Dr. G Rajeswari
Professor & HOD,
Department of Biochemistry,
Rangaraya Medical College,
Kakinada, Andhra Pradesh,
India.

Dr. P Satya Gopal
Assistant Professor,
Department of Pharmacology,
Rangaraya Medical College,
Kakinada, Andhra Pradesh,
India.

Dr. B Veerabhadrudu
Post Graduate,
Department of Biochemistry,
Rangaraya Medical College,
Kakinada, Andhra Pradesh,
India.

Dr. E Suresh
Post Graduate,
Department of Biochemistry,
Rangaraya Medical College,
Kakinada, Andhra Pradesh,
India.

Study of magnesium levels in polycystic ovarian syndrome

Dr. G Rajeswari, Dr. P Satya Gopal, Dr. B Veerabhadrudu, Dr. E Suresh

Abstract
Introduction: Polycystic ovarian syndrome is the most common endocrinopathy in the women of reproductive age with a prevalence of approximately 7-10% worldwide. It reflects multiple potential aetiologies and variable clinical manifestations. This syndrome is characterised by serious health implications such as diabetes, coronary heart disease and also leads to infertility.
Methods: Magnesium, uric acid, fasting blood sugar were estimated in 80 clinically diagnosed patients of PCOS who were between the age group of 18-40 years. Results were compared with a group of 40 normal subjects having same age group.
Results: In our study, fasting blood sugar levels were significantly increased and serum magnesium levels were significantly decreased in PCOS patients suggesting increased urinary excretion of magnesium in the presence of elevated insulin. Magnesium showed a significantly negative correlation with FBS, TC, TGL, LDL, uric acid and non-significant positive correlation with HDL. Serum uric acid levels were significantly increased and showed significant positive correlation with FBS, TC, TGL, LDL and VLDL & significant negative correlation with magnesium
Conclusion: Administration of magnesium is acts as a beneficial effect on dyslipidaemia of PCOS patients by through the activation of LCAT and suppression of adrenergic activity. So, magnesium acts as a prognostic biomarker in PCOS patients

Keywords: PCOS- polycystic ovarian syndrome, insulin resistance, dyslipidemia, Lecithin cholesterol acyltransferase

Introduction

Polycystic ovarian syndrome is the most common endocrinopathy in the women of reproductive age with a prevalence of approximately 7-10% world-wide [1]. Caribbean, Hispanic women, migrant Asian Indians & Mexican Americans have a great prevalence of PCOS. It reflects multiple potential aetiologies and variable clinical manifestations. This syndrome is characterised by serious health implications such as diabetes, coronary heart disease and also leads to infertility. This syndrome was first described by stein and Leventhal in 1935 [2]. According to the new Rotterdam criteria, two out three criteria have at least to be met in order to fit the diagnosis of PCOS [3]. These criteria are anovulation, androgen excess and polycystic ovarian morphology in ultrasound assessment [4].

One of the major biochemical features of PCOS is insulin resistance [5] accompanied by compensatory hyperinsulinemia; that hyperinsulinemia produces hyperandrogenism of PCOS by increasing ovarian production particularly testosterone and by decreasing serum SHBG concentration. The high levels of androgenic hormones interfere with the pituitary ovarian axis leading to increased LH levels, anovulation, amenorrhea, recurrent pregnancy loss and infertility. Hyperinsulinemia has also been associated with high blood pressure and increased clot formation and appears to be a major risk factor for the development of heart disease. Insulin resistance effects 15-20% of women with PCOS leading to a number of comorbidities including metabolic syndrome, hypertension, dyslipidaemia, glucose intolerance, and diabetes [6]. Mental health disorders including depression, anxiety, bipolar disorder and binge eating disorder also occur more frequently in women with PCOS. Approximately, 25% to 30% of women with PCOS will show impaired glucose tolerance by the age of 30 and 8% of affected women will develop type 2 diabetes annually [7]. Women with PCOS are seen to have more extensive coronary artery disease by angiography [8]. It is well known that obesity is observed in about 60% of women with PCOS [9].

Correspondence
Dr. E Suresh
Post Graduate,
Department of Biochemistry,
Rangaraya Medical College,
Kakinada, Andhra Pradesh,
India.

Due to complexity of the syndrome, a number of metabolic and other implications of women health will have to be confronted in the near future. PCOS seem to have a long prodromal phase with detectable abnormalities throughout the life cycle of affected women and represents a major health and economic burden. Proper diagnosis and management of PCOS is essential to prevent future metabolic, endocrine, psychiatric and cardiovascular complications. The increased incidence of cardiovascular disease in women with PCOS has prompted researchers to look for indicators of early metabolic changes in these patients. The studies available at present on Sr. Uric acid and Magnesium levels in PCOS patients are very less and led to controversial results. With this background case control study was undertaken to analyse and correlate the biochemical parameters FBS, Magnesium, Sr. uric acid and lipid profile that may help to identify women with PCOS who are at risk of cardio- metabolic syndrome.

Methods
The study was conducted in the Department of Biochemistry, Rangaraya Medical College, Kakinada, Andhra Pradesh, India. The study was undertaken to determine biochemical changes in polycystic ovarian syndrome patients. Venous blood was collected to analyse the parameters magnesium, uric acid, fasting blood sugar, lipid profile. The study includes 80 cases between the age group of 18-40 years. These values are compared with 40 control groups having same age group. All of these samples were taken from the department of Obstetrics and Gynaecology, Government General Hospital, Kakinada after the consent was obtained both from cases and controls

The study group consists of premenopausal women diagnosed to have polycystic ovarian syndrome (PCOS) by the Gynaecology department. The control group consists of healthy female volunteers with regular menstrual cycles.

Inclusion criteria
Age group: between 18-40 years. Body mass index. Presence of polycystic ovaries on ultra sound scan, Oligo menorrhoea/amenorrhea, Clinical/Biochemical signs of hyperandrogenism a. Hirsutism b. Acne

Exclusion Criteria
Diabetes mellitus, Hypertension, Cardiovascular diseases Thyroid disorders, renal diseases, Pregnant or lactating women Oral contraceptive medication, Hormonal medication within previous 2 months Lipid lowering drugs medication, all the subjects' height and weight were recorded without shoes using standard apparatus.

Statistical analysis
The observed values were compared with control group for statistical analysis. All data were expressed as mean ± SD. Statistical analysis was done by student T test. Differences with 'p' value less than 0.05 were considered to be statistically significant. The following methods were used for analysing the serum sample Serum magnesium by calmagite method, Serum uric acid by uricase method
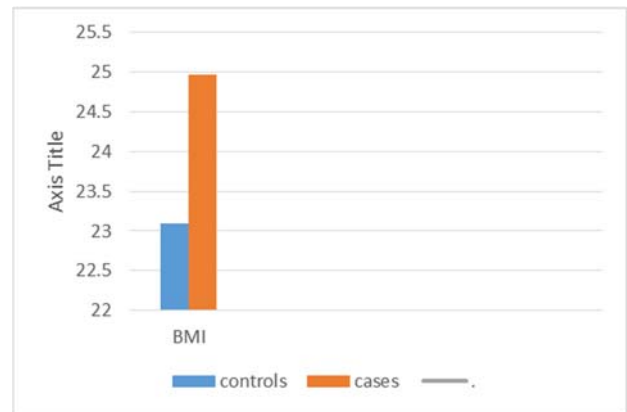
Observations and Results
The present study comprises of 80 patients with polycystic ovarian syndrome between the age group 18 – 40 years and 40 normal healthy women as controls. All the study group and control group are from the outpatient department of the

obstetrics and gynaecology, Government General Hospital, Kakinada. The following parameters were analysed, BMI, Fasting blood sugar, Uric acid, Magnesium, TC, TGL, HDL-C, LDL-C, and VLDL-C.

Table 1: Mean, Standard deviation and P values of BMI in PCOS patients.

Parameters	Controls(N=40) Mean ± Sd	Patients(N=80) Mean ± Sd	P Value
BMI(kg/m^2)	23.10 ± 2.24	24.97 ± 2.34	0.0001*

The above data shows PCOS patients had significantly higher BMI.

Table 2: Mean, Standard deviation and P values of Biochemical parameters in PCOS patients and control groups.

Parameter	Controls (N=40) Mean ± Sd	Patients (N=80) Mean ± Sd	P Value
FBS	89.10 ± 5.89	116.65 ± 11.15	0.0001*
Total cholesterol	166.5 ± 8.03	228.3 ± 24.00	0.0001*
Triglycerides	145.9 ± 8.13	203.5 ± 27.30	0.0001*
HDL-C	37.45 ± 1.63	28.55 ± 3.56	0.0001*
LDL-C	99.95 ± 8.86	159.31 ± 24.28	0.0001*
VLDL-C	29.10 ± 1.66	40.46 ± 5.50	0.0001*

Table shows a significantly higher fasting blood sugar, Total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol levels in PCOS Patients than the control group PCOS patients had significantly lower HDL-C levels when compared to the controls (P value<0.0001)
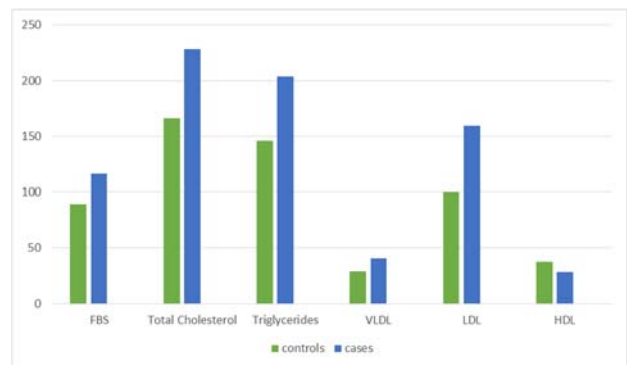

Table 3

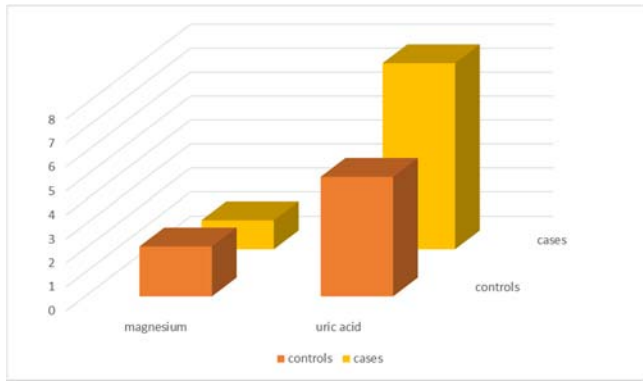| Parameter	Controls (N=40) Mean ± Sd	Cases (N=80) Mean ± Sd	P Value
Magnesium	2.087 ± 0.189	1.210 ± 0.239	0.0001*
Uric acid	4.972 ± 0.641	7.754 ± 0.816	0.0001*

Table shows a significantly higher, serum uric acid, levels in PCOS Patients than the control group PCOS patients and had significantly lower serum magnesium levels when compared to the controls

Table 4: correlation of magnesium & uric acid in patients with PCOS

	r value	P value
FBS	-0.4121	0.0001
TC	-0.3396	0.002
TGL	-0.2881	0.009
LDL	-0.2865	0.01
HDL	0.1012	0.3717
VLDL	-0.282	0.01
Uric acid	-0.362	0.0009

Table summarises the correlation coefficient and p values of magnesium and other parameters in the study group. Magnesium showed a significantly negative correlation with FBS, TC, TGL, and LDL. & non-significant positive correlation with HDL.

Discussion

PCOS is a common female endocrine disorder with prevalence ranging from 2.2% to 26% in India [10]. This draws attention to the issue of early diagnosis in adolescent girls. It is multisystem endocrinopathy in women of reproductive with the ovarian expression of various metabolic disturbances. PCOS is not only the reproductive endocrinopathy but also metabolic disorder. Hypergonadism was thought to be a main underlying factor. Women with PCOS are known to be at increased risk of insulin resistance. There is a risk factor for developing type 2 diabetes mellitus, in these women. Adiposity plays a crucial role in the development and maintenance of PCOS and strongly influences the severity of both its clinical & endocrine features in many women with this condition. Women with PCOS have disturbed lipid profile the causes of dyslipidaemia in PCOS are multifactorial. PCOS is a chronic disease with manifestation across the lifespan and represents a major health and economic burden.

In this study FBS, T.C, TGL, HDL-C, LDL-C, VLDL-C, serum magnesium and serum uric acid, were analysed and compared with control groups to know the values of these parameters in PCOS.

In this study, serum uric acid levels in PCOS were significantly raised when compared to healthy controls. The raise was statistically significant (p value < 0.0001). Similar results were observed by N. Swetha *et al* in their correlative study of biochemical parameters in PCOS [11]. It is due to endothelial dysfunction and chronic inflammation. Uric acid exerting prooxidant and pro inflammatory action at the endothelial cell. The main determinant of serum uric acid level was the BMI. In PCOS, androgens may increase serum uric acid levels by inducing hepatic metabolism of purine [12]. In this study, Serum magnesium levels in PCOS were decreased when compared to controls. The decrease was statistically highly significant (p value<0.0001). Similar results were observed by N.Swetha *et al*, pourteymour Fard tabrizi and Kauffman RP *et al*.

Magnesium, a cofactor for many enzymes is induced in glucose metabolism. It is required for proper glucose utilization and insulin signalling. It has been shown that magnesium plays an important role of 2nd messenger for insulin action [13]. Low magnesium concentration are associated with impaired glucose tolerance and increased risk of type 2 diabetes mellitus. Present study showed negative correlation between glucose and magnesium which were statistically significant. ($r=-0.412$, $p=0.0001$). Therefore, intracellular magnesium deficiency may affect the development of insulin resistance.

In this study, FBS levels were increased when compared to controls. The increase was statistically highly significant (p value <0.0001). Similar results were observed by N. Swetha *et al*. In PCOS, because of insulin resistance, FBS levels were increased.

In this study T.C, TGL, LDL-C & VLDL-C shows increased levels when compared to controls. The increase was statistically highly significant (p value<0.0001) in all these parameters. HDL-C level shows decreased when compared to controls. The decrease was statistically highly significant (p value < 0.0001). Similar results were observed by N.Swetha *et al* in their study.

Women with PCOS have disturbed lipid profile. PCOS cause dyslipidaemia. The causes are multifactorial. Insulin resistance appears to have major role. Insulin resistance may cause lipolysis, altered expression of lipoprotein lipase and hepatic lipase [14].

As per study of N.Swetha *et al*, no correlation was found between uric acid and magnesium, TC, TGL. But, as per our study, uric acid showed significant positive correlation with FBS ($r=0.41$; $P=0.0001$), TC ($r=0.32$; $P=0.002$), TGL ($r=0.37$;$p= 0.0005$) & significant negative correlation with magnesium($r=-0.36$;$P=0.0009$). In the present study, as shown in table 6 magnesium showed a significant negative correlation with FBS ($r=-0.41$; $P=0.0001$), TC($r=-0.33$;$P=0.002$), TGL($r=-0.28$;$P=0.009$), ($r=-0.28$; $P=0.001$), VLDL($r=-0.28$;$P=0.01$), uric acid($r=-0.36$;$P=0.0009$) and non-significant positive correlation with HDL($r=0.10$;$P=0.37$).

In PCOS, uric acid, FBS and lipid profile except HDL and magnesium shows increased levels, which was statistically highly significant. PCOS patients are prone for diabetes mellitus due to insulin resistance. Because of dyslipidaemia, they are prone for vascular diseases.

Conclusion

Fasting blood sugar levels were significantly increased in PCOS patients suggesting impaired glucose tolerance and impaired fasting glucose levels.

Serum magnesium levels were significantly decreased in PCOS patients suggesting increased urinary excretion of magnesium in the presence of elevated insulin. Impaired oxidative metabolism contributed by in adequacies of magnesium. Magnesium showed a significantly negative correlation with FBS, TC, TGL, LDL, uric acid and non-significant positive correlation with HDL.

Serum uric acid levels were significantly increased due to pro-oxidant nature. Measurements of uric acid levels may predict non classic cardiovascular risk in PCOS patients. Uric acid showed significant positive correlation with FBS, TC, TGL, LDL and VLDL & significant negative correlation with magnesium

Lipid profile levels were significantly increased when compared to controls. The major lipid abnormality showed in PCOS patients is that triglycerides, total cholesterol, LDL-C, were significantly increased but HDL was significantly decreased, as well as decreased insulin response to glucose challenge and marked decrease activity of the LCAT, that clears the triglycerides from the blood. Daily supplementation of magnesium may improves insulin mediated glucose uptake and insulin secretion in patients who have established with PCOS.

Present study conclude that the administration of magnesium is acts as a beneficial effects on dyslipidaemia of PCOS patients by through the activation of LCAT and suppression of adrenergic activity. So, Magnesium acts as a prognostic biomarker in PCOS patients.

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