

## Association of Estrogen and Progesterone with Ovarian Cancers

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### ABSTRACT

**Objective:** To find an association between estrogen and progesterone with ovarian cancer progression.

**Study Design:** Cross-sectional study

**Place and Duration of Study:** Department of Obstetrics & Gynaecology, Islam Teaching Hospital, Sialkot from 1<sup>st</sup> January 2021 to 31<sup>st</sup> December 2021.

**Methodology:** One hundred participants were enrolled. Ovarian cancer women were placed in Group A while healthy woman in Group B. The study was approved from the review board. The age of the patients was between 18-45 years. Demographic details as well as clinical and relevant familial history was documented of each patient. The blood sampling was done on same menstrual day 12 in each patient. Each patient 4 cc blood was withdrawn for analysis if their estrogen and progesterone levels. The blood was collected in serum vials and serum was separated by centrifugation at 3000rpm. The patients who were confirmed for ovarian cancer CA 125 were confirmed through clinical diagnosis in addition to their MRI and CT scan imaging.

**Results:** The mean age of the patients was 33.3±2.1 years of ovarian cancers while 21.5±3.4 years of normal controls. Majority of the females were from low socioeconomic class. The values of progesterone and estrogen were significantly higher in CA 125 cases such as Group A in comparison with group B respectively. The analytes were assessed in the follicular phase and showed higher frequency in 96% and 94% of cases with ovarian cancer. The mean value was 2±0.4ng/ml and 119.1±2.9 pg/ml respectively.

**Conclusion:** In ovarian cancer, level of estrogen was very higher during follicular phase.

**Keywords:** Ovarian cancer, Advanced epithelial cancer, Estrogen, Progesterone, Abnormal secretion

### INTRODUCTION

Ovarian cancer is considered as the deadliest gynecological malignancy and ranked on number fifth in most common types of cancer. It mostly encounters in postmenopausal women as almost 80% of the cases have been observed in older aged women. Due to advance research and new therapeutic interventions, falling trend of ovarian cancer is observed among women and life expectancy has also greatly improved from 34% to 45% from year 1975 to 2010. High rate of mortality and lethal consequences are greatly attributed to the false or late diagnosis of this cancer.<sup>1-3</sup> More than half of the new ovarian cancer cases are detected as advanced epithelial cancer (EOC).

Epidemiological and experimental data demonstrated that, ovarian cancer has strong association with estrogen metabolism and exposure. The ovarian cancer cells and estrogen regulation shared common metabolic and regulation pathways which exacerbates the chances of other cancers as well including endometrial cancer.<sup>4,5</sup> Ovaries carry out two main functions including ovulation and secretion and maintenance of estrogen and progesterone secretion. These two are the steroid hormones and their synthesis and metabolic pathway require number of enzymes which need to modify cholesterol molecule. Estrogen is measured as the primary sex hormones in females and it is present in three main types such as estriol, estrone and estradiol, out of which, estradiol is the ovarian estrogen. Alternatively, progesterone promotes breast growth and regulate uterine cycle. Studies proved that progesterone provides protection against ovarian carcinogenesis.<sup>6-8</sup> In abnormal circumstances like cancerous condition, ovarian function become changes and hormone secretion by ovaries also got change.

Despite of the presence of reliable and effective screening tools and diagnostic method, ovarian cancer still not diagnosed at early stage due to variety of non specific symptoms. Ovarian cancer cells determined and appeared when tumor reaches at advance stage. Another cause of high mortality rate is development of resistance by cancer cells to different chemotherapeutic regimens which leads to early relapse and tumor progression.<sup>9,10</sup> Present study was designed to determine the association of females' sex hormone; estrogen and

progesterone with the progression and onset of ovarian cancer. Result of present study will prove beneficial in the early diagnosis and treatment plan for ovarian cancer by considering these two hormones as major contributor.

### MATERIALS AND METHODS

This cross-sectional study conducted at Department of Obstetrics & Gynaecology, Islam Teaching Hospital, Sialkot from 1<sup>st</sup> January 2021 to 31<sup>st</sup> December 2021 and 100 conveniently selected women were enrolled as participants after their informed consent. The women were either those who were confirmed for ovarian cancer or those who were healthy without any development of ovarian or any other type of cancer. Ovarian cancer women were placed in Group A while healthy woman in Group B. Those ovarian cancer women who were suffering from other type of disease or pregnant women or women on hormone replacement therapy or endocrinological disorders were excluded. The age of the patients was between 18- 45 years. Demographic details as well as clinical and relevant familial history was documented of each patient. The blood sampling was done on same menstrual day 12 in each patient. The sample size was calculated through WHO calculator with 80% power of test and 95% CI. Each patient 4 cc blood was withdrawn for analysis if their estrogen and progesterone levels. The blood was collected in serum vials and serum was separated by centrifugation at 3000rpm. The serum was stored at -20°C until analysis. Enzyme linked immune sorbent assay was used for analyzing the estrogen and progesterone value through human available kits (Calbiotech UK). The patients who were confirmed for ovarian cancer CA 125 were confirmed through clinical diagnosis in addition to their MRI and CT scan imaging. Data was analyzed using SPSS version 26.0 by representation into frequencies and percentages and mean as well as standard deviations of qualitative and quantitative data respectively. Chi square tool was opted for analysis with a p value less than 0.05 as significant.

### RESULTS

The mean age of the patients was 33.3±2.1 years while 21.5±3.4 years of normal controls. Majority of the females were from low

socioeconomic class suffering from CA125 while normal controls were from middle socioeconomic class with 66% (Table 1).

There was no significant difference within the age of menarche of group A and Group B with slight variance in the age of menarche as greater than 12 years where Group A had 20% cases while group B has 14% of the normal control participants (Table 2).

The values of progesterone and estrogen were significantly higher in CA 125 cases such as Group A in comparison with group B respectively. The analytes were assessed in the follicular phase and showed higher frequency in 96% and 94% of cases with ovarian cancer. The mean value was 2±0.4ng/ml and 119.1±2.9 pg/ml respectively (Table 3).

Table 1: Demographic distribution of both groups (=100)

Variable	Group A (n=50)	Group B (n=50)
Age (years)	33.3±2.1	21.5±3.4
Socioeconomic class		
Low class	22 (44%)	6 (12%)
Middle class	12 (24%)	33 (66%)
High class	16 (32%)	11 (22%)

P<0.05

Table 2: Comparison of age of menarche in both groups (n=100)

Age of Menarche	Group A	Group B	P value
<12 years	40 (80%)	43 (86%)	0.612
>12 years	10 (20%)	7 (14%)	0.055

Table 3: Mean values of estrogen and progesterone in both groups (n=100)

Age of Menarche	Group A	Group B	P value
Progesterone (ng/ml)			
Follicular Phase (0.15-0.70)	0.6±0.03	2±0.4	<0.05
Estrogen (pg/ml)			
Follicular phase (30-100)	63.7±2.3	119.1±2.9	<0.05

## DISCUSSION

Ovarian cancer is one the most common type of cancer and the leading cause of death among women. This equally hits developed and under developed countries. Effective treatment regimen and early diagnosis could increase the survival chances and life expectancy of the patient. Present screening test has low predictive value which further worsens the situation. High incidence of recurrence has also been observed after initial treatment. Statistical data of 2020 showed that, 1.2% of all cancer cases has been reported out of which, 48% of the patients had local stage cancer whereas in 58% of the patient, cancer was metastasized. Higher frequency and incidence rate was observed in non-Hispanic followed by Americans and Indians.<sup>10-14</sup>

In present study, sex hormones including estrogen and progesterone were assessed in ovarian cancer patients to find their role in progression and severity of the disease. Results suggest that, progesterone provide protection against ovarian carcinogenesis. Its secretion was also higher during follicular phase. Increased level of progesterone in ovarian cancer has also reported by other various studies.<sup>15-17</sup> Likewise, estrogen level was very higher during follicular phase in both groups. This proves that, estrogen secretion gets alter by ovaries malfunctioning and ovarian cancer cells itself are producing estrogen. Other studies also highlighted that ovarian tumors and epithelial ovarian tumors have the ability to produce estrogen.<sup>18,19</sup>

The results of the present study suggest that estrogen and progesterone has strong association with the ovarian cancer development. Its high frequency and deadly consequences are

due to various factors including advanced age in which person is already immunocompromised, ineffective screening test, inappropriate diagnostic tool and smoking. Considering these two hormones value as an important indicator, it will help medical practitioners and health care workers to timely diagnose this disease to combat its deadly consequences and mortality rate.

## CONCLUSION

In ovarian cancer, level of estrogen was very higher during follicular phase while progesterone remained unchanged. Therefore, alteration in hormonal secretion would prove an important parameter for identifying ovarian cancer.

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