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RESEARCH ARTICLE

EFFECT OF TAMOXIFEN ON FASTING SERUM LIPID PROFILE IN BREAST CANCER PATIENTS

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Key words:-
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Abstract

Background: Tamoxifen acts as a selective estrogen receptor modulator by binding to the estrogenreceptors on mammary epithelium andblockingtheproliferative action of estrogen on mammaryepithelium. In contrast to that it has a weak estrogen agonistic effect on bone, liver and endometrium.Tamoxifen therapy has favorable effects on serum lipid profile by decreasing serum levels of Total cholesterol and low density lipoprotein (LDL), while its effect on high density lipoprotein (HDL) and triglyceride (TG)is still controversial. So this study is to evaluate the effects of tamoxifenTherapy on fasting serum lipid profile in patients with breast cancer.

Results: Mean age was 43.56±3.53yrs , most common BMI was 30-34.9. Patient serum TG levels were raised from baseline after 3 months of tamoxifen with p values of (0.000) which was statistically significant while HDL levels were raised but with p value of (0.008) which was statistically insignificant. Serum LDL and total cholesterol were reduced from baseline after 3 month with p value of (0.000) and (0.000) respectively.

Conclusion: This study concludes that tamoxifen has effects on serum lipid profile by increasing TG levels and lowering TC and LDL levels so this should be in consideration while prescribing tamoxifen to the patients having other risk factors for cardiovascular abnormalities.

Introduction:-

Background:

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer related deaths in women worldwide. Data of breast cancer incidence in 2012 shows an estimate of 1.7million new cases and 521,900 breast cancer related deaths. Breast cancer accounts for 25% of all cancers and 15% of all cancer related deaths among women, which signifies huge burden of disease.[1]

According to world health organization (WHO) figures, more than 1.2 million people are diagnosed with breast cancer globallyper year.Breast cancer is one of the most commoncancers in Pakistan as well. According to (WHO), one in nine Pakistani women suffers from breast cancer, which is highest incidence in Asia.[2]According to a recent study reported from Shaukat Khanum Memorial Cancer hospital Pakistan, incidence of breast cancer is 21.5% among both male and female population, however it accounts for 45.9% among female patients only.[2]

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Breast cancer can be treated with different modalities including surgery, cytotoxic chemotherapy, radiotherapy, endocrine therapy or combination of these modalities.[3][4]

Endocrine therapy for breast cancer targets estrogen and progesterone receptors in breast cancer cells.[5] Tamoxifen is one of the endocrine therapies and has been used as a standard modality for many years.[6] Tamoxifen acts as a selective estrogen receptor modulator by binding to the estrogen receptors on mammary epithelium and blocking the proliferative action of estrogen on mammary epithelium.[7] In contrast to that it has a weak estrogen agonisticeffect on bone,liver and endometrium.[8] In addition to that it has also been observed that Tamoxifen affects various biochemical profiles of the patients including fasting lipid profile and plasma lipoprotein concentrations.[9][10][11]

Tamoxifen therapy has favorable effects on serum lipid profile bydecreasing serum levels of Total cholesterol and low density lipoprotein(LDL), while its effect on high density lipoprotein (HDL) is stillcontroversial.[12]][14]So this study is to evaluate the effects of tamoxifen Therapy on fasting serum lipid profile in patients with breast cancer.

Objective:-

The objective of this study is
To study the effects of Tamoxifen on fasting serum lipid profile of breast cancer patients.

Operational Definition:
Fasting Serum Lipid Profile:
Defined as lipid profile of patients taken after overnight fast. It will include LDL, HDL and total cholesterol.

Hormone receptor positive breast tumors:
Defined on the basis of the immuno-histochemical expression of Estrogen receptor (ER) and Progesterone receptor (PR) on biopsy specimen of breast cancer patients.

Methods:-

Duration of study:
24 months starting from date of approval.

Ethical approval:
Study was approved by ethical review committee of my institution

Sample size:
45 patient were selected that fulfill the inclusion and exclusion criteria of the study.

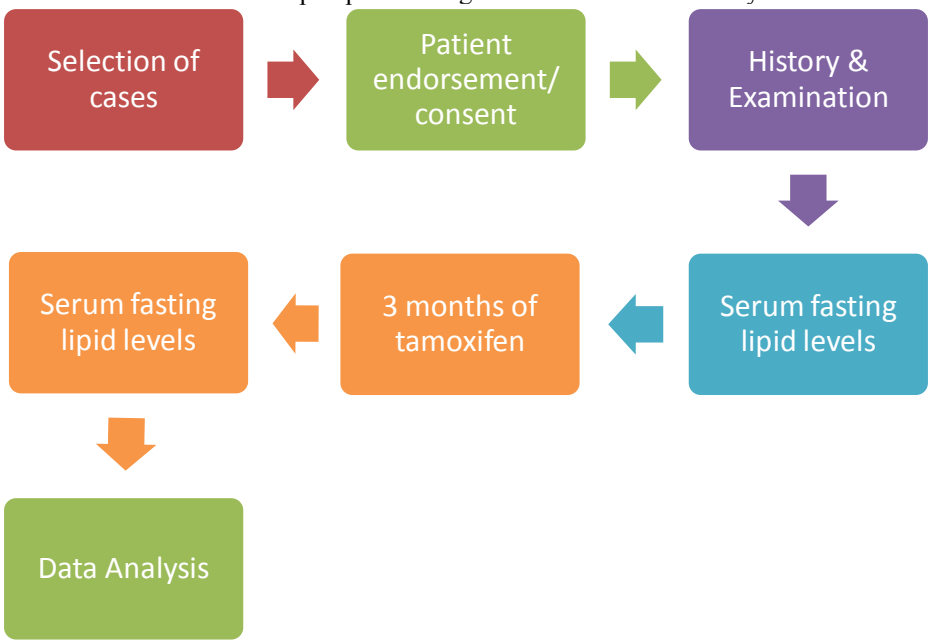
Sampling Techniques:
Patients enrolled in study using consecutive non probability sampling method.

Sample Selection:
Inclusion Criteria:
1. Patient aged 25 -75yrs
2. Histopathologic evidence of breast carcinoma.
3. Hormone receptor positive patients.
4. Baseline lipid profile.
5. Baseline echocardiography showing Ejection Fraction of > 50 %.
6. Normal blood counts, liver and kidney function tests.

Exclusion Criteria:
1. Patients with established diabetes mellitus,hypertension,coronary heart disease,liver diseases andchronic kidney disease.
2. Patients who received previous endocrine therapy.
3. Pregnancy.
4. Concomitant other malignancy

Study Design:

It was a prospective single arm interventional study



Data Collection:

In this study, patients with histological proven carcinoma breast with positive hormone receptor statuswere recruited from Oncology out-patient. After taking an informed consent, selection of patients was carried out on the basis of non-probability consecutive sampling technique. After enrolling the patients in the study, detailed history, examination, and base line fasting serum lipid profile were done. Thereafter, tamoxifen 20mg will be given orally daily for 3 months and fasting serum lipid profile were repeated at 3 months. These results were compared with the baseline fasting serum lipid profile results.

Data Analysis:-

SPSS 23 was used to analyze data. Descriptive analysis was done by including frequencies and ranges for qualitative variables like age and gender. Means,range and standard deviationswas used for quantitative variable i.e. fasting serum lipid profile. Statistical analysis was done by paired t- test to compare the baseline and post tamoxifen fasting serum lipid profile levels. p-value of less than 0.05 is taken as significant.

Results:-

Mean age was 43.56±3.53yrs , most common BMI was 30-34.9.Patient serum TG levels were raised from baseline after 3 months of tamoxifen with p values of (0.000) which was statistically significant while HDL levels were raised but with p value of (0.008) which was statistically insignificant. Serum LDL and total cholesterol were reduced from baseline after 3 month with p value of (0.000) and (0.000) respectively.

Discussion:-

Tamoxifen a nonsteroidal antiestrogenic selective estrogen receptor modulator (SERM)synthesized in 1966 was initially developed as an antifertility agent but currently is used as antineoplastic agent in breast carcinoma . As their name says, SERMs are “selective” this means that a SERM that blocks estrogen's action in breast cells can activate estrogen's action in other cells, such as bone, liver, and uterine cells. [4]In our study we analyzed effects of tamoxifen on serum lipid profile pre and post 3months of tamoxifen .In our study serum Total cholesterol(TC) and low density lipoprotein (LDL) were decreased from baseline after 3months of tamoxifen this is in comparison with studies done by hossein et al,y.hozumi et al and gupta et al, these comparable results are due to SERM effect of tamoxifen and the other factor leading to this effect could be the type of chemotherapy as it is noted that anthracycline based chemotherapy reduces serum TC and LDL[14][8][5][4]and in our patients most commonly anthracycline based chemotherapy was used ,so this could augment the effect of tamoxifen on lowering TC and LDL in our study population.

Triglyceride levels (TG) were raised from baseline in our study this can be explained by SERM effect of tamoxifen other factor in my study is baseline raised BMI of patients which could also lead to initially raised TG levels at baseline which strengthens the effect of tamoxifen in altering TG levels in our study it has same results as study done by hossein et al [5](3) but it has contrasting results with studies done by gupta et al and chilen et al which showed no alteration in serum TG levels this difference could be explained due to apolipoprotein *APOE* polymorphism .TG levels are modified by *APOE* polymorphism ,Patients with the *APOE4* allele have lower serum TG levels [4].The genomic differences between races might explain the different TG levels found in this study. APOE 4 levels are lower in western population and high in Asian population [15]which could be reason of baseline raised TG levels in Asian population [15] and could explain raised TG levels in our study .

HDL cholesterol was raised in my study from baseline but p value was insignificant which is in comparable to studies done previously.

Figure legends:

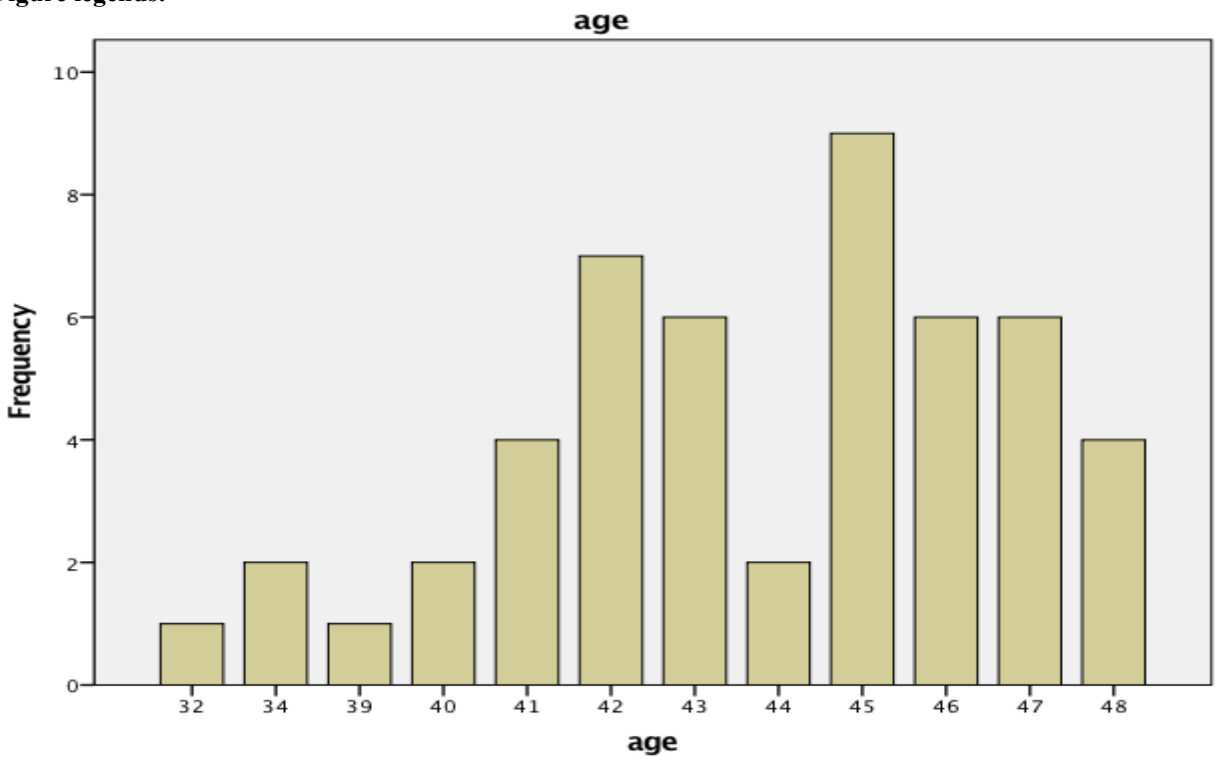


Figure 1:-

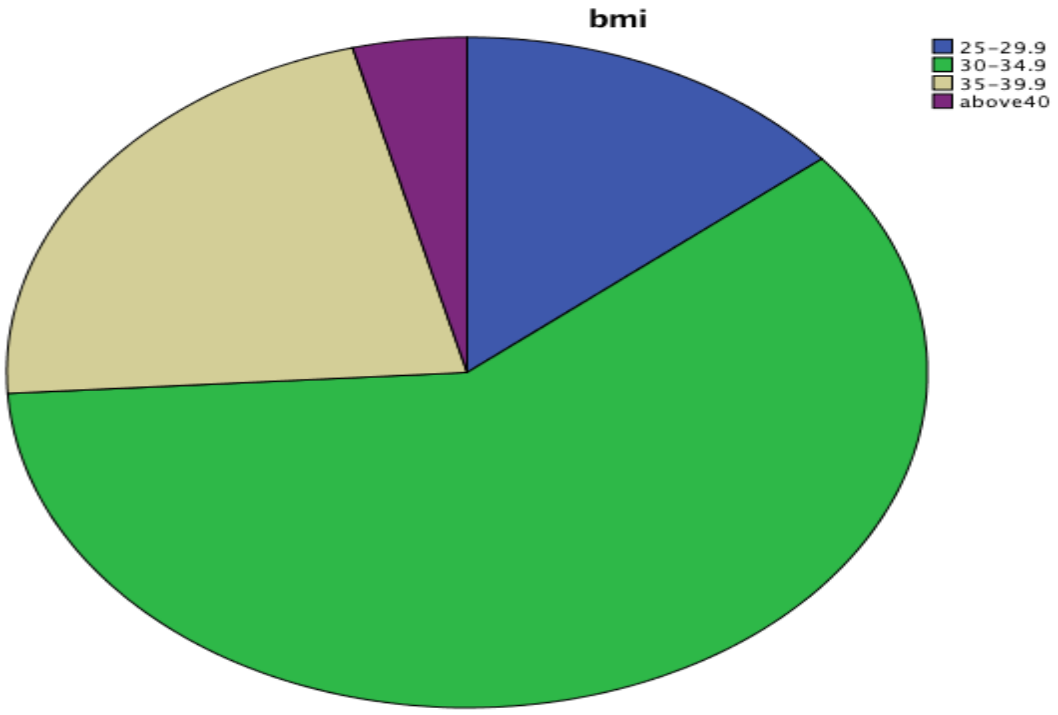


Figure 2:-

2 tailed sig value is significant < 0.05

Table 1:- Serum lipid profile in 3months pre and post tamoxifen.

	Pre tamoxifen	Post tamoxifen	P value
TG	1.43±0.22	2.45±0.61	0.000
HDL	1.04 ± 0.21	1.16 ± 0.28	0.008
LDL	2.89 ± 0.48	2.25 ± 0.53	0.000
Cholesterol	4. ± 0.41	4.19 ± 0.58	0.000

Conclusion:-

Thus my study concludes that tamoxifen has effects on serum lipid profile by increasing TG levels and lowering TC and LDL levels so this should be in consideration while prescribing tamoxifen to the patients having other risk factors for cardiovascular abnormalities .

Abbreviations:-

Estrogen receptor (ER) ,Progesterone receptor (PR),apolipoprotein *APO,* Total cholesterol (TC)Low density lipoprotein (LDL). Triglycerides (TG),High density lipoprotein (HDL)

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