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Study of Changes in Biochemical Parameter Cholesterol in Ovarian Tumors before and after Chemotherapy

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Abstract: ***Introduction: The cancer burden in India is given in gynaecological cancers occur in about 6.8% population. The lifetime risk of developing sporadic epithelial ovarian cancer is approximately 1.7% although patients with a familial predisposition have a much higher lifetime risk in the range of 10 to 40%. Methodology: Cholesterol in tissue and blood has consistently been found to have a prime role in the pathogenesis of coronary artery disease, but an association of cholesterol with cancers such as colorectal and breast cancer and leukemia has also been reported. The cholesterol content of cell membranes is tightly regulated, and this process of regulation involves the uptake of cholesterol-rich low-density lipoprotein (LDL). The present study designed with an aim to explore the changes in the biochemical profile Cholesterol of malignant and benign ovarian tumours pre therapy and post therapy. A case study control was conducted on 40 patients suffering from ovarian tumors (Benign and Malignant) who had reported to Rangaraya Medical College and hospital, Kakinada. Results: All stastical analysis was done using SPSS software and results were obtained The mean age of the patients were found to be 44.77 ± 11.66. Mean age of the patients with malignant tumors (n=29) was 47.7 to ± 9.26 years whereas for benign tumors (n=11) it was only 37± 4.34 years. hical committee clearance and informed the concent from the patients.***

Keywords: Ovarian neoplasm, Cholesterol, epithelial ovarian cancers

1. Introduction

Ovarian cancer is the malignant proliferation of ovarian cells arising from the ovary. It represents a spectrum of disease entities which arise from various cells such as epithelial, germ cell or sex cord stromal cells. Epithelial ovarian cancer arises from epithelial cells and typically occurs in postmenopausal women. In contrast, most germ cell tumours present at a younger age while sex cord stromal tumours may occur at any age. Approximately 90% of ovarian tumours are epithelial in origin. Managing these cancers poses significant therapeutic challenges as they present at an advance stage and tend to recur in majority of the cases. In contrast other malignant ovarian tumours like germ cell and sex cord stromal tumours are often localized in distribution, and amenable to complete surgical resection thus having a favorable prognosis.

Although majority of the ovarian cancers arise from the surface epithelium of the ovaries. However, a minority of these tumours also arise from the epithelial lining of the fallopian tube.

Early ovarian cancer is diagnosed by surgical evaluation of an adnexal mass. The decision to subject a patient to surgical exploration is difficult to make. However, Ultrasonography evaluation of adnexal masses has not only improved the ability to distinguish patients who should have surgical exploration from patients who can be further evaluated through observation, but it also has resulted in an increasing number of patients who are found to have an asymptomatic ovarian cyst. This result is of particular concern in postmenopausal women.

Cholesterol in tissue and blood has consistently been found to have a prime role in the pathogenesis of coronary artery disease, but an association of cholesterol with cancers such as colorectal, breast cancer and leukemia has also been reported. The cholesterol content of cell membranes is tightly regulated, and this process of regulation involves the uptake of cholesterol-rich low-density lipoprotein (LDL). However, interestingly, cholesterol accumulation has been reported in various solid tumours, especially oral and prostate cancers (Freeman MR, Solomon KR. Cholesterol and prostate cancer[1,2,3]. In addition, cholesterol metabolism is dysregulated in many malignancies, including myeloid leukemia, lung and breast cancers. Although a high level of serum triglycerides (TGs) does not appear to be mechanically involved in the development of most cancers, reduction of serum TGs and intensive surveillance with total colonoscopy in colon cancer may have benefit in men with hypertriglyceridemia[4,5,6]. An association between high serum TGs and colon cancer has also been reported by McKeown–Eyssen et al. Several case–control and cohort studies have found positive association between ovarian cancer and an intake of foods with high levels of saturated fats or cholesterol, such as red meat, eggs, and dairy products. It has been reported that ovarian cancer risk is positively associated with higher consumption of dietary cholesterol and eggs, and inversely associated with a higher intake of vegetables overall and of cruciferous vegetables and with supplementation of vitamin E, beta-carotene, and vitamin B complex[7,8].

High consumption of fats may increase circulating estrogen levels, thus increasing the possibility of cell damage and proliferation that is responsible for cancerous growth Risch *et al.* suggested that dietary cholesterol may influence

the risk of ovarian cancer through elevated circulating estrogen or progesterone. The repeated rupture of the follicle associated with ovulation is believed to expose the ovarian epithelium to hormones in the surrounding fluid; high estrogen concentrations may increase the likelihood of tumour development[9]. However, Bertone *et al.* found that the association of fat-rich food intake and ovarian cancer risk was not significant, although an increase in risk with frequent intake of eggs was observed. A weakly positive, but nonlinear association was observed for saturated fat intake and ovarian cancer[10] risk in an Italian case–control study in which intake of monounsaturated and polyunsaturated fatty acids was inversely correlated with ovarian cancer[11,12,13].

2. Review of Literature

Kang, et al. has evaluated **Alteration in lipid ovarian cancer, similarity to breast cancer.** He found that lipid profiles accurately distinguished ovarian cancer from adjacent normal tissue samples.

Gadomska H et al. estimated Lipids in serum of patients with Malignant Ovarian Neoplasms. It was found out that low levels of esterified and total Cholesterol and low levels of HDL Cholesterol properly differentiated affected subjects from healthy ones whereas proper values of these parameters cannot exclude a neoplasm.

Nosov et al studied 358 serum samples (control, benign adnexal masses, and early-stage and late-stage ovarian cancer) obtained from the National Cancer Institute identified 3 serum proteins (apolipoprotein A-1, transthyretin, and transferrin) for the detection of ovarian cancer and reported them combined with CA-125 to effectively detect early-stage mucinous tumors.

Aims and Objectives

- To explore the changes in the biochemical profile Cholesterol of malignant and benign ovarian tumours pre therapy and post therapy[15].
- To explore the differences in the biochemical profile Cholesterol, between healthy individuals and patients with ovarian tumours.

3. Materials and Methods

Study type: case control study
Place of study: Rangaraya Medical College & General Hospital, Kakinada
Study Period: March 2019 to January 2020

Selection criteria:

Exclusion criteria:
1) Patients diagnosed with other malignant tumors
2) Patients older than 65 years

Inclusion criteria: patients diagnosed with ovarian tumors

4. Procedures

Cholesterol – CHOD –PAP method using EM-200(ERBA-TRANSASIA)fully automated analyser

The present study was conducted in the Department of Biochemistry, Rangaraya Medical College, Kakinada, Andhra Pradesh. The present study was undertaken to study the various changes in the biochemical parameters in the serum of patients with ovarian tumors before and after therapy (Surgery and/or chemotherapy[16,17,18,19]). The serum of 40 patients of ovarian tumors was taken out of which 11 were benign tumors and 29 were malignant tumours. The values were compared with the values of 40 healthy women taken as Control groups. All the subjects were accrued from the department of Gynaecology, Govt. General Hospital who were admitted for treatment. Demographic and clinical data were collected at routine Gynaecology visits. Blood samples were obtained by venous puncture from the antecubital vein of each woman before and after therapy (Surgery and/or Chemotherapy). The control group denied any history of chronic disease and of same age group and test group. Consent was obtained from both the cases and control groups. Serum was separated and analyzed by using standard methods. The observed values were compared with control group for statistical analysis. All data were expressed as Mean $\pm$ Standard deviation and standard error of mean. Differences with a P-value of less than 0.05 were considered to be stastically significant.

Serum cholesterol levels were estimated by CHOD/POD method

5. Observation and Results

The study was approved by the institutional scientific and review committee. We present our observations on the demographic, treatment and biochemical profile ovarian tumours (benign and malignant) pretreatment and post treatment and compared them with matched healthy individuals. We accrued 40 healthy female individuals and 40 patients with ovarian tumours of which 29 patients had malignant ovarian cancers (epithelial and non epithelial) and 11 patients had benign ovarian cysts) over a period of 1.5 years.

Table 1: Demographic profile of Patients with Tumours and treatment parameters

Patient and tumour profile		Frequency	%
Age (N =40)	Mean age :44.77 years Median Age: 48 years Mean ± SD: 44.77± 11.76 Mean± SEM:44.77 ± 1.86		
	Range:13- 65yrs		
Duration of symptoms For all patients (N =40)	Mean duration 12. 6 weeks Median duration: 6.5 weeks		

	Mean ± SD:12.61± 20.89 Mean± SEM: 12.61± 3.30		
	Range :0.4 -104 weeks		
Duration of symptoms for patients with malignant tumours (N = 29)	Mean duration: 8.62 weeks Median Duration: 6 weeks Mean ± SD:8.62 ± 12.50 Mean± SEM:8.62 ± 2.32		
	Range: 0.6 -52 weeks		
Duration of symptoms for patients with benign tumours (N = 11)	Mean Duration: 23.1 weeks Median duration: 8 weeks Mean ± SD:23.1 ± 33.1 weeks Mean ± SEM:23.1 ± 9.98 weeks		
	Range: 0.4 - 104 weeks		
Histology of tumour (N =40	Benign Cyst Serous Cystadenocarcinoma Mucinous Cystadenocarcinoma Granulosa cell tumour Yolk sac tumour Cyst adenoma	10 12 15 1 1 1	25 30 37.5 2.5 2.5 2.5
Type of tumour (N = 40)	Benign	11	27.5
	Malignant	29	72.5
Age of pts with malignant tumours (N = 29)	Mean Age: 47.72 years Median Age: 49 years Mean ± SD: 47.72 ± 9.26 years Mean± SEM:47.72 ± 1.72 years		
	Range:15- 65 years		
Age of pts with Benign Tumours (N = 11)	Mean Age: 37 years Median Age: 40 years Mean ± SD: 37 ± 14.4 years Mean ± SEM : 37 ± 4.34 years		
	Range: 13—56 years		
Medical history (N = 40)	Hypertension Diabetes Anemia Hypertension with hypothyroidism No Medical history History Not available	3 1 1 2 29 4	7.5 2.5 2.5 5.0 72.5 10.0
Treatment profile		**Frequency**	**%**
No of Chemotherapy cycles in patients with malignant tumours (N = 29)	Mean : 5.4 cycles Median: 6 cycles Mean ± SD: 5.4 ± 1.27 cycles Mean± SEM:5.4 ± 0..23 cycles Range: 1 – 6 cycles		
No of chemotherapy cycles (N = 29)	Pts who had 6 cycles Pts who had 5 cycles Pts who had 3 cycle Pts who had 1 cycle	23 2 3 1	79.3 6.9 10.3 3.5
Surgery	Complete Incomplete No surgery	35 3	87.5 7.5 5.0
Patients with Malignant tumours (N = 29)	Chemotherapy only Neoadjuvant chemotherapy +Surgery Surgery +Adjuvant Chemotherapy	2 1 26	6.9 3.5 89.6

Table 2: Biochemical profile of healthy female individuals (N = 40)

Parameters	Mean	Median	Mean ± SEM	Mean ± SD	Range
Age (years)	44.02	44	44.02±1.47	44.02±9.36	27-70
Cholesterol (Mg/dl)	182.65	179.5	182.65±3.09	182.65±19.59	148-228

Table 3: Biochemical profile of patients for all Ovarian Tumours (pre-treatment and Post treatment) [N= 40]

Parameters	Pretreatment/ Post treatment	Mean	Median	± SEM	± SD	Range
Cholesterol (mg/dl)	Pre	182.55	178.50	10.14	64.17	101-471
	Post	164.57	154.00	6.09	38.52	111-300

Table 4: Changes in Pretreatment and post treatment biochemical parameters in benign ovarian tumours

Parameters	Pretreatment/Post treatment	Mean	Median	± SEM	± SD	Range	P- Value
Cholesterol (mg/dl)	Pre	195.8	171	31.09	103.1	101-471	0.52
	Post	164.5	146	15.97	52.96	111-300	
	Post	2.66	2.90	0.28	0.95	1-4.6	

Table 5: Changes in Pretreatment and post treatment biochemical parameters in ovarian tumours (benign & Malignant)

Parameters	Pretreatment/ Post treatment	Mean	Median	± SEM	± SD	Range	P- Value
Cholesterol (mg/dl)	Pre	189	178	10.28	64.17	101-471	0.02
	Post	163.3	152	6.10	38.10	111-300	
	Post	7.29	5.9	0.63	3.93	3.3-20.0	
	Post	2.88	2.6	0.22	1.41	1-9.8	

Table 6: Biochemical profile of healthy female individuals (controls) vs. females with ovarian tumours. (N = 40)

Parameters	Controls/ Tumours	Mean	Median	± SEM	± SD	Range	P-Value
Cholesterol (mg/dl)	Controls	182.65	179.5	3.09	19.59	148-228	0.99
	Ovarian tumours	182.55	178.50	10.14	64.17	101-471	
	Ovarian tumours	4.36	3.35	0.38	2.45	2.00-14.80	

6. Discussion

A study was conducted on 40 patients suffering from ovarian tumors (Benign and Malignant) who had reported to Rangaraya Medical College hospital, Kakinada. The demographic and treatment profile of patients with ovarian tumours are illustrated in tables 6 &7. The mean age of the patients were found to be 44.77 ± 11.66. Mean age of the patients with malignant tumors (n=29) was 47.7 to ± 9.26 years whereas for benign tumors (n=11) it was only 37± 4.34 years. A similar finding of mean age of 49.9 ± 17.5 years was found in a study conducted in ovarian cancer patients by Umran Kucukgoz Gulec, et al [(76)]

The mean duration of symptoms was 12.6 ± 20.89 weeks (range 0.4- 104 weeks) and the median was 6.5 weeks in our cohort of patients. The mean duration of symptoms for benign (n=11) tumors was 23.1 ± 33.1 weeks whereas for malignant (n=29) tumors the duration of symptoms was 8.62 ± 12.50 weeks. As expected the symptomatology in malignant tumours was more aggressive than benign tumours.

Platinum based chemotherapy using cisplatin or carboplatin in combination with paclitaxel is the standard adjuvant therapy in ovarian cancers. In our study, the number of chemotherapy cycles in patients with malignant ovarian tumours was 5.4 ± 1.27 cycles with a compliance rate of 79.3%. (Table-6) In a study of 218 ovarian cancer patients reported from india, the compliance to chemotherapy was extremely poor at 45%. [(79)].In our study, 87.5% had complete surgery for their condition. 89.6% of patients required surgery + adjuvant chemotherapy and 6.9% took only chemotherapy as a palliative treatment due to advance stage of the disease.

The main objective of the study was to explore the changes in the biochemical parameters in pre and post therapy in both benign and malignant ovarian tumours. Moreover, we sought to study the differences in these parameters between the afflicted patients and the healthy controls. We also did a subset analysis to study the correlation of other biochemical parameters with the main tumour marker CA-125 in patients with both benign and malignant ovarian tumours.

The mean cholesterol levels did not vary between healthy control (182.65) [table7], patients with benign ovarian tumours (182.55) [table-9] and patients with malignant ovarian cancers (177.5). Furthermore, the post treatment levels of cholesterol did not change significantly from the pre treatment levels in both patients with benign tumours (p =0.5) or in patients with malignant ovarian cancer (p =0.08) Although there is some data which dysregulated lipid/cholesterol metabolism to be associated with ovarian tumours.[(99)] Several case–control and cohort studies have found positive associations between ovarian cancer and high levels of saturated fats or cholesterol [(26,100,101)]. However, it has been shown in some studies that the elevation of phospholipids especially choline phospholipid metabolism is associated with increased risk of ovarian cancer.

Phospholipids have been found to be involved in ovarian cancer in several forms, including lysophosphatidic acid (LPA), phospholipase A2 (PLA2), phospholipase D (PLD), and autotoxin (ATX), among others. although we did not study these biochemical markers, but considering their strong association with risk of ovarian cancers, these markers could be an area of focused biomarker research for early diagnosis of ovarian cancer. Even after extensive literature search we could not find any study related to the prognostic significance of cholesterol.

7. Limitations of Study

Lack of follow up of patients, factors like life style,diet,lipid lowering drugs may also effect the study out come.

8. Conclusion

The cholesterol levels changed insignificantly in both benign and malignant tumors.

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