How to Cite:
Poonguzhali, B., Sowndharya, J., Prabha, T., & Suganya, K. (2022). A study of lipoprotein (a) and biochemical parameters of metabolic syndrome among younger population. *International Journal of Health Sciences*, *6*(S1), 14435–14448. https://doi.org/10.53730/ijhs.v6nS1.8721

A study of lipoprotein (a) and biochemical parameters of metabolic syndrome among younger population

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***Abstract*---**Metabolic syndrome is a cluster of conditions that occur together, increasing your risk of heart disease, stroke and type 2 diabetes. Aim & Objective: Due to the scarcity of studies about the epidemiological behaviour of Lp(a) in our country, the main aim of our research is to study the relationship between Lp(a) and the metabolic syndrome and its components in younger population Materials & Methods: A total of 136 subjects were enrolled into the study. A pre-structured and pretested proforma was used to collect the data. Baseline data including age, gender, religion, detailed medical history, clinical examinations and relevant investigations such as HDL-cholesterol, triglyceride, lipoprotein (a) and fasting glucose were done in the study. Analysis was done by SPSS version 18. In our study, 46.2% males and 43.1% females were affected by metabolic syndrome with no significant correlation with sex. Lipoprotein (a) level is increased in themetabolic syndrome category by Modified NCEP ATP III Criteria and IDF Criteria. Lipoprotein (a) level has significant correlation with the metabolic syndrome according to their p values (<0.01). It has significantly correlated with the individual components of metabolic syndrome and age category too (p value <0.01).

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
Manuscript submitted: 18 March 2022, Manuscript revised: 9 April 2022, Accepted for publication: 27 May 2022

***Keywords*---**Metabolic syndrome, Lipoprotien (a), HDL-cholesterol, triglycerides, fasting glucose.

Introduction

Metabolic syndrome is a cluster of conditions that occur together, increasing your risk of heart disease, stroke and type 2 diabetes. These conditions include increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels[1] Metabolic syndrome is identified by the guidelines provided by World Health Organization (WHO), National Cholesterol Education Program – Adult Treatment Panel III (NCEP-ATP III) and International Diabetes Federation (IDF). ATP III viewed cardio vascular disease as the primary clinical outcome of MS. The people affected by the MS have increased chance of getting Type 2 diabetes mellitus and CVD[1]. South Asians have high numbers of diabetes and highest numbers of premature CAD in the world, both occur about 10 years early compared to other populations.

This increased risk is due to South Asian dyslipidemia. It is characterized by high levels of apolipoprotein B, lipoprotein (a), triglycerides in the serum and low levels of apolipoprotein A_1 and HDL cholesterol.[2] Lipoprotein (a) has emerged nowadays as a powerful genetic risk factor for CAD.[3] Nowadays Clinical interest in Lp(a) has increased more times, because the studies has explained the relationship between plasma Lp(a) concentrations (reported as ≥ 30mg/dL) and coronary and cerebro vascular disease, peripheral artery disease, and also the early origin of atherosclerosis in children and adolescents. The scarcity of studies about the epidemiological behaviour of Lp(a) in our country, the main aim of our research is to study the relationship between Lp(a) and the metabolic syndrome andits components in younger population .[4]

Materials and Methods

Sources of data

Patients and bystanders who attended the general medicine OPD for routine medical check up formed the subjects for the present cross-sectional study. The total of 136 subjects were enrolled into the study.

Diagnostic criteria

Metabolic syndrome was diagnosed according to the NCEP-ATP III criteria (Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults – Adult Treatment Panel III) and IDF criteria.

Inclusion criteria

- Patients and bystanders attending general medicine OPD
- Age between 24-39 years.

Exclusion criteria

- Pregnancy, Congenital diseases, patients with chronic diseases.
- Those who are not willing to participate.

Method of collection of data

Informed consent was taken from the all subjects. A pre-structured and pretested proforma was used to collect the data. Baseline data including age, gender religion, detailed medical history, clinical examinations and relevant investigationswere included as part of the methodology.

The following parameters were collected: age, gender, religion, waist circumference, blood pressure and fasting clinical chemistry parameters. Waist circumference was measured using a non-stretchable fibre measuring tape. The subjectswere asked to stand erect in a relaxed position with both feet together on a flat surface. Waist circumference was taken at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. Blood pressure was recorded in the sitting position in the right arm to the nearest 2 mmHg using the mercury sphygmomanometer (Diamond Deluxe BP apparatus, Pune, India). Two readings were taken 5 min apart and the mean of the two was taken as blood pressure. Blood samples were collected from each participant after a 9-hour overnight fasting and employing standard infection prevention procedures. The collected blood samples were used to determine the concentrations of HDL-cholesterol, triglyceride, lipoprotein (a) and fasting glucose.

Estimation of lipoprotein (a) by latex turbidimetry

Lp(a) is a low density lipoprotein-like particle containing apolipoprotein B-100 disulphide-linked to one large glycoprotein called apolipoprotein (a). The Lp(a)-turbilatex is a quantitative turbidimetric test for the measurement of Lp(a) in human serum or plasma. The quantification of Lp(a) in serum or plasma is important for identification of individuals at risk for developing atherosclerosis [5].

Estimation of blood glucose
Using Colorimetric enzymatic method GOD-POD (Glycerol phosphate oxidase – peroxidase) blood glucose was estimated [6].

Estimation of serum triglycerides
Using Colorimetric enzymatic method GOD-POD serum triglycerides were estimated in the serum[7].

Estimation of serum HDL-cholesterol
Bio systems kit was used for the measurement of serum HDL cholesterol. HDL cholesterol is spectrophotometrically measured by direct detergent method[8].

Statistical analysis

Analysis was done by SPSS version 18.Simple proportion, Percentage, Mean, Standard deviation, and Pearson correlation co-efficient were calculated. Appropriate test of significance like chi-square test and “t”test were done. Values of $p < 0.05$ were considered statistically significant.

Result

Table 1: Parameters of metabolic syndrome including Lp(a)

Descriptive Statistics					
	Number	Minimum	Maximum	Mean	Std. Deviation
WC	136	78	104	91.92	5.46
SBP	136	100	160	131.56	11.77
DBP	136	70	100	84.07	7.11
FBS	136	82	170	106.82	13.32
TGL	136	112	204	155.71	22.18
HDL	136	25	54	40.50	6.88
Lp(a)	136	13.12	90.91	43.36	21.77

According to the parameters of metabolic syndrome, minimum waist circumference is 78 cm and maximum is 104 cm with the mean and standard deviation of 91.92 ± 5.46. Minimum systolic BP is 100 mmHg and maximum is 160 mmHg with the mean and standard deviation of 131.56 ± 11.77, followed by diastolic BP, minimum is 70 mmHg and maximum is 100 mmHg with the mean and standard deviation of 84.07 ± 7.11.About fasting blood sugar, minimum is 82 mg/dl and maximum is 170 mg/dl with the mean and standard deviation of 106.82 ± 13.32. In lipids, minimum triglyceride is 112 mg/dl and maximum is 204 mg/dl with the mean and standard deviation of 155.71 ± 22.18, followed by High density lipoprotein cholesterol, minimum is 25 and maximum is 54 with the mean and standard deviation of 40.50 ± 6.88. According to the lipoprotein (a) values, minimum is 13.12 and maximum is 90.91 with the mean and standard deviation of 43.36 ± 21.77.

Table 2: Distribution of Metabolic Syndrome Parameters among Age Category

AGE.CAT		WC	SBP	DBP	FBS	TGL	HDL
24 - 29 Years	N	43	43	43	43	43	43
	Mean	88.00	119.67	77.81	96.33	133.44	44.51
	SD	4.018	7.596	4.447	6.951	10.664	4.930
30 - 34 Years	N	28	28	28	28	28	28
	Mean	91.57	132.14	84.86	106.36	163.89	40.57
	SD	5.666	7.075	7.271	8.274	17.635	5.909
35 - 39 Years	N	65	65	65	65	65	65
	Mean	94.66	139.17	87.88	113.97	166.92	37.82
	SD	4.560	8.916	5.476	13.691	18.487	7.137
Total	N	136	136	136	136	136	136
	Mean	91.92	131.56	84.07	106.82	155.71	40.50
	SD	5.462	11.772	7.107	13.316	22.180	6.877
F - Value		26.659	73.895	42.067	33.782	59.525	14.776
p- Value		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*

* Significant at 0.01 level

Table 2 shows the metabolic syndrome parameters like waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood sugar, abnormal

triglycerides and abnormal HDL levels, individually has significant correlation with the age category, according to their p-value <0.01 level.

Table 3: Distribution of Metabolic Syndrome Parameters among Sex Category

SEX		WC	SBP	DBP	FBS	TGL	HDL
Male	N	78	78	78	78	78	78
	Mean	93.63	135.18	85.97	109.95	159.40	37.35
	SD	5.604	10.999	6.610	14.710	22.872	5.564
Female	N	58	58	58	58	58	58
	Mean	89.62	126.69	81.52	102.62	150.76	44.74
	SD	4.344	11.079	7.002	9.814	20.371	6.186
Total	N	136	136	136	136	136	136
	Mean	91.92	131.56	84.07	106.82	155.71	40.50
	SD	5.462	11.772	7.107	13.316	22.180	6.877
F – Value		20.490	19.696	14.379	10.806	5.203	53.404
p- Value		0.000*	0.000*	0.000*	0.001*	0.024**	0.000*

* Significant at 0.01 level ** Significant at 0.05 level

Table 3 shows that the MS parameters waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood sugar, abnormal HDL levels, individually has significant correlation with the age category, according to their p-value <0.01 level and abnormal triglycerides have significant correlation with the sex category, according to their p- value <0.05 level.

Table 4: Distribution of Parameters among MS Category by Modified NECP ATP III

MS.BY. NECP. ATPIII		AGE	WC	SBP	DBP	FBS	TGL	HDL
Yes	N	64	64	64	64	64	64	64
	Mean	35.58	95.50	139.91	89.25	114.69	172.70	36.97
	SD	2.984	4.704	7.932	5.595	13.509	16.898	6.907
No	N	72	72	72	72	72	72	72
	Mean	27.92	88.74	124.14	79.47	99.83	140.61	43.64
	SD	3.931	3.907	9.437	4.759	8.362	13.805	5.133
Total	N	136	136	136	136	136	136	136
	Mean	32.60	91.92	131.56	84.07	106.82	155.71	40.50
	SD	5.040	5.462	11.772	7.107	13.316	22.180	6.877
F - Value		165.525	83.825	109.736	121.250	60.855	148.347	41.422
p- Value		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*

* Significant at 0.01 level

Table 4 shows the distribution of parameters among metabolic syndrome category by NCEP ATP III Criteria with their mean and standard deviation. All the parameters waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood sugar, abnormal triglycerides and abnormal HDL levels, individually

has significant correlation with the metabolic syndrome category, according to their p-value <0.01 level.

Table 5: Distribution of Parameters among MS Category by IDF

MS.BY.IDF		AGE	WC	SBP	DBP	FBS	TGL	HDL
Yes	N	61	61	61	61	61	61	61
	Mean	35.76	95.7	140.33	89.31	115.11	171.59	37.11
	SD	2.967	4.663	7.951	5.315	13.680	17.553	6.785
No	N	75	75	75	75	75	75	75
	Mean	28.21	88.84	124.43	79.81	100.08	142.80	43.25
	SD	3.908	3.922	9.307	5.314	8.306	16.459	5.640
Total	N	136	136	136	136	136	136	136
	Mean	32.60	91.92	131.56	84.07	106.82	155.71	40.50
	SD	5.040	5.462	11.772	7.107	13.316	22.180	6.877
F - Value		163.978	86.965	111.701	107.456	62.383	96.965	33.199
p - Value		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*

* Significant at 0.01 level

Table 5 shows the distribution of parameters among metabolic syndrome category by IDF Criteria with their mean and standard deviation. All parameters had significant correlation with the metabolic syndrome category, according to their p-value <0.01 level.

Table 6: Lp(a) and Age, Sex, Religion Categories

Factors	Category	Number	Mean	SD	F- Value	p- Value
Age	24 - 29 Years	43	21.3681	5.66707	70.471	0.000*
	30 - 34 Years	28	45.6282	14.11606		
	35 - 39 Years	65	56.9342	19.49907		
Sex	Male	78	46.2577	24.53144	3.292	0.072
	Female	58	39.4662	16.81050		
Religion	Hindu	82	43.8849	22.73297	1.080	0.343
	Christian	42	40.3057	18.83605		
	Muslim	12	50.4783	24.40403		

* Significant at 0.01 level

In our study population, maximum amount of lipoprotein (a) is present in the age group of 35-39 years with the mean and standard deviation of 56.93 ± 19.49, followed by 30-34 years with the mean and standard deviation of 45.62 ± 14.11 and then 24-29 years with the mean and standard deviation of 21.36 ± 5.66. Amount of lipoprotein (a) among various age categories has significant correlation according to their p-value 0.000 (<0.01). In sex category, maximum amount of lipoprotein (a) is present in the males with the mean and standard deviation of 46.25 ± 24.53 compared to the females with the mean and standard deviation of 39.46 ± 16.81. Amount of lipoprotein (a) among sex

category has no significant correlation according to their p- value 0.072 (>0.05).In religion category, maximum amount of lipoprotein (a) is present in Muslims with the mean and standard deviation of 50.47 ± 24.40 followed by Hindus with the mean and standard deviation of 43.88 ± 23.73 and then Christians with the mean and standard deviation of 39.46 ± 16.81. Amount of lipoprotein (a) amongreligion category has no significant correlation according to their p-value 0.343 (>0.05).

Table 7: Lp(a) and Metabolic Syndrome

MS Category		Number	Mean	SD	F –Value	p- Value
Modified NECP ATP III	Yes	64	58.5331	18.54920	103.137	0.000*
	No	72	29.8753	14.27932		
IDF	Yes	61	58.6128	18.60316	90.136	0.000*
	No	75	30.9568	15.37194		

* Significant at 0.01 level

Amount of lipoprotein (a) is present in the metabolic syndrome category, by Modified NECP ATP III Criteria with the mean and standard deviation of 55.65 ±18.30 and IDF Criteria with the mean and standard deviation of 56.07 ± 18.10. Metabolic syndrome category by either Modified NECP ATP III Criteria or IDF Criteria has significant correlation with lipoprotein (a) according to their p-value 0.000 (<0.01).

Table 8: Correlation of Lp(a) with Other Parameters

	Number	Correlation Coefficient	Significance
AGE	136	0.751	0.000*
WC	136	0.681	0.000*
SBP	136	0.691	0.000*
DBP	136	0.644	0.000*
FBS	136	0.668	0.000*
TGL	136	0.668	0.000*
HDL	136	-0.636	0.000*

* Correlation is significant at 0.01 level.

In our study, lipoprotein (a) with the age category has significant correlation according to the correlation coefficient 0.751 and p-value 0.000 (<0.01) and the lipoprotein (a) with the waist circumference has significant correlation according to the correlation coefficient 0.681 and p-value 0.000 (<0.01). Lipoprotein (a) with the systolic blood pressure has significant correlation according to the correlation coefficient 0.691 and p-value 0.000 (<0.01) and diastolic blood pressure has significant correlation according to the correlation coefficient 0.644 and p-value 0.000 (<0.01).Lipoprotein (a) with the fasting blood sugar has significant correlation according to the correlation coefficient 0.668 and p-value 0.000 (<0.01) and also with the triglyceride level has significant correlation according to the correlation coefficient 0.668 and p-value 0.000 (<0.01). Finally, lipoprotein (a) with HDL cholesterol has

significant negative correlation according to the correlation coefficient -0.636 and p- value 0.000 (<0.01).

Table 9: Correlation of Age with Other Parameters

	Number	Correlation Coefficient	Significance
WC	136	0.579	0.000*
SBP	136	0.723	0.000*
DBP	136	0.627	0.000*
FBS	136	0.624	0.000*
TGL	136	0.628	0.000*
HDL	136	-0.443	0.000*

* Correlation is significant at 0.01 levels.

Table 9 shows correlation of age with metabolic syndrome parameters. Waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood sugarand triglycerides have significant correlation with the age category according to their correlation coefficients (and p-values) respectively 0.579 (0.000) ,0.723 (0.000), 0.627
(0.000), 0.624(0.000), 0.628 (0.000).HDL cholesterol has significant negative correlation with the age category according to their correlation coefficient -0.443 and p-value 0.000.

Table 10: Correlation of Other Parameters

Control Variables	Other Variables	WC	SBP	DBP	FBS	TGL	HDL
AGE & Lp(a)	WC	1.000	.406**	.357**	.401**	.292**	-.392**
	SBP	.406**	1.000	.573**	.423**	.318**	-.416**
	DBP	.357**	.573**	1.000	.297**	.350**	-.216*
	FBS	.401**	.423**	.297**	1.000	.165	-.233**
	TGL	.292**	.318**	.350**	.165	1.000	-.247**
	HDL	-.392**	-.416**	-.216*	-.233**	-.247**	1.000
**. Correlation is significant at 0.01 level							
*. Correlation is significant at 0.05 level							

Age and lipoprotein (a) is taking as control variables, correlation of other parameters of metabolic syndrome individually shows significant correlation except systolic and diastolic blood pressure. HDL has negative correlation with all otherparameters of metabolic syndrome.

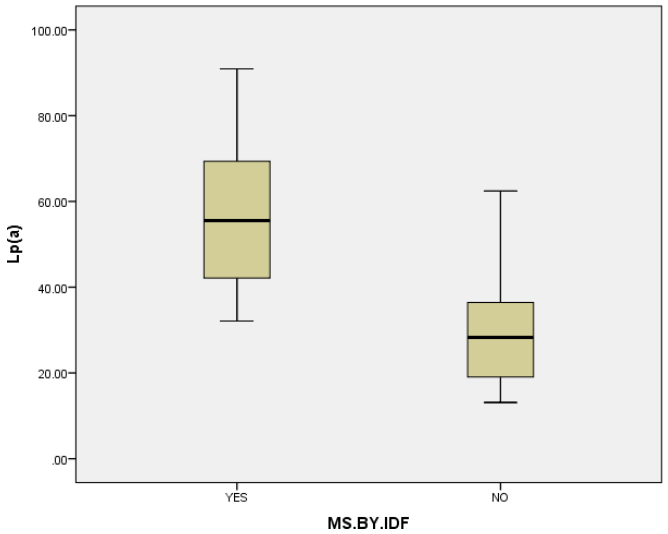

Figure 1: Lp(a) in MS by modified NCEP ATP III category

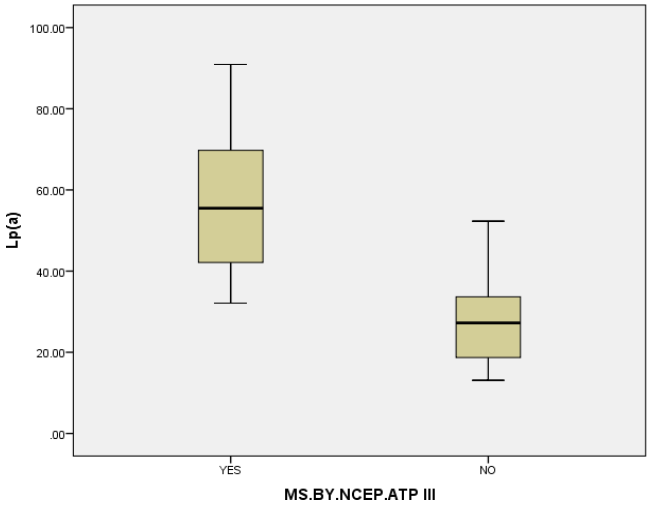

Figure 2: Lp(a) in ms by IDF category

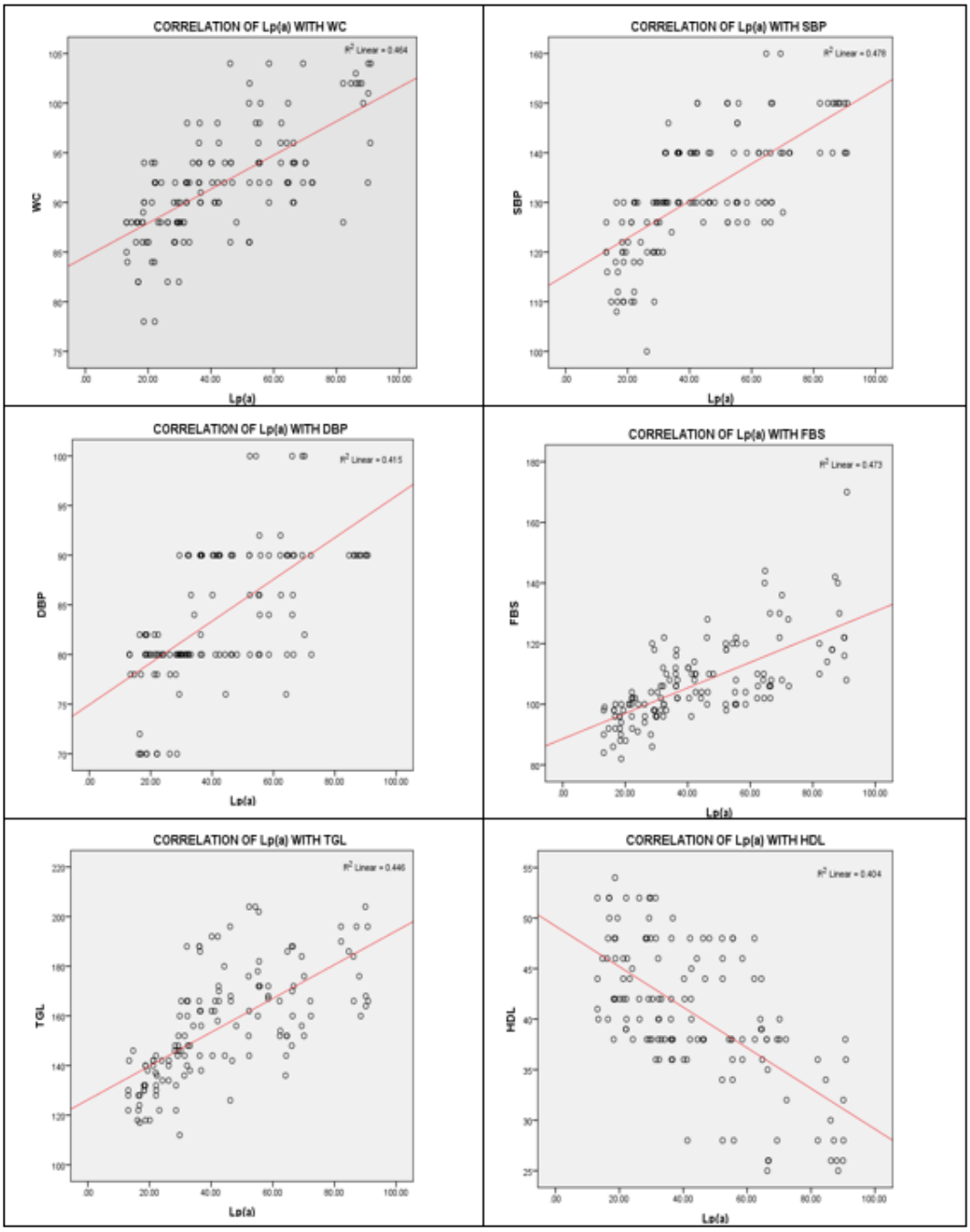

Figure 3: Correlation of Lp (a) with MS parameters

Discussion

Metabolic syndrome (MS), major components of which include central obesity, hypertriglyceridemia, low high-density lipoprotein levels, elevated BP and fasting hyperglycaemia has emerged as an important determinant of CV risk. Nowadays

metabolic syndrome prevalence is increasing in the childhood and adolescent population[9].

According to waist circumference cut off criteria, Rajeev Gupta et al stuty[10]was 108cm (M) and 80cm (F). Dongfeng Gu et al[11] and Pandit Vinodh et al[12] studies used 90cm (M) and 80 cm (F) as a cut off criteria. We also used 90cm (M) and 80 cm (F) as a cut off criteria similar to above studies. Different studies uses different criteria, in this analysis, we have used the ATP III criteria, with a modification to the value for waist circumference (WC) that is more applicable to the Asian Indian population. The waist circumference criteria followed in this study is comparable with A.Ramachandranet al[13], Dongfeng Gu et al[11] and Pandit Vinodh et al[12]

G.P.Parale et al[14] study shows 13.22% of males and 7.36% of females are affected by diabetes mellitus. Rajeev Gupta et al[10] (16.9% males, 16.1% females), Pandit Vinodh et al[12] (18.4% males, 11.2% females) also shows maximum numbers of males are affected by diabetes compared to females. However Sarkar et al[15] study shows 20.7% males and 41.3% females, which is contradictory to other three studies.

In our study, incidence of diabetes mellitus in males was higher than the females because women mainly develop peripheral adiposity with gluteal fat accumulation, whereas men are more prone to development of central or android obesity. (However, concentrations of lipoproteins as well as body fat distribution in women shift to a male pattern after menopause).

Shahbazian et al[16] study (13.7% males & 16.9% females), Kamble et al[17] study (53.5% males & 54.2% females) shows females are maximum affected by hypertension compared to males. Pandit Vinodh et al[12] (21.6% males & 18.4% females), Surana et al[18] (75.1% males & 71.01% females) shows males are affected mostly by hypertension.

The percentage of hypertension in our study (52.6% males and 34.5% females) is similar to Kamble et al[17] study in rural wartha, central India. Males are more affected by hypertension than the females because of android type obesity and smoking. Smoking leads to narrowing of blood vessels and increases the blood pressure.

al[19]study (47.8% in males & 34.2% in females), Surana et al[18] study (58.32% in males &57.25% in females) show abnormal triglyceride levels more in males compared to females. Pandit . However our study substantiates Kamble et al[17], Shahbazian et al[19] and Surana et al[18] study results. The value of our study is similar to Surana et al study (53.8% in males and 37.9% in females).

Pandit Vinodh et al[12] studies show decreased HDL levels 22.4% in males and 20.8% in females. Here decreased HDL levels are more or less similar in males and females. The other studies show decreased HDL levels more in females compared to males. Shahbazian et al[19] study shows decreased HDL 28.5% in males and 50.7% in females, Surana et al[18] study shows 43.05% in males and 64.59% in females, and Kamble et al[17] study shows 50% in males and 70.2% in

females. Likewise our study also shows HDL levels decreased more in females compared to males. The values are similar to Shahbazian et al[19] study.

Metabolic syndrome category by either Modified NECP ATP III Criteria or IDF Criteria has significant correlation with lipoprotein (a) according to their p-value 0.000 (<0.01). Lipoprotein (a) and individual parameters of metabolic syndrome has also significant correlation according to their p-value (<0.01) levels. Among them HDL has negative correlation with lipoprotein (a). Subjects with MS have increased levels of Lp(a) compared to the normal subjects. Our result is similar to the study of Bermudez et al[20] and Bozbas et al[21]. This association differs from the study done in older Japanese adults[22] where Lp(a) and MS have no significant correlation.

There are not much of studies explaining the relationship between individual components of MS and Lp(a)[23]. Only few studies dealt about this relationship. In our study, every individual component of the MS has significant correlation with Lp(a) like Bermudez et al[20] study. Our results differ from the study done by Candido et al[24] in 400 Brazilian individuals (here, no significant correlation between MS and Lp(a)).

In our population, age and sex has significant correlation with Lp(a).so, age also is the main risk factor for presenting elevated Lp(a), similar to previous studies on Swedish subjects [25]and on Taiwanese population[26]. According to sex, males have higher Lp(a) levels than females similar to Kotani et al study[22]. One limitation of our study was that, this study was cross sectional that does not allow us to draw any causal interference. Therefore in the future large prospective studies should be used to confirm the association between above mentioned factors and metabolic syndrome.

Conclusion

In our study, according to gender, 46.2% males and 43.1% females were affected by metabolic syndrome with no significant correlation in the sex. Lipoprotein (a) level is increased in the metabolic syndrome category by Modified NCEP ATP III Criteria and IDF Criteria. Lipoprotein (a) level has significant correlation with the metabolic syndrome according to their p values (<0.01). It has significantly correlated with the individual components of metabolic syndrome and age category also (p value <0.01).

The significant increase in the prevalence of metabolic syndrome is primarily a major risk factor for coronary heart disease and diabetes mellitus. Health education and awareness among individuals about nutrition, physical exercise and waist circumference maintenance from the younger age group is needed to prevent major non-communicable health disorders in the age of increased life expectancy. The detection of one component of the metabolic syndrome should lead to a search for and management of the other components.

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