ORIGINAL ARTICLE e-ISSN: 2349-0659 p-ISSN; 2350-0964

Comparative Evaluation of Circulating Serum Hormone Assays in Patients with Ovarian Malignancies: A Case–Control Analysis

Narayan Ashok Madrasi[1], Shahid Akbar Mujawar[2]*, Abhaykumar Sudhakar Sardeshmukh[1], Amitkumar Bapuso Pandav[3], Madhav Govind Kalekar[4], Ulhas Shankar Mali[5]

Abstract

Background: Ovarian malignancy develops within a complex endocrine environment, and alterations in reproductive hormones may reflect changes in ovarian function, reproductive aging, and tumor-related biology. However, the combined circulating profile of gonadotropins, progesterone (P4), and prolactin (PRL) in ovarian cancer remains incompletely characterized. **Objective:** This study aimed to compare serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), P4, and PRL concentrations between women with ovarian cancer and healthy controls and to evaluate their correlations and discriminatory performance. **Materials and Methods:** This case–control study included 100 women at a tertiary care center in Western Maharashtra, comprising 50 women with ovarian cancer and 50 healthy controls. Serum LH, FSH, P4, and PRL were measured using standard immunoassay techniques. Group differences were assessed using the Mann–Whitney U test, associations using Spearman's rank correlation, and discriminatory performance using receiver operating characteristic (ROC) analysis. **Results:** FSH and PRL were significantly higher in women with ovarian cancer, whereas P4 was significantly lower; LH showed no significant between-group difference. Age correlated positively with LH ($\rho = 0.528$, $P < 0.001$) and FSH ($\rho = 0.749$, $P < 0.001$) and negatively with P4 ($\rho = -0.714$, $P < 0.001$). The strongest inter-hormonal association was the inverse correlation between FSH and P4 ($\rho = -0.778$, $P < 0.001$). PRL showed the highest discriminatory performance (area under the curve [AUC] = 0.780), followed by FSH (AUC = 0.636), whereas LH showed poor discrimination and P4 demonstrated an inverse ROC pattern. **Conclusion:** Ovarian malignancy was associated with a distinct endocrine profile characterized by higher FSH and PRL and lower P4 levels. PRL showed the strongest discriminatory ability, although its specificity was limited. These findings suggest that reproductive hormones may provide complementary insight into the endocrine milieu of ovarian cancer but should not be used as stand-alone diagnostic markers.

Keywords: Endocrine profile, Follicle-stimulating hormone, Luteinizing hormone, Ovarian cancer, Progesterone, Prolactin, Receiver operating characteristic analysis

Asian Pac. J. Health Sci., (2026); DOI: 10.21276/apjhs.2026.13.3.35

Introduction

The ovary is a central reproductive and endocrine organ that is responsible not only for oocyte development and ovulation but also for the coordinated production of hormones that regulate female reproductive function across the lifespan. This activity is governed by the hypothalamic–pituitary–ovarian axis, in which gonadotropin-releasing hormone controls pituitary secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and ovarian steroids provide feedback to the hypothalamus and pituitary.[1] Disturbance of this finely regulated axis may accompany changes in ovarian function, reproductive aging, and ovarian pathology.

In ovarian malignancy, endocrine regulation becomes particularly relevant because ovarian tumors may arise within or interact with hormonally responsive tissues. Experimental and clinical evidence indicates that gonadotropins and steroid hormones can influence ovarian tumor biology through receptor-mediated pathways, whereas malignant ovarian cells may themselves retain responsiveness to endocrine signals.[2] FSH and LH regulate normal ovarian follicular and steroidogenic activity, whereas progesterone (P4) participates in ovarian and endometrial physiology and may exert context-dependent effects on ovarian cancer cells through P4-receptor signaling.[2,3] Recent evidence has also highlighted the FSH–FSH receptor axis as a potential contributor to ovarian cancer growth and progression, although its biological effects appear to depend on tumor type and cellular context.

[1]Department of Biochemistry, Government Medical College, Miraj, Maharashtra, India.

[2]Department of Biochemistry, B. J. Government Medical College, Pune, Maharashtra, India.

[3]Department of Pathology, Government Medical College, Miraj, Maharashtra, India.

[4]Department of Biochemistry, V. M. Government Medical College, Solapur, Maharashtra, India.

[5]Modern Diagnostics, Sangli, Maharashtra, India.

Corresponding Author: Dr. Shahid Akbar Mujawar, Department of Biochemistry, B. J. Government Medical College, Pune - 411001, Maharashtra, India. E-mail: dr.shahidmujawar@gmail.com

How to cite this article: Madrasi NA, Mujawar SA, Sardeshmukh AS, Pandav AB, Kalekar MG, Mali US. Comparative Evaluation of Circulating Serum Hormone Assays in Patients with Ovarian Malignancies: A Case–Control Analysis. Asian Pac. J. Health Sci., 2026;13(3):):176-180.

Source of support: Nil.

Conflicts of interest: None.

Received: 25/07/2026 **Revised:** 30/08/2026 **Accepted:** 04/09/2026

Prolactin (PRL) adds another dimension to this endocrine network. Although primarily secreted by the anterior pituitary, PRL also participates in ovarian physiology through endocrine, paracrine, and autocrine mechanisms.[4] Its possible relationship with ovarian cancer has gained renewed interest. In a pooled

prospective analysis, Hathaway *et al*. reported a trend toward higher epithelial ovarian cancer risk with increasing circulating PRL, whereas other experimental studies have demonstrated expression of PRL receptors in ovarian cancer tissues and potential involvement of PRL signaling in tumor-cell survival and progression.[5]

Despite growing interest in hormonal influences on ovarian carcinogenesis, most studies have examined individual hormones, receptor pathways, or specific histological subtypes. The combined circulating profile of LH, FSH, P4, and PRL in women with established ovarian malignancy remains less clearly defined, particularly with regard to age-related changes, inter-hormonal relationships, and comparative discriminatory performance.

Therefore, the present study aimed to compare serum LH, FSH, P4, and PRL concentrations between women with ovarian cancer and healthy controls, examine their relationships with age and with one another, and evaluate their discriminatory performance using receiver operating characteristic (ROC) analysis.

Materials and Methods

Study Framework and Participants

A hospital-based case–control study was undertaken at a tertiary care center in Western Maharashtra. The study included 100 women, comprising 50 women with ovarian cancer and 50 healthy controls. Women with confirmed primary ovarian malignancy and complete clinical, pathological, and hormonal data were included in the study group. The control group comprised apparently healthy women without evidence of malignancy or major systemic illness likely to influence the biochemical parameters.

Women with a history of smoking, severe hepatic, renal, or cardiac disease, other significant systemic illnesses, incomplete clinical or laboratory records, or unwillingness to provide informed consent were excluded. The study methodology followed accepted principles for reporting observational case–control research.[6]

Clinical Characterization

Relevant demographic and clinical information was recorded for all participants. Age was documented in both groups, whereas the site of ovarian involvement was recorded as right-sided, left-sided, or bilateral in women with ovarian malignancy. The diagnosis of ovarian cancer was based on the clinical and pathological records available for each participant. In the ovarian cancer group, 42% had right-sided, 36% left-sided, and 22% bilateral ovarian involvement.

Hormonal Profiling

The endocrine assessment included serum LH, FSH, P4, and PRL. Hormone concentrations were measured using standard immunoassay-based laboratory techniques with commercially available reagents and validated analytical platforms. The same laboratory procedures were applied to samples from both study groups to maintain analytical comparability.

Statistical Analysis

Continuous variables were summarized as mean ± standard deviation or median with interquartile range, as appropriate, whereas categorical variables were expressed as frequencies and percentages. Serum LH, FSH, P4, and PRL concentrations between the ovarian cancer and control groups were compared using the Mann–Whitney U test.

Within the ovarian cancer group, relationships between age and individual hormones and inter-hormonal associations were examined using Spearman's rank correlation coefficient (ρ). ROC curve analysis was used to assess the ability of each hormone to discriminate ovarian cancer cases from healthy controls. The area under the curve (AUC), cutoff value, sensitivity, and specificity were determined.[7] A two-sided $P < 0.05$ was considered statistically significant.

Ethical Considerations

The study was conducted after approval from the relevant Institutional Ethics Committee. Written informed consent was obtained from all participants, and confidentiality of clinical and laboratory information was maintained throughout data collection, analysis, and reporting.

Results

A total of 100 women were included in the analysis, comprising 50 women with ovarian cancer and 50 healthy controls. The ovarian cancer group showed a distinct endocrine profile characterized by higher FSH and PRL concentrations and lower P4 levels, whereas LH did not differ significantly between the groups. Significant age-related and inter-hormonal relationships were also observed. ROC analysis showed that PRL had the greatest discriminatory ability among the evaluated hormones, followed by FSH, whereas LH showed poor discrimination and P4 demonstrated an inverse ROC pattern.

A total of 100 participants were included in the study, comprising 50 age-matched healthy controls and 50 individuals with ovarian cancer [Table 1]. The mean age was 36.90 ± 17.89 years in the age-matched healthy control group and 48.12 ± 14.36 years in the ovarian cancer group. The median age was 30.50 years (interquartile range [IQR]: 23.75–50.25) among age-matched healthy controls and 50.00 years (IQR: 39.50–60.00) among the

Table 1: Demographic and clinical characteristics of the study participants

Variable	*Age-matched healthy controls (n=50)*	*Ovarian cancer (n=50)*
Age (years)		
Mean±SD	36.90±17.89	48.12±14.36
Median (IQR)	30.50 (23.75–50.25)	50.00 (39.50–60.00)
Min–Max	12–80	13–70
Age group, *n* (%)		
≤20	4 (8.0)	4 (8.0)
21–30	21 (42.0)	3 (6.0)
31–40	10 (20.0)	7 (14.0)
41–50	3 (6.0)	14 (28.0)
51–60	4 (8.0)	14 (28.0)
>60	8 (16.0)	8 (16.0)
Site of ovary, *n* (%)		
Right	-	21 (42.0)
Left	-	18 (36.0)
Bilateral (B/L)	-	11 (22.0)
Total (%)	50 (100.0)	50 (100.0)

Continuous variables are presented as mean±SD, median (interquartile range), and minimum–maximum. Categorical variables are presented as *n* (%)

ovarian cancer group. Regarding age-group distribution, the age-matched healthy controls were predominantly in the 21–30-year group (42.0%), whereas the ovarian cancer group was most frequently represented in the 41–50-year and 51–60-year groups (28.0% each). The ≤20-year group accounted for 8.0% in both groups, whereas those aged >60 years accounted for 16.0% in both groups. Among individuals with ovarian cancer, the ovarian tumor was located on the right side in 42.0%, the left side in 36.0%, and bilaterally in 22.0%.

Serum hormone levels differed between the two groups for FSH, P4, and PRL, whereas LH did not show a statistically significant difference [Table 2]. FSH was significantly higher in the ovarian cancer group than in the age-matched healthy controls (35.65 vs. 13.30, $P = 0.019$). P4 was significantly lower in the ovarian cancer group (0.65 vs. 1.15, $P = 0.006$). PRL was markedly higher in the ovarian cancer group (19.40 vs. 10.15, $P < 0.001$). In contrast, LH levels were not significantly different between the groups (13.40 vs. 20.75, $P = 0.299$).

Spearman correlation analysis showed several significant associations between age and serum hormone levels in the ovarian cancer group. Age was positively correlated with LH ($\rho = 0.528$, $P < 0.001$) and showed a strong positive correlation with FSH ($\rho = 0.749$, $P < 0.001$) [Table 3]. In contrast, age demonstrated a strong negative correlation with P4 ($\rho = -0.714$, $P < 0.001$), whereas no significant correlation was observed between age and PRL ($\rho = -0.030$, $P = 0.838$). Among the hormones, FSH showed a strong positive correlation with LH ($\rho = 0.592$, $P < 0.001$) and a strong negative correlation with P4 ($\rho = -0.778$, $P < 0.001$). LH also showed a significant negative correlation with P4 ($\rho = -0.402$, $P = 0.004$) and a weak negative correlation with PRL ($\rho = -0.297$, $P = 0.036$). No significant correlations were observed between FSH and PRL or between P4 and PRL. Overall, the strongest association was observed between FSH and P4 ($\rho = -0.778$, $P < 0.001$), followed by the positive correlation between age and FSH ($\rho = 0.749$, $P < 0.001$) and the negative correlation between age and P4 ($\rho = -0.714$, $P < 0.001$).

ROC analysis showed that PRL had the highest discriminatory performance among the four hormones (AUC = 0.780, $P < 0.001$). At the selected cutoff of 9.65, PRL showed 96.0% sensitivity and 48.0% specificity [Table 4]. FSH demonstrated limited discriminatory ability (AUC = 0.636, $P = 0.019$), with 76.0% sensitivity and 56.0% specificity at a cutoff of 15.25. LH showed poor discriminatory performance (AUC = 0.440, $P = 0.299$), whereas P4 showed an inverse ROC direction (AUC = 0.341, $P = 0.006$). Overall, PRL demonstrated the strongest discriminatory performance, followed by FSH, whereas LH and P4 showed lower AUC values in the reported ROC direction.

ROC analysis showed that PRL had the highest discriminatory performance (AUC = 0.780, $P < 0.001$) [Figure 1], followed by FSH (AUC = 0.636, $P = 0.019$). LH showed poor discrimination (AUC = 0.440, $P = 0.299$), while P4 had an AUC of 0.341 ($P = 0.006$) in the reported ROC direction.

Table 2: Comparison of serum hormone levels between age-matched healthy controls and the ovarian cancer group

Hormone	Age-matched healthy controls	Ovarian cancer	*P*-value
LH	20.75 (8.83–48.25)	13.40 (7.88–34.73)	0.299
FSH	13.30 (8.38–37.88)	35.65 (14.03–61.88)	0.019*
P4	1.15 (0.68–7.35)	0.65 (0.30–2.03)	0.006**
PRL	10.15 (6.18–17.45)	19.40 (14.20–98.78)	<0.001***

*P< 0.05; **P< 0.01; ***P< 0.001. Values are presented as median (interquartile range). Mann–Whitney U test was used for between-group comparison. P<0.05 was considered statistically significant. P4: Progesterone, PRL: Prolactin, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

Table 3: Spearman correlation analysis of age and serum hormone levels in the ovarian cancer group

Variable 1	*Variable 2*	*Spearman's ρ*	*P-value*
Age	LH	0.528	<0.001*
Age	FSH	0.749	<0.001*
Age	P4	−0.714	<0.001*
Age	PRL	−0.030	0.838
LH	FSH	0.592	<0.001*
LH	P4	−0.402	0.004*
LH	PRL	−0.297	0.036*
FSH	P4	−0.778	<0.001*
FSH	PRL	−0.065	0.656
P4	PRL	0.113	0.436

Spearman's rank correlation was used. P<0.05 was considered statistically significant; P<0.01 was considered highly significant. n=50, P4: Progesterone, PRL: Prolactin, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

Discussion

The present study identified a distinct but selective endocrine pattern in women with ovarian cancer. As shown in Table 1, women with ovarian cancer were older overall than the healthy controls, with the highest proportions occurring between 41 and 60 years. This difference is important because reproductive aging itself influences circulating gonadotropins and ovarian steroids and should therefore be considered when interpreting the observed endocrine changes. Large longitudinal data from Soares *et al*. demonstrated progressive increases in both FSH and LH across the menopausal transition,[8] whereas Ganie *et al*. also showed substantial age-related variation in reproductive hormones among healthy Indian women.[9]

As presented in Table 2, FSH was significantly higher in ovarian cancer patients, whereas LH did not differ significantly. Parchwani *et al*. similarly reported significantly higher FSH concentrations in women with epithelial ovarian cancer than in healthy controls, whereas no significant association was identified for LH.[10] Their findings closely support the present pattern and suggest that FSH may have a more prominent relationship with ovarian carcinogenesis than LH. Nevertheless, hormonal behavior differs across ovarian histologies; Matsuoka *et al*. demonstrated markedly different gonadotropin and steroid profiles in granulosa-cell tumors compared with other ovarian tumors,[11] emphasizing the biological heterogeneity of ovarian malignancy.

P4 was significantly lower in the ovarian cancer group (0.65 vs. 1.15 ng/mL; $P = 0.006$). However, this finding must be interpreted alongside age and reproductive status. Santoro *et al*. demonstrated declining serum P4 as women approached the final menstrual period.[12] Thus, the lower P4 observed in the present cancer cohort

Table 4: ROC analysis of serum hormones for discrimination between age-matched healthy controls and the ovarian cancer group

Hormone	*AUC*	*Cutoff*	*Sensitivity (%)*	*Specificity (%)*
LH	0.44	5.15	94	16
FSH	0.636	15.25	76	56
P4	0.341	26.5	8	100
PRL	0.78	9.65	96	48

P4: Progesterone, PRL: Prolactin, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, AUC: Area under the curve, ROC: Receiver operating characteristic

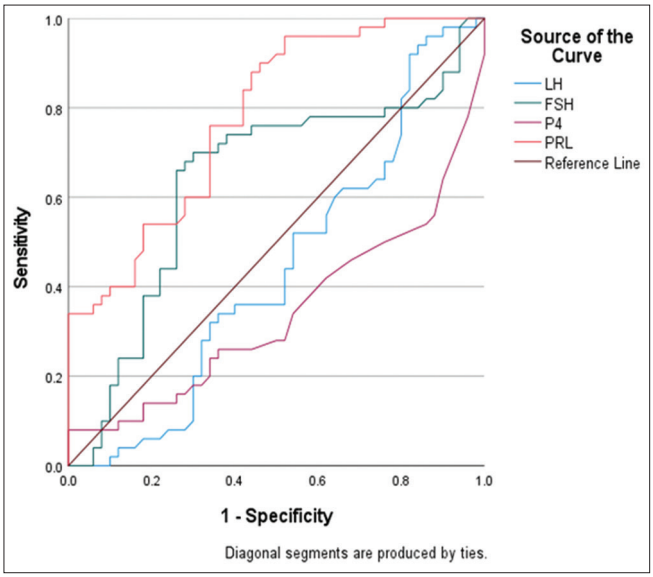

Figure 1: Receiver operating characteristic curves of serum hormones for discrimination between age-matched healthy controls and the ovarian cancer group

may reflect both altered ovarian endocrine function and the older age distribution rather than malignancy alone.

PRL showed the most striking endocrine elevation, increasing from 10.15 ng/mL in controls to 19.40 ng/mL in ovarian cancer patients. This finding is supported by Hathaway *et al*. (2021), who reported a positive trend between circulating PRL and epithelial ovarian cancer risk.[5] Alkharusi *et al*. further demonstrated PRL-receptor expression in 72% of ovarian cancer tissues and showed that PRL signaling could activate pathways involved in ovarian cancer-cell behavior.[13] In addition, Hasenburg *et al*. found that plasma PRL differed between benign and malignant ovarian masses and contributed to a multiprotein model for malignancy prediction.[14]

The correlation pattern in Table 3 showed strong positive relationships of age with FSH and negative relationships with P4, whereas the strongest inter-hormonal association was the inverse FSH–P4 correlation ($\rho = -0.778$). These findings are consistent with the endocrine transition accompanying reproductive aging[8,12] and indicate that age-related hormonal physiology remains closely intertwined with ovarian cancer-associated endocrine changes.

Finally, Table 4 and Figure 1 demonstrated that PRL provided the strongest discrimination (AUC = 0.780), followed by FSH (AUC = 0.636). Despite its high sensitivity of 96%, PRL specificity was only 48%, limiting its value as a stand-alone marker. P4 had an AUC of 0.341 because lower rather than higher concentrations characterized ovarian cancer; therefore, this should be interpreted as inverse discrimination, not absence of an association. Overall, the findings suggest that ovarian malignancy is accompanied by a complex endocrine profile, but these hormones should be interpreted in conjunction with age, reproductive status, and established clinical and pathological parameters.

Strengths, Limitations and Future Directions

A major strength of the present study was the simultaneous evaluation of LH, FSH, P4, and PRL, together with correlation and ROC analyses, allowing a broader assessment of the endocrine environment associated with ovarian malignancy. The study identified clear hormonal differences, particularly higher FSH and PRL concentrations and lower P4 levels in the ovarian cancer group. However, the relatively small sample size, single-center design, heterogeneous ovarian malignancies, and the difference in age distribution between cases and controls may limit the generalizability of the findings. Menopausal status, menstrual-cycle phase, tumor stage, histological subtype, tumor burden, and use of hormonal medications were not available for detailed stratified analysis and may have influenced circulating hormone concentrations. Future multicenter studies with larger, age-balanced cohorts should evaluate endocrine profiles according to menopausal status, histological subtype, and disease stage and explore whether combining hormonal parameters with established tumor markers improves clinical discrimination.

Conclusion

The present study demonstrated that ovarian malignancy is associated with a distinct endocrine profile characterized by significantly higher FSH and PRL concentrations and lower P4 levels, whereas LH did not differ significantly from healthy controls. Strong positive relationships of age with FSH and LH, together with the marked inverse association between FSH and P4, further highlight the interaction between reproductive aging and ovarian endocrine function. Among the evaluated hormones, PRL showed the greatest discriminatory performance, although its limited specificity indicates that it should not be considered a stand-alone diagnostic marker. Overall, these findings suggest that hormonal alterations may provide useful insight into the endocrine milieu of ovarian malignancy, but their interpretation should remain integrated with clinical, radiological, pathological, and established biomarker assessment.

AI Declaration

No generative AI was used for conceptualization, analysis, or content generation. AI use was limited to language refinement, and the authors remain fully responsible for the accuracy, originality, validity, and integrity of the manuscript's content.

References

1. Mikhael S, Punjala-Patel A, Gavrilova-Jordan L. Hypothalamic-pituitary-ovarian axis disorders impacting female fertility. Biomedicines 2019;7:5.
2. Li H, Liu Y, Wang Y, Zhao X, Qi X. Hormone therapy for ovarian cancer: Emphasis on mechanisms and applications (Review). Oncol Rep 2021;46:223.
3. Mauro LJ, Spartz A, Austin JR, Lange CA. Reevaluating the role of progesterone in ovarian cancer: Is progesterone always protective? Endocr Rev 2023;44:1029-46.
4. Szukiewicz D. Current insights in prolactin signaling and ovulatory function. Int J Mol Sci 2024;25:1976.
5. Hathaway CA, Rice MS, Townsend MK, Hankinson SE, Arslan AA, Buring JE, *et al*. Prolactin and risk of epithelial ovarian cancer. Cancer Epidemiol Biomarkers Prev 2021;30:1652-9.
6. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, *et al*. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. BMJ 2007;335:806-8.
7. Obuchowski NA, Bullen JA. Receiver operating characteristic (ROC)

curves: Review of methods with applications in diagnostic medicine. Phys Med Biol 2018;63:07TR01.
8. Soares AG, Kilpi F, Fraser A, Nelson SM, Sattar N, Welsh PI, *et al*. Longitudinal changes in reproductive hormones through the menopause transition in the Avon longitudinal study of parents and children. Sci Rep 2020;10:21258.
9. Ganie MA, Chowdhury S, Suri V, Joshi B, Bhattacharya PK, Agrawal S, *et al*. Normative range of various serum hormonal parameters among Indian women of reproductive age: ICMR-PCOS task force study outcome. Lancet Reg Health Southeast Asia 2023;15:100226.
10. Parchwani D, Dholariya SJ, Takodara S, Singh R, Sharma VK, Saxena A, *et al*. Analysis of prediagnostic circulating levels of gonadotropins and androgens with risk of epithelial ovarian cancer. J Lab Physicians 2022;14:47-56.
11. Matsuoka A, Tate S, Nishikimi K, Kobayashi T, Otsuka S, Shozu M. Serum FSH as a useful marker for the differential diagnosis of ovarian granulosa cell tumors. Cancers (Basel) 2022;14:4480.
12. Santoro N, El Khoudary SR, Nasr A, Gold EB, Greendale G, McConnell D, *et al*. Daily luteal serum and urinary hormone profiles in the menopause transition: Study of women's health across the nation. Menopause 2020;27:127-33.
13. Alkharusi A, AlMuslahi A, AlBalushi N, AlAjmi R, AlRawahi S, AlFarqani A, *et al*. Connections between prolactin and ovarian cancer. PLoS One 2021;16:e0255701.
14. Hasenburg A, Eichkorn D, Vosshagen F, Obermayr E, Geroldinger A, Zeillinger R, *et al*. Biomarker-based early detection of epithelial ovarian cancer based on a five-protein signature in patient's plasma-a prospective trial. BMC Cancer 2021;21:1037.