IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 9 Ver. 14 (September. 2018), PP 38-43
www.iosrjournals.org

A Hospital Based Study Correlating the Prevalence of Fatty Liver Disease in Polycystic Ovary Syndrome using Ultra Sound as Screening Modality

Sonica Sharma[1], Bhamidipaty Kanaka Durgaprasad [*2], Pilli Hemaprakash Kumari [3], Payala Vijayalakshmi[4]

[1]*Assistant Professor, Department of Radiodiagnosis*
[*2] *Head of the Department and Professor, Department of Radiodiagnosis,*
[3] *Head of the Department and Professor, Department of Microbiology,*
[4] *Tutor, Department of Microbiology,*
GITAM Institute of Medical sciences and Research, GITAM (Deemed to be University),
Visakhapatnam-530045 (A.P), India.
Corresponding author: Dr. Bhamidipaty Kanaka Durgaprasad

Abstract:
Background: *Women with PCOS had a higher prevalence of fatty infiltration of liver compared to women with out PCOS. In a Hospital set up ultrasonography is the most widely used screening modality for detection of fatty infiltration of liver and for PCOS, due to its low cost, non invasiveness, easy availability, mobility and reasonable level of sensitivity.* ***Aim and Objectives:*** *The main aim of the present study was to identify the prevalence of fatty liver as seen on ultrasonography in patients with PCOS, corroborating with laboratory and physical parameters to determine the efficacy of Ultra sound as a screening modality, as fatty liver is precursor for chronic disease like cirrhosis and hepatocellular carcinoma in some patients and PCOS is associated with increased risk of type-2-diabetes and cardiovascular diseases.* ***Materials and Methods:*** *It is a Prospective study using existing records, conducted at the Department of RadioDiagnosis and imaging of the GIMSR (GITAM Institute of Medical Sciences and Research), Visakhapatnam. It is a tertiary level hospital and the study was performed on total 100 numbers of samples. The patients referred to the Radiology department with complaints of amenorrhea or oligomenorrhea, belonging to the adolescent, young and adult population for PCOS diagnosis. The abdomino pelvic scan was performed on PHILIPS HD15 Ultrasound machine, using a 3 MHz curvilinear probe and transvaginal probe in married obese females, where transabdominal visualization was suboptimal, after verbal consent from the patient. No patients had a history of alcohol consumption.The presence of fatty liver in each patient was evaluated by an expert radiologist using abdominal ultrasonography (USG). The degree of fatty liver on abdominal USG was stratified as mild, moderate, or severe. The diagnosis was also based on the measurement of SGOT, SGPT levels, Lipid profile and liver enzyme aminotransferase levels. Statistical analysis: Mean, median, and standard deviations were calculated for continuous variables. Pearson's Chi-square test was used to assess differences in the groups for categorical data. The P < 0.05 was considered statistically significant.* ***Results:*** *The women with PCOS had significantly higher visceral fat indicated by higher waist-hip ratio, higer alanine aminotransferase (ALT) or serum glutamic pyruvic transaminase (SGPT), aspartate aminotransferase (AST) or serum glutamic oxaloacetic transaminase (SGOT), alkaline phosphatase (ALP) levels and higher lipid profile values. Table-1 showed the clinical and biochemical characteristics of PCOS patients with or without fattyliver. It was found that BMI and waist-hip ratio was significantly (P<0.001) higher in PCOS patients with hepatic liver than patients without fatty liver. The lipid profile values of total cholesterol, triglycerides, VLDL, LDL were also high where as HDL was lower comparitively than patients without fatty liver. The serum enzymatic levels of SGOT, SGPT and ALP were also observed to be in higher concentrations in patients with fattyliver than patients without hepato steatosis.* ***Conclusion:*** *The non invasive and widely available screening methods can be used in large patient populations with NAFLD and PCOS for early detection and intervention to prevent the progression and reduce or prevent the morbidity and mortality.*

Date of Submission: 20-09-2018 Date of acceptance: 08-10-2018

I. Introduction

Polycystic ovarian syndrome (PCOS) is a complex endocrinologic disorder of abnormal estrogen and androgen production resulting in chronic anovulation. The serum LH (Luteinizing harmone) level is elevated and the FSH (Follicle stimulating harmone) level is depressed; an elevated LH/FSH ratio is a characteristic finding [1]. PCOS is a common cause of infertility and a higher-than-usual rate of early pregnancy loss. Clinical manifestations of PCOS range from mild signs of hyperandrogenism in thin, normally menstruating women to the classic Stein-Leventhal syndrome (oligomenorrhea or amenorrhoea, hirsutism, and obesity) [2]. The typical sonographic findings of polycystic ovaries are bilaterally enlarged ovaries containing multiple small follicles and increased stromal echogenicity. Transvaginal sonography is more sensitive in detecting the small follicles. Using transvaginal sonography, increased stromal echogenicity is believed to be the most sensitive and specific sign of polycystic ovaries [3]. In a small number of patients, the sonographic findings may be unilateral. Diagnosis of polycystic ovaries should have either 12 or more follicles measuring 2 to 9 mm in diameter or increased ovarian volume greater than 10cc. These criteria are not considered to be valid if the patient is taking oral contraceptive pills or there is a dominant follicle greater than 10 mm because ovulation does not occur, the follicles will persist on serial studies [4, 5]. Long-term follow-up is recommended in patients with PCOS because the unopposed high estrogen levels appear to be associated with an increased risk of endometrial and breast carcinoma. The criteria for the diagnosis of PCOS are based on NIH/NICHD and Rotterdam criteria [6, 7, 8].

Waist-hip ratio (WHR) is used as measure of body fat distribution or more specifically abdominal obesity. Generally WHR is above 0.85 in females and above 0.90 for males or a BMI > 30.0. According to National Institute of Health (NIH) WHR greater than 1.0 is indicative of higher risk of developing heart disease. It is a good indicator of visceral fat, localized in the abdominal area, and is closely linked to chronic diseases such as coronary heart disease, hypertension, and diabetes even in people with normal BMI [9]. WHR is a better gauge of obesity in older people whose WHR $\leq$ 0.80 are at low risk and WHR is in between 0.81 to 0.85 are at moderate risk and WHR is greater than 0.85 are at high risk.

Ultrasonograph is a widely accessible technique for diagnosis of PCOS as well as fatty liver. Ultrasound for detection of fatty liver is qualitative, in terms of diagnosing fatty infiltration as increase in hepatic parenchymal echogenicity as well as fairly quantitative by grading the fat infiltration as mild, moderate and severe [10, 11]. Minimal diffuse increase in hepatic echogenicity with normal visualization of diaphragm and intrahepatic vessel borders is seen in mild fatty liver cases. Moderate diffuse increase in hepatic echogenicity with slightly impaired visualization of intrahepatic vessels and diaphragm is seen in moderate fatty liver cases. In severe fatty liver patients, marked increase in echogenicity with poor penetration of posterior segment of right lobe of liver and poor or no visualization of hepatic vessels and diaphragm is present.

Fatty liver is an acquired, reversible disorder of metabolism, resulting in an accumulation of triglycerides within the hepatocytes, due to stimulation of lipolysis. Fatty liver is recognized as a significant component of the metabolic syndrome, which has recently increased in significance. The most common cause likely is obesity other causes include excessive alcohol intake, poorly controlled hyperlipidemia, diabetes, excess exogenous or endogenous corticosteroids, pregnancy, total parenteral hyper alimentation, severe hepatitis, glycogen storage disease, jejunoileal bypass procedures for obesity, cystic fibrosis, congenital generalized lipodystrophy, several chemotherapeutic agents, including methotrexate, and toxins such as carbon tetrachloride and yellow phosphorus. It is now recognized that fatty infiltration of the liver is the precursor for significant chronic disease and hepatocellular carcinoma in some patients.

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease comprising a spectrum of liver damage from fatty liver infiltration to end-stage liver disease, in patients without significant alcohol consumption. Increased prevalence of NAFLD has been reported in patients with polycystic ovary syndrome (PCOS), one of the most common endocrinopathies in premenopausal women, which has been redefined as a reproductive and metabolic disorder after the recognition of the important role of insulin resistance in the pathophysiology of the syndrome. PCOS patients, particularly obese patients with features of the metabolic syndrome, should be submitted to screening for NAFLD comprising assessment of serum aminotransferase levels and of hepatic steatosis by abdominal ultrasound. Long-term follow up studies are needed to clarify clinical implications, appropriate diagnostic evaluation and optimal treatment for PCOS patients with NAFLD. Lifestyle modifications including diet, weight loss and exercise are the most appropriate initial therapeutic interventions for PCOS patients with NAFLD.

The main aim of the present study was to identify the prevalence of fatty liver as seen on ultrasonography in patients with PCOS, corroborating with laboratory and physical parameters to determine the efficacy of Ultra sound as a screening modality, as fatty liver is precursor for chronic disease like cirrhosis and hepatocellular carcinoma in some patients and PCOS is associated with increased risk of type-2-diabetes and cardiovascular diseases [12].

II. Materials and Methods

It is a prospective study using existing records, conducted at the Department of RadioDiagnosis and imaging, GIMSR (GITAM Institute of Medical Science and Research), Visakhapatnam. It is a tertiary level hospital and the study was performed on total 100 numbers of samples. The study was conducted from July 2017 to July 2018, following approval of Institutional Ethics Committee. A purposive and convenient sampling technique was used for the data collection from the study population, who satisfied inclusion criteria to participate in the study.

The patients referred to the Radiology department with complaints of amenorrhea or oligomenorrhea, belonging to the adolescent, young and adult population for PCOS diagnosis. The abdomino pelvic scan was performed on PHILIPS HD15 Ultrasound machine, using a 3 MHz curvilinear probe and transvaginal probe in married obese females, where transabdominal visualization was suboptimal, after verbal consent from the patient. The height was measured in meters and weight in kilograms to calculate the BMI in Kg/m^2, to classify patients into normal, underweight, overweight and obese categories according to World health organization. The WHR or Abdominal circumference (AC) was measured to the nearest millimeter using a tapeline at each child's maximum waist girth in a standing position. Generally WHR is above 0.85 in females. Among the screened individuals, those who had normal menustral cycles were clinically normal including BMI and no PCO morphology on USG were considered as non PCOS group. Individuals with underlying organic causes of liver disease or drug history within the prior 3 months were excluded from the study. No patients had a history of alcohol consumption.The presence of fatty liver in each patient was evaluated by an expert radiologist using abdominal ultrasonography (USG). The degree of fatty liver on abdominal USG was stratified as mild, moderate, or severe. The diagnosis was also based on the measurement of SGOT, SGPT levels, Lipid profile and liver enzyme aminotransferase levels.

Statistical analysis: Data were analyzed using SPSS software version 22.0. Frequencies and percentages were used for categorical data. Mean, median, and standard deviations were calculated for continuous variables. Pearson's Chi-square test was used to assess differences in the groups for categorical data. The $P < 0.05$ was considered statistically significant.

III. Results

A group of 100 patients with ultrasound picture of polycystic ovary were checked for fatty infiltration of liver who were referred to the department of Radiodiagnosis, from various other departments of our hospital with complains of oligomenorrhoea. The physical parameters like height and weight were measured to calculate BMI, waist and hip measurements were taken to calculate WHR (Figure-1). The women with PCOS had significantly higher visceral fat indicated by higher waist-hip ratio, higer alanine aminotransferase (ALT) or serum glutamic pyruvic transaminase (SGPT), aspartate aminotransferase (AST) or serum glutamic oxaloacetic transaminase (SGOT), alkaline phosphatase (ALP) levels and higher lipid profile values. Table-1 showed the clinical and biochemical characteristics of PCOS patients with or without fattyliver. It was found that BMI and waist-hip ratio was significantly ($P<0.001$) higher in PCOS patients with hepatic liver than patients without fatty liver. The lipid profile values of total cholesterol, triglycerides, VLDL, LDL were also high where as HDL was lower comparitively than patients without fatty liver (Figure-2). The serum enzymatic levels of SGOT, SGPT and ALP were also observed to be in higher concentrations in patients with fattyliver than patients without hepato steatosis (Figure-3).

Table 1: Clinical and Biochemical characteristics of polycystic ovary syndrome patients with or without fatty liver.

Variables	PCOS with hepatic liver	PCOS	t-value	P-value
Age	30.15 ± 3.29	30.43 ± 3.99	0.39	0.70
BMI	27.85 ± 3.14	23.76 ± 4.34	5.45	<0.001*
Waist - Hip ratio	0.81 ± 0.07	0.71 ± 0.05	7.60	<0.001*
Total cholesterol	184.74 ± 43.96	126.63 ± 15.43	8.53	<0.001*
HDL	39.78 ± 4.84	55.7 ± 10.31	9.61	<0.001*
LDL	112.09 ± 18.27	85.59 ± 17.6	7.35	<0.001*
VLDL	27.94 ± 8.28	16.33 ± 6.51	7.70	<0.001*
TG	131.65 ± 31.4	80.91 ± 14.8	10.04	<0.001*
SGOT	29.3 ± 7.1	19.22 ± 4.6	8.26	<0.001*
SGPT	34.28 ± 9.36	24.09 ± 7.5	5.94	<0.001*
ALP	125.35 ± 32.28	80.5 ± 27.85	7.37	<0.001*

Figure 1: Distribution of PCOS cases based on Age, Body mass index and Waist-hip ratio

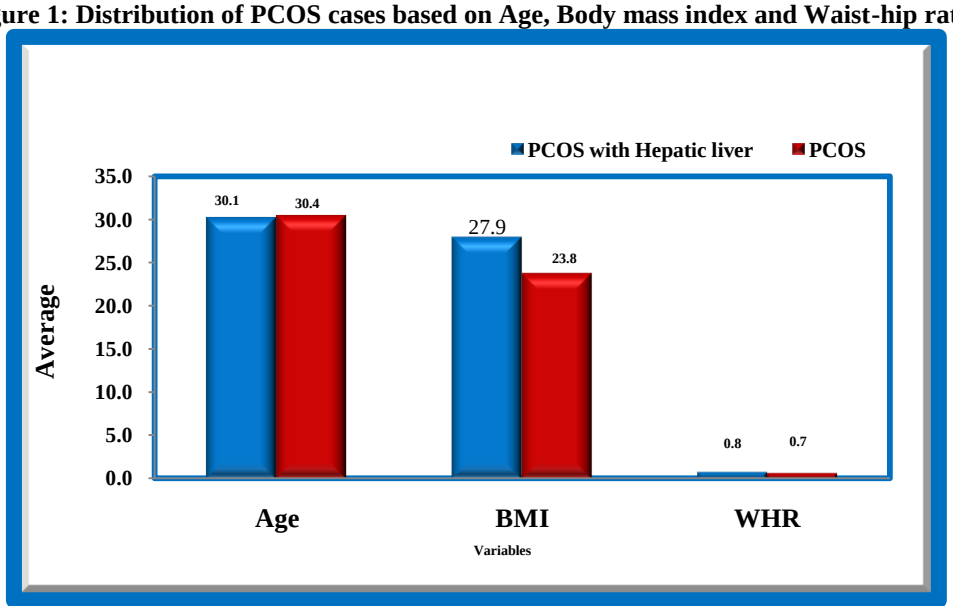


Figure 2: Distribution of PCOS cases based on Lipid profile

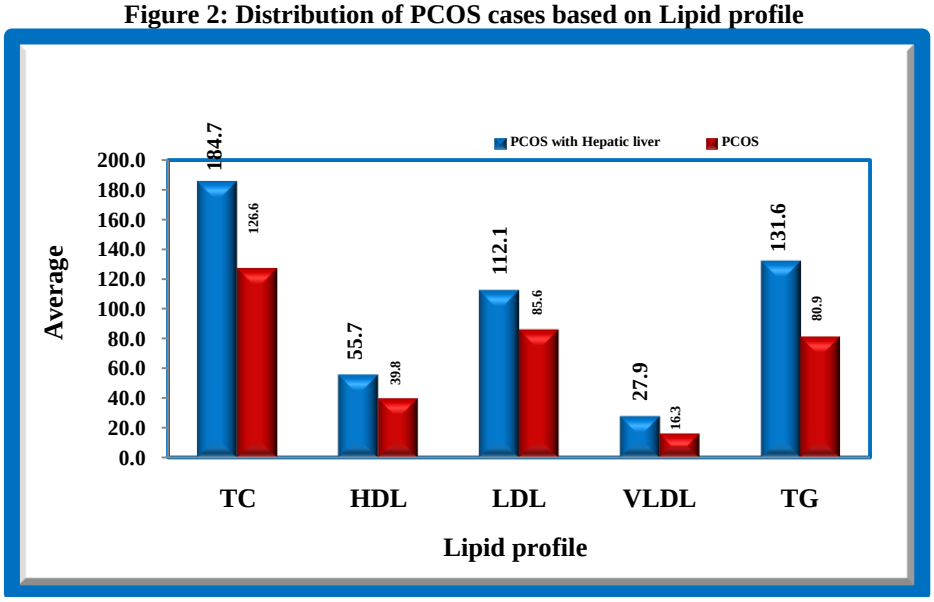
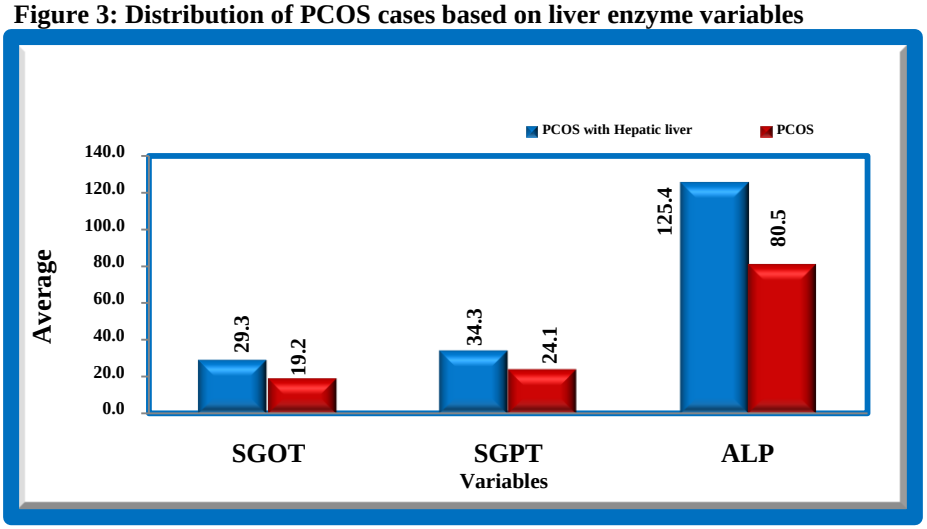


Figure 3: Distribution of PCOS cases based on liver enzyme variables



IV. Discussion

Women with PCOS had a higher prevalence of fatty infiltration of liver compared to women without PCOS. In a Hospital set up ultrasonography is the most widely used screening modality for detection of fatty infiltration of liver and for PCOS, due to its low cost, non invasiveness, easy availability, mobility, reasonable level of sensitivity as compared to more expensive imaging modalities like CT, or MRI, which have issues like radiation, exposure, contrast reactions in additions to their high cost. Fatty liver or hepatic steatosis is the accumulation of fat within the liver parenchyma due to various causes like obesity, alcohol and hyperlipidemia. NAFLD is closely related to obesity, dyslipidemia and hypertension and is regarded as a hepatic manifestation of metabolic syndrome [9, 10]. Hepatic steatosis on USG appears as a diffuse increase in hepatic echogenicity or brightness, as compared to echogenicity of the renal parenchyma.

It has been found that NAFLD is more prevalent in PCOS patients, suggesting a strong correlation between the PCOS and NAFLD. PCOS patients are at greater risk metabolic abnormalities such as glucose intolerance, dyslipidemia and metabolic syndrome. There is a strong relation between NAFLD and PCOS exists as evidenced by their higher (as high as 40- 55%) prevalence in females with PCOS than in females without PCOS. Converse is also true as proved by a study by Brzozowska *et al.* (2009) [13] reporting that PCOS was more prevalent in females with NAFLD (histologically diagnosed) than those with normal liver, further strengthening the PCOS and NAFLD interrelationship. PCOS and NAFLD combination also has a strong association with metabolic syndrome (MS), insulin resistance and obesity, exposing them to greater risk of cardiovascular diseases and spectrum of NAFLD.

Our present study corroborates the presence of both PCOS and NAFLD, particularly in obese (high BMI) females in reproductive age group, with central adiposity, as indicated by waist hip ratio (WHR), by noting elevated liver transaminase levels and presence of fatty liver on USG, suggesting that NAFLD along with dyslipidemia is relatively more common in obese females, probable etiological factors could be insulin resistance and higher levels of testosterone. The subgroup analysis between PCOS patients with fatty liver and without fatty liver showed that age, obesity, central adiposity (increased visceral fat), and dyslipidemia were the factors associated with fatty liver, corroborating the findings of other studies. Gutierrez-Gorbe *et al.* (2010) [14] in their study found higher prevalence of NAFLD in post menopausal women with PCOS than in premenopausal women, attributed to increased androgen levels and reduced estrogen levels that might have had a protective effect against NAFDL in reproductive age group. Baranova *et al.* (2011) [15] observed that insulin resistance, a marker of MS is also observed in 50-80% of patients having PCOS with NAFLD. Therefore NAFLD can be considered as hepatic manifestation of metabolic syndrome, predicting emergence of metabolic complications and increased risk of cardiovascular diseases.

Similarly, PCOS can also be appropriately considered as ovarian manifestation of metabolic syndromes. Since both these conditions if coexisting can respond to similar treatment strategies, there is need to screen patients with either of the conditions i.e. PCOS or NAFLD to prevent liver and cardiovascular system related morbidities and mortalities. There causes are treatable; therefore screening for these conditions should be included in the clinical protocol. Since both PCOS and NAFLD are assuming epidemic proportions, the population at risk to be screened also has increased manifold. Hence there is a need for recognizing widely and easily available non invasive, cost effective screening techniques to identify patients at risk for progression of liver and cardiovascular diseases. Our study was limited by small sample size and mostly obese patients. Larger studies with broader sample base are needed for most appropriate screening method in larger population. Our study used ultrasonography and lipid profile as a screening tool, instead of liver biopsy. Even though liver biopsy is regarded as the Gold standard for assessment of NAFLD, its invasive nature and not so wide availability limits its use as a screening procedure or for follow up in large populations at risk. Hence USG meets the needs as a non invasive and reasonably accurate screening and follow up tool, due to its acceptable level of sensitivity in detection of fatty liver (sensitivity 80% in the presence of >30% of fatty infiltration), wide availability, short examination time, easy to perform and cost effectiveness. Its diagnostic efficacy is enhanced when combined with elevation of liver enzyme levels. But liver biopsy may still be required to accurately grade severity of fat infiltration, inflammation and for confirmation of hepatic malignancy. The non invasive and widely available screening methods can be used in large patient populations with NAFLD and PCOS for early detection and intervention to prevent the progression and reduce or prevent the morbidity and mortality [16].

V. Conclusion

Ultrasonography allows for reliable and accurate detection of moderate to severe fatty liver, compared to histology. Because of its low cost safety and accessibility USG is likely the imaging technique of choice for screening of fatty liver in clinical and population setting. NAFLD is more prevalent in PCOS, which has been refined as a reproductive and metabolic disorder. Obesity and insulin resistance are the main factors related to NAFLD in PCOS. Limited data imply that advanced stage of liver disease is possibly more frequent in obese PCOS patients with NAFDL. PCOS patients, in particular obese patients with features of metabolic syndrome,

should be submitted to liver evaluation comprising assessment of aminotransferase levels and abdominal ultrasound. Life style modification including diet, weight loss and exercise are the most appropriate initial therapeutic interventions for PCOS patients with NAFLD. Long-term follow up studies would help to clarify clinical implications and guide appropriate diagnostic evaluation, follow-up protocol and optimal treatment for PCOS patients with NAFLD.

The authors declared “No conflict of interest”

References

[1]. Balen AH, Tan SL, Jacobs HS. Hypersecretion of luteinising hormone: a significant cause of infertility and miscarriage. Br J Obstet Gynaecol. 1993;100:1082-108.
[2]. Eden JA, Warren P. A review of 1019 consecutive cases of polycystic ovary syndrome demonstrated by ultrasound. Australas Radiol. 1999; 43:41-46.
[3]. Yeh HC, Futterweit W, Thornton JC. Polycystic ovarian disease: ultrasound features in 104 patients. Radiology. 1987; 163:111-116.
[4]. Hann LE, Hall DA, McArdle CR, Seibel M. Polycystic ovarian disease: sonographic spectrum. Radiology. 1984; 150:531-534.
[5]. Pache TD, Wladimiroff JW, Hop WC, Fauser BC. How to discriminate between normal and polycystic ovaries: transvaginal ultrasound study. Radiology 1992; 183:421-423.
[6]. Ardaens Y, Robert Y, Lemaitre L, et al. Polycystic ovarian disease: contribution of vaginal endosonography and reassessment of ultrasonic diagnosis. Fertil Steril. 1991; 55:1062-1068.
[7]. Battaglia C, Regnani G, Petraglia F, et al. Polycystic ovary syndrome: it is always bilateral Ultrasound Obstet Gynecol. 1999; 14:183- 187.
[8]. Balen AH, Laven JS, Tan SL, et al. Ultrasound assessment of the polycystic ovary: international consensus definitions. Hum Reprod Update. 2003; 9:505-514.
[9]. Jonard S, Robert Y, Dewailly D, et al. Revisiting the ovarian volume as a diagnostic criterion for polycystic ovaries.Hum Reprod. 2005;20 :2893-2898.
[10]. Zakim D. Metabolism of glucose and fatty acids by the liver. In: Zakim D, Boyer TD, editors. Hepatology: A textbook of liver disease. Philadelphia: Saunders; 1982: 76-109.
[11]. Wilson SR, Rosen IE, Chin-Sang HB, Arenson AM. Fatty infiltration of the liver–an imaging challenge. J Can Assoc Radiol. 1982; 33: 227-232.
[12]. Quinn SF, Gosink BB. Characteristic sonographic signs of hepatic fatty infiltration. AJR Am J Roentgenol. 1985; 145:753-755.
[13]. Brzozowska MM, Ostapowicz G, Weltman MD. An association between non-alcoholic fatty liver disease and polycystic ovarian syndrome. J Gastroenterol Hepatol. 2009; 24:243–24.
[14]. Gutierrez-Grobe Y, Ponciano-Rodríguez G, Ramos MH, Uribe M, Méndez-Sánchez N. Prevalence of non alcoholic fatty liver disease in premenopausal, postmenopausal and polycystic ovary syndrome women. The role of estrogens. Ann Hepatol. 2010; 9:402–9.
[15]. Baranova A, Tran TP, Birerdinc A, Younossi ZM. Systematic review: Association of polycystic ovary syndrome with metabolic syndrome and non-alcoholic fatty liver disease. Aliment Pharmacol Ther. 2011; 33:801–14.
[16]. Wieckowska A, Feldstein AE. Diagnosis of nonalcoholic fatty liver disease: Invasive versus noninvasive. Semin Liver Dis. 2008; 28:386–95.

Dr. Sonica sharma , " A Hospital Based Study Correlating The Prevalence Of Fatty Liver Disease In Polycystic Ovary Syndrome Using Ultra Sound As Screening Modality "IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 9, 2018, pp 38-43.