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Study of Highly Sensitive C-Reactive Protein Level in Medical Students with Metabolic Syndrome

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Abstract: ***Background: Metabolic syndrome is considered proinflammatory state, and measurement of inflammatory markers like high-sensitivity C-reactive protein (hs-CRP) can improve the prediction of cardiovascular disease in subject with metabolic syndrome. Methods: We prospectively studied the relationship of high-sensitivity C-reactive protein (hs-CRP) with various components of metabolic syndrome in 50 medical students with metabolic syndrome at our tertiary care centre. Results: The mean age of patients was 22.18 ± 1.22years; with 26(52%) males and 24(48%) females. On univariate analysis, hs-CRP was found to be significantly increased in subjects with abnormal waist circumference (p= 0.0001), with deranged fasting glucose levels(p=0.0430) and those with hypertension(p=0.022) There was no significant association between hs-CRP and high triglycerides and reduced high density lipoprotein cholesterol. hs-CRP increased significantly with increasing number of components of metabolic syndrome (p=0.0074). Conclusions: High concentration of hs-CRP was present in subjects with metabolic syndrome. Thereforehs-CRP can be used as a maker of inflammation in metabolic syndrome.***

Keywords: Metabolic Syndrome,Highly Sensitive C-Reactive Protein,Obesity, Medical students

1. Introduction

Metabolic syndrome, is a cluster of abnormalities characterized by central obesity, high triglycerides, hypertension or high normal blood pressure, low high-density lipoprotein (HDL) cholesterol and diabetes or high fasting glucose. Subjects having this condition are at increased risk for developing cardiovascular disease and diabetes mellitus as well as increased mortality from other causes [1,2]. Publication of the Third Report of United States (US) National Cholesterol Education Program Adult Treatment Panel-III (NCEP-ATP-III)[3]data of the US Third National Health and Nutrition Survey (NHANES-3) were evaluated for prevalence of metabolic syndrome[4]. Prevalence in the US was reported as 23.7% with prevalence being similar for women(23.4%) and men (24.0%). An ethnic difference in its prevalence was reported with a higher prevalence among Mexican-Americans than other groups in the US[4].

India is a major contributor to the global cardiovascular mortality[5,6]and there is increasing trends in prevalence of various components of the metabolic syndrome [7–9].Studies across urban south India documented prevalence's ranging from 22.1% to 41%,[10–12] Likewise, a prevalence study of urban community in northern India reported a prevalence of 22.37% for metabolic syndrome.[13] On the contrary, a lower prevalence of 19.52% was reported in an urban population in western India.[14]

Inflammation plays a pivotal role both in the development of insulin resistance and metabolic syndrome.[15] Developing a robust biomarker that can predict metabolic syndrome instead of examining individual variable features will be important from a population standpoint of view in screening, monitoring the natural history of the disease, and measuring the response to therapeutic interventions.[15]There is now abundant evidence that high concentrations of high sensitivity C-reactive protein (hs-CRP), a proinflamatory cytokine is associated with insulin resistance and metabolic syndrome and may predict onset of diabetes mellitus and cardiovascular events.[15]There are suggestions to include hs-CRP as one of the diagnostic criteria for metabolic syndrome.[16]

It is already known that atherosclerosis begins early in life [17] and the cardiovascular risk factors in childhood track into adulthood and can predict future CVD[18].

In this study, we had measured the value of hs-CRP in medical students with metabolic syndrome and have correlated various components of metabolic syndrome with hs-CRP levels.

2. Materials and Methods

The present study entitled "Study of Highly Sensitive C-Reactive Protein Level in Medical Students with Metabolic Syndrome**"** was carried out in dept. of medicine, AcharyaVinobhaBhave Rural Hospital of Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha during the period of 2 years (September 2015 to September 2017).

50 medical students fulfilling criteria of metabolic syndrome according to modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and consideringabdominal obesity as per World Health Organization (WHO) guidelines for South Asians were enrolled in the present study.Subjects with acute and chronic infections , malignancy and chronic liver disease were excluded from the study.

The study was initiated only after obtaining permission from the institutional ethics committee, DattaMeghe Institute Of Medical Sciences (DU) Sawangi(Meghe) Wardha.Sample size were calculated on the basis of prevalence of metabolic

syndrome 33.5% and level of significance at 5%.[19]

Sample size

N= Z 2 α/2 * P*(1-P)/ d2
Z α/2= Level of significance at =5%
= 1.96
P= prevalence of metabolic syndrome=31.6=0.316
d = error of margin=13%

$$n = \frac{1.96^2 \times 0.316\ (1-0.316)}{(0.13 \times 0.13)}$$

n = 49.13
n=50

Anthropometric measurement

Waist circumference was measured using a non-elastic measuring tape at the highest level of iliaccrest with the patient standing with feet 1 foot apart.[20]

Blood Pressure Measurement:

Blood pressure were measured using a mercury sphygmomanometer, a minimum of two times in every participant in a sitting position and the mean of the readings will be used for analysis. Participants were classified as normotensive, prehypertensive and hypertensive as per the JNC - 7 criteria.[21]

Biochemical Parameter Estimation

Fasting plasma glucose was estimated by the GOD / POD method by the machine RobonicSemi Automatic Chemical Analyzer.Serum triglycerides were estimated using a LIQUID STABLE GPO – PAP method by machine RobonicSemi Automatic Chemical Analyzer. Direct Enzymatic Method estimated serum HDL by machine RobonicSemi Automatic Chemical Analyzer.

Method of measuring hs-CRP

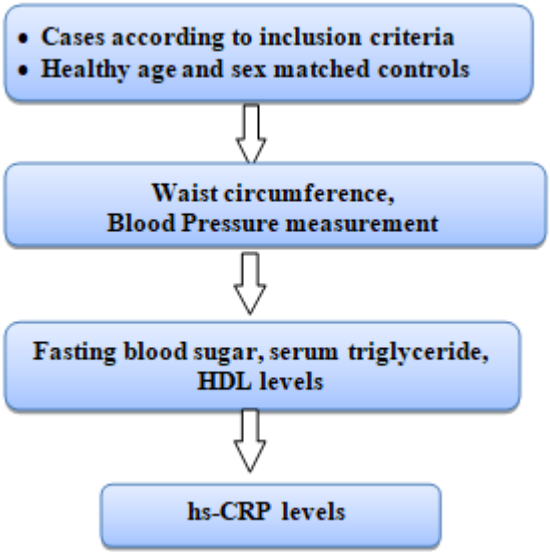
Principle: The latex particle coated with anti-CRP is agglutinated, when it reacts with the sample that contains C-reactive protein (CRP). The latex particles agglutinated is proportional to the concentration of the CRP in the sample and it can be measured by turbidimetry.

Method

- Under all aseptic precautions 2 ml of blood sample was collected from the vein of the subject.
- This sample was immediately centrifuged and serum was separated.
- This serum was preserved at -20 degree Celsius.
- All measurements were done in RANDOX DAYTONA random analyser available in AVBRH by turbidimetry method
- hs-CRP level>3mg/dl was considered as elevated.
- **KIT NAME-**Spinreact Ultrasensitive CRP kit.

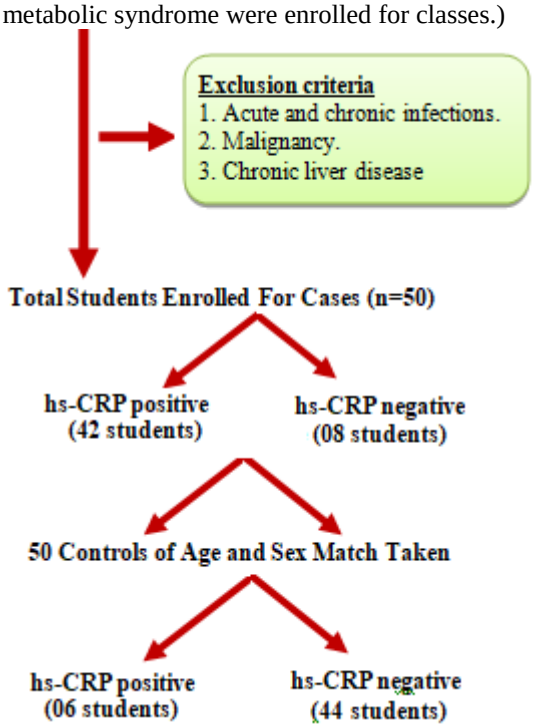
Study Process

Image no 1
Study Process



3. Flow Chart

Total Students Screened (n= 400)
(50 Students fulfilling at least 3 criteria of **-NCEP-ATP III**of metabolic syndrome were enrolled for classes.)



4. Statistical Analysis

Statistical analysis was done by using descriptive and inferential statistics using the student's unpaired t test, chi square test and Odd's ratio and software used in the analysis were SPSS 22.0 version and Graph Pad Prism 6.0 version and $p<0.05$ is considered as level of significance.

5. Result and Observation

In our study out of 50 medical students, mean age was 22.18 (0.78) and that of controls was 21.96 (1.40). Cases included 26 (52) % males and 24 (48) % females. Controls include 28 (56) % males and 22 (44) % females. There was **no**

statistical significant difference found in gender of subjects in both the groups ($p > 0.05$). Base line characteristics are shown in Table no 1. Mean hs-CRP concentration of cases was 4.14mg/l and that of controls were 2.15mg/l which was **statistically significant**. **P=0.0001 [**Table no 2**]**.There was a **significant association** between hs-CRP and the components of the metabolic syndrome. This was more so with central obesity (4.14 vs 2.15, p = **0.0001**), than with diabetes mellitus (4.23 vs 3.07, p = **0.043**) and with an elevated blood pressure level (4.90 vs 3.97, **p= 0.022**). Present study has no significant relationship of hs-CRP with low HDL levels (4.20 vs 3.87, p=0.43) and high triglyceride levels (4.07 vs 4.41,p=0.40) . Abdominal obesity showed more positive correlation with hs-CRP Levels.[Table no 3].In present study, we also found that there was higher median concentration of hs-CRP with increasing number of components of the metabolic syndrome. Patients fulfilling 3 and 4 criteria had a median hs-CRP of **4.04mg/l** and **5.14mg/l** respectively. As expected, there was a significant positive linear association with a number of abnormal features of the syndrome ,**p = 0.0001**[Table no 4 and figure no 1]. In present study the odds of having a high hs-CRP Levels were **38.50** [odds ratio (OR), confidence interval (CI) **(12.31-120.4)]** times higher in obese patients than that ofnon obese individual which is **statistically significant. [**Table no 5]. The odds of having a high hs-CRP Levels were **2.22** [odds ratio (OR), confidence interval (CI) **(0.19-25.02)]** times higher in deranged glucose level individuals than that of normal glucose level individual which is **statistically significant. [**Table no 6**]**.The odds of having a high hs-CRP Levels were **4.82** [odds ratio (OR), confidence interval (CI) **(0.25-91.42)]** times higher in individuals with raised blood pressure level than that of individuals with normal blood pressure level which is **statistically significant.[** Table no 7**]**. The odds of having a high hs-CRP Levels were **0.60, CI** (**0.06-5.66**) times higher in subjects with high triglyceride levels compared to normal triglyceride level subjects which is **statistically non-significant**. [Table no 8]. The odds of having a high hs-CRP Levels were **0.75**,**CI** (**0.12 – 4.52)** times higher in individuals with low HDL levels than that of individuals with normal HDL level which is **statistically non-significant. [**Table no 09]

Table 1: Baseline Characteristics

Total no of patients n = 50	Cases (mean)	SD	Controls (Mean)	SD	p-value
Age	22.18	1.22	21.98	1.30	0.79 p=0.43,NS
Sex Male=26 Female=24	26 24	52% 48%	28 22	56% 44%	0.16, p=0.68, NS
hs-CRP (mg/l)	4.14	1.10	2.15	0.29	11.55, p=0.0001, S
Waist circumference (cm)	106.46	13.45	84.9	3.17	10.29, p=0.0001,S
Triglyceride level(mg/dl)	159.26	11.36	98.50	33.25	12.22, p=0.0001, S
HDL Level(mg/dl)	54.42	9.16	51.00	9.46	1.83, P=0.069,NS
Fasting glucose(mg/dl)	105.44	5.52	93.56	5.90	10.38, p=0.0001,S
Blood pressure Systolic BP(mmHg) Diastolic BP(mmHg)	123 77.68	10.87 8.00	121.92 76.92	6.89 9.40	0.59, p=0.55, NS 0.43, p=0.63, NS

Table 2: Comparison of hs-CRP level between cases and controls

	Metabolic syndrome (Cases)	Controls	p-value
Mean hs-CRP(mg/l)	4.14(1.10)	2.15(0.29)	11.55,
Standard Deviation	1.10	0.29	p=0.0001,S

Table 3: Univariate Comparison of hs-CRP levels between various components of metabolic syndrome

Metabolic syndrome component	Mean hs-CRP level(mg/l)	p value
Obesity (Waist circumference >90cm-male, >80cm-female) Yes (n=50) No (n=50)	4.14±1.10 2.15±0.29	11.55 P=0.0001, S
Fasting glucose (>100mg/dl) Yes (n=46) No(n=04)	4.23±1.10 3.07±0.18	2.08, p=0.043,S
Low HDL (<50mg/dl –Female) (<40mg/dl – Male) Yes(n=12) No(n=38)	4.20±1.13 3.87±0.097	0.79, p=0.43,NS
High TG (>150mg/dl) Yes(n=41) No(n=09)	4.07±1.14 4.41±0.91	0.84, p=0.40,NS
Hypertension (135/80mmhg) Yes=09 No=41	4.90±0.96 3.97±1.07	2.36, p=0.022,S

Table 4: Distribution of subjects according to fulfilling 3 and 4 criteria of metabolic syndrome

Metabolic Syndrome	hs-CRP LEVEL(mg/l)	P-value
Fulfilling 3 criteria	4.04 ±0.91	3.46,p=0.0074,S
Fulfilling 4 criteria	5.14 ±0.95	

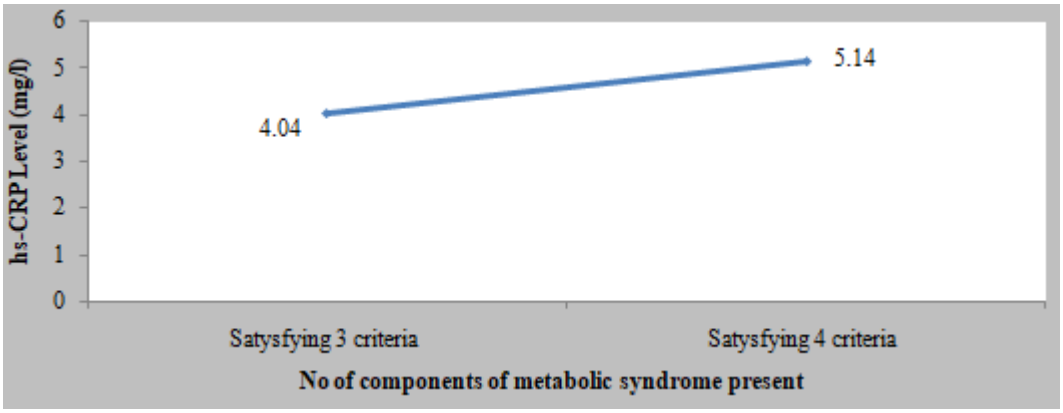


Figure 1: Distribution of subjects according to fulling 3 and 4 criteria

Table 5: Association Of hs-CRP with Abdominal Obesity

hs-CRP Levels	Obese (n=50)	Non obese (n=50)	2ϰ-value	p-value	Odd's Ratio
Increased(>3mg/l)	42	6	51.92	0.0001,S	38.50 (12.31-120.4)
Normal (<3mg/l)	08	44			

Table 6: Association of hs-CRP with Fasting Glucose Level

hs-CRP Levels	Impaired fasting glucose (n=46)	Normal fasting glucose levels(n=4)	2ϰ-value	Odd's Ratio
Increased (>3mg/l)	40	3	0.43	2.22 (0.19-25.02)
Normal (<3mg/l)	6	1		

Table 7: Association of hs-CRP with Blood Pressure

hs-CRP Levels	Raised Blood Pressure(n=9)	Normal Blood Pressure(n=41)	2ϰ-value	Odd's Ratio
Increased (>3mg/l)	9	33	2.09	4.82 (0.25-91.42)
Normal (<3mg/l)	0	08		

Table 8: Association of hs-CRP with Triglyceride Level

hs-CRP Level	Impaired Triglyceride Levels(n=41)	Normal Triglyceride Level(n=09)	2ϰ-value	Odd's Ratio
Increased (>3mg/l)	34	08	0.19	0.60 (0.06-5.66)
Normal (<3mg/l)	07	01		

Table 09: Association of hs-CRP with HDL level

hs-CRP Levels	Low HDL Levels(n=12)	Normal HDL Levels(n=38)	2ϰ-value	Odd's Ratio
Increased (>3mg/l)	10	33	0.09	0.75 (0.12-4.52)
Normal (<3mg/l)	2	5		

6. Discussion

In the current study, we compared the value of hs-CRP Level in metabolic syndrome subjects with controls and we evaluated the relationship of hs-CRP with various components of metabolic syndrome in medical students of our college.

In the present study, no statistical difference was found in gender in various components of metabolic syndrome. Similar findings were seen in study by Huffman et al **in** 2009 where the metabolic syndrome was present in 41% of participants, and no differences were seen by sex.[22]

In the present study, the mean concentration of hs-CRP was significantly higher (4.14mg/dl) than that of controls (2.15mg/l), **p value=0.0001**. Similar findings were seen by H. H. El Shorbagy*et al* in2010stating that Obese group had significantly higher (hs-CRP) levels than control group, ($p <$ 0.01) and significantly higher LDL-C, triglyceride (TG), and lower HDL-C than the control group.[23]

Our analysis revealed that there was a significant association between hs-CRP and the components of the metabolic syndrome. This was more so with central obesity (4.14 vs 2.15, p = 0.0001), then with diabetes mellitus(4.23 vs 3.07, p = 0.043) and with elevated blood pressure level(4.90 vs 3.97,p= 0.022). However our study has no significant relationship of hs-CRP with low HDL levels(4.20 vs 3.87, p=0.43) and high triglyceride levels(4.07 vs 4.41,p=0.40) . Similar findings were seenbySudhaVidyasagar et alin2013,2014. There was a significant association between hs-CRP and the components of the metabolic syndrome. This was highest with central obesity(1.4 vs 0.8 mg/L, p = 0.013), and with diabetes mellitus,(1.3 vs 0.7 mg/L, p=0.027). However there was no association between hypertension and elevated hs-CRP level in this study[24].

We also found that there was higher median concentration of hs-CRP with increasing number of components of the metabolic syndrome. Patients fulfilling 3 and 4 criteria had a median hs-CRP of 4.04mg/dl and 5.14mg/dl respectively. As expected, there was a significant positive linear association with a number of abnormal features of the syndrome **(p = 0.0001).**Similar findings were seenbySudhaVidyasagaret alin2013,2014. There was higher median concentration of hs-CRP with increasing number of components of the metabolic syndrome. Patients fulfilling 3, 4, and 5 criteria had a median hs-CRP of 1.21, 1.80, and 2.29 mg/L respectively. There was a significant positive linear association with a number of abnormal features of the syndrome (p = 0.008).[24]

We also found that the odds of having a high hs-CRP Levels were **38.50**[odds ratio (OR), confidence interval (CI) **(12.31-120.4)]** higher in obese subjects with metabolic syndrome compared to non-obese subjects.

Our study also revealed that the odds of having a high hs-CRP Levels were **2.22** [odds ratio (OR), confidence interval (CI) **(0.19-25.02)]** higher in impaired fasting glucose level subjects compared to normal glucose level subjects.

In present study, we also found that the odds of having high hs-CRP Levels were **4.82** [odds ratio(OR),confidence interval(CI) **(0.25-91.42)]** higher in hypertensive subjects compared to normal subjects.

Similar findings were seenby Antônio C. Oliveira et alin 2008 stating that excessive weight (odds ratio (OR), 7.9; confidence interval (CI), 4.7–13.4; P = 0.000), hypertension (OR, 2.3; CI, 1.3–4.2; P = 0.003), and hypertriglyceridemia (OR, 2.3; CI, 1.5–3.7; P < 0.001) were independently associated with hs-CRP.[25]

7. Conclusion

High concentration of hs-CRP is present in subjects with metabolic syndrome as compared to controls.A positive correlation was found between hs-CRP and the components of metabolic syndrome like central obesity, diabetes mellitus and hypertension. The highest significant correlation was present between central obesity and hs-CRP.There was a linear increase in hs-CRP with increasing number of metabolic syndrome components. This suggests that the higher the number of components of metabolic syndrome in a subject, higher the risk of cardiovascular events.Therefore hs- CRP can probably be used as a surrogate marker of chronic inflammation in patients with metabolic syndrome.

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