLDL, LDL are raised and HDL level declined in group 4 MetS subjects as compared to healthy controls.

Graphs 1 and 2 shows that comparison between components of metabolic syndrome (group 2, 3 and 4) between healthy controls (group 1), increases. There was no significant difference in creatinine, urea, and eGFR.

Figures 1-5, CysC was positively correlated with waist circumference, SBP, DBP, fasting plasma glucose and triglycerides (p=<0.0001) and negatively correlated with HDL, which were statistically significant.

CysC was significantly higher in MetS subjects than in controls (p value <0.005) and it was significantly higher in group 4 as compared to group 3 and in group 3 as compared to group 2 (p value <0.005).

DISCUSSION

In the present study we have observed that there was a significant increase in BMI, Systolic BP, waist circumference, fasting blood glucose, total cholesterol, Triglyceride, LDL and serum Cystatin C level in group 2, 3, 4 as compared to the group 1 (healthy control) and a significant decrease in serum HDL level in group 2, 3 and 4 as compared to group 1 (healthy control).

Our findings were in agreement with positive correlation of Cystatin C with waist circumference, BMI, SBP, Fasting blood glucose and Total cholesterol and T.G in MetS Groups. Correlation of Cystatin C with HDL shows negative correlation in MetS Groups.

The observation of this study also revealed that positive correlation between BMI and serum CysC level in MetS subjects. Our finding were in agreement with the study of Retnakaran et al and Vigil et al. **(24, 25)** Our study also observed a positive correlation between waist circumference and serum CysC level in MetS subjects and finding were in agreement with the study of Vivien SS et al. **(23)** In relation to age, no clear association was seen and it doesn't directly affect the mechanism of metabolic syndrome. In our study, CysC was proportionately associated with Systolic and diastolic blood pressure and our finding were in agreement with the study of Kestenbaum et al. **(26)** Our study shown a positive correlation between fasting blood sugar and CysC level in MetS subjects and the finding agree with the study of Richard P et al, where CysC level was closely related with fasting plasma glucose level and was associated with progression to Prediabetic level as found in various patients. **(27)**

Present study revealed a positive correlation of Cystatin C with total cholesterol, triglycerides level, LDL and VLDL level and a negative correlation with HDL; HDL is protective in nature in cardiovascular disease resulting from oxidative damage. Oxidative stress induces the synthesis of Cystatin C. Our findings are in agreement with Nishiyama et al. **(30)** and Kim SY et al. **(31)**

Obesity, dyslipidemia and hypertension, which were components of MetS, associated with certain degree of renal disease. Obesity was associated with an increase in cytokines related with production of inflammation and compression of renal hilum due to increased deposition of adipose tissue **(28)** which was associated with renal damage. In obese patients the level of Cystatin C was also increased as seen in the study of Deepa et al. **(29)**

Lieu et al **(32)** had found a positive correlation between waist circumference, fasting plasma glucose level, triglyceride level and systolic and diastolic blood pressure but in case of HDL a negative correlation was found.

Hashemi et al **(33)** also found a correlative study as compared to our study and indicated that increased Cystatin C level may be associated with certain degree of renal dysfunction even when serum creatinine level does not exceeded the normal level in patients with metabolic syndrome.

CONCLUSION

The present study shows that the level of Cystatin C is raised in metabolic syndrome subjects. The Present study has also revealed a positive correlation between the serum Cystatin C with waist circumference, BMI blood pressure, fasting plasma glucose, Cholestrol, Triglyceride and negative correlation with the HDL. Therefore CysC can be used as early marker of metabolic syndrome and renal dysfunction.

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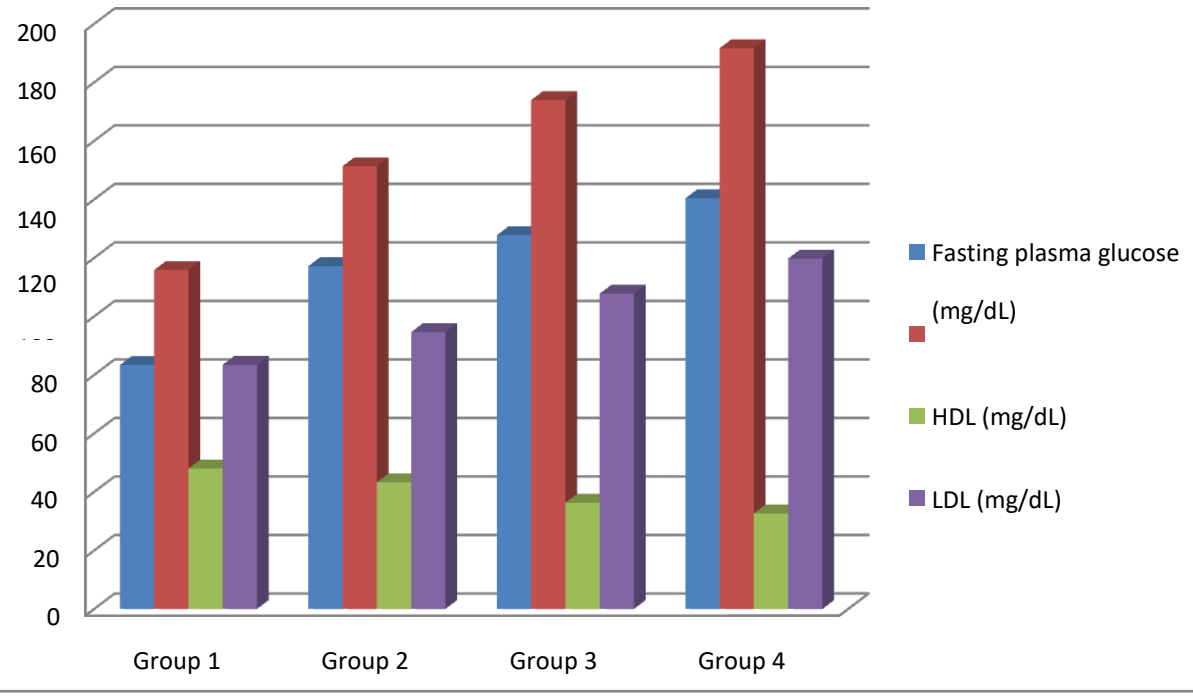
Table 1: Demographic Characters in studied groups

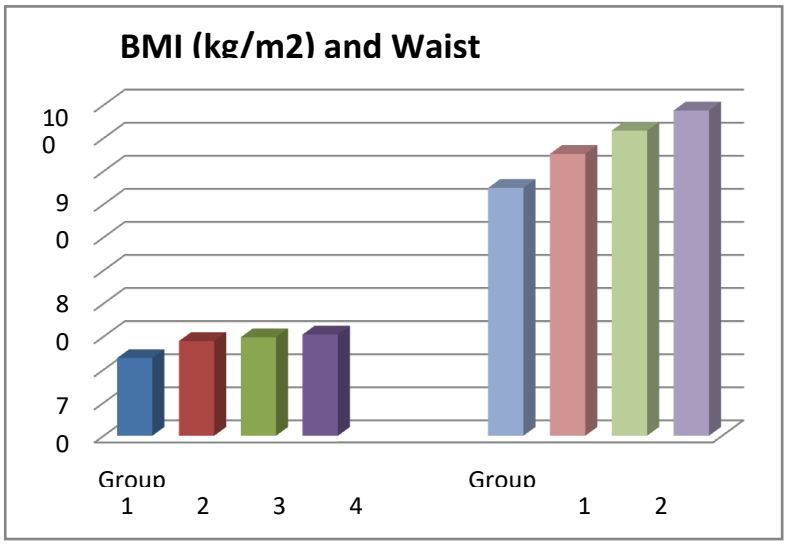
Parameter	Group 1 (n = 30)	Group 2 (n = 30)	Group 3 (n = 30)	Group4 (n = 30)	p value
	Mean ± SD				
Age (years)	41.02±4.92	39.07±5.06	40.55±5.62	40.97±5.03	0.385
Height (m)	1.54±0.06	1.52±0.03	1.53±0.04	1.53±0.03	0.314
Weight (kg)	61.81±6.14	73.53±3.75	77.12±4.49	79.80±4.43	<0.0001*
BMI (kg/m2)	23.48±2.24	28.60±1.93	29.77±1.81	30.60±1.23	<0.0001*
Waist Circumference (cm)	74.94±5.46	85.24±8.67	92.27±7.95	98.35±4.02	<0.0001*

Table 2: Clinical and biochemical parameters in studied groups

Parameter	Group 1 (n = 30)	Group 2 (n = 30)	Group 3 (n = 30)	Group4 (n = 30)	p value
	Mean ± SD				
SBP (mm Hg)	109.60±6.66	118.88±13.64	125.52±10.34	136.22±5.70	<0.0001*
DBP (mm Hg)	70.84±4.97	75.27±8.38	81.83±7.26	88.13±4.15	<0.0001*
CysC (mg/L)	0.66±0.12	1.08±0.27	1.58±0.18	1.73±0.09	<0.0001*
Fasting plasma glucose (mg/dL)	83.38±7.30	117.19±14.69	127.76±21.65	140.38±13.36	<0.0001*
Total cholesterol (mg/dL)	154.22±12.93	167.88±15.05	178.52±21.08	190.56±26.17	<0.0001*
Triglycerides (mg/dL)	115.86±15.35	151.34±14.23	173.95±17.89	191.68±33.82	<0.0001*
VLDL (mg/dL)	22.77±3.03	29.96±2.98	34.48±3.63	38.13±6.71	<0.0001*
LDL (mg/dL)	83.47±12.56	94.63±17.44	107.78±17.29	119.77±23.91	<0.0001*
HDL (mg/dL)	47.98±6.49	43.31±9.00	36.31±8.49	32.67±4.85	<0.0001*
Urea (mg/dL)	26.43±5.34	24.88±6.26	24.86±4.27	26.11±5.56	0.716
Creatinine (mg/dL)	0.73±0.11	0.73±0.10	0.74±0.12	0.76±0.11	
eGFR (mL/min/1.73m2)	94.04±22.50	91.25±12.48	89.87±11.80	87.13±9.28	

Graph 1: Comparison of Fasting Blood Glucose,TG,HDL,LDLin studied groups





Graph 2 Comparison of BMI (kg/m2) and Waist Circumference (cm) among control (Group 1) and metabolic syndrome Groups

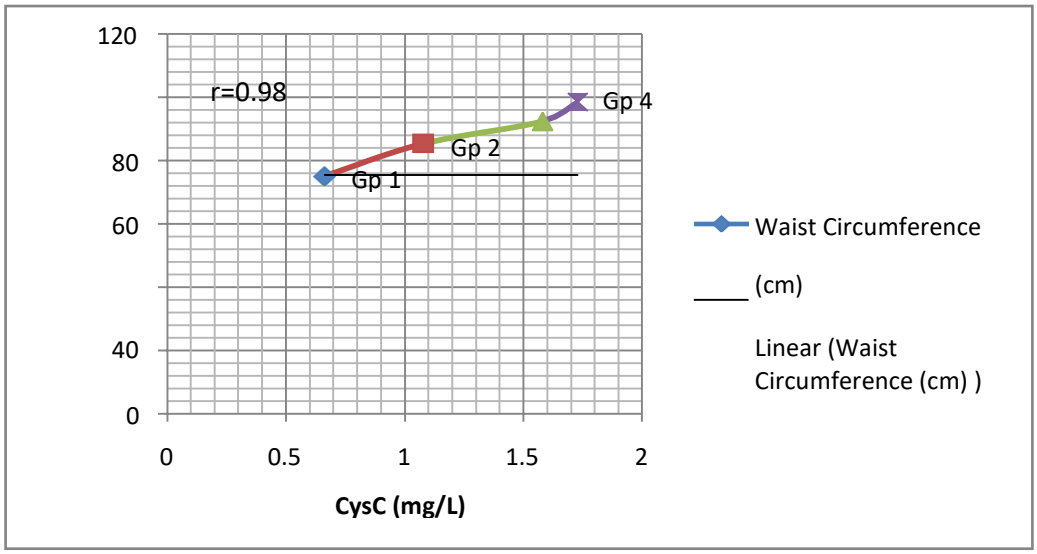


Fig-1 Correlation of CysC with Waist Circumference (cm) in MetS Groups (Group1, 2, 3, 4) (r=0.98)

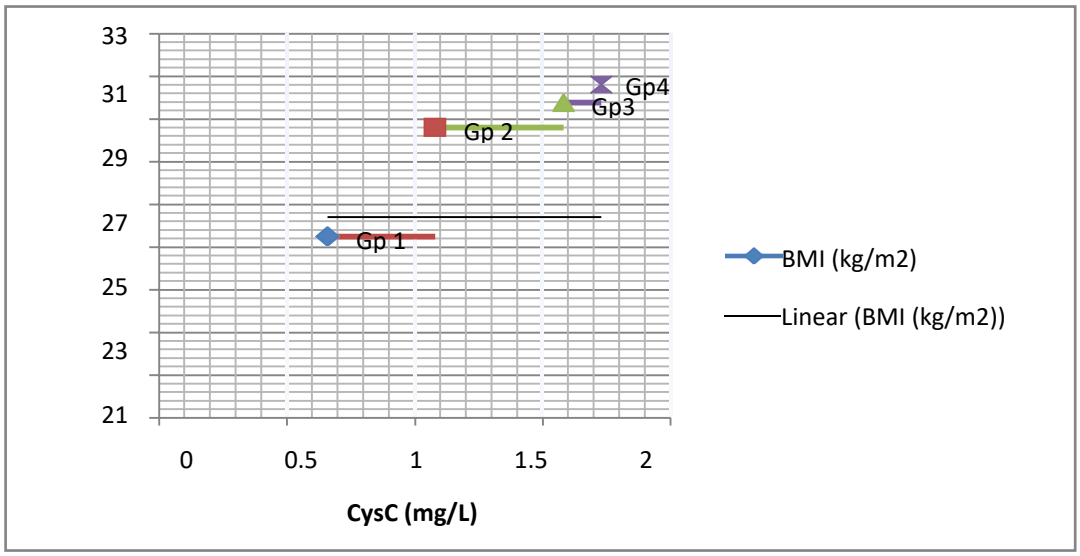


Fig-2 Correlation of CysC with BMI (kg/m2) in MetS Groups (Group1, 2 ,3 ,4) (r=0.94)

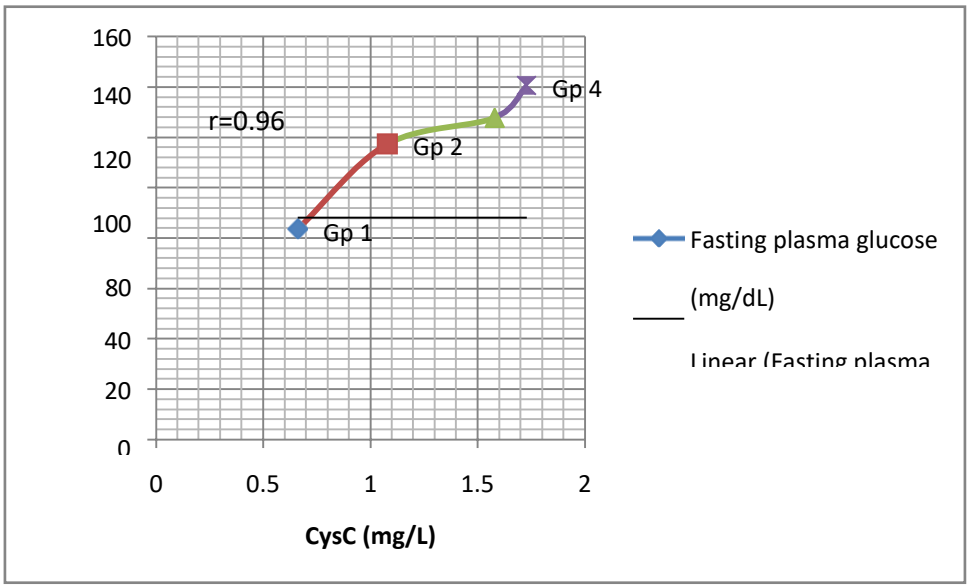


Fig-3 Correlation of CysC with Fasting plasma glucose (mg/dL) in MetS Groups (Group1, 2, 3, 4) (r=0.96)

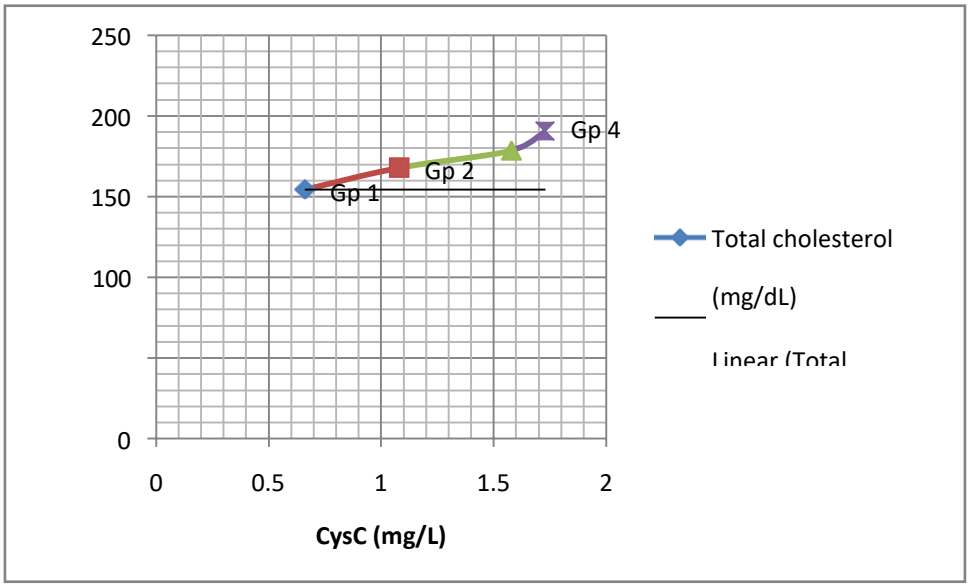


Fig-4 Correlation of CysC with Total cholesterol (mg/dL) in MetS Groups (Group1, 2, 3, 4) (r=0.98)

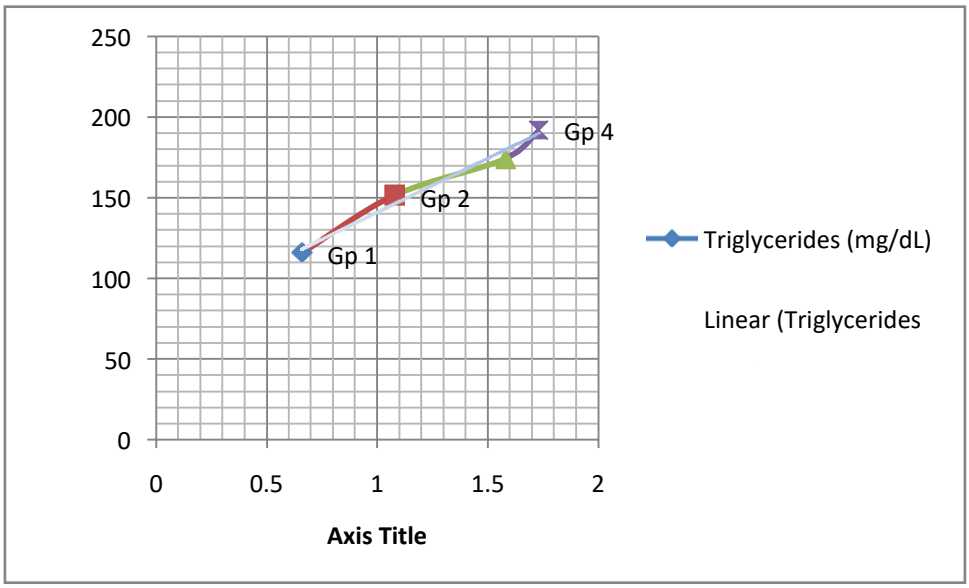


Fig-5 Correlation of CysC with Triglycerides (mg/dL) in MetS Groups(r=0.98)

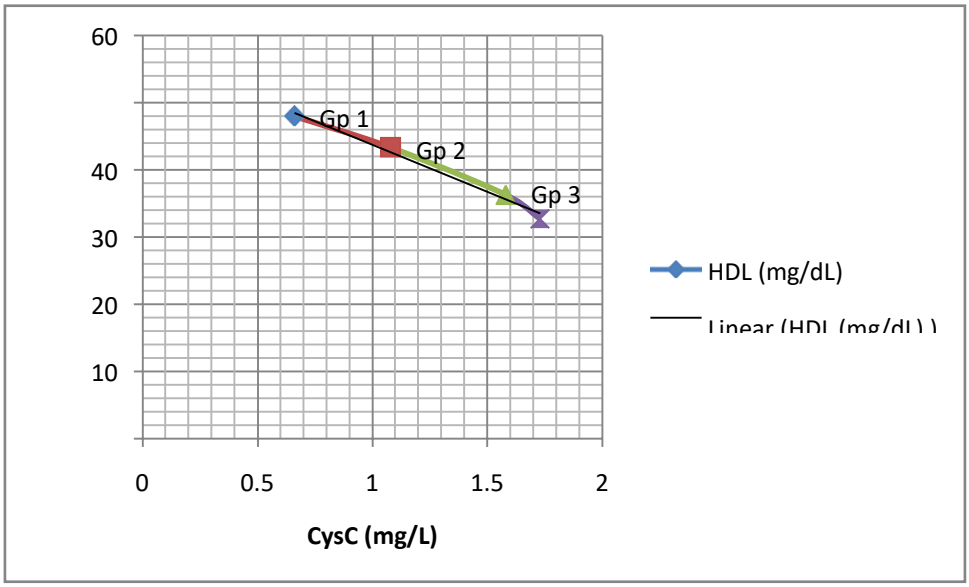


Fig-6 Correlation of CysC with HDL (mg/dL) in MetS Groups (Group1, 2, 3, 4) (r= -0.99)

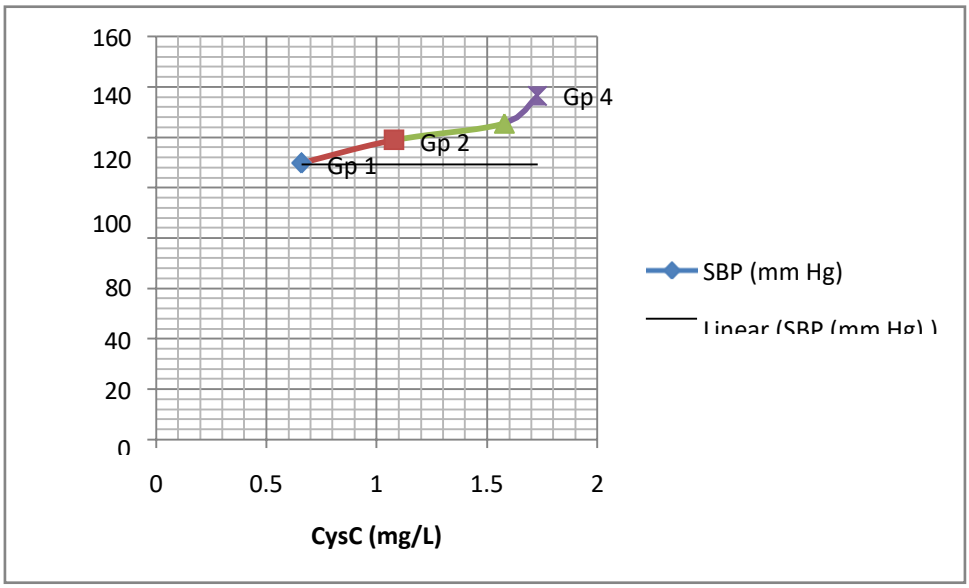


Fig-7 Correlation of CysC with SBP (mm Hg) in MetS Groups (Group1,2,3,4) (r=0.96)