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ORIGINAL RESEARCH

Correlation of adiponectin and resistin, triglyceride and HDL cholesterol, Homeostatic model assessment-insulin resistance and bodymass index in polycystic ovarian syndrome

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Abstract

Background: PCOS, considered to be a common endocrinological disorder of females of reproductive age is often associated with obesity, dyslipidemia, hyperandrogenism, metabolic syndrome and infertility. Adipokines levels in PCOS is also reported to be altered may play a key role in obesity and dyslipidemia and insulin resistance. This study explored the relation among Adiponectin to Resistin Ratio , Tryglyceride to HDL cholesterol ,HOMA IR and BMI. **Materials & Methods:** In this cross sectional comparative study 144 PCOS patients were included. Anthropometric and Biochemical parameters were evaluated. Patient population was categorized into Obese and No-obese groups depending on BMI and all the parameters were compared. Correlation among Adiponectin to Resistin Ratio , Triglyceride to HDL cholesterol ,HoMA IR and BMI was assessed. **Result:** Significant difference was observed between lipid profile of Obese and Non-Obese groups. TG: HDL Ratio also had strong association (r = 0.79) with BMI. A:R Ratio and TG: HDL Ratio correlated significantly (r= - 0.78). HOMA IR had moderate correlation with BMI (p = 0.54), A:R Ratio (r = -0.41) and TG: HDL Ratio (r = 0.59). **Conclusion:** In Obese PCOS patients Adiponectin and Resistin decrease significantly and A:R Ratio decrease significantly exposing the subjects to the more cardio-metabolic risk. TG:HDL Ratio can predict A:R Ratio, independent of HOMA IR.

Key words: Adiponectin : Resistin Ratio, PCOS, TG:HDL Ratio, HOMA IR

Introduction

Polycystic Ovarian Syndrome is a very common endocrinological disorder of women of reproductive age.Studies have shown that dyslipidemia, Insulin resistance, oxidative stress,obesity and metabolic syndrome are common in PCOS patients [1]. Lipid level derangement is one of the most common observable phenomena in PCOS patients [2]. Prevalence of PCOS is higher in overweight to obese women. Different PCOS phenotypes show different lipid profile associated with phenotype specific androgen level led to an assumption that androgen may play a role in hyperlipidemia [3]. Ethnic and regional

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variations are observable in degrees of obesity, dyslipidemia and other metabolic abnormalities among PCOS population [4].Hyperandrogenemia due to insulin resistance leading to hyperlipidemia turns into a vicious cycle during the course of the disease [5]. Accumulated fat mass act as a potential endocrine organ and secrete Adipokines [6]. Adiponectin and Resistin two widely studied adipokines are having opposite effect on Insulin function and former have an inverse relationship with Adipocity. Ratio of triglyceride and High-density Lipoprotein fraction of Cholesterol(TG:HDL Ratio) is a marker for Insulin resistance, dyslipidemia and major cardiovascular outcomes. However, the relationship between the TG/HDL-C ratio and IR varies according to ethnicity and gender.[7,8].The present study explored the relationship between anthropometric variable Body mass Index and three metabolic indices as Adiponectin Resistin Ratio, TG to HDL ratio and HOMA IR. In obese and non-obese PCOS Patients.

Material methods

This Cross-sectional Comparative Study was conducted in the Mayo Institute of Medical Sciences, Barabanki, India. 144 female subjects aged between 18 – 40 years already diagnosed with PCOS as per Rotterdam criteria were included from OPD of department of Obstetrics and Gynecology Mayo Institute of Medical Sciences, Barabanki India. To be diagnosed as per Rotterdam criteria the subjects had undergone clinical examination, sonography, Biochemical and Hormonal Assays. The study was approved by institutional ethical committee and written informed consent was obtained from all participants.

Exclusion criteria: Subjects less than 18 yrs and more than 40 yrs of age, with late onset congenital adrenal hyperplasia, thyroid disease, hyper prolactinemia, androgen secreting tumors were excluded from the study. Subjects using medication (including Oral Contraceptives), a hormonal intrauterine device and pregnant or lactating subjects were excluded from the studies.

Procedure methodology: Height and weight was measured using standard stadiometer and BMI was calculated using standard formula. Waist and hip circumference were recorded for all the subjects to calculate Waist Hip ratio (WHR). Overnight fasting blood sample was collected for estimation of biochemical parameters. Lipid Parameters are measure using enzymatic method using BS 240 Mindray Fully automated analyzer. LDL was estimated using formula (LDL = Total Cholesterol – HDL-(TG/5)[9].Enzyme-linked Immunosorbent Assay method was used for estimation of serum Insulin, Adiponectin and Resistin levels. Human Insulin ELISA Kit, Diametra, Italy , Adiponectin Elisa kit, Demeditec ,Germany, Human Resistin Elisa kit, Sincere Biotech China were used for the study. Homeostasis Model Assessment (HOMA) was calculated for estimate of Insulin Resistance.

Statistical Analysis: Data were analyzed using Microsoft Excel 365 Statistical plugin software. Results are expressed as Mean, Standard Deviation. T Test was performed find the difference of mean values. Pearson's correlation was performed to find out the association between the selected variables. Results were considered statistically significant whenever $p < 0.05$.

Results

Descriptive base line data for PCOS subjects (N=144) is expressed as Table 1.

VARIABLE (N= 144)	VALUES

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AGE (Years)	25.01 ± 4.11
HEIGHT (Centimeters)	156.53 ± 4.82
WEIGHT (Kgs)	64.63 ± 10.48
BMI (Kg/m^2)	26.37 ± 3.20
ADIPONECTIN(µg/ml)	10.28 ± 3.27
RESISTIN (ng/ml)	5.41 ± 1.09
A: R RATIO	2.08 ± 0.97
FASTING SUGAR (mg/dl)	90.20 ± 9.05
INSULIN (µIU/ml)	9.62 ± 2.03
HOMA IR	2.16 ± 0.56
TRIGLYCERIDE (mg/dl)	144.93 ± 19.27
CHOLESTEROL (mg/dl)	162.07 ± 15.61
HDL (mg/dl)	38.49 ± 2.27
LDL (mg.dl)	77.45 ± 16.43
VLDL (mg/dl)	28.99 ± 3.85
TG: HDL RATIO	3.79 ± 0.62

Table 1: Table Descriptive statistics showing the base line data of PCOS Patients (N=144)

Subjects were categorized into two groups of Obese (n = 71 ,BMI≥25) and Non-Obese (n = 73, BMI<25) for the comparative studies. Observations from Obese and Non Obese groups of PCOS patients shows significant differences ($p<0.05$) Between the groups. All the anthropometric parameters and biochemical parameters were significantly high for obese group except HDL cholesterol and Adiponectin . HDL Cholesterol was found to be higher among non obese group ($p< 0.0001$)Adiponectin levels were significantly low($p<0.0001$ in Obese groups (7.58±2.11) when compared to Non-Obese group (12.99± 1.39) [Table 2]

PARAMETERS	OBESE (n = 71)		NON-OBESE (n = 73)		T TEST
	MEAN	SD	MEAN	SD	
BMI (Kg/m^2)	28.83	2.67	23.84	0.86	p<0.0001*
INSULIN (µIU/ml)	10.18	1.68	9.13	2.18	0.0006*
FASTING BLOOD SUGAR	94.21	8.42	86.07	7.76	p<0.0001
HOMA IR	2.37	0.46	1.97	0.55	p<0.0001
ADIPONECTIN (µg/ml)	7.58	2.11	12.99	1.39	p<0.0001
RESISTIN (ng/ml)	6.22	0.84	12.99	0.52	p<0.0001
A:R RATIO	1.27	0.52	2.89	0.50	p<0.0001
TRIGLYCERIDE (mg/dl)	158.58	16.15	131.18	9.74	p<0.0001
CHOLESTEROL (mg/dl)	171.84	12.36	151.85	11.82	p<0.0001
HDL (mg/dl)	37.36	1.82	39.62	2.13	p<0.0001
LDL (mg/dl)	89.50	12.83	65.32	8.50	p<0.0001
TG/HDL	4.25	0.45	3.32	0.32	p<0.0001

Table 2: Table Descriptive statistics showing the base line data of Obese and Non-Obese PCOS PatientsAlong with Comparison. Difference is significant at $p<0.05$

Correlation Studies showed that, among all the indices A:R ratio had shown a significant negative corelation with BMI ($r = -0.81$, $p <0.0001$) .TG:HDL ratio correlated strongly, while HOMA IR has a moderate correlation. All the correlations were significant (Table 3).

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Table 3: Correlation Statistics Showing the association between BMI and A:R Ratio, TG:HDL Ratio,HOMA IR

	r	r^2	p
A: R RATIO	- 0.81	0.66	<0.00001
TG:HDL RATIO	0.78	0.61	<0.00001
HOMA IR	0.54	0.30	<0.00001

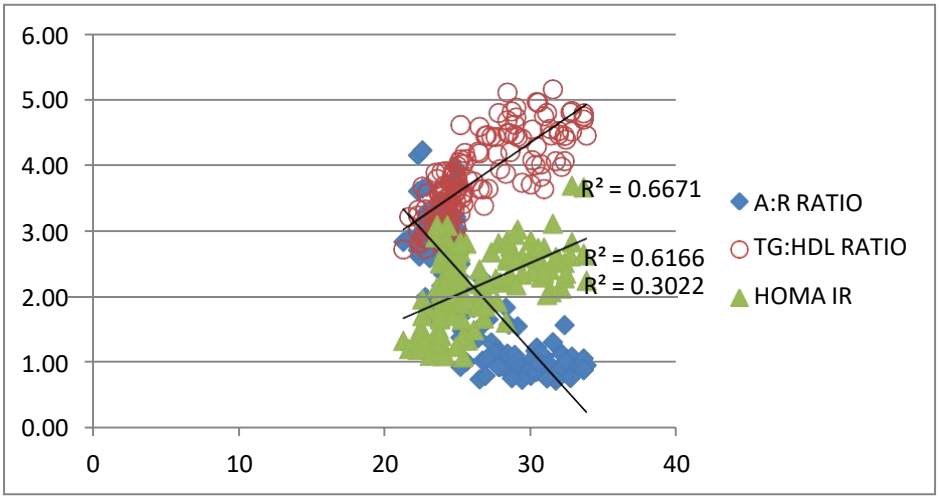

Figure 1: Correlation Between BMI and A:R Ratio, TG:HDL Ratio , HOMA IR

Correlation between BMI and A:R Ratio, TG:HDL Ratio, HOMA IR was also performed For Obese and Non Obese groups. Adiponectin to Resistin Ratio (A:R Ratio) showed a significant negative association among the obese, but the correlation was insignificant (p=0.112) among the non-obese. Surrogate of dyslipidemia, TG: HDL Ratio correlated significantly in both the groups having non-significant stronger association among Obese group (Z = 0.75, p =0.45). HOMA IR also correlated significantly among both the groups but the association is non significantly weaker among Obese group. (Table 4).

Table 4: Correlation Statistics Showing the association between BMI and A:R Ratio, TG:HDL Ratio,HOMAIR ain Obese and Non Obese PCOS patients

	OBESE (n=73)		NON OBESE (n=71)		Fisher r-to-z transformation
	r	p	r	p	
TG : HDL RATIO	0.51	<0.00001	0.41	.000384	Z=0.75,p=0.45
A:R RATIO	-0.61	<0.00001	-0.19	0.112	Z=3.03,p=0.0024
HOMA IR	0.47	.000035	0.59	< .00001	Z= -0.98, p = 0.32

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Fig 2: Correlation Between BMI and A:R Ratio, TG:HDL Ratio , HOMA IR among Obese PCOS patients

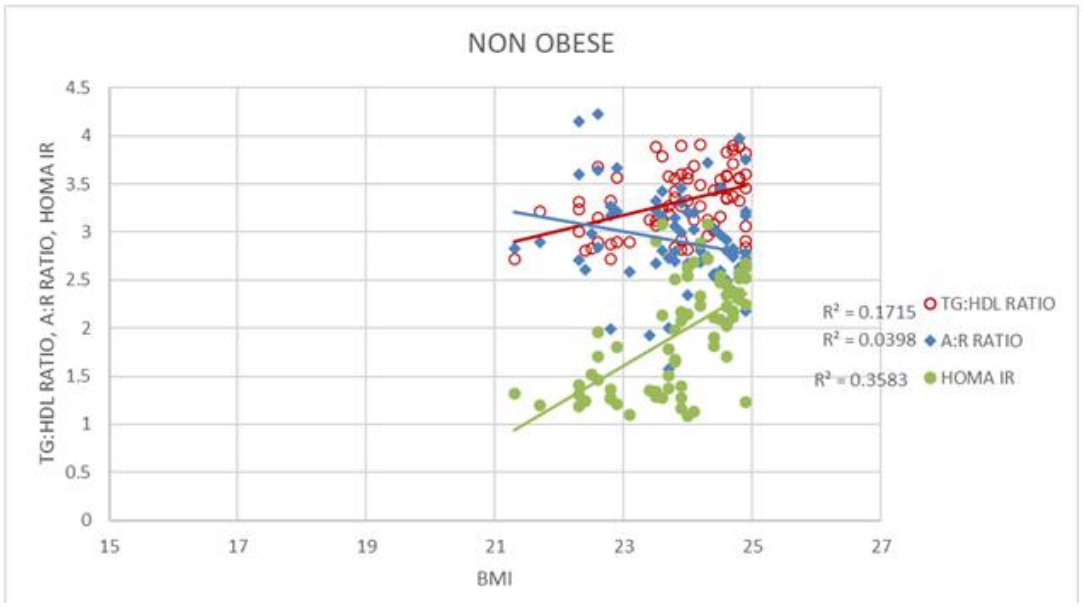

Fig 3: Correlation Between BMI and A:R Ratio, TG:HDL Ratio , HOMA IR among Obese PCOS

Patients Over all correlations of 3 Biochemical indices of Insulin Resistance, Dyslipidemia and Adipokine
status and BMI are expressed in Table 5. Our Observation suggested that A:R Ratio negatively correlated most strongly(r= - 0.82) with BMI which is also a proxy of adiposity . TG : HDL Ratio also had strong association (r
= 0.79) with BMI. A:R Ratio and TG: HDL Ratio correlated significantly (r = - 0.78). HOMA IR had moderate correlation with BMI (p = 0.54), A:R Ratio (r = -0.41) and TG: HDL Ratio (r = 0.59).

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Table 5: Overall Correlation Statistics (r value) Showing the association between BMI, A:RRatio,TG:HDL Ratio, and HOMAIR in PCOS patients

	A:R RATIO	TG:HDL RATIO	HOMA IR	BMI
A:R RATIO	1	-0.78	-0.41	-0.82
TG: HDL RATIO	-0.78	1	0.59	0.79
HOMA IR	-0.41	0.59	1	0.54
BMI	-0.82	0.79	0.54	1

Discussion

In both obesity and Type 2 diabetes mellitus the level of serum Adiponectin was found to be low among the case subjects when compared with controls [10] . Studies have shown Adiponectin level had a strong independent positive correlation to HDL levels and were also positively related to TG levels.[11].In our study we observed that Among PCOS population Adiponectin level in obese patients decrease significantly when compared to non – obese patients. The observation is concurrent with previous studies observing that Serum Adiponectin decrease in obese PCOS patients and may play a role metabolic abnormalities and pathogenesis of Insulin resistance in obese women with PCOS.[12] . Resistin is also thought to have a potential association with obesity and insulin resistance[13]. Association between Resistin and BMI is still controversial [14,13]. Our study shows that Resistin level appears to be significanty less in Obese PCOS patients. We observed that Adiponectin to Resistin ratio negatively correlated with BMI and HOMAIR . [15]. Adiponectin/Resistin ratios found to be negatively correlated with BMI, insulin, and HOMA-IR, along with testosterone, SHBG, and hirsutism in PCOS patients.[15] TG/HDL Ratio, found to be directly correlated with insulin levels and can be used as a marker of IR (HOMA-IR) in infertile PCOS patients [16] . In our study we observed that the association is moderate and TG/HDL ratio has a more stronger association with BMI. The present observations of the study revealed that BMI may have an Association adipokine index (A:R Ratio) & Lipid index (TG:HDL)

.TG:HDL Ratio which is a surrogate marker of dyslipidemia has a significant positive association with BMI . HOMA IR also correlated with BMI but the strength of association is more robust with Lipid index. Several work with Adiponectin: Leptin Ratio and dyslipidemia and Insulin Resistance have been observed during the literature search . Adiponectin : Resistin ratio appeared to be less explored with dyslipidemiain PCOS. In our study we observed TG:HDL Ratio can predict A:R Ratio($p<0.000$) independent of HOMA IR ($p = 0.25$).We observed that in PCOS patients A:R Ratio and TG:HDL ratio correlate significantly . Both Adiponectin and Resistin values are significantly less in Obese PCOS than Non -obese counterpart. But Interestingly the A:R Ratio appears to be significantly less in Obese PCOS population. Adiponectin to Resistin ratio correlate significantly among the obese group where as the association is non- significant among non obese PCOS group.

Conclusion

Study conclude that Dyslipidemic marker TG:HDL Ratio correlate significantly with Adiponectin To Resistin Ratio and BMI in PCOS patients. In Obese PCOS patients Adiponectin and resistin decrease significantly and A:R Ratio decrease significantly exposing the subjects to the more cardio-metabolic risk.

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