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ASSOCIATION OF CARIOVASCULAR RISK FACTORS AMONG REPRODUCTIVE AGE GROUP WOMEN WITH PCOS IN KASHMIR VALLEY ,AN ANALYTICAL AND PRESPECTIVE CASE CONTROL STUDY.

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ABSTRACT
Polycystic Ovarian Syndrome (PCOS) is associated with reproductive and metabolic abnormalities.PCOS is one of the most common endocrine diseass in women ,affectingupto 10% of women in reproductive age .PCOS is characterized by chronic anovulatory cycles ,oligo – or amenorrhea, hirsutism,an insulin resistance ; obesity is also common .PCOS not only has a negative effect on fertility,but it is also considered aclear cutplurimetabolic syndrome ,being associated with type 2 diabetes mellitus ,hypertension and dyslipidemia. Insulin resistance is probably the major risk factor for the occurance of cardiovascular disease (CVD) in PCOS.The risk of coronary artery disease and myocardial infarction has been reported to be increased in patients with PCOS compared with regularly cycling women even if mortality because of circulatory disease does not seem to be increased .In PCOS women , endothelial and diastolic dysfunction have been shown and associated with both elevated androgen levels and insulin resistance .
Recently ,together with classic Cardio vascular (CV) risk factors ,such as Total Cholesterol (TC) and High Density Lipoproteincholesterol (HDL –C) levels ,obesity ,homocysteine ,and left ventricular hypertrophy LVH have been shown to be independently associated with CV risk . LVH is an important predictor of CV morbidity and mortality.
KEY WORDS:- POLYCYSTIC OVARIAN SYNDROME , HYPERTENTION , DYSLIPIDEMIA , CARDIOVASCULAR DISEASES, DIABETES MILLITUS , IMPAIRED GLUCOSE TOLERANCE , OBESITY .

1 .AIMS AND OBJECTIVES :-

A .The aim of this study was to investigate the cardiovascular CV risk of reproductive age group women with PCOS in Kashmir valley and studied the prevalence of diastolic filling and systolic performance by echocardiography .

B. To analyse any potential association between Cardiac and Metobolic parameters ,such as insulin secretion anlipid profile in a selected group of 220 young women.

2. INTRODUCTION :-

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder in women of reproductive age with a prevalence of 7 to 21 %(depending on the criteria used for the definition of PCOS), while Cardiovascular Disease (CVD) is the most common cause of death in the world both in women and men .Many studies have demonstrated relationships between CVD risk factors such as abdominal obesity ,dislipidemia ,glucose intolerance ,diabetes and hypertension and signs of PCOS .However, the existence of risk factors does not mean the same thing as increased risk .Therefore, the connection between PCOS and increased risk of developing CVD is debatable. Many factors in PCOS ,including both metabolic and hormonal, affect Cardiovascular .

3 .MATERIALS AND METHODS:-

3 .1 RECRUITMENT OF SUBJECTS :-

This was an analytical andprespective case control study involving a total of 120 PCOS women and 100 age matched controls between the age group of 18 .5 to 30.5 years were recruited for study .The women visiting SDH ChadooraBudgam, LD Hospital Srinagar and Skims Soura Srinagar endocrinological Out patient clinic , for PCOS related symptoms such as hirsutism ,acne ,obesity ,infertility or menstrual irregularities from march 2021 to December 2023 were evaluated for PCOS.Controles were recruited from different High schools, Higher secondary schools and from Different Departments of university of Kashmir.The controls had no history of any endocrinological disorder. To evalvate the Cardiovascular risk of Polycystic Ovarian Syndrome (PCOS),we investigated lipid profile ,metabolic pattern and echocardiography in these subjects .PCOS women had higher fasting glucose and insulin levels, homeostasis model assessment score of insulin sensitivity, total cholesterol(TC) and low density lipoprotein cholesterol (LDL –C) Levels ,and TC / high density lipoprotein cholesterol(HDL –C) ratio and lower HDL –C levels than controls .PCOS women had higher left atrium size (33.02±5.02 vs 28.02 ±2.6 mm;P< 0.0001) and left ventricular mass index (LVM i) (81.5 ± 19.2 vs.57.2 ± 6.4 g/m2 ; P <0.0001) and lower left Ventricular ejection fraction (65.4 ± 5.1 vs. 68.1 ± 3.6 %P=0.003)thancontrols. When patients and controls were grouped according to BMI [normal weight (BMI >18 .5 and< 25 kg /m2) , overweight (BMI , 25.5 to 30 ,5 kg /m2) ,and obese (BMI , > 30 Kg /m2), the difference between PCOS women and controls were maintained in overweight and obese women .In normal weight PCOS women ,a significant increase in the left ventricular mass index and a decrease in diastolic filling were observed . No change in TC,LDL,HDL, TC/HDL –C ratio ,and triglycerides compared with controls.

3.2 .ETHICS STATEMENT:-

This study was approved by Institutional ethics committee under ethical approval no.
B.M.O /CHA/890 ,dated :-20.09.2022.subjects were recruited after written informed consent consent was obtained from them.

3.3 . STUDY PROTOCOL:-

3.3. A . ANTTHROPOMETRIC AND CLINICAL STUDY :-

Height ,weight ,BMI, waist to hip ratio,and measurements of heart rate ,systolic blood pressure and diastolic blood pressure were evaluated by standard methods.BMI was measured as the ratio between the weight and square of the height .A BMI between 25.5 and 30.5 kg/m2was considered an index of overweight where as BMI greater than 30 kg/m2 was considered as index of obesity.

3.3 .B. BIOCHEMICAL STUDY:-

Fasting glucose, triglycerides TG, total cholesterol TC,low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) levels were measured by standard procedures in the morning between 10 to 12 hours after an overnight fast and resting in bed during early follicular phase 3rd to 5th day. Sampling was performed under aseptic conditions for the biochemical and hormonal analyses were permormed 10 minutes after needle insertion in duplicate and immediately centrifuged.And the serum was stored at -80 C until analysis. Hypertriglyceridemia was diagnosed when triglyceride levels were greater than 250mg/dl ,where as hypercholesterolemia was diagnosed after an oral glucose tolerance test (OGTT) .75 g of oral anhydrous glucose diluted in 300ml of water ,measuring blood glucose after every 30 minutes for 2 hours .

3.3..C .MEASUREMENT OF CARDIOVASCULAR AND METABOLIC RISK FACTORS:-

ECHOCARDIOGRAPHIC STUDY:-

M-mode two dimensional ,and pulsed Doppler echocardiography studies were performed by one operator.
Waist –hip ratio (WHR circumference).The free androgen index (FAI)was derived using formula :-

FAI =Total testeronenmol/L /SHBG nmol/L × 100
The homeostasis model assessment (HOMA)index ,which is considered an index of insulin resistance was calculated using formula :-
Fasting glucose mg/dl × fasting insulin(Uiu/ml)/405.

TABLE :- 1 . Anthropometric Parameterand BP in PCOS and control women .Values are given as mean ± SD

AMETER	S (n= 120)	NTROLS (n= 100)	
	± 4.5	: 3.5	
	± 7.5	± 4.9	01
olic blood pressure (mmHg)	95 ± 16	± 10.6	1
tolic blood pressure(mmHg)	± 11	± 8.1	01
ertension (%)	22)	2.1)	001
% androgen index.	: 5.2	1.4 ± 0.8	0001
omenorrhea	%	%	0001

TABLE:- 2 . Lipid and fasting blood glucose in PCOS and control groups .Values are given as mean ± SD

AMETERS	S (n=120)	trols (n= 100)	
l Cholesterol mol/L)	± 1.5	3 ± 1.03	
– Cholesterol (m /L)	± 1.O2	) ± 1 .07	001
–Cholesterol hol/L)	6 ± 0. 92	4 ± 0.96	001
–Cholesterol / Cholesterol mol/L)	0.66	: 0.39	001
lycerides (m mol/L)	±1.92	± 0.93	
ng blood glucose ol/L)	± 1.01	± 0.94	
ired fasting blood glucose	(5)	3.9)	

STATISTICAL ANALYSIS :-
Results were statistically anaysed and data was expressed as mean ±Sd .A p value of <0.05 was used as a criteria for statististicalsignificance.For the analysis ,Statistical Graph Pad Prism Version 5.0 was used. Stepwise linear regression analysis was performed to evaluate the associative importance of LVM I,as a dependent variable ,against age , BMI ,HOMA ,FAI ,lipid profile ,systolic and diastolic BP and daily smoking habbit .Smoking habbit were evaluated using x2 test.

TABLE 4 :- ECHOGRAPHIC FINDING IN PCOS AND CONTROLS.

diastolic diameter (mm)	*±4.1*	*2±1.92*	
ystolic diameter (mm)	*±4.8*	*±1.94*	*1*
(mm)	*1.6*	*±1.01*	*001*
osterior wall thickness)	*1.8*	*1.01*	*001*
I (g/m2	*1±15.2*	*±5.8*	*001*
T atrium size (mm)	*1±4.6*	*±2.4*	*001*
a size (mm)	*±3.8*	*±1.6*	
to late mitral flow velocity	*0.6*	*0.3*	*001*

IST :- inter ventricular septum thikness.

RESULTS :-

As expected,PCOS patients had significantly (p<0.05),higher LH ,testosterone ,and SHBG level than controls .Diastolic blood pressure and mean blood pressure were also significantly (P<0.05) ,higher in patients than in the controls ,where as systolic blood pressure and heart rate were a bit similar in both patients and controls. The free androgen index FAI was (P < 0.05),higher in patients than in controls.

BIOCHEMICAL:-

Biochemical study shows PCOS patients had significantly (P <0.05)higher fasting glucose and insulin levels , HOMA ,TC ,LDL –C ,and TC /HDL –C ratio ,where as HDL – levels were significantly (P < 0.05) lower in patients than controls . TC levels were similar in both patients and controls. Both PCOS patients were having normal triglycerides and cholesterol levels .

ECHOCARDIOGRAPHY:-

Echocardiography study shows that the women with PCOS had a cardiac size significantly increased (P < 0.05) than controls .there was a progressive impairment of metabolic profileand cardiac finding .

The findings of this analytical and prespective case controlled study in selected reproductive age group women with PCOS showed a significant impairement of glucose and lipid profile with an increased LVM (Left ventricular Mass) and decreased LV (Left Ventricular performance and diastolic fiiling. These abnormalities persisted even in young patients with normal weight ,suggesting that the pathogenesis of cardiac abnormalities in PCOS is not only dependent on BMI ,but LVM is significantly correlated with both BmI and HOMA (Homeostasis Model Assessment) index.

TABLE :- 4. Main cardiovascular risk factors and echocardiographic findings in patients and controls according to BMI .

	BMI 18 .5 -25.5 kg/m2			*BMI 25.6 -30.1 kg/m2*			*BMI>30.1kg /m2*		
	PCOS	*Controls*	*P*	*PCOS*	*Controls*	*P*	*PCOS*	*Controls*	*P*
NO.	*35*	*30*		*35*	*30*		*50*	*40*	
FAI%	*9.2±6.3*	*1.1±0.6<0.0001*		*10.9±2.6*	*0.9±0.6<0.0001*		*7.2±5.1*	*1.2±0.5< 0.0001*	
Fasting Insulin pmol/L	*9.1±4.4*	*2.3±0.9<0.0001*		*10.4±3.1*	*2.8±1.4<0.0001*		*18.1±7.4*	*2.4±1.0<0.0001*	
HOMA	*1.9±0.9*	*0.4±0.2<0.0001*		*2.6±1.3*	*0.4±0.3*	*0.001*	*5.01±0.6*	*0.4±0.2<0.0001*	
TC mmol/L	*3.7±0.5*	*3.5±0.4*	*0.180*	*4.7±0.7*	*3.6±0.6*	*0.006*	*2.6±0.6*	*3.8±0.5<0.0001*	
LDL-C mmol/L	*2.1±0.5*	*1.8±0.4*	*0.142*	*2.4±0.4*	*1.9±0.3*	*0.007*	*2.7±0.6*	*2.01±0.5*	*0.004*
HDL-C mmol/L	*2.5±0.8*	*2.8±0.4*	*0.136*	*2.6±0.4*	*3.1±1.01*	*0.022*	*1.9±0.4*	*3.1±0.5*	*0.011*
TC/HDL-C	*1.6±0.5*	*1.3±0.4*	*0.050*	*1.9±0.0.6*	*1.3±0.5*	*0.045*	*1.9±0.4*	*1.3±0.6*	*0.002*

Ratio									
TG mmol/l	*1.4±0.3*	*1.3±0.4*	*0.347*	*1.6±0.4*	*1.5±0.3*	*0.512*	*1.7±0.3*	*1.6±0.3*	*0.234*
LVM i (g/m2)	*70.4±19.2*	*56.4±4.6*	*0.021*	*78.1±9.1*	*56.4±8.8*	*0.001*	*92.4±14.2*	*56.01±5.01*	*<0.0001*
LVEF (%)	*66±4.1*	*68.1±4.1*	*0.183*	*65.7±5.1*	*66.4±2.8*	*0.760*	*62.4±3.9*	*66.9±2.01*	*0.001*

PCOS Women represent an intriguing biological model illustrating hormonal effects on cardiovascular risk .In fact ,several findings indicate association between heart diseases and PCOS.,i.e .dyslipidemia ,insulin resistance,increased Left ventricular mass (LVM) ,and diastolic dysfunction.PCOS .We designed the study to investigate different variables affecting heart structure and function.we selected young (reproductive age group women)patients to better understand the role of increased BMI frequent in PCOS ,we included a group of lean patients and controls .

PCOS women were reported to have higher Total Cholesterol TG leves and lower HDL Cholesterol values .Because insulin is major positive regulator of liproteinlipasethat is involved in pathway of HDL –C production.,dyslipidemia is probably secondary to insulin resistance.

CONCLUSION:- Our study shows the detrimental effect of PCOS on the cardiovascular system even in young (reproductive age group women).women with PCOS have increased basal serum insulin secretion and at tissue level show selective insulin resistance for metabolic pathways. Hyperinsulinemia plays role in multiple factors involved in pathogenesis of PCOS and severity of its symptoms .Women with high fasting insulin have higher values of markers of cardiovascular disease such as (high sensitive C Reactive Protein ,LVM ,Systolicand Diastolic BP)and metabolic risk ,such as (LDL –Cholesterol, Total Cholesterol ,Low HDL –Cholesterol).besides hypertension,diabetes, dyslipidemia .Insuline resistance is probably the major risk factor of the occurance of Cardiovascular disease (CVD) in PCOS.

CONFLICT OF INTREST STATEMENT :-

The Authors stated that they have no conflicts of intrest regarding the publication of this case control study.

CONSENT FOR PUBLICATION :-

All Authors have approved the manuscript for submission.

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