DYSLIPIDEMIA AND BENIGN BREAST DISEASES

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ABSTRACT

Background: Benign breast disorders are the most common abnormalities found in women as far as breast disease is concerned. The study's goal was to see if there is a link between serum dyslipidemia and benign breast diseases in women.

Subjects and Methods: This is a case-control study, that involved 70 patients with benign breast diseases (cyclical mastalgia, fibrocystic breast disease and fibroadenoma) and 70 control healthy women and all of them had been selected randomly, aged (20-45 years) in a period between 1st September. 2021- 30th June. 2022. It is hospital-based study, The patients' group was carried out at the breast clinic at Azadi teaching hospital, while healthy participants in control group had been recruited in this study from different places in Duhok city such as governmental institutions, camps and universities with matching ages.

Results: The mean age of patients and control groups was 33.5±7.6 and 33.1±6.5 respectively. Fibrocystic breast disease constitutes 40 % of patients with benign breast diseases, while 38 % of them had cyclical mastalgia and only 21% had fibroadenoma. Seventy-Eight percent of patients had a normal lipid profiles and it is also normal in 80 % of a control group (P value less than <0.8). There was a significant difference in total cholesterol and VLDL between patients and control groups (P value less than <0.004 and 0.0005 consequently). Regarding the relationship of a lipid profile to the different etiologies of benign breast diseases, all parameters were not significant between different groups except for LDL and VLDL, as it was significant when we compare fibroadenoma to fibrocystic breast diseases with the P-value of 0.0001 and 0.0002 consequently. Also, when we compare fibroadenoma and cyclical mastalgia, there was a significant difference between LDL and VLDL with P values of 0.0001 and 0.01consequently.

Conclusion: There is a clear association between benign breast diseases and some parameters of lipid profile such as total cholesterol and VLDL. We do recommend measuring lipid profiles in these groups of patients especially those with fibroadenoma

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The breast is a dynamic organ that goes through cyclical changes[1]. One of the most complicated endocrine organs is the mammary gland. Developmental abnormalities, inflammatory lesions, epithelial and stromal proliferations all fall under the umbrella of benign breast disorders. The great majority of lesions found in the breast are harmless (benign) diseases[2]. It affects around 25% of all asymptomatic women. A fibroadenoma is a benign lump that is painless, solid, firm and rubbery. It is most common in women between the ages of 14 and 35, but it can affect anyone at any age. The exact cause of fibroadenoma is unknown, but experts believe that is caused by the female reproductive hormone (estrogen).

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The evaluation of fibroadenoma is by history and physical examination... Physically, it is characterized by some features such as non-painful or non-tender mobile mass, rubbery substance and regular borders. For further assessment diagnostic mammography is needed for imaging, which has some characteristic features such as a well-circumscribed discrete oval mass hypodense or isodense of breast glandular tissue. On ultrasound fibroadenoma appears as a well-circumscribed, spherical to oval, or macrolobulated mass with homogeneous hypoechogenicity. In some situations, may need FNAC/tru-cut biopsy[3].The majority of fibroadenoma do not require treatment, but if their size is excessive and they may squeeze other breast tissues, they should be excised. While Rapid growth, a size more than 3 cm, and a patient request are all indications for surgical intervention[4].

Fibrocystic disease (FBD) is caused by an overreaction of breast tissue to cyclical hormonal fluctuations, and it is more common in the third to fifth decades of life[5]. Experts estimate that roughly 90% of women have some form of fibrocystic alteration during their reproductive years [6]. The etiology of FBD and mastalgia is based on some apparent associations with endocrine and other variables or processes such as variation in the level of estrogen and progesterone[7]. Change in Prolactin levels has shown high levels in cases with FBD[8]. From a pathological point of view, FBD affects the terminal duct lobular unit (TDLU)[9] . Breast tenderness or mastalgia, as well as a lump, are common symptoms of FBD. Another distinguishing feature is diffuse nodularity with multiple, movable lumps (cystic dilatations) that are compressible[5]. The diagnosis of fibrocystic breast disease is usually based on clinical evidence. The essential clinical signs to diagnose the disease are cyclical breast discomfort, nodularity, lumpiness with fluctuating lump sizes, the multiplicity of lesions, and bilateral involvement. Ultrasonography (USG), mammography, and fine needle aspiration cytology (FNAC) may use to confirm the diagnosis in dubious cases [10-11].

Cyclical mastalgia, during their reproductive life almost two-thirds of women, experience cyclical mastalgia. Although it is usually harmless, worry of underlying breast cancer has become one of the most common reasons for seeking medical advice. This type of pain usually affects both breasts. The pain is normally the worst just before a menstrual cycle, and it subsides once the period is over [12]. Mastalgia is linked to premenstrual syndrome (PMS), fibrocystic breast illness, psychologic distress, and, in rare cases, breast cancer. A clinical assessment can reassure the vast majority of women. Evaluation is done by history and clinical examination. First-line treatments include mechanical breast support, a low-fat, high-carbohydrate diet, and topical non-steroidal anti-inflammatory medications. Bromocriptine, tamoxifen, and danazol are hormonal medications that have shown success in the treatment of mastalgia [13].

Recently many researches have been conducted on the relationship between benign breast illnesses and lipid profile, because lipid contents are an essential substance in the cell membrane for a variety of biological tasks, including cell development and division in both normal and malignant tissues. Several researchers have investigated the effectiveness of variations in tissue/blood cholesterol levels in the diagnosis and treatment of various disorders and even malignancies [1]. The

incidence of benign breast illnesses is higher in countries with a higher fat intake, particularly fat from animal sources such as meat and dairy products. Fat intake has been linked to an increased risk of proliferative benign breast disorders, particularly atypical hyperplasia, in numerous studies[14].

PATIENTS AND METHODS

This is a case-control study that involved (70) patients with benign breast diseases (cyclical mastalgia, fibrocystic breast disease, and fibroadenoma), and 70 of control healthy women and all of them are selected randomly. The consent was taken from all patients who attended the Breast Clinic in Azadi teaching hospital, while healthy participants in the control group were recruited in this study from different places in Duhok city such as governmental institutions, camps, and universities with matching ages (20-45 years) in a period between 1st September. 2021- 30th June. 2022. A 5 ml of blood aspirated from both control and patient groups has been sent for serum lipid profile after 12 hours of fasting. The lipid profile included total cholesterol, triglyceride, LDL, VLDL, HDL and Non-HDL. BMI was also recorded in both groups. The cases that were suffering from benign breast diseases will be diagnosed by clinical examination, imaging, and histopathology whenever it's clinically indicated. Both control and patients group should have no medical history of certain diseases which may alter serum lipid profile such as (Type 2diabetes, hepatocellular disease, chronic renal failure, hypothyroidism, familial hyperlipidemia, polycystic ovarian syndrome...etc.), with no history of smoking, alcohol intake and certain drugs such as (Diuretics, Glucocorticoids, Ciclosporins, Androgen,B blockers and Retinoids).

Dyslipidemia cut points based on American association of clinical endocrinologists (AACE) guidelines which include; total cholesterol is considered high when it's ≥ 200 mg/dl, HDL – cholesterol: is considered dyslipidemic when it's < 40 mg/dl in males and < 50 mg/dl in females. LDL -cholesterol: is considered high when it's ≥ 130mg/dl, Triglyceride: is considered high when it's ≥ 150 mg/dl. Lastly for Non-HDL which is total cholesterol minus HDL is considered high when it's >130 mg/dl for both men and women[15].

STATISTICAL ANALYSES

For statistical analyses regarding the categorical data, frequencies and percentages are used, whereas for continuous data, mean and standard deviation are being used. The Chi-square test is being used to examine the relationships between the variables, with p-values of less than or equal to 0.05 considered significant. The Statistical Package for Social Sciences is being used to examine the data (SPSS 25 IBM: USA).

RESULTS

Fibrocystic breast disease constitutes 40 % of patients with benign breast diseases, while 38 % of them had fibroadenoma and only 21% had cyclical mastalgia (table 1). Seventy-Eight percent of patients had normal lipid profiles and it's also normal in 80 % of the control group (P value less than <0.8). Almost one-third of participants in both groups were overweight and 13 % of them were obese (see table 1). The mean age of subjects in the patients' group and control groups was

33.5±7.6 and 33.1±6.5 respectively (table 2).

Table (1): Showing the general characteristics of the participants.

Parameters	Patients N (%)	Controls N (%)	*p*-value
Complain			
fibroadenoma	27(38.6%)	----------	
fibrocystic	28(40.0%)	----------	
disease	15(21.4%)	----------	
cyclical mastalgia			
Lipid Profile			
Normal	55(78.6%)	56(80.0%)	0.8
Isolated HyperTG	7(10.0%)	9(12.9%)	0.5
Isolated	5(7.1%)	4(5.7%)	0.7
hyperCho	3(4.3%)	1(1.4%)	0.3
Combined			
Dyslipidemia			
BMI			
<25	23(32.9%)	20(28.6%)	0.6
25-30	32(45.7%)	30(42.9%)	0.7
30-35	12(17.1%)	14(20.0%)	0.6
35-40	2(2.9%)	5(7.1%)	0.2
>40	----------	1(1.4%)	
Non-HDL			
Normal	50(71.4%)	53(75.7%)	0.5
Elevated	20(28.6%)	17(24.3%)	0.5

There was a significant difference in total cholesterol and VLDL between patients and control groups (P value less than <0.004 and 0.0005 consequently). However this was not the case for other parameters in lipid profile as there was no significant difference between both groups (table 2). Also, there was no significant difference regarding subclassification of lipid profile such as isolated hypercholetrolemia,isolated hypertriglcerdemia, and combined dyslipidemia (figure 1).

Table 2: Lipid between patients and controls

Parameters	Patients mean±SD	Controls mean±SD	*p*-value
Age	33.5±7.6	33.1±6.5	0.7
Total cholesterol	170.1±31.1	163.8±31.1	0.004
LDL	100.7±27.5	94.0±26.9	0.1
HDL	54.5±11.7	51.1±13.8	0.2
TG	94.3±41.9	106.8±59.6	0.1
VLDL	15.8±6.1	21.5±12.0	0.0005
Non-HDL	115.6±31.7	112.7±28.6	0.5

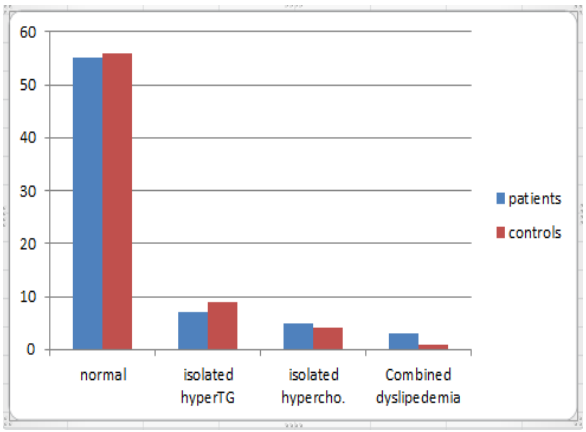

Figure1: Lipids profile normal and abnormal between patients and controls

Regarding the relationship of a lipid profile to the different etiologies of benign breast diseases, all parameters were insignificant between different groups (table 3), however when we compare fibroadenoma to fibrocystic breast disease there was a significant difference between both groups regarding LDL and VLDL with P value of 0.0001 and 0.0002 consequently (table 4). Also when we compare fibroadenoma and cyclical mastalgia, there was a significant

difference between LDL and VLDL with P values of 0.0001 and 0.01 consequently (table 5), meanwhile, when we compare fibrocystic and cyclical mastalgia there was no significant difference regarding all lipid parameters (table 6).

Table 3: The classification of lipid profile According to the etiology of benign breast disease (BBD)

Etiology of BBD	Normal Lipid Profile	Isolated Hyper TG	Isolated Hyperch	Combined Dyslipidemia	Total
Fibro-adenoma	24	1	2	0	27
Fibro-cystic disease	21	3	3	1	28
Cyclical mastalgia	10	3	0	2	15
Total	**55**	**7**	**5**	**3**	**70**

Table 4: Comparison between fibroadenoma and fibrocystic disease of the breast

	Fibro-adenoma N=27 mean±SD	Fibrocystic disease N=28 mean±SD	*p*-value
Total cholesterol	161.2±31.0	177.1±28.0	0.05
LDL	192.3±32.0	106.3±20.6	<0.0001
HDL	54.7±10.1	55.3±11.8	0.8
TG	80.4±34.6	101.3±36.9	0.03
VLDL	12.8±4.1	17.5±4.5	0.0002
Non-HDL	106.5±31.1	121.8±26.9	0.05

Table 5: Comparison between fibroadenoma and cyclical mastalgia

	Fibroadenoma N=27 mean±SD	Cyclical mastalgia N=15 mean±SD	*p*-value
Total cholesterol	161.2±31.0	173.1±35.0	0.2
LDL	192.3±32.0	105.8±27.9	<0.000
HDL	54.7±10.1	52.6±14.5	0.5
TG	80.4±34.6	105.9±56.5	0.07
VLDL	12.8±4.1	18.1±9.2	0.01
Non-HDL	106.5±31.1	120.5±38.8	0.2

Table 6: Comparison between fibrocystic breast disease and cyclical mastalgia

	Fibrocystic disease N=28 mean±SD	Cyclical mastalgia N=15 mean±SD	*p*-value
Total cholesterol	177.1±28.0	173.1±35.0	0.6
LDL	106.3±20.6	105.8±27.9	0.9
HDL	55.3±11.8	52.6±14.5	0.5
TG	101.3±36.9	105.9±56.5	0.7
VLDL	17.5±4.5	18.1±9.2	0.7
Non-HDL	121.8±26.9	120.5±38.8	0.8

DISCUSSION

This study is the first to look for an association between serum lipid profile and benign breast diseases in the Kurdistan region, Iraq. Our result shows a significant association between benign breast diseases and total cholesterol along with VLDL, while there was no association between benign breast diseases and triglycerides, HDL, and NON-HDL. In a study carried out from June 2018 to November 2018 in the department of general surgery at Medical College in Chennai, India, which included 75 cases aged between 16-35 years, had been chosen randomly who had benign breast disorders of one of three categories, fibroadenoma., fibrocystic breast disease and mastalgia. In that study revealed serum LDL cholesterol levels in

patients with benign breast disease did not arise, however, serum triglyceride levels were high in 21.3 % of women with benign breast disease had increased serum triglyceride levels suggestive of hyperlipidemia[16].

In another study, Gonenc et al.2006, found that total cholesterol and HDL levels increased in patients with benign breast disease. He also found no increase in serum LDL cholesterol[17]. Khanna et al.2002 also found that all patients with benign breast disease had higher serum triglyceride levels than the control group[18]. Another study has been done in the department of biology, faculty of Science, Kufa University, Najaf, Iraq. This study involved 80 women divided into two groups: the control group which included 40 healthy women and the benign group which contained 40 women with benign breast tumors aged between 20-60 years, The results clarify a significant $P \leq 0.05$ increase in the levels of cholesterol, high-density lipoprotein HDL and triglycerides TG in women in the benign group in compared with healthy women although the LDL level was similar [19] but our result shows no association between isolated hypertriglcerdemia and benign breast diseases.

When it comes to subtypes of benign breast diseases there was a strong association of fibroadenoma, LDL, and VLDL. Meanwhile, there was no association of other benign breast diseases such as fibrocystic and mastalgia to any parameters of lipid profile. There is similar study had been done in India from August 2012 to July 2014 they selected 50 cases randomly and they diagnosed with different benign breast lesions like fibroadenoma, breast abscess, mastalgia and fibrocystic disease with 30 control cases. That study revealed total cholesterol and HDL level and triglyceride were significantly higher than controls[20].

CONCLUSION

As far as there is an association between benign breast diseases and some parameters of lipid profile such as total cholesterol and VLDL, we do recommend measuring lipid profile in these groups of patients especially those with fibroadema, however more researches are needed in this field especially to look for the impact of lipid lowering therapy on the improvement of such conditions.

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CONFLICT OF INTEREST

The authors declared that they have no conflict of interest

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پوختە

نەخۆشییە بێهۆشکەرەکانی مەمک لە باوترین نەخۆشییەکانی ژنانن.

ئامانج: لەم توێژینەوەیە دۆزینەوەی پەیوەندییە لە نێوان بەرز ڕێژەی چەوری لە خوێندا و ڕوودانی هەندێک نەخۆشی بێهۆشکەر کە کاریگەری لەسەر مەمک هەیە.

بابەتەکان و شێوازەکان: ئەمە توێژینەوەیەکی کەیس-کۆنترۆڵە کە لەسەر ١٤٠ ژن ئەنجامدراوە، ٧٠ نەخۆش کە نەخۆشییە بێهۆشەکانی مەمکیان هەیە (ڕیشاڵی گەدە، نەخۆشی ڕیشاڵی کیسی مەمک و ئازاری وەرزی مەمک) بەراورد دەکرێن لەگەڵ گروپێک لە ٧٠ ژن کە لە ڕووی کلینیکیەوە تەندروستن و ئەم دوو گروپە هاوتا دەکرێن لە ڕووی تەمەنەوە، لە نێوان ٢٠ بۆ ٤٥ ساڵدایە، توێژینەوەکە لە ماوەی ١ی ئەیلوولی ٢٠٢١ تا ٣١ی حوزەیرانی ٢٠٢٢ ئەنجامدراوە، توێژینەوەکە لە نەخۆشخانەی فێرکاری ئازادی / دۆهوک ئەنجامدراوە، لەکاتێکدا حاڵەتی تەندروست لە ناوەندە جیاوازەکانی حکومەت کۆکراونەتەوە و دامەزراوە و کۆلێژ و کەمپەکان.

دەرەنجامەکان: مامناوەندی تەمەن بۆ هەردوو گروپەکە بە ڕێککەوت 7.6 ± 33.5 و 6.5 ± 33.1 بووە، نەخۆشی لەگەڵ نەخۆشی ڕیشاڵی کیسی نزیکەی 40% پێکدەهێنێت و ڕیشاڵی گەدە بە نزیکەی 38% مەزەندە دەکرێت، لە کاتێکدا ئازاری خولیی لە مەمکدا تەنها نزیکەی 21% پێکدەهێنێت. لە سەدا حەفتا و هەشتی ئەو ژنانەی کە نەخۆشی بێهۆشکەری مەمکیان هەبووە و لە سەدا هەشتا لە نەخۆشە تەندروستەکانی کلینیکی ئاستی کۆلیسترۆلیان ئاسایی بووە ($P < 0.8$) جیاوازییەکی بەرچاو و ڕوون لە کۆی کۆلیسترۆڵ و چەوری پڕۆتینی چڕی زۆر نزم (VLDL)دا هەبوو. لە نێوان دوو گروپدا، کە ڕێژەکە لە نەخۆشەکاندا زیاتر بوو لە گروپی تەندروست لە ڕووی کلینیکیەوە بە بەهای ئەگەری کەمتر لە 0.004 و 0.0005، بە ڕێککەوت. سەبارەت بە پەیوەندی نێوان کۆلیسترۆڵ و هۆکارە جیاوازەکانی نەخۆشییە بێهۆشەکانی مەمک، هیچ جیاوازییەک لە پێوانەکاندا نەبووە جگە لە چەوری پڕۆتینی چڕیی نزم (LDL) و چەوری پڕۆتینی چـڕیی زۆر نـزم (VLDL)، کە ئاسـتەکانیان بـەرز بـووە لە ژنانی تووشبوو بە ڕیشاڵی گەدە کە a بەهـای ئەگـەری کەمـتر لە 0.0001 و 0,004 بەڕێککەوت.

دەرەنجامەکان: بەپێی توێژینەوەکە پەیوەندییەک هەیە لە نێوان ئەو ژنانەی کە نەخۆشییە بێهۆشەکانی مەمکیان هەیە و جیاوازی هەیە لە ڕێژەی کۆی کۆلیسترۆڵ و چەوری پڕۆتینی چڕی زۆر نزم (VLDL) هەروەها ئەم توێژینەوەیە دەریخستووە بەرزبوونەوەی ئاستی چەوری پڕۆتینی چڕیی نزم (LDL) و چەوری پڕۆتینی چڕیی زۆر نزم (VLDL) لە ژنانی تووشبوو بە ڕیشاڵی گەدە، بۆیە پێشنیار دەکەین ئاستی چەوری بۆ ئەو خانمانە بپێورێت کە بەدەست نەخۆشییە بێهۆشەکانی مەمکەوە دەناڵێنن، بەڵام... لەم توێژینەوەیەدا پێویستە لێکۆڵینەوەی زیاتر بکرێت، ئەم بابەتە بۆ ئەوەیە کە لێکۆڵینەوە لە کاریگەری چارەسەری دابەزاندنی چەوری لەسەر باشترکردنی نیشانەکان و یارمەتیدانی چارەسەرکردنیان بکرێت.

الخلاصة

عسر شحميات الدم وأمراض الثدي

الخلفية والأهداف: تعد الامراض الثدي الحميدة من اكثر الامراض شيوعا لدى النساء. الهدف من هذه الدراسة هي ايجاد علاقة بين ارتفاع نسبة الدهون في الدم والاصابة ببعض الامراض الحميدة التي تصيب الثدي .

المواضيع و طرق البحث: هذه دراسة تشمل الحالات و الشواهد التي اجريت على 140 امراة .سيتم مقارنة 70 مريضة لديهن الامراض الحميدة في الثدي (الاورام الغدية الليفية,الامراض الكيسي الليفي في الثدي و الالم الدوري في الثدي) مع مجموعة من 70 امراة اصحاء سريريا و تتم مطابقة هاتين المجموعتين من حيث العمر و التي تتراوح ما بين 20الى 45 سنة.الدراسة اجريت في الفترة من 1 ايلول 2021 الى 31 حزيران 2022.الدراسة اجريت في مستشفى ازادي التعليمي/ دهوك بينما الحالات الاصحاء تم جمعهم من المراكز والمؤسسات الحكومية المختلفة و الكليات و المخيمات.

النتائج: متوسط العمر لكلا المجموعتين كان7,6±33,5 و6,5± 33,1 على التوالي .يشكل المرض المصابين ب مرض الكيسي الليفي حوالي 40% والاورام الغدية الليفية يقدر حوالي 38% بينما الالم الدوري للثدي تشكل حوالي 21% فقط. ثمانية وسبعون بالمائة من المصابات بالامراض الحميدة في الثدي وثمانون بالمئة من الاصحاء سريريا كانت نسبة الكوليسترول في الدم طبيعية (القيمة الاحتمالية اقل من (0,8). كان هناك فرق كبير وواضح في نسبة الكوليسترول الكلي والبروتين الدهني منخفض الكثافة للغاية (VLDL) بين مجموعتين، حيث كانت النسبة مرتفعة لدى المرضى أكثر من مجموعة الاصحاء سريريا بقيمة احتمالية اقل من 0,004 و0,0005 على التوالي. وبخصوص العلاقة بين نسبة الكوليسترول والمسببات المختلفة لامراض الثدي الحميدة لم يكن هناك اختلاف في القياسات ما عدا البروتين الدهني منخفض الكثافة (LDL) والبروتين الدهني منخفض الكثافة للغاية (VLDL) كانتا مستواهما مرتفعة لدى المصابات بالاورام الغدية الليفية بقيمة احتمالية اقل من 0,0001 و0,004 على التوالي.

الاستنتاجات: حسب الدراسة الحالية هناك علاقة بين المصابات بامراض الثدي الحميدة و اختلاف في نسبة الكوليسترول الكلي و البروتين الدهني منخفض الكثافة للغاية. (VLDL) واتضح من هذه الدراسة ايضا ارتفاع في نسبة البروتين الدهني منخفض الكثافة (LDL) ونسبة البروتين الدهني منخفض الكثافة للغاية (VLDL) لدى المصابات بالاورام الغدية الليفية ولهذا فاننا نوصي بقياس مستوى الدهون للواتي يعانين من امراض الثدي الحميدة ولكن هناك حاجة الى المزيد من الابحاث في هذا الموضوع من اجل بحث عن تاثير العلاج الخافض للدهون على تحسين الاعراض و المساعدة في علاجها