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Plasma Adiponectin Is An Independent Predictor Of Metabolic Syndrome

Y. Premchandra singh[1], L. Tilakeswari Devi[2],L. Joshita[3],
Th. Romola Devi[4], S. Ranabir [5] M. Amuba [6], Th. Premchand[7],
W. Gyaneshwar Singh[8]

[1,]*Fellow,Diabetes Mgt(CMC Vellore)and ex-PGT,Dept .of Biochemistry,RIMS ,Imphal.*
[2]*MPH,MD(Anaesthesiology)student,Dept of Anaesthesiology,RIMS,Imphal*
[3,4] *MD(Biochemistry) student,Dept.Of Biochemistry,RIMS*
[5]*DM (Endocrinology),AIIMS,Assistant Professor, Dept of Medicine ,RIMS*
[6,8] *Professor,Dept.of Biochemistry ,RIMS,Imphal*
[7]*Professor,Dept.of Medicine ,Regional Institute of Medical Sciences,Imphal*

Abstract:Objective: *To evaluate the relationship between serum adiponectin level and metabolic syndrome and to identify factors influencing adiponectin level.*

Methods: *A cross-sectional study was performed for a period of 2 years, employing 90 subjects including 60 type 2 Diabetes Mellitus patients and 30 apparently normal individuals in Dept of Biochemistry RIMS in collaboration with Department of Medicine, RIMS Imphal. Metabolic syndrome was identified in both groups according to International Diabetes Federation Criteria (IDF).General characteristics,lipid parameters, HbA1c value were obtained for each subject.*

Results: *In this first study of adiponectin value in the IndianManipuri population, the mean ±SD value of adiponectin is 8.76 ±2.38 µg/ml in non metabolic group and is significantly decreased in metabolic syndrome individuals ,i.e 5.92 ±1.13 µg/ml (p=0.000). Serum adiponectin level was correlated negatively with waist circumference ,triglyceride, and positively with HDL-cholesterol level. Both sexes with the lowest adiponectin quartile had a higher prevalence of Metabolic Syndrome and its components than that with the highest quartile. Females have higher level of adiponectin which was independently predicted by waist circumference. A cut off value of hypoadiponectinemia (<7.425 µg/ml)is proposed to predict future occurrence of metabolic syndrome in this ethnic population. Adiponectin reduce the risk of having metabolic syndome (0.405 times less chance,p<0.001)*

Conclusions: *Hypoadiponectinemia is strongly associated with Metabolic Syndrome. Our results suggest that the level of adiponectin may act as predictor of metabolic syndrome.*

Key Words *: Adiponectin ,Diabetes ,Metabolic Syndrome*

I. Introduction

Owing to rapid economic growth and change in diet and lifestyle, metabolic syndrome has become one of the most widespread health challenges in India[1]. Metabolic syndrome is a cluster of multiple metabolic abnormalities including central obesity, hypertension, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, and elevated fasting glucose and insulin resistance that identify individuals at increased risk for type 2 diabetes and progression of cardiovascular disease.

Adipose tissue has been recognized as an active endocrine organ in addition to its role as the main storage depot for triglycerides. While free-fatty acids released from adipose tissue have long been implicated in the development of these obesity-related complications , there is growing evidence that adipocyte-derived cytokines such as tumor necrosis factor-α (TNF α) , plasminogen activator inhibitor type 1, interleukin 6 ,and complement C3 may also have a role[2].

More recently, a novel adipose-specific protein, adiponectin,has been discovered [3,4] . Adiponectin, the gene product of the adipose most abundant gene transcript-1 (*apM1*) gene which is exclusively and abundantly expressed in white adipose tissue, is a 244-amino acid protein with high structural homology to collagen VIII, X, and complement C1q[3,4] as well as TNFα [5].

Adiponectin is the only adipose-specific plasma protein that is decreased in individuals with obesity, type 2 diabetes and coronary artery disease[6]. It has been shown to be an insulin-sensitizing hormone and has drawn substantial attention in research on metabolic syndrome.It suppresses hepatic glucose production, promotes lipid oxidation in muscle and may have a protective role against atherosclerosis. A single nucleotide polymorphism in the adiponectin gene was shown to be associated with hypoadiponectinaemia, insulin resistance and increased risk of type2 diabetes mellitus. Moreover the protective effect of adiponectin was

supported by human cohort studies in which hypoadiponectinaemia apparently predicted the development of Type 2 diabetes in Pima Indians[7].

A growing body of evidence suggests that hypoadiponectinemia may play a significant role in the development of Metabolic Syndrome[8]. However, very few studies have assessed the ability of Adiponectin to detect the presence of Metabolic Syndrome or to predict individual Metabolic Syndrome components.

Developing a robust biomarker that can predict Metabolic Syndrome instead of examining individual features will be important from a population standpoint in screening, monitoring the natural history of the disease, and measuring the response to therapeutic interventions[9], and this is endorsed by International Diabetes Federation[10] for arriving a platinum definition of Metabolic syndrome, which is so far not yet satisfactory due to ethnic variations.

Nevertheless, Adiponectin levels varied depending on gender, age and ethnic background and it is therefore necessary to clarify its threshold for increased disease risk in specific groups before it can be considered in clinical practice. Ample evidence suggested that close association between Adiponectin and Metabolic syndrome in different ethnic groups such as Whites, Asian Indians, Koreans, and Japanese[11]. However, currently no data on adiponectin levels related to metabolic syndrome criteria and diabetes are available for the Indian Manipuri population, presumed to be of Mongoloid origin. This is an important omission, given the increased focus on the prevalence of metabolic syndrome, diabetes and CVD in this region[12].

Aims And Objects:

Thus, this study was conducted to determine the baseline level of adiponectin in this population and to assess the correlation of plasma adiponectin value with various components of the metabolic syndrome among diabetes subjects and apparently healthy individuals (whether obese or not) in the Manipuri population.

We also tested whether adiponectin is a valid robust biomarker that can predict Metabolic Syndrome.

II. Material And Methods

Subjects:

This cross sectional study involved ninety subjects comprising sixty already diagnosed type 2 diabetic patients that were recruited randomly from the Diabetes Clinic, Medicine Department, Regional Institute of Medical Sciences, Imphal from September 2009 to August 2010 and another thirty non-diabetic apparently healthy control volunteers from the Biochemistry Department, RIMS Imphal .Interested persons were required to perform oral glucose tolerance test (OGTT) to exclude undiagnosed diabetes. The study was performed according to the principles expressed in the Declaration of Helsinki. Informed consent was obtained from each subject after full explanation of the purpose, nature, and risk of all procedures used. Approval from the Institutional Ethics committee was taken for the study.

The ninety studied subjects were subdivided into two groups based on fulfillment of criteria of Metabolic syndrome as per International Diabetes Federation (2005) definition. Diabetes mellitus was diagnosed as per WHO definition. A standardized medical history was obtained. Patients were excluded from the study if they had CAD or history of CAD or clinical evidence of atherosclerosis, severe hepatic or renal impairment. Also subjects on thiazolindiones medication and insulin therapy were excluded from the study.

Anthropometry and Abdominal Fat Distribution :

Standardised protocols were used to measure body weight, height and waist circumference. Height was measured without shoes on a stadiometer affixed to the wall .Measurements were recorded to the nearest cm. Weight was measured on a digital scale wearing light clothing, without shoes. Weight was recorded to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight (kg) divided by the square of the height (m^2).

Waist circumference is measured at a level midway between the lower rib margin and iliac crest with the tape all around the body in horizontal position.

Hip circumference was measured as the maximal circumference over the buttocks. Waist Hip ratio is also calculated by dividing the waist circumference measurement by the hip circumference measurement. BP was defined as the average of the last two measurements with a standard mercury sphygmomanometer taken at intervals longer than 2 minutes after the participants had been sitting for at least 30 minutes according to the American Heart Association guidelines.

III. Biochemical Measurements

After an overnight fasting, blood samples were withdrawn at 9-10 am and analyzed for various parameters. Aliquots of these samples were used for the biochemical analysis immediately, but aliquots for plasma adiponectin were stored at $-80^{O}C$ until collection of the desired samples for study.

Total cholesterol was measured by CHOD PAP Method [13], HDL cholesterol was measured by Precipitation technique using Human Cholesterol Liquicolor Test kit[14].Serum Triglyceride was measured by GPO-PAP Method with calorimetric determinations[15]. Low-density lipoprotein cholesterol (LDL-C) level was estimated using the Friedewald formula[16]. Fasting glucose was determined by a glucose oxidase-based assay. HbA_{1C} was measured by Ion Exchange Resin method [17] using Glycosylated Haemoglobin Test Kit manufactured by Human Wiesbaden, Germany. Adiponectin was measured by a validated sandwich enzyme linked immunosorbent assay [18](Mercodia cat no 10-1193-01) using ELISA reader.

IV. Definition of metabolic syndrome:

There is not a standard definition of the metabolic syndrome in India. In the present study, we tentatively defined it by IDF (International Diabetes Federation) criteria as recommended by an Indian consensus statement [19] that is, a person having Central obesity (defined as waist circumference ≥ 90 cm for Asian men and ≥ 80 cm for Asian women ,with ethnic specific values for other groups) plus any two of the following four factors : i)Raised TG level ≥ 150 mg/dl or specific treatment ii)Reduced HDL cholesterol < 40 mg/dl (men) and <50 mg/dl (women) or specific treatment iii) Raised BP : Systolic BP ≥ 130 or Diastolic BP ≥ 85 mm Hg or specific treatment iv)Raised fasting Plasma Glucose (FPG ≥ 100 mg/dl,or previously diagnosed type 2 Diabetes.

V. Statistical Analysis

All statistical analyses were performed using the SPSS program for Windows (version 16 statistical software; Texas Instruments, IL, USA). Data was explored for outliers, skeweness, and normality. For continuous variables, results were expressed as mean ± SD or median (minimum, maximum).Category variables were represented by frequency counts, and comparisons between 2 groups were analyzed by the chi-square test. Significant group differences in the parameters were compared by one-way ANOVA. Intergroup and intra-group differences in the parameters were performed using student t, or Mann-Whitney test when appropriate. The Pearson correlation coefficient was used to evaluate the strength association between two variables. Multiple linear regression analysis was employed to further quantify the strengths of associations between plasma adiponectin and the variables of interest; BMI, fasting glucose, waist circumference, triglycerides and HDL-C, BP etc. The level of $p < 0.05$ was considered as cut-off value for significance.

VI. Results

Prevalence of the Metabolic Syndrome:

Based on IDF criteria, 37 subjects (47.11%) are having metabolic syndrome . Out of this 37.77% are (n=34) diabetic patients and 3.33% (n=3) are apparently healthy control. These prevalence of metabolic syndrome is more in females viz., 64.9% as compared to males viz. 35.15%. The prevalence of metabolic syndrome is seen more in urban population than rural (56.8% vs 43.25). The prevalence increased from 15.1% among subjects aged 31–40 years to 28.3% among those aged 41–50 years, and 32.1% among 51-60 years but decreased to 7.5% among 61-70 years. Therefore, the prevalence of the metabolic syndrome was highest in 51-60 years age group.

Comparison of the baseline variables in the metabolic and non metabolic subgroups is shown in Table1.

Table 1. Comparison of the baseline variables in the metabolic and non metabolic syndrome

Parameter	Non-metabolic syndrome n=53) Mean±SD	metabolic syndrome n=37) Mean±SD	Df	t-value	P-value
Age(yr)	50.04 ± 12.85	54.30 ± 8.62	87.9	1.9	0.063
Weight (Kg)	56.78 ± 7.75	60.14 ± 10.18	63.8	1.7	0.096
Systolic BP (mm Hg)	126.36 ± 9.00	132.05 ± 11.27	66.1	2.6	0.013
Diastolic BP (mm Hg	82.30 ± 6.13	84.32 ± 7.25	88.0	1.4	0.157
Fasting blood sugar	101.15 ± 25.96	115.92 ± 30.17	88.0	2.5	0.015
HbA1c (%)	6.25 ± 1.32	7.79 ± 1.42	88.0	5.3	0.000
Waist circumference	81.91 ± 9.19	89.16 ± 7.11	88.0	4.7	0.000
WHR	0.86 ± 0.06	0.90 ± 0.05	88.0	3.1	0.003
BMI	22.56 ± 2.51	24.13 ± 3.32	63.4	2.4	0.018
TG (mg /dl)	127.02 ± 45.71	184.43 ± 67.99	58.3	4.5	0.000
TC (mg /dl)	197.66 ± 34.01	232.49 ± 55.06	55.0	3.4	0.001
VLDL (mg /dl)	25.34 ± 9.36	37.16 ± 13.43	88.0	4.9	0.000
HDL (mg /dl)	65.15 ± 11.39	57.81 ± 13.76	88.0	-2.8	0.007
LDL (mg /dl)	107.80 ± 31.54	136.79 ± 49.03	56.5	3.2	0.002
Adiponectin (µg/ml)	8.76 ± 2.38	5.92 ± 1.13	79.0	-7.5	0.000

The plasma level of adiponectin were lowered in the subjects with metabolic syndrome as compared with those without the syndrome viz.,5.92±1.12 µg/dl vs 8.76± 2.38 µg/dl (p=0.000). The adiponectin value for male and female metabolic syndrome subject was 5.81±1.16 µg/ml and 5.98±1.15 µg/ml respectively.

A significant increasing trend ($p<0.05$) was noted with increased proportion of higher ranges of Triglyceride, total cholesterol, LDL Cholesterol and Glycated Hb in metabolic syndrome than in non metabolic .The mean± SD BMI of metabolic syndrome case is 24.13± 3.32 and the control is 2256.±2.51 ($p <0.05$). Only 11.3% of metabolic syndrome has BMI range > 25. However, waist circumference and waist hip ratio increase significantly in metabolic syndrome.

Total Cholesterol is significantly higher in metabolic syndrome (232.49± 55.0 6mg/dl) than non metabolic (197.66 ± 34.01 mg/dl). Low density lipoprotein (LDL) significantly increases from non metabolic (107.80± 31.54 mg/dl) to metabolic (136.79 ± 49.03 mg/dl). VLDL cholesterol significantly increases from 25.34 ± 9.36mg/dl (non metabolic) to 37.16 ±13.43 mg/dl in metabolic syndrome.

Table 2. Adiponectin levels as means ± SD in subjects positive to individual components of metabolic syndrome according to IDF criteria, and in those not having the components of Metabolic syndrome

Parameter	Metabolic syndrome (n) Plasma Adiponectin (µg/ml) Mean±SD	Non metabolic syndrome(n) Plasma Adiponectin (µg/ml) Mean±SD	P-value
metabolic syndrome	n=37 5.92±1.12	n=53 8.76±2.38	0.000
Systolic BP (> 130mmHg)	n=24 6.00 ±1.25	n=18 9.05±2.77	0.000
Diastolic BP(>80 mm Hg)	n=23 5.99 ± 1.18	n=16 9.08 ±2.74	0.000
Waist circumference (female>80 cm)	n=23 5.98 ± 1.18	n=13 9.9 ±2.7	0.000
Waist circumference (male> 90 cm)	n=13 5.81 ±4.10	n=24 7.90 ± 0.05	0.000
Fasting blood sugar(>100mg/dl)	n=26 6.07 ± 1.02	n=24 7.48 ± 1.91	0.003
TG(>150 mg/dl)	n=27 5.97 ±1.18	n=14 7.28 ± 2.03	0.011
HDL (male , 40 mg/dl)	n=0	n=1 8.80	NA
HDL (female ,50 mg/dl)	n=16 6.09±1.16	n=27 9.60 ±2.41	0.000

Adiponectin levels were compared with different components of the metabolic syndrome defined by IDF. Table 2 reveals the mean adiponectin concentration in relation to the clinical features and components of metabolic syndrome. It is observed that adiponectin levels were associated with most features ($p< 0.05$).

Table 3. Group-wise correlation between adiponectin and other parameters

Parameter	metabolic syndrome (n= 37) (r)*	Non-metabolic syndrome (n= 53) (r)*
Age	0.078	-0.334
Weight	-0.276	0.047
Waist circumference	-0.287	0.054
WHR	-0.262	-0.088
Systolic BP	0.010	0.104
Diastolic BP	0.059	0.093
Fasting BS	0.118	-0.482
HbA1c	-0.159	-0.614
BMI	-0.223	0.012
TG	0.178 +	-0.469
TC	-0.091	-0.352
VLDL	0.143	-0.449
HDL	0.065	0.579
LDL	-0.146	-0.455

** Pearsons Correlation coefficient , + p > 0.05 ,others p < 0.05*

Generally any correlation coefficient is considered only when correlation is > 0.4 or < -0.4. Any Sig. (1-tailed) p-value < 0.05 is said to be significant for that estimate like Pearson Correlation coefficient in Correlations

. The correlation coefficient between plasma adiponectin and various parameters of the Metabolic syndrome is shown in Table 3.

In univariate analysis, the dependent variable in total study subjects HbA1c, gender, glucose, waist size, waist-hip ratio, DBP, HbA1c, TG, HDL-C predicted the variability in adiponectin significantly ($p < 0.05$). In total number of the subjects (90), simple linear regression analysis yielded highest correlation of serum adiponectin to to HbA1c ($r = -0.615$; $p = 0.000$), HDL-C ($r = 0.474$; $p = 0.000$), LDL cholesterol ($r = -0.429$;$p = 0.000$), serum triglyceride ($r = -0.427$; $p = 0.000$), fasting blood glucose ($r=-0.379$; $p= 0.000$) waist hip ratio ($r=-0.278$;$p=0.004$) and BMI ($r = -0.194$;$p = 0.033$).

The presence of insulin and thiazolinedione group of drugs may influence the plasma value of adiponectin and relation with blood glucose and other lipid parameters in diabetes patient. Therefore, those patients receiving these group of drugs were excluded.

In metabolic syndrome group, adiponectin levels were negatively and statistically significantly correlated with BMI, waist circumference, waist to hip ratio, LDL cholesterol and Total Cholesterol in decreasing strength. HDL cholesterol ($r= 0.065$, $p< 0.05$), age were positively correlated with adiponectin.

In non metabolic syndrome subjects, Adiponectin is found to be positively correlated with HDL cholesterol and negatively correlated with triglyceride ,total cholesterol ,HbA1c, waist hip ratio and age.

Adiponectin at different quartiles:

The interquartile cut off points of plasma adiponectin concentration were determined in the study population (n=90) and found to be 5.8, 6.95, and 9.2 µg/ml .Accordingly four categories are made :category 1:3.8- < 5.8 µg/ml ; category 2 : ≥ 5.8 -< 6.95 µg/ml ; category 3 : ≥ 6.95 - < 9.2 µg/ml; category 4: ≥ 9.2-14.21 µg/ml . The median value was 6.2 µg/ml and the effective range was 3.8-14.21 µg/ml.

Distribution of adiponectin quartiles in Diabetes with metabolic syndrome

There is more prevalence of diabetes in the first, second and third quartile. 91.3% of diabetes fall in lowest adiponectin quartile range, whereas maximum percentage of highest adiponectin quartile is seen in 87 % of apparently healthy individuals.Diabetes cases with metabolic syndrome have lower range of adiponectin (first and second quartile). Fourth quartile is absent among those diabetes with metabolic syndrome.

Multiple Linear regression analysis was done using Adiponectin as a dependent variable in total subjects

Table 4. Multiple Linear regression using Adiponectin as dependent variable

Coefficients[a]

Model		Unstandardized Coefficients		t	Sig.
		B	Std. Error		
7	(Constant)	17.871	2.878	6.210	.000
	Glycated HB %	-.420	.163	-2.584	.011
	Age	-.044	.016	-2.770	.007
	Hdlch	.064	.018	3.599	.001
	Whratio	-7.168	2.942	-2.437	.017
	total cholesterol (mg/dl)	-.013	.005	-2.864	.005

a. Dependent Variable: total adiponectin level ug/ml

Excluded Variables[h]

Model		Beta In	T	Sig.
7	Bmi	-.102[g]	-1.365	.176
	Fasting blood glucose(mg%)	.158[g]	1.616	.110
	LDL Cholesterol (mg/dl)	.266[g]	.940	.350
	S Triglyceride (mg/ dl)	-.087[g]	-.968	.336
	VLDL (mg/dl)	-.081[g]	-.879	.382

g. Predictors in the Model: (Constant), Glycated HB %, age, hdlch, whratio, total cholesterol (mg/dl)

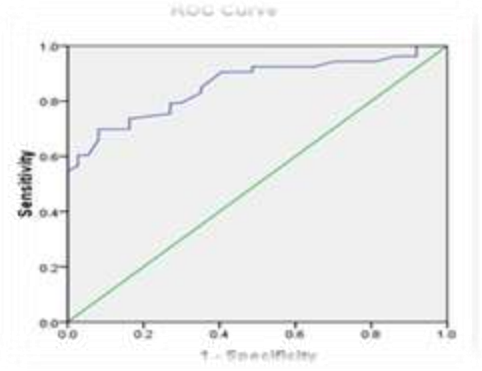
h. Dependent Variable: total adiponectin level ug/ml

Table 4 represents the results of multiple linear regression analysis carried out using serum adiponectin as the dependent variable in all the subjects. In this analysis, only those variables were considered which had a significant correlation in the simple linear regression analysis.

In all the total subjects, When multiple regression enter method , is applied for variables that were significant in simple regression, followed by stepwise regression for all studied parameters, HbA1c ,age, waist hip ratio , serum HDL cholesterol and total cholesterol were parameters predicting plasma adiponectin levels.

The receiver operating characteristic (ROC) analysis of the criteria for metabolic syndrome by serum adiponectin level was performed .

Fig 1. ROC Curves of Plasma total adiponectin levels for the prediction of Metabolic syndrome (fig 1-A) and Simultaneous presence of diabetes (fig1-B)



se

Fig.1(A)

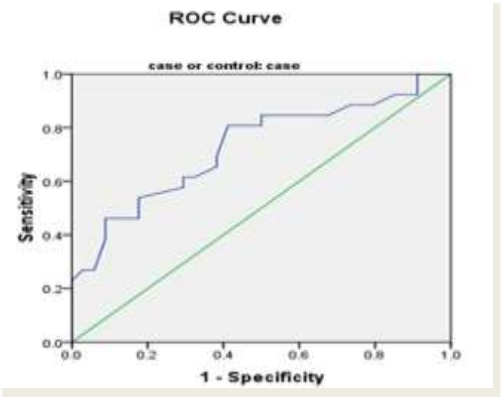


fig.1(B)

Figure 1(A) depicts the ROC curve for the criteria of metabolic syndrome according to the serum adiponectin level (irrespective of presence of diabetes). The area under the ROC curve for serum adiponectin level was 0.859±0.039. The cut-off value was 7.425 µg/ml, the sensitivity was 69.8%, and the specificity was 91.9%.

The ROC curve of plasma adiponectin for prediction of metabolic syndrome is further analysed with respect to simultaneous presence of diabetes fig 1(B). The area under the ROC curve for serum adiponectin level as a criteria of metabolic syndrome was 0.728±0.068 (in case of patient already suffering from diabetes). The cut-off value was 6.15 µg/ml, the sensitivity was 80.8%, d the specificity was 58.80 %.

Multiple logistic regression analysis was done employing **Hosmer and Lemeshow Test.** While doing Logistic regression analysis for Metabolic syndrome we omitted the variables which are used to calculate the Metabolic syndrome Based on the results it is better to use simple logistic regression for adiponectin as predictor variable for Metabolic syndrome. The other variables are excluded because of non-realistic results. The simple logistic regression shows that, for a unit increase in the adiponectin there is 0.405 times (less chance) of having metabolic syndrome. That is, increase in the adiponectin reduces the risk of having metabolic syndrome. This risk reduction is statistically significant (P<0.001).

VII. Discussion

This is the first study conducted in the Indian Manipuri to evaluate the adiponectin level in diabetic, metabolic syndrome and normal individuals.

In this study the prevalence of metabolic syndrome was 47.11 % by IDF, males constitute 35.13 % and females constitute 64.87 %.This is in agreement with published data from North Indians, where it is reported that metabolic syndrome (IDF) is found in 47.4 % subjects and it was more prevalent among females (59.6%) [20].

Although there have been various reports about the prevalence of metabolic syndrome in the general population, this study have evaluated the prevalence of Metabolic Syndrome in diabetic subjects. This study demonstrates that metabolic syndrome is common among diabetic patients (37.77%), making it a risk factor for the development of diabetes and, subsequently, its complications. It is however, having a lower incidence than a recent study in urban India [21] ,where the prevalence of Metabolic syndrome (ATP III) among urban Indian diabetic patients was 77.2% and was significantly higher in women (87.71%) as compared to men (69.33%) (p<0.001).

The mean level of adiponectin with corresponding BMI in the normal subjects of this ethnic population is relatively lower than the other published reports of adiponectin level in European (9.85 ± 2.33 vs 10.89 ±0.86 µg/ml; 23.47 vs 27.5) or even from the mainland India(9.85 ± 2.33 Vs 16.7 ±7.6 µg/ml; 23.47 vs 26.1) [22]. However the mean value of adiponectin and mean BMI is almost similar with those reported from Chinese (9.85 ± 2.33 vs 8.52±0.57 µg/ml; 23.47 Vs 23.8) and South Asian population (9.85 ± 2.33 vs 8.26 ±0.45 µg/ml; 23.47 Vs 26.1. Several reports showed that adiponectin is significantly lowerin South Asians than in European [23].

Glycemic foods are known to induce both hyperglycemia and hyperinsulinemia. South Asian populations including this present study population largely consume a diet consisting of foods with a high glycaemic index. It has been recognized that glycaemic foods influence body fat, which suggests that the effects could be at least partly mediated by adipose tissue–related pathways[24].

The present study agrees previous findings that type II diabetes and metabolic syndrome were associated with low serum adiponectin concentrations [6,8,25-27].

Following the need for establishment of criteria appropriate for Asian populations ,recently application of lower cutoff of body mass index (BMI) (Asian criteria of overweight: 23–25 kg/m2 and obesity:>25kg/m2) [28] has led to increase in prevalence figures of obesity in several Asian countries .

However, our data showed that central obesity was an independent negative predictor of serum adiponectin and reaffirms the concept that adiponectin may represent a link between central obesity and type II diabetes. It have been suggested that adipose tissue-derived cytokines negatively regulate adiponectin synthesis and release. In particular, TNF-α and interleukin-6 have been shown to reduce adiponectin mRNA content and inhibit adiponectin release in 3T3-L1 cells. Some authors have suggested that a parcrine loop exist in the adipose tissue by demonstrating that adipocytes co-cultured with macrophages upregulate proinflammatory cytokines (TNF-α) and in counterpart, those inflammatory proteins downregulate adiponectin expression[29,30].

In this study, the relationship of adiponectin with WHR, and waist circumfernce appeared to be stronger than other obesity indices or BMI, indicating that central fat distribution (visceral obesity) is a better determinant of circulating adiponectin than total fat mass.

Similar to the findings of this study, Cnop et al [31] have reported recently that intra-abdominal fat (but not BMI) was significantly and independently associated with adiponectin, whereas a Japanese study [32] has reported an inverse association between adiponectin and WHR in morbidly obese patients but not in overweight and moderately obese patients.

This study considered sex specific differences in adiponectin levels and their interaction with diabetes. As expected, the adiponectin levels were higher in women than in men. Sex hormones, including estrogen, progesterone and androgen may affect the plasma adiponectin level [32]. Androgens decreased the plasma adiponectin level and that androgen-induced hypoadiponectemia may be related to a high risk of insulin resistance and atherosclerosis in men [33].

There was a positive and strong correlation between serum adiponectin and HDL-cholesterol in the two groups, as previously reported in Japanese subjects [34]. Such a strong correlation between adiponectin and HDL cholesterol levels may likely be explained by the activation of peroxisome proliferator- activated receptor-α which influences the expression of genes encoding for proteins involved in HDL metabolism [32].

In the present study, the plasma concentration of adiponectin was significantly correlated with each component of the metabolic syndrome. Plasma adiponectin may therefore become a useful biomarker for the metabolic syndrome The major finding of our study was that in both the sexes, those subjects in the lowest adiponectin quartile exhibited a significantly higher probability of having MS when compared with those in the highest quartile.

Kumada M et al [35] reported that subjects with plasma adiponectin concentration less than 4.0µg/ml in Japanese population had a 2-fold increase in the incidence of CAD.

In this study it is proposed to set up a plasma adiponectin concentration of less than 7.425 µg/ml, (sensitivity 69.8%, specificity 91.9%) as the cut-off point for hpoadiponectinemia to predict metabolic syndrome. And another cut off point of plasma adiponectin concentration less than 6.15 µg/ml (sensitivity 80.8%, specificity 58.80 %) is proposed to predict metabolic syndrome in presence of diabetes.

Weight reduction increases the plasma adiponectin concentration; 21% reduction in BMI resulted in a 46% increase of plasma adiponectin concentration in obese subjects. Therapeutic agents (ie, adiponectin promoters) can elevate the plasma adiponectin concentration. In mice and humans adiponectin promoters have a non classical peroxisome proliferator responsive element, which activates receptor gamma ligands, thiazolidinediones, promoting adiponectin activity and raise its plasma concentration. It has also been reported, still controversially, that blockade of the renin – angiotensin system and the sulfonylurea reagent, glimepiride, increase the plasma adiponectin value [36].

Limitation : This study is cross-sectional, which does not allow inferring causality from its results. Total adiponectin and not high molecular weight fraction which has been proposed to have a stronger correlation with insulin resistance is estimated in this study.

The strength of our study include a relatively homogeneous cohort comprising of diabetic patients.

VIII. Conclusion

Adiponectin level in Indian Manipuri population is similar to the values of South Asians and Chinese, but lower than Europeans. The study agrees previous findings that type II diabetes and metabolic syndrome were associated with low serum adiponectin concentrations .This study demonstrates that metabolic syndrome is extremely common among diabetic patients, making it a risk factor for the development of diabetes and, subsequently, its complications. Adiponectin is significantly and independently associated with several components of metabolic syndrome and can therefore be an independent predictor of Metabolic syndrome

IX. Recommendations

Because of the epidemic of obesity and a sedentary lifestyle worldwide, metabolic syndrome is becoming increasingly commonly recognised. Development of a method for convenient prediction of metabolic syndrome in daily clinical practice presents a major challenge for physicians and public health policy makers. The present study provided evidence of the usefulness for estimation of total adiponectin level as a convenient and sensitive biomarker for the prediction of metabolic syndrome. Prospective and population based studies along with interventions to increase adiponectin level are however required to confirm the associations.

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