International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article.

Women Affected with PCOS and Evaluation of Liver Function Tests To Predict Liver Fibrosis: A Non-Invasive Method

Shabir Ud Din Lone[1], Sheikh Junaid Aziz[2*], Humairah Shafi[3], Hilal Ahmad Wani[4]

[1]Associate Professor, [2]Lecturer, [3]Post Graduate,
Department of Physiology, Government Medical College, Srinagar, J&K, India.
[4]Assistant Professor, Department of Biochemistry, Government Degree College, Sumbal, J&K, India.

ABSTRACT

Introduction: PCOS is common in the women of reproductive age group. It is consistent with hyperandrogenism and anovulatory cycles. The female generally presents with features of menstrual disturbances, acne, hirsutism and obesity. The women with PCOS are prone to cardiovascular morbidity and hepatic disorder like NAFLD. The increased risk of obesity in these patients make them vulnerable to the insulin resistance and ultimately to the development NAFLD and Diabetes mellitus.

Materials and Methods: The present study was designed to determine the effect of PCOS on Liver in the development of fibrosis. We included 40 women with PCOS in the study group and 20 healthy women of the same age group without PCOS as the Control. The various anthropometric measurements along with some serum biochemical analysis were done.

Results and Observations: We found that BMI, LDL, WC, FPG, OGTT were higher in the PCOS group than the control group and the difference was statistically significant. The HDL was significantly lower in the PCOS group than the control. Our results showed the comparison between the subgroups of PCOS. The cases having PCOS with steatosis and cases having PCOS without steatosis classified on the basis of non-invasive measurements like FIB and NAFLD scoring. The statistically significant difference was found in FPG and GGT, AST. Though the difference in the OGTT was not statistically significant but the values were outside the 90% confidence interval. The short coming of this study was of short sample size and that if a large enough sample is taken they might also become statistically significant.

Conclusion: We conclude that in women with PCOS the prevalence of metabolic disorder is more and women with this Syndrome evaluation for hepatic steatosis should be done.

Key words: PCOS, NAFLD, Obesity, Diabetes Mellitus, Liver Fibrosis.

***Correspondence to:**

Dr. Sheikh Junaid Aziz,
Lecturer, Department of Physiology,
Government Medical College, Srinagar, J&K, India.

Article History:

Received: 06-06-2021, **Revised:** 02-07-2021, **Accepted:** 26-07-2021

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2021.7.4.017	

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a gynaecological endocrine disorder that affects approximately 5-10% of women in reproductive age. It is characterized by hyperandrogenism and anovulation with signs and symptoms of menstrual cycle disturbances, acne, hirsutism and obesity.[1] Women with PCOS have long term risk of developing metabolic syndrome associated with increasing cardiovascular morbidity and non-alcoholic fatty liver disease (NAFLD). NAFLD typically characterised by more than 5% accumulation of hepatocellular lipids comprises disease stages ranging from hepatic steatosis (HS) to non-alcoholic steato-hepatitis (NASH). Several techniques have been developed for non-invasive study of diagnosis and staging of NAFLD, such as ultrasonography, computerized tomography (CT) and MRI to clinically assess but has a limitation because of radiation and observer bias and lack of accessibility.[2] A new ultrasound based technique for measuring fat content in the liver using signals acquired by transient elastography probe called controlled attenuation parameter (CAP). Karlas and Colleagues reported the cut-offs of CAP were 248dB/mm for those above steatosis grade S0.[3] The new body fat indices such as lipid accumulation product (LAP) index, Visceral adiposity index (VAI), and the product of triglycerides and glucose (TyG) accurately predict insulin resistance (IR), prediabetes and type 2 diabetes mellitus (T2DM).[4-7]

Obesity mainly central obesity and IR are the main factors related to NAFLD in PCOS. Androgen excess, a main feature of PCOS is also related to IR. It may be an additional contributing factor to development of NAFLD. Thus, this study was conducted to determine non-invasive fibrosis staging of NAFLD in hospital coming women with PCOS.

MATERIALS AND METHODS

The study was conducted in the department of physiology GMC Srinagar in collaboration with endocrinology, department of super-speciality hospital. We enrolled 40 non pregnant patients aged between 20-40 years who attended regular OPD for PCOS management between Jan 2018 and Jan 2020. Also, in addition to that 20 non-pregnant women in reproductive age attending general medicine OPD were enrolled to serve as controls. The study group PCOS was defined according to the Rotterdam criteria, that is by the presence of atleast two out of following three factors, clinical or biochemical hyper-androgenism, chronic oligo-anovulation or polycystic ovarian morphology.[8] The study was approved by ethical committee GMC Srinagar. The subjects were excluded if with the history of alcoholism, chronic liver disease, dyslipidaemia, or any drugs that could cause fibrosis.

Anthropometric and Laboratory Data

Following a 12 hour overnight fasting subjects underwent weight, height and waist circumference (WC) measurement by calibrated scale after removing heavy shoes and clothes. WC was measured at the midpoint between the inferior costal margin and superior border of the iliac crest in the mid axillary line. BMI was calculated as the weight in Kgs divided by square of height in meters. Obesity was defined as a BMI >= 30kgs/m^2 and central obesity as a WC >= 80cms. Clinical and laboratory data were recorded. Arterial BP was measured after sitting for atleast 15 min. Three readings were taken at 5 min interval and mean was recorded. Phenotypic sub-group of PCOS and fasting blood samples were used to measure fasting plasma glucose (FBG), transaminases, lipid profiles and hormones. All biochemical measurements were tested in biochemistry central laboratory of GMC Srinagar. The standard methods like enzymatic, hexokinase and electro Chemiluminescence immunoassay were used to measure serum AST, ALT and FPG and Insulin respectively. The levels of fasting plasma glucose, insulin, oral glucose tolerance tests OGTT, total testosterone (TT), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TGs), Serum alanine amino transaminase (ALT), aspartate amino transaminase (AST), y-glutamate transaminase (GGT), were recorded from all the participants.

Subjects with PCOS were classified into four phenotypes (methodology of the national institute of health 2012).[9]

A. Hyperandrogenism (HA) plus ovulatory dysfunction (OD) plus polycystic ovary (PCOM)
B. (HA plus OD)
C. (HA plus PCOM)
D. (OD plus PCOM)

Impaired fasting glucose (IFG) was defined as a FPG >=100 mg/dL but < 126mg/dL.[10]

LAP (lipid accumulation product) and VAI (visceral adiposity index) were calculated using published formula:

LAP = (WC – 58) * TG (mmol/L)[12] and

VAI as WC/ {36.58 + (1.89 * BMI)} * (TG/0.81) * (1.52/HDL) (13)

LAP>= 34.5; and VAI > 1.67.[11-13]

The clinical and biochemical hyperandrogenism was assessed by the modified Ferriman-Gallwey score. Subjects with score >= 8 were considered to be hirsute.[14] Oligomenorrhea was defined as the occurrence of <8 menstrual cycles/year. Levels of ALT, AST and GGT were deemed elevated if above normal reference level of >69IU/L, >46IU/L and >43IU/L respectively.[15]

NAFLD and Staging

Women with PCOS and steatosis were assessed by a Hepatologist who evaluated the patient clinically and took a laboratory evaluation and measurements of liver enzymes, viral hepatic serology, iron studies, platelet count, 25-hydroxylated D, and accordingly NAFLD scoring and FIB-4 index were calculated.

NAFLD score = -1.675 + 0.037 × age (years) + 0.094 × BMI (kg/m^2) + 1.13 × IFG/diabetes (yes = 1, no = 0) + 0.99 × AST/ALT ratio - 0.013 × platelet (×10^9/L) - 0.66 × albumin (g/dL).[16]

FIB-4 = Age (years) x AST (U/L) / Platelets (×10^9/L) x √ALT (U/L).[17]

Hepatic steatosis was considered absent when the echogenicity in the hepatic parenchyma was equal to that of the renal cortex. Fatty liver was determined in the presence of higher echogenicity in the hepatic parenchyma compared with renal cortex and impaired visualization of the intra hepatic vessels and the diaphragm.[18]

Statistical Analysis

Statistical analysis done using the SPSS software (version 23). Continuous variables were taken as means and standard deviations. The independent t test was used to find the association between the cases and controls and also between the subgroups.

The Levenes test was used to find the equality of variance between the groups and subgroups and the p value was adjusted according to the significance value of Levenes test. The P value <0.05 was considered statistically significant.

Table 1: Clinical, anthropometric and laboratory characteristics of the participants in the PCOS and control groups:

Parameter	control (n=20)	PCOS (n=40)	Signif. by Levene's Test for Equality of Variances	P value (2 tailed)
Age (years)	25.90±3.68	26.73±4.60	0.142	0.488
BMI (kg/m^2)	24.65±1.95	28.03±2.49	0.099	0.000
WC (cms)	100.88±1.44	104.36±5.11	0.000	0.000
TG (mg/dL)	109.39±22.86	140.01±32.28	0.020	0.000
LDL (mg/dL)	71.91±11.86	98.93±20.53	0.251	0.000
HDL (mg/dL)	40.58±4.61	35.88±5.13	0.040	0.001
FPG (mg/dL)	86.96±7.96	97.86±9.34	0.867	0.000
ALT (U/L)	27.15±10.71	27.38±12.78	0.425	0.945
AST (U/L)	21.80±8.31	25.87±7.86	0.720	0.069
GGT (U/L)	8.95±2.01	11.63±6.62	0.001	0.023
OGTT (mg/dL)	178.69±13.00	197.98±21.43	0.437	0.000
Albumin (g/L)	.	3.57±0.29.	.	
Platelet (*10^9)/L	.	206.98±41.44		

Table 2: Clinical, anthropometric and laboratory data of the participants with pcos with or without hepatic steatosis:

Parameter	PCOS without Hepatic Steatosis (n=29)	PCOS with Hepatic Steatosis (n=11)	Signif. by Levene's Test for Equality of Variances	P value (2 tailed)
Age (years)	26.48±4.21	27.36±5.66	0.514	0.810
BMI (kg/m^2)	27.97±2.56	28.18±2.40	0.069	0.115
WC (cms)	105.14±5.34	102.28±3.94	0.662	0.118
TG (mg/dL)	144.94±31.99	127.00±30.71	0.180	0.116
LDL (mg/dL)	102.08±22.64	90.61±10.14	0.190	0.957
HDL (mg/dL)	35.86±5.00	35.95±5.72	0.482	0.213
FPG (mg/dL)	96.72±9.45	100.87±8.74	0.080	0.033
ALT (U/L)	30.00±13.24	20.45±8.58	0.688	0.985
AST (U/L)	25.86±7.87	25.91±8.22	0.009	0.002
GGT (U/L)	13.00±7.19	8.00±2.53	0.523	0.641
OGTT (mg/dL)	198.97±17.84	195.36±29.83	0.442	0.065
VAI	9.07±2.45	7.54±1.42	0.074	0.060

RESULTS AND OBSERVATIONS

The anthropometric and laboratory parameters of the cases with PCOS and control groups in the table 1, the average age of cases were 26.27 with SD 4.60 and of the control group was 25.90 with SD 3.68. The values of BMI, with Waist circumference (WC), Triglycerides (TGs), Low density lipoproteins (LDL), Fasting Plasma glucose (FPG) in cases as compared to control group were statistically significant. The Prevalence of hyper-triglycerides and impaired fasting glucose was higher in PCOS group than another.

The clinical anthropometric and laboratory parameters of the subjects with PCOS and without associated NAFLD in table 2. On analysis, WC, serum TGs, AST, ALT, IGF levels were associated with hepatic fibrosis. FIB-4 index was significant in subjects while as NAFLD score was calculated in subjects with PCOS and Hepatic steatosis. In 5 subjects the score was lower. In 2 subjects the score was higher suggesting of severe fibrosis.

DISCUSSION

In this study (table 1) we compared subjects who presented as cases with PCOS with control group without PCOS and noted they have different BMI and WC which are statistically significant. The associated additional factors were also analysed and found that subjects with PCOS have higher rate of obesity and thereby higher prevalence of metabolic syndrome.

In table 2 we observed insignificance by Levenes test for equality of variances in cases with PCOS with hepatic steatosis (n=11) and PCOS without hepatic steatosis (n=29), not any significant differences were found in BMI and WC, maybe it is because of younger age group, which is inconsistent with the previous studies[19,20] but statistically significant difference was found as far their serum TGs and Liver enzymes were considered. We observed high prevalence of fatty liver changes in subjects with PCOS, Levenes test for equality of variances confirmed TG, ALT, AST, GGT, VAI as independent factors associated with non-alcoholic fatty liver and hepatic steatosis in cases with PCOS. But in our study, there was high prevalence of obesity in cases with PCOS as compared to control group without PCOS, which sends an alarm for an observation of growing obesity in our society to rule out PCOS and thereby NAFLD and steatosis.[21]

With the development of liver disease the investigation of metabolic abnormalities in patients with PCOS is of great importance in clinical practice. In our study subjects with the PCOS phenotype A were predominant but association of steatosis was not detected in the study among the various phenotypic representations possibly because of classic hyper-androgenism.

CONCLUSION

In conclusion, our study found association between metabolic changes and PCOS in a set of subjects selected in our OPD and have demonstrated a high prevalence of fatty liver changes, steatosis to fibrosis in patients with PCOS with similar BMI and WC.

ACKNOWLEDGEMENTS

The authors would like to thank all the persons who participated in this study. Without their cooperation this work would not have been possible. Lastly authors are thankful to all the staff members of the Department of Physiology for their help in the data collection and compilation and provision of some valuable suggestions.

REFERENCES

1. Conway G, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Franks S, Gambineri A et al. The polycystic ovary syndrome: a position statement from the European Society of Endocrinology.European Journal of Endocrinology2014;171:1–29.

2. Leoni S, Tovoli F, Napoli L, Serio I, Ferri S & Bolondi L. Current guidelines for the management of non-alcoholic fatty liver disease: a systematic review with comparative analysis. World Journal of Gastroenterology 2018; 24: 3361–73. https://doi.org/10.3748/wjg.v24.i30.3361.

3. Karlas T, Petroff D, Sasso M, Fan JG, Mi YQ, de Ledinghen V, Kumar M, Lupsor-Platon M, Han KH, Cardoso AC, et al. Individual patient data meta-analysis of controlled attenuation parameter (CAP) technology for assessing steatosis. Journal of Hepatology 2017; 66: 1022–30.

4. Roriz AK, Passos LC, de Oliveira CC, Eickemberg M, Moreira Pde A & Sampaio LR. Evaluation of the accuracy of anthropometric clinical indicators of visceral fat in adults and elderly. PLoS ONE 2014; 9: e103499.

5. Nusrianto R, Ayundini G, Kristanti M, Astrella C, Amalina N, Muhadi, Riyadina W, Tahapary DL & Soewondo P. Visceral adiposity index and lipid accumulation product as a predictor of type 2 diabetes mellitus: the Bogor cohort study of non-communicable diseases risk factors. Diabetes Research and Clinical Practice 2019; 155: 107798.

6. Ahn N, Baumeister SE, Amann U, Rathmann W, Peters A, Huth C, Thorand B & Meisinger C. Visceral adiposity index (VAI), lipid accumulation product (LAP), and product of triglycerides and glucose (TyG) to discriminate prediabetes and diabetes. Scientific Reports 2019; 9: 9693.
7. Mazidi M, Kengne AP, Katsiki N, Mikhailidis DP & Banach M. Lipid accumulation product and triglycerides/glucose index are useful predictors of insulin resistance. Journal of Diabetes and its Complications 2018; 32: 266–70. (https://doi.org/10.1016/j.jdiacomp.2017.10.007)
8. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertility and Sterility 2004; 81: 19–25. (https://doi.org/10.1016/j.fertnstert.2003.10.004)
9. Johnson TRB, Kaplan, LK, Ouyang P, Rizza RA. National Institute of Health Evidence-based Methodology Workshop on Polycystic Ovary Syndrome. Nat Institutes Heal. 2012;1-14.
10. Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, Pratley R, et al. Impaired Fasting Glucose and Impaired Glucose Tolerance. Implications for care. Diabetes Care. 2007;30(3):753-59.
11. Geloneze B, Repetto EM, Geloneze SR, Tambascia MA, Ermetice MN. The threshold value for insulin resistance (HOMA-IR) in an admixture population IR in the Brazilian Metabolic Syndrome Study. Diabetes Res Clin Pract. 2006;72(2):219-20.
12. Wiltgen, D, Benedetto IG, Mastella LS, Spritzer PM. Lipid accumulation product index: A reliable marker of cardiovascular risk in polycystic ovary syndrome. Hum Reprod. 2009;24:1726-31.
13. Bron8czyk-Puzon8 A, Jagielski P, Kulik-Kupka K, Koszowska A, Nowak, J, Zubelewicz-Szkodzin8ska B. Usefulness of a new anthropometric indicator – VAI (Visceral Adiposity Index) in the evaluation of metabolic and hormonal disorders in women with polycystic ovary syndrome. Adv Clin Exp Med. 2017;26:825-28.
14. Hatch R, Rosenfield RL, Kim MH, Tredway, D. Hirsutism: Implications, etiology, and management. Am J Obstet Gynecol. 1981;140:815-30.
15. Fauser BCJM. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81:19-25.
16. Angulo P, Hui JM, Marchesini, G, Bugianesi E, George J, Farrell GC, et al. The NAFLD fibrosis score: A noninvasive system that identifies liver fibrosis in patients with NAFLD. Hepatology. 2007 Apr;45(4):846-54. doi: 10.1002/hep.21496.
17. Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J,et al. Development of a Simple Noninvasive Index to Predict Significant Fibrosis in Patients With HIV/HCV Coinfection. Hepatology, June 2006;43(6):1317-25.
18. Castera L, Forns X, Alberti A. Non-invasive evaluation of liver fibrosis using transient elastography. J Hepatol. 2008;48:835-47.
19. Zhang J, HU J, Zhang C, Jiao Y, Kong X, Wang W. Analyses of risk factors for polycystic ovary syndrome complicated with non-alcoholic fatty liver disease. Exp Ther Med. 2018;15: 4259-64.
20. Kim JJ, Kim D, Yim JY, Kang JH, Han KH, Kim SM, et al. Polycystic ovary syndrome with hyperandrogenism as a risk factor for non-obese non-alcoholic fatty liver disease. Aliment Pharmacol Ther. 2017;45:1403-12.
21. Zheng SH, Li XL. Visceral adiposity index as a predictor of clinical severity and therapeutic outcome of PCOS. Gynecol Endocrinol. 2016;32:177-83.

Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Shabir Ud Din Lone, Sheikh Junaid Aziz, Humairah Shafi, Hilal Ahmad Wani. Women Affected with PCOS and Evaluation of Liver Function Tests To Predict Liver Fibrosis: A Non-Invasive Method. Int J Med Res Prof. 2021 July; 7(4): 77-80. DOI:10.21276/ijmrp.2021.7.4.017