

# Non-Alcoholic Fatty Liver Disease and Polycystic Ovary Syndrome

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## ABSTRACT

**Background:** Non-alcoholic fatty liver disease (NAFLD) is common in patients with increasing obesity and metabolic syndrome (MS). Because both these features are prevalent in polycystic ovary syndrome. It appears that study of NAFLD in PCOS may be a good indicator of MS or presence of some of its features. There are two stages of NAFLD, one is steatosis which appears as increased fat in hepatocytes and other more severe form is non-alcoholic fatty liver steatohepatites with necrosis and inflammation (NASH). It may progress to cirrhosis and hepatocellular carcinoma.

**Aim:** To evaluate liver in patients with polycystic ovary syndrome for non-alcoholic fatty liver disease and abnormal aminotransferase activity

**Methods:** 30 patients diagnosed as PCOS according to Rotterdam Criteria 2003 will be compared with 16 healthy patients matched with age and BMI. Anthropometric features such as BMI, waist circumferences will be measured. Abdominal ultrasonography for grade of fatty liver will be performed on study as well as control subjects. Biochemical analysis such as fasting blood sugar and alanine aminotransferase levels will be performed.

**Design:** A case controlled cross sectional study.

**Setting:** Gynaecology and Radiology Departments, Shalamar Hospital, Lahore

**Results:** Features of higher BMI, and increase waist circumference in PCOS are associated with NAFLD and abnormalities of ALT. Results will be presented by applying SPSS version 21.

**Conclusion:** The increased prevalence of NAFLD IN PCOS patients suggests an association between these two conditions. In fact NAFLD is emerging as marker of metabolic syndrome. This makes it necessary to evaluate these young patients for liver disease, so effective measures can be taken to prevent to this progressive problem.

**Keywords:** Fatty liver disease, polycystic ovary syndrome, NAFLD

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## INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is recognized increasingly as accumulation of fat in the liver. It resembles chronic liver disease - histologically in patient without intake of alcohol and other disorders which are nutritionally induced by ingestion of drugs. It also excludes the chronic liver disorder caused by other diseases<sup>1</sup>. There are two stages 1) Steatosis which involves increased fat accumulation in liver and is a reversible condition and 2) it may progress to more severe condition called, nonalcoholic steatohepatites (NASH). In few patients this may lead to development of fibrosis and cirrhosis<sup>2</sup>.

NAFLD, clinical relevance is related to high prevalence in general population (10-30%) and its possible progression to more severe condition but evolution to hepatocellular carcinoma is very rare<sup>3</sup>.

In PCOS underlying pathophysiology is insulin resistance and it has repercussions on reproductive,

metabolic and cardiovascular system, it has rekindled the interest of scientific community to study this group with broader approach<sup>4</sup>. As studies have found that insulin resistance is also responsible for development of NAFLD, the most common liver disease now a days<sup>4</sup>.

Several studies have pointed to increased prevalence of developing metabolic syndrome or some of its components, such as density, glucose intolerance and dislipidemia<sup>5</sup>. Because of potential of progression of NAFLD with metabolic syndrome, It is essential that early interventions for diagnosis and therapeutic intervention are carried out in such patients<sup>6,7</sup>.

The objective of this study is to identify risk of NAFLD in patients with PCOS as compared to general population and to make aware scientists that it is emerging as marker of metabolic syndrome.

## METHOD & PATIENTS

It is prospective case control cross sectional study patients were inducted from Gynaecology OPD at Shalamar Hospital from 01 July, 2016 till 31 December, 2016. Thirty women aged between 18-

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45yrs with confirmed diagnosis of PCOS based on 2003 rotterdam<sup>8</sup>criteria. Diagnosis of PCOS was based upon the presence of hyperandrogenesim (clinical and/or biochemical) combined with either oligo/amenorrheor polycystic ovarian morphology on ultrasound.

Diseases causing androgen excess and disordered ovulation, Cushing syndrome, CAH hyperprolactinemia, untreated thyroid disease and androgen secreting tumors were excluded by appropriate tests. Previous history of chronic liver disease or using drugs that are risk factors for NAFLD such as steroids, tamoxifen, diliazem, amiodarone& consumption of alcohol were also excluded. Sixteen age and weight matched premenopausal apparently healthy control were also recruited from outpatient department who presented with obesity or others general problems. Controls had normal menses and no clinical signs of hyperandrogensim

Patients and control underwent a clinical examination, anthropometric measurements such as (weight, height, waist circumference) and blood pressure were recorded. Liver and pelvic ultrasounds were carried out. Biochemical analysis including fasting blood sugar serum alanine aminotransferase and carried done. Metabolic syndrome was diagnosed in patients and control based on the presence of three or more of the following findings: (waist circumference >80cm, serum fasting glucose  $\geq$  100mg, blood pressure  $\geq$ 135/85hg, Serum triglycerides  $\geq$  150mg/d or HDL<50mg proposed by American Heart Association. All patients were submitted to ultrasonography of the liver with 3.5MHz convex transducer for the screening of hepatic steatosis. Hepatic parenchymal echotexture was evaluated and compared with echotexture of the Spleen. When Isoechoic, the liver parenchyma is considered normal, the presence of hyperechoic hepatic parenchyma (bright liver) is considered as hepatic steatosis.

Mild hepaticsteatosis is diffuse increase of fine echoes in the liver parenchyma but allows good view of its vessels. Moderate hepaticsteatosis is defined when diffuse increase of echogenic liver parenchyma makes it difficult to view the vascular walls and diaphragm. Severe hepaticsteatosis is significant increase of fine echoes and intense posterior attenuation preventing the view of vascular walls and diaphragm. Statistical analysis was carried out by applying SPSS version 21.

Results of continuous variables are presented as mean and  $\pm$ SD and for categorical variables as absolute number and as percentages. P value <0.05 is considered significant.

## RESULTS

Clinical and laboratory characteristics of 30 patients with PCOS and 16 age, weight matched healthy control are shown in table I. Patients with PCOS had significant abdominal obesity (P= 0.001). The markers of metabolic syndrome for e.g., BMI, fasting blood glucose and systolic and diastolic, B.P were on higher side in PCOS Patients. In table II the hepatic steatosis was present in 22(73.10%) patients as compared to 5(31.25%) controls with P value 0.011 which was significantly higher. Table III compares the characteristics of patients with NAFLD and PCOS with subgroup of PCOS patients who did not had NAFLD. Both had abdominal obesity as depicted by waist circumference and BMI which were significantly higher in PCOS with NAFLD, P value.003 &.001 respectively as compared to sub group.

Table III: PCO patients with hepatic steatosis were older, had higher BMI, more abdominal adiposity, and biochemical tests fasting blood sugar and ALT were higher.

Figure I shows the graphical representation of PCOS and control patients. Elevated aminotransferase was present in 33% PCOS patients as compared to 6% of controls. They were all obese.

Table 1: Comparison between patient with polycystic ovary syndrome group and control group.

	PCOS n=30	Control n=16	P value
Age Years	25.87 $\pm$ 6.17	30.6 $\pm$ 6.97	0.041
BMI	31.94 $\pm$ 5.73	29.22 $\pm$ 5.53	0.128
Waist Circumference	101.91 $\pm$ 13.11	89.87 $\pm$ 15.29	0.01 s
ALT IU/L	37.07 $\pm$ 20.84	20.38 $\pm$ 7.04	0.004 s
Fasting Glucose	93.6 $\pm$ 16	88.31 $\pm$ 10.23	0.048
SBP	115.0 $\pm$ 9.0	119.37 $\pm$ 29	0.128
DBP	74.0 $\pm$ 8.14	76.88 $\pm$ 6.02	0.221

P<0.05 significant

Table 2: Comparison of prevalence of nonalcoholic fatty liver disease between polycystic ovary syndrome and control group.

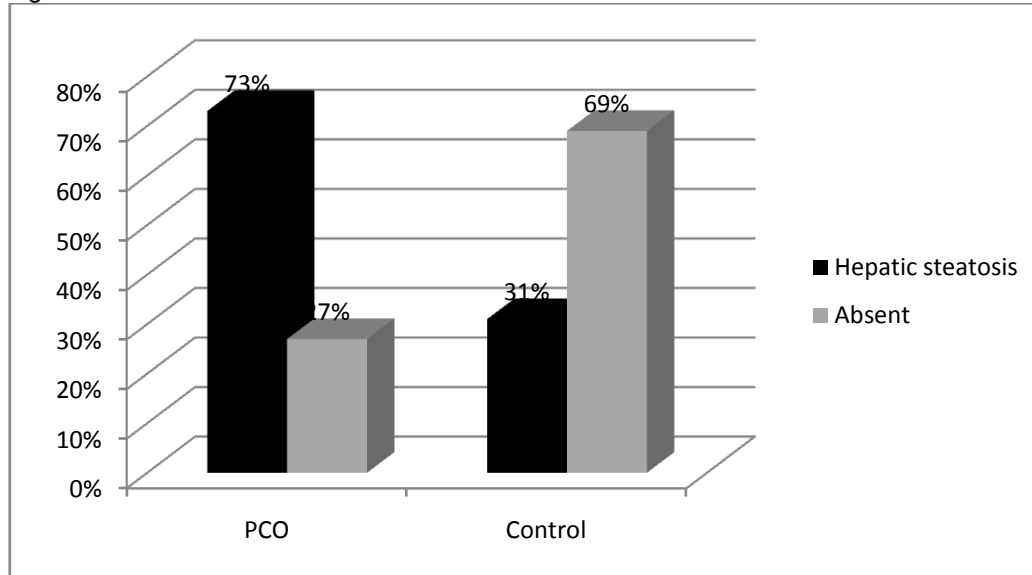
NAFLD	PCOS Group n=30	Control Group n=16	P value
Present	22 (73.10%)	5 (31.25%)	0.011
Absent	8 (26.67%)	11 (68.75%)	

Table III: Comparison between patient with polycystic and NAFLD sub group with patients only with PCOS.

	Sub Group PCOS+NAFLD (n=22)	Sub Group PCOS+NonNAFLD(n=8)	P value
Age	26.20 ± 6.35	24.20±5.44	0.518
BMI	33.39 ± 4.69	24.3	0.001
Waist Circumference	104.94 ± 12.02	86.78 ± 5.9	0.003
Fasting Glucose	82.68 ± 14.24	77.32 ± 16.6	0.460
SBP	116.0 ±9. 13	110.0 ± 7.1	0.61
DBP	76.2 ± 12	74.5 ± 12	0.18
ALT	74.40. ± 8.70	72.0 ±4.47	0.56

Pvalue<0.05=significant

Fig.1: NAFLD in PCO and controls



## DISCUSSION

In the literature studies available to show association between PCOS and NAFLD are still scarce and recent. There studies results are different from our population because of difference in life style and genetic back ground. Our study found 73.3% hepatic steatosis in PCO patients (P Value.001) which is highly significant. This is in agreement with a study which showed a prevalence of 71% in a population of patient with diagnosis of PCOS.<sup>9</sup> However this value is higher as compared to previous studies, which depicted 55% and 41.5% respectively. These differences can be explained due to ethnic differences. Cerda studied Hispanic and gambarine investigated population compared of several ethnicity whereas our study involved only Asians. Other studies have shown that southeast Asians have higher incidence of PCOS and they are more obese.

In present study the PCO patient had significantly higher abdominal adiposity (P.011). The markers of metabolic syndrome for e.g., BMI, fasting glucose and systolic and diastolic were higher in patients with PCO and hepatic steatosis.

Several studies indicate more frequency of metabolic syndrome (MS) in women with PCOS as compared to normal population<sup>6</sup>.Insulin resistance is a underlying denominator of both conditions. These women if not monitored and counselled have propensity to develop NAFLD is future.

Younger and leaner patient may develop NAFLD, but incidence is low. In my study 2 lean patients with PCOS had hepatic steatosis.

In the cohort subgroup when patients with PCOS and NAFLD were compared with those without NAFLD obesity, abdominal adiposity were factors predominantly significant.

Serum alanine aminotransferase has been used as a biochemical marker, indicative of presence of NAFLD after excluding other chronic liver diseases. Some studies have reported raised ALT in PCOS patients ranging between 15-39%<sup>12,13</sup>.

In the present study using cutoff level of ALT ≥40iu/L, 33% of patients with PCOS had abnormal levels. As most of patients were obese, increasing the prevalence of NAFLD. However elevated ALT is a crude method of detecting NAFLD, as 2/3<sup>rd</sup> of patient with NAFLD did not had abnormal ALT level. Ultrasonography is a sensitive, cost effective with

short examination time in detecting fatty liver infiltration. Although hepatic steatosis is a relatively benign condition, but it has a potential for progression and it is a reversible condition. Life style modification have beneficial effect.

## CONCLUSION

This study provides strong indication that NAFLD is common in PCOS obese patients, so these patients should undergo evaluation by ultrasound of their liver earlier on so that to establish diagnosis of fatty infiltration with repercussion on their health.

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