How to Cite:
Dhari, Z. A., Sultan, A. H., Shubber, L. A., & Al_Ameri, H. D. (2022). Association between polycystic ovary and fibrocystic breast by ultrasound. *International Journal of Health Sciences*, *6*(S2), 11420–11428. https://doi.org/10.53730/ijhs.v6nS2.7435

Association between polycystic ovary and fibrocystic breast by ultrasound

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***Abstract*---**Background: Polycystic ovary syndrome is one of the most gynecologic, endocrine cases affect approximately 5-15%of women during reproductive age. Polycystic ovary syndrome (PCOS) is a multifactorial and polygenic pathology that manifests itself with a wide spectrum of signs and symptoms. The study aims to find out the association between PCOS and fibrocystic disease of the breast according to finding detected by ultrasound. Method: Across sectional study with 140 patients were enrolled in this study collected from the gynecologic and infertility clinic in Al-Imameen Al-Kadhymian Medical City, Iraq, Baghdad during the period from march 2021 to January 2022.Information was taken from patients through interview, inclusion criteria includes female gender, age between 20-50 years old not using oral contraceptive drug, pelvic and breast ultrasound report. SPSS version 24 was used to examine the frequency association between variable. Result: There were 140 female cases of PCOs, fifty-five (39%) were fibrocystic disease of breast. The prevalence of fibrocystic disease of breast in patient with PCOs in current study were fifty-five (39%).there were significant association between fibrocystic disease of breast with age, education level, BMI, age of monarch, hirsutism, history of infertility and history of pain with p value ≤ 0.05.

***Keywords*---**fibrocystic disease, breast, PCOS, patient, ultrasound**.**

Introduction

Polycystic ovary syndrome is one of the most gynecologic, endocrine cases affect approximately 5-15%of women during reproductive age [1]. Polycystic ovary syndrome (PCOS) is a multifactorial and polygenic pathology that manifests itself with a wide spectrum of signs and symptoms [2]. The main factors involved in PCOs patient was increase androgen levels and insulin resistance, but genetic, developmental and environmental factors also play a role in its etiology [3]. Other factor is defect in the hypothalamus-pituitary-ovarian axis. The enhanced-gonadotropin releasing-hormone (GnRH) pulse frequency results from the disruption of negative feedback of sex steroids in the hypothalamus. This disruption subsequently leads to increases in both luteotropin (LH) amplitude and pulse frequency and an increased LH to folliculotropin (FSH) ratio. Augmentation of the GnRH axis may also stimulate via GABAergic neurons, which paradoxically display positive not negative effects under androgen exposure [4, 5]. Insulin resistance can be found both in lean and overweight and obese women, is responsible for some PCOS phenotypes and increases the risk of infertility [6]. Adams criteria had become a standard in diagnosing PCOS: the finding of 10 or more peripherally located follicles, between 2 and 8mm in diameter, together with an increased amount of stroma and an overall ovarian volume greater or equal to 9mm3 [7-10]. PCOS was diagnosed when one or more of the following signs and symptoms: menstrual pattern disturbances (amenorrhea, oligomenorrhea), hirsutism, overweight or obesity, infertility, associated to at least one biochemical endocrine disturbance [11]. Polycystic ovary (PCO) or polycystic-appearing ovaries (PAO) is an alteration of ovarian morphology, commonly detected by ultrasound pelvic scan, that occurs in a variety of endocrinepathies [11]. Fibrocystic disease of the breast is the most common benign breast abnormality, found in up to 60-70% of women. It is thought to be caused by an exaggerated response of the breast tissue to hormones. From a clinical point of view, the symptoms range from mastalgia (cyclic or persistent) pain comes in many forms, including sharp, burning, or a feeling of tightness in the breast tissue [12, 13]. To mass (cysts or nodules) appear mainly in the upper outer quadrants of the breast. Cyst is the most common clinical symptom and a common source of concern in the patient [14] it is often undergoing change in size during the menstrual cycle, upon examination it appears as hard or floppy lump and sometimes painful [15] although most of lesions are benign, the study is essential to confirm their benign nature [16]. Symptom may not require specific treatment, just painkillers, and information intended to reassure the patient in case of mastalgia [14]. On the other hand, presence of mass which MAY BE complex cysts or atypical in appearance, need further evaluation by FNA or biopsy to establish a definitive pathological diagnosis [17]. Proliferative and non-proliferative are types of fibrocystic disease in which Proliferative type is associated with increased risk of developing breast cancer reaching 50 % under certain histopathological and clinical circumstances [18]. While Non-proliferative lesions are seen in 70% of all biopsies taken in breast cancer screening cases. Estrogens increase the proliferation, differentiation and mitosis of breast cells. Studies show that progesterone can have various proliferative and inhibitory effects on epithelial breast cells [19]. Hyperestrogenism and anovulation are involved in the etiology of benign breast disease; the growth of mammary gland is influenced by a critical imbalance between estrogens and progesterone action [20, 21]. The study aims to find out the association between

PCOS and fibrocystic disease of the breast according to finding detected by ultrasound.

Method

Cross sectional study carried out at gynecologic and infertility clinic in AL-Immamain AL-Kadhymain hospital from March 2021 to June 2022. Total cases were 140 patients with polycystic ovary syndrome from age 20 -50 year, patient use oral contraceptive were excluded from study. The data collected after taken agreement from patient to enrolled in this cross section study. PCOs diagnosed by ultrasound done by professional radiology with following diagnostic criteria: cardinal features of hyperandrogenism: hirsutism (elevated serum total testosterone) and clinical evidence of ovarian dysfunction: oligoamenorrhea, infertility from anovulation and abnormal ultrasound finding (PCO appearance at ultrasound) [14]. The following standard criteria were used for the ultrasound diagnosis of PCO/PAO and PCOS: each woman had to have evidence on both ovaries of 10 or more peripherally oriented follicles (2–8mm in diameter) on a sonographic plane, increased ovarian volume and increased stromal density. Fibrocystic breast disease diagnosed by breast ultrasound done by professional radiology with diagnostic criteria Sonography of breast disease examined the cyst's shape, diameter and margins, the presence of lateral shades, posterior reinforcement, length/thickness ratio and atypical vascularization by color Doppler flow. All cases were examined using GE ultrasound machine with 3.5-MHz and 10-MHz probes for the pelvic and breast scans, respectively. The frequency table, association table were done by using SPSS version 24.

Results

The study sample were 140 female cases of PCOS, from these fifty-five (39%) were fibrocystic disease of breast. The demographic characteristic of study sample was fifty-seven (40.7%) at age 20-29 years old while lower percentage 28.6% with age 30-39 years old & thirty-five percent with secondary education while twelve's percent were illiterate. The highest percentage of females 69 (49.3%) presented with BMI (25-29.9), while the lowest percentage of female 9(6.4%) presented with BMI (35-40). There were sixty (42.9%) female's multipara between 1-3 and fifty percent of sample were with chronic diseases & fifty percent with drug uses history. Nearly fifty-nine percentage of female with menarche less than 13 years old & eighty-five (60.7%) with history of less than seven-day menstrual cycle & twenty-four (17.1%) were with regular cycle. Highest frequency of patients 107 (76.4%) presented without history of infertility & highest frequency of female 86 (61.4%) without of hirsutisms. Nearly twenty-one percent of female presented with pain, thirteen 9.3% presented with solitary cyst, forty-one (29.3%) presented with prominent fibro glandular tissue& forty-two (30%) presented with multiple cysts, as shown in table 1:

Table 1: distribution of variables

Variables		No.	percentage
Age	*20-29*	57	40.7
	30-39	40	28.6

	40-50	43	30.7
Education level	*illiterate*	17	12.1
	primary	39	27.9
	secondary	49	35
	higher	35	25
BMI	*Less than 18.9*	9	6.4
	18.9-24.9	23	16.4
	25-29.9	69	49.3
	30-34.9	30	21.4
	35-40	9	6.4
GPA	*0*	49	35
	1-3	60	42.9
	More than 3	31	22.1
Chronic disease	*yes*	67	47.9
	no	70	50
Drug history	*yes*	70	50
	no	70	50
History of menses regularity	*yes*	24	17.1
	no	116	82.9
Date of bleeding	*Less than 7 days*	85	60.7
	7 days and more	55	39.3
Age at menarche	*Less than 13 years*	82	58.6
	13 and more	58	41.4
History of hirsutism	*Yes*	54	38.6
	No	86	61.4
History of infertility	*No*	107	76.4
	primary	22	15.7
	secondary	11	7.9
History of pain	*Yes*	29	20.7
	No	111	79.3
Solitary cyst	*Yes*	13	9.3
	No	127	90.7
Fibroglandular	*Yes*	41	29.3
	No	99	70.7
Multiple cyst	*yes*	42	30
	No	98	70

There were significant association between age and fibrocystic disease p=0.00 with highest frequency 26 (65%) at age (30-39) years. In higher education group there were 21 (60%) were fibrocystic disease p=0.0001. There were significant association between age of menarche and fibrocystic disease of breast p=0.002, as female with menarche less than 13 were more predispose to fibrocystic disease than female with menarche more than 13 years old. Females with history of hirsutism and fibrocystic disease were 33(61.1) with significant association p=0.0001. There were significant association between history of infertility and fibrocystic disease of breast p=0.006 with higher frequency 14 (63.6%) with primary infertility. One hindered percent of female with history of pain were

fibrocystic disease with p=0.0001. There were significant association between BMI and fibrocystic disease with highest percentage 56.5% at BMI (18.9-24.9) & lowest (22.2%) at BMI (35-40), p=0.04. There were no significant association between gravida, chronic disease, regularity of menses, history of drug uses & date of bleeding with fibrocystic disease of breast p>0.05, as shown in table 2:

Table 2: association between variables and fibrocystic

Variables		fibrocystic		Not fibrocystic		P value
		No.	%	No .	%	
Age	20-29	10	17.5	47	82.5	0.001
	30-39	26	65	14	35	
	40-50	19	44.2	24	55.8	
GPA	0	17	34.7	32	65.3	0.275
	1-3	22	36.3	38	63.3	
	>3	16	51.6	15	48.4	
Chronic disease	yes	26	38.8	41	61.2	0.911
	No	29	39.3	44	60.3	
education	illiterate	0	0	17	100	0.001
	primary	17	43.6	22	56.4	
	secondary	17	34.7	32	65.3	
	higher	21	60	14	40	
Regular mense	yes	10	41.7	14	58.3	0.793
	No	45	38.8	71	61.2	
menarch	less than 13	41	50	41	50	0.002
	13 and more	14	24.1	44	75.9	
hirsutism	yes	33	61.1	21	38.9	0.001
	no	22	25.6	64	74.4	
infertility	primary	14	63.6	8	36.4	0.006
	no	40	37.4	67	62.6	
	secondary	1	9.1	10	90.9	
pain	yes	29	100	0	0	0.001
	no	26	23.4	85	76.6	
BMI	< 18.9	5	55.6	4	44.4	0.048
	18.9-24.9	13	56.5	10	43.5	
	25-29.9	20	29	49	71	
	30-34.9	15	50	15	50	
	35-40	2	22.2	7	77.8	
USE DRUG	yes	25	35.7	45	64.3	0.387
	no	30	42.9	40	57.1	
Day of bleeding	< 7	30	35.5	55	764	0.229
	≤ 7	25	45.5	30	54.5	

P-value ≤0.05 (significant).

Discussion

The results of our study showed that there was a statistically significant association between fibrocystic breast changes and PCOS as well as people with PCOS had a higher chance of producing fibrocystic breast changes than people without this syndrome. The positive relationship between PCOS and fibrocystic breast changes can be attributed to several mechanisms. Because there is a distinct degree of hyperandrogenism in PCOS, this hyperandrogenism cause inhibitory effects on progesterone and consequently leads to increase mammary epithelial cell proliferation, breast growth, and fibrocystic breast formation [22, 23]. The next mechanism is the possibility of converting androgens to estrogen and the stimulatory effects of estrogen on the growth and division of the mammary epithelium [24] besides, the lack of ovulation in patients with PCOS can be considered as the next mechanism. The incidence of fibrocystic breast disease is 7% in the general population. Statistically significant association between a PCOS and fibrocystic breast disease has been shown in Gumus et al study [25]. Frequency of fibrocystic breast disease was 39% in patient with PCOs in this study, this figure is similar to that reported in Turkeya [25]. Lower figures were reported in USA (NSABP center) that is inconsistent to higher figure announced in Rome, Italy [26]. This difference might be explained by variation in methods of study, sampling and ethnic groups. Age was positively associated to fibrocystic disease in this current study (p value=0.001) in which 65% of patient aged between 30-39 years had fibrocystic disease, this finding is similar to that reported in New Mexico, USA [27]. slightly lower figures were noticed in Poland. This seems to be logic due to more hormonal disturbance was between 30-50 years old. Direct relation was noticed between parity status and frequency of fibrocystic breast disease increasing fibrocystic disease, but still it was not significant associated p value (0.28), this finding in inconsistent with that in Mexico, USA that showed marked cystic ductal dilation was less common in parous than in nulliparous women, this difference might be due to parity lead to changes in breast morphology, histology and biochemistry. Education had positivity significant association with fibrocystic breast disease in this study p value=0.001 this due to more follow up and good seeking for medical advice in higher education patient. No significant relationship was observed between regularity of menses, its duration and fibrocystic disease it was concordance with that of Lavecchia [28]. Direct correlation between menstrual disturbance and fibrocystic breast disease was stated in other literature [26]. Early menarche ≤13 years had direct significant association with fibrocystic breast disease (ie: those with early menarche have more change to fibrocystic disease) It is in agreement with that of American study [29, 30]. This might be due to demonstration of early ovulation after early menarche, so more hormonal effect on breast. It was found that hirsutism was significant associated with fibrocystic breast disease p value=0.001. This figure is higher than that noticed in other Turkish studies [25]. PCOs patients with hyperandrogenemia (hirsutism) phenotype have more chance to develop fibrocystic breast disease due to hormonal imbalance [31]. It was in agreement with other literature's patient Ozkaya [32]. Mastalgia (ie pain in single or both breast) was directly significant association with fibrocystic breast p value=0.001, similar result was shown in other studies carried out in Nigeria, it seems to be logic because fibrocystic breast changes were the most common cause of breast pain due to hormonal imbalance that affect breast tissue by

increasing in milk producing glands, an enlarged of cells and scarring of breast tissue [33]. BMI was inversely related to fibrocystic breast disease, this finding is consistent with that of Italian study but it was in agreement with other studies in America [34]. That showed an increasing in risk of fibrocystic disease occur in fatty women due to conversion of estradiol to androgen that lead to hormonal imbalance. The study carried out in University of Alabama Medical Center, Birmingham, Alabama documents the relation between estradiol and androgen [35].

Conclusion

High frequency (39%) of fibrocystic disease from patient with polycystic ovary disease. There were significant association between fibrocystic breast and age, BMI, infertility, hirsutism, education, age at menarche.

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