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# Association of Interleukin-6 rs1800795 and Interleukin-1A rs1800587 Genetic Variants and Their Serum Levels with the Risk of Endometrial Carcinoma in Egyptian Women

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**Abstract**

**BACKGROUND:** Endometrial carcinoma (EC) is the most common gynecological malignancy in women globally. Interleukin-6 (IL-6) and interleukin-1A (IL-1A) are pro-inflammatory cytokines that play a role in immune response against EC. Several genetic variations, such as polymorphism, may alter interleukins expression and influence the risk of EC susceptibility.

**AIM:** The objective of this study is to investigate the association of IL-6 (rs1800795) and IL-1A (rs1800587) polymorphisms and their serum levels with the development of EC versus healthy controls, as well EC prognosis by distribution of these polymorphisms in stages, grades, and histotypes of EC patients in Egyptian women.

**METHODS:** One hundred EC patients and 100 cancer-free controls were recruited in this case–control study. Polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) was used for genotyping of IL-6 rs1800795 and IL-1A rs1800587 polymorphisms in both groups. ELISA was performed to measure the levels of IL-6 and IL-1A in all participants.

**RESULTS:** The proportions of C allele, homozygous CC genotype, and heterozygous GC genotype of IL-6 rs1800795 polymorphism were significantly elevated in EC patients when compared with the control individuals. IL-6 rs1800795 CC genotype was significantly greater in the advanced stage than in the early stage of EC. However, IL-1A rs1800587 polymorphism's T allele and genotypes (TT and CT) were not associated with EC patients versus healthy controls. Furthermore, EC patients exhibited significantly higher serum levels of IL-6 and IL-1A than the healthy controls. The genotypes' distribution of IL-6 rs1800795 and IL-1A rs1800795 was not significantly associated with their serum levels in EC patients and controls.

**CONCLUSIONS:** IL6 rs1800795 CC genotype was associated with EC, particularly in the advanced stage, and this suggests that this genotype represents a prognostic biomarker for EC. In addition, both IL-6 and IL-1A serum levels were significantly elevated in EC patients when compared with healthy individuals, suggesting a potential value in differential diagnosis of the disease.

## Introduction

Approximately 382,000 new cases of endometrial carcinoma (EC) are diagnosed worldwide each year, among whom around 90,000 women die from this disease [1]. Egypt and South Africa have the highest rates of EC in Africa [1]. The tumorigenesis of EC is a complicated process involving numerous dysregulated genes [2]. Moreover, EC can be caused by genetic disorders, and serum levels of various tumor markers are increased in 20%–30% of EC patients [3], [4]. EC patients' survival is significantly associated with several accepted prognostic factors such as stage, grade, and histotype of the disease established by Buchman classification [5] and FIGO (International Federation of Gynecology and Obstetrics) [6].

Interleukin-6 (IL-6) is a cytokine produced by a variety of cells including cancer cells, and it plays a crucial role in tumor growth and cell differentiation [7]. IL-6 promoter polymorphism (rs1800795) at position 174 has been associated with a variety of cancer risks in a number of previous investigations [8], [9], [10]. IL-6 rs1800795 polymorphism is thought to enhance the incidence of gynecological cancers, including EC [11], [12]. Furthermore, high levels of circulating IL-6 have been associated with EC, according to a recent Chinese study [13].

Interleukin 1A (IL-1A) belongs to the interleukin 1 cytokine family, which plays a role in tumor proliferation, invasion, metastasis, as well as interactions of the malignant cells with the host's immune system [14]. Moreover, IL-1A would create an immune memory for tumor cells, allowing the immune system to attack them [15]. Of interest, numerous studies found association between several polymorphisms of IL-1A and several gynecological diseases, such as endometriosis [16], polycystic ovary syndrome [17], and

cervical cancer [18]. Besides, rs1800587 polymorphism, which is located at position -889 of the IL1A promoter region, has been associated with gynecological cancer [19] and could affect IL-1A expression [20].

This is the first study to investigate the association of IL-6 rs1800795 and IL-1A rs1800587 polymorphisms and their serum levels with the incidence of EC in Egyptian population. In addition, the study sought to link the distribution of the genotypes of both investigated polymorphisms with clinical and pathological parameters among EC patients.

## Subjects and Methods

### *Subjects*

A case–control study was conducted on 200 women who were divided into two groups. Group I included 100 patients, with pathological proven EC, who were recruited from the Obstetrics and Gynecology Department and the Oncology Center, Mansoura University, Egypt, from November 2021 to April 2022. Group II included an equal number of age- and body mass index (BMI)-matched healthy control subjects, who had undergone pelvic ultrasonography that showed no evidence of malignancy or diseases of the uterus.

General abdominal and pathological evaluations after patient endometrial biopsy or after hysterectomy were used to ascertain surgical staging, grading, and histological classifications. The clinical or pathological disease stage, grade, and histotype during the diagnosis were determined using the FIGO staging system revised 2018 [6].

### *Exclusion criteria*

Patients with other types of malignancy, inflammation, or infectious diseases and those with injury or suffering from any active disease were excluded from the study. Pregnant women and women with alcohol intake or smoking history were also excluded from the study.

### *Ethical consideration*

All participants provided written informed consent agreements in correspondence to the ethical principles of the Declaration of Helsinki. The study followed protocols approved by the Research Ethics Committee of Faculty of Pharmacy, Suez Canal University, Egypt (code #201706PHDH1). The study protocol was also approved by the Institutional Review Board (IRB) (approval number: R.20.10.14) on October 22, 2020, provided by the Research Ethics of the Faculty of Medicine, Mansoura University, Egypt.

### *Sample collection and preparation*

Venous blood samples (5 mL) were drawn; 2 mL of whole blood was collected in ethylenediaminetetraacetic acid (EDTA) tubes and used for total genomic DNA extraction, while 3 mL was collected in plain tubes for serum separation. Serum was prepared by allowing the whole blood to clot for 30 min at room temperature, followed by centrifugation at 2500 rpm for 15 min. The serum supernatant was used to determine the IL-6 and IL-1A levels. The samples were immediately stored at −80°C until analysis.

### *Extraction of genomic DNA and genotyping*

Determination of IL-6 rs1800795 and IL-1A rs1800587 polymorphisms was performed by polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP) analysis. Genomic DNA was extracted from the leukocyte portion of whole blood using the GeneJET Whole Blood Genomic DNA Purification Mini Kit (Thermo Fisher, Vilnius, Lithuania; Cat. No. K0781).

Approximately 100 ng of DNA as a template in PCR, flanking the −174 G/C polymorphism (rs1800795) of the IL-6 gene, using forward primer 5'-TTGTCAAGACATGCCAAAGTG -3' and reverse primer 5'-TCAGACATCTCCAGTCCTATA-3', and the temperature profile: 94°C, 56°C, and 72°C for 30 s each, for a total of 30 cycles was used. The amplified PCR product of 300 bp was restricted with endonuclease *NIa III* restriction enzyme (Waltham, MA, USA; Cat. No ER1831) for 2 h at 37°C then the PCR products were verified on 2% agarose gel along with a 50 base pair (bp) DNA size marker (GeneDireX, Taiwan), visualized by ultraviolet transillumination, and photographed after staining with ethidium bromide, which yielded 13 + 54 + 233 bp fragments in the GG homozygous state, 13+54+111+122 bp fragments in the CC homozygous genotype, and 13+54+111+122+233 bp fragments in GC heterozygous [19].

For IL-1A −889 C/T (rs1800587), forward primer 5'-GCATGCCATCACACCTAGTT-3' and reverse primer 5'-TTACATATGAGCCTTCCATG-3' were employed and the following temperature profile was used: 92°C for 30 s for denaturation, and 56°C and 60°C for 1 min each for annealing and extension, for a total of 40 cycles. The amplified product of 193 bp was analyzed using Fast Digest NcoI as a restriction enzyme (Waltham, MA, USA; Cat No. FD0574) for 5 min at 37°C, which was verified on 2% agarose gel along with a 50 bp DNA size marker (GeneDireX, Taiwan). The products were visualized by ultraviolet transillumination and photographed after staining with ethidium bromide to visualize allele-specific fragments, which yielded 174 + 19 bp fragments in the CC homozygous state, while allele T had no recognition site [21].

### *Serum IL-6 and IL-1A levels*

Determination of the serum levels of IL-6 and IL-1A was carried out using commercially available enzyme-linked immunosorbent assay (ELISA) kits [(Boster Co., USA) (Cat No. EK0389) and (Cat No. EK0410), respectively].

### *Statistical analysis*

Data were analyzed using IBM-SPSS software (IBM Corp., released 2017, IBM SPSS Statistics for Windows, Version 25.0; IBM Corp., Armonk, NY, USA). Qualitative data were expressed as frequencies and percentages and compared using the Chi-square test. Quantitative data were initially tested for normality using Shapiro–Wilk test, with data being normally distributed if $p > 0.05$. The presence of significant outliers was tested for by inspecting boxplots. Quantitative data were expressed as mean ± standard deviation (SD) if normally distributed or expressed as median and interquartile range (IQR) if not normally distributed, and compared using Mann–Whitney U-test for two groups comparisons, Kruskal–Wallis for three groups comparisons, or one-way analysis of variance (ANOVA) was used for multiple groups. For any of the used tests, results were considered statistically significant if $p \leq 0.05$. For statistical analysis of single-nucleotide polymorphism (SNP), data were analyzed using SNPStats software (https://www.snpstats.net/start.htm).

## Results

Age and BMI in the EC patients were not significantly different when compared with the control group ($p = 0.323$ and $p = 0.401$, respectively). Stage, grade, and histotype of tumors were collected from the patient database. Most cases of EC were diagnosed at early stages (IA, IB, and II), low grade (1 and 2), and histotype (1), while a few cases were at advanced stages (IIIA, IIIB, and IIIC), high grade (3), and histotype (2). The frequencies of different EC stages, grades, and histotypes are presented in Table 1. Endometrial tumors were classified histologically according to FIGO [14], [22].

In all patients and controls, IL-6 rs1800795 genotype frequencies were in Hardy–Weinberg equilibrium (HWE), whereas IL-1A rs1800587 genotype frequencies were not.

Regarding to IL-6 rs1800795 polymorphism, Table 2 shows that in EC patients, the proportion of C allele, when compared to G allele, was statistically significantly greater in EC than in control individuals. Patients with the C allele had 2.19 times higher likelihood of developing EC than those with the G allele (OR = 2.19, 95% CI = 1.38–3.5, $p = 0.001$). Furthermore, the heterozygous GC genotype and the rare homozygous CC genotype were significantly higher in the EC patients versus the control when compared to the common GG genotype [(OR = 2.12, 95% CI = 1.15–3.89, $p = 0.015$), and (OR = 4.34, 95% CI = 1.32–14.28, $p = 0.016$), respectively] (Table 2). On the other hand, for the IL-1A rs1800587 polymorphism, there was no statistically significant difference between EC patients and controls for the proportion of T allele compared to C allele, and for CT and TT genotypes compared to CC genotype [(OR=1.04, 95% CI = 0.64-1.6, $p = 0.834$), (OR=1.4, 95% CI = 0.78-2.5, $p = 0.25$), and (OR = 0.65, 95% CI = 0.2–2.14, $p = 0.48$), respectively] (Table 2).

**Table 1: Clinical and biochemical parameters of EC patients and healthy control subjects**

| Parameter | Group | | Test of significance | |
|---|---|---|---|---|
| | EC (n = 100) | Control (n = 100) | Z | p |
| Age (years) | 58 (52.5–62) | 56.5 (52.3–60) | −0.989 | 0.323 |
| BMI (kg/m$^2$) | 34.5 (30.8–37.9) | 35 (30.9–39) | −0.840 | 0.401 |
| Stages (%) | | | | |
| Early stage | | | | |
| I A | 46 | | | |
| I B | 33 | | | |
| II | 6 | | | |
| Advance stage | | | | |
| III A | 7 | | | |
| III B | 6 | | | |
| III C | 2 | | | |
| Grades (%) | | | | |
| Low grade | | | | |
| Grade 1 | 73 | | | |
| Grade 2 | 10 | | | |
| High grade | | | | |
| Grade 3 | 17 | | | |
| Types | | | | |
| Type I (endometrioid adenocarcinoma) | 80 | | | |
| Type II (papillary serous clear cell carcinoma) | 20 | | | |

Comparison by Mann–Whitney U-test; data expression: Frequency (percentage). BMI: Body mass index, Z: z value, EC: Endometrial carcinoma

**Table 2: Allele frequencies and genotype distribution of interleukin-6 rs1800795 and interleukin-6A rs1800587 polymorphisms in the endometrial carcinoma patients and healthy control subjects**

| SNP | Alleles/ genotypes | Group | | OR (95% CI) | p value of OR |
|---|---|---|---|---|---|
| | | EC (n = 100), n (%) | Control (n = 100), n (%) | | |
| IL-6 rs1800795 | G | 135 (74) | 164 (82) | R | |
| | C | 65 (26) | 36 (18) | 2.19 (1.38–3.50) | 0.001* |
| | GG | 47 (47) | 68 (68) | R | |
| | GC | 41 (41) | 28 (28) | 2.12 (1.15–3.89) | 0.015* |
| | CC | 12 (12) | 4 (4) | 4.34 (1.32–14.28) | 0.016* |
| IL-1A rs1800587 | C | 129 (64) | 131 (66) | R | |
| | T | 71 (36) | 69 (34) | 1.04 (0.64–1.6) | 0.834 |
| | CC | 34 (34) | 40 (40) | R | |
| | CT | 61 (61) | 51 (51) | 1.40 (0.78–2.5) | 0.25 |
| | TT | 5 (5) | 9 (9) | 0.65 (0.2–2.14) | 0.48 |

Comparisons of column proportions with Bonferroni adjustment, data expression: Frequency (percentage). p value of OR by simple binary logistic regression. *p value is significant if ≤ 0.05. OR: Odds ratio, CI: Confidence interval, R: Reference category, EC: Endometrial carcinoma, IL: Interleukin, SNP: Single-nucleotide polymorphism

The serum levels of IL-6 and IL-1A were measured using ELISA. Significantly higher IL-6 and IL-1A levels were found in the EC patients compared with the control subjects ($p < 0.0005$ for both) (Table 3).

**Table 3: Interleukin-6 and interleukin-1A serum levels in the endometrial carcinoma patients and healthy control subjects using enzyme-linked immunosorbent assay**

| ILs | Groups | | Test of significance | |
|---|---|---|---|---|
| | EC (n = 100) | Control (n = 100) | Z | p |
| IL-6 | 1.1 (0.9–1.3) | 0.9 (0.7–1.1) | −3.562 | < 0.0005* |
| IL-1A | 3.5 (3.0–3.8) | 2.5 (1.9–2.8) | −10.389 | < 0.0005* |

Comparison by Mann–Whitney U-test. *p value is significant if ≤ 0.05. EC: Endometrial carcinoma, IL: Interleukin.

**Table 4: Association between levels of interleukin-6 and interleukin-1A and the genotypes of their corresponding polymorphisms in the endometrial carcinoma patients and healthy control subjects**

| Gene/genotypes | EC | | | p | Control | | | p |
|---|---|---|---|---|---|---|---|---|
| IL-6 rs1800795 | CC | GC | GG | | CC | GC | GG | |
| n | 12 | 41 | 47 | 0.823 | 4 | 28 | 68 | 0.243 |
| Mean ± SD | 1.1 ± 0.25 | 1.1 ± 0.29 | 1.07 ± 0.32 | | 0.75 ± 0.13 | 0.85 ± 0.32 | 0.96 ± 0.38 | |
| Eta (η) | 0.063 | | | | 0.170 | | | |
| Gene/genotypes | EC | | | p | Control | | | p |
| IL-1A rs1800587 | CC | CT | TT | | CC | CT | TT | |
| n | 40 | 51 | 9 | 0.821 | 34 | 61 | 5 | 0.742 |
| Median (IQR) | 3.5 (3.0–3.8) | 3.4 (3.0–3.9) | 3.5 (3.1–4.0) | | 2.5 (1.9–2.9) | 2.5 (2.0–2.8) | 2.3 (1.3–2.9) | |
| Eta (η) | 0.083 | | | | 0.080 | | | |

p value: One-way ANOVA for IL-6 and Kruskal–Wallis for IL-1A; Eta values assess the association between genotypes (nominal variable) and IL-6/IL-1A levels (interval variable). IQR: Interquartile range, SD: Standard deviation, EC: Endometrial carcinoma, IL: Interleukin, ANOVA: Analysis of variance.

In both EC patients and control groups, there was no statistically significant difference between IL-6 and IL-1A levels and the genotypes of the corresponding polymorphisms [(p = 0.823, p = 0.243), and (p = 0.821, p = 0.742), respectively] (Table 4).

Table 5 shows that the rare homozygous CC genotype of IL-6 rs1800795 was significantly more frequent in those with advanced stage versus early stage of the disease (OR = 6, 95% CI = 1.37–26.2, p = 0.017). However, the heterozygous GC genotype of IL-6 rs1800795 was not significant in the early and advanced stages (p = 0.819). In addition, there was no statistically significant difference between early and advanced stages of disease with regard to the genotypes (CT and TT) of IL-1A rs1800587 polymorphism (p = 0.552 and p = 0.898, respectively).

**Table 5: Distribution of the interleukin-6 rs1800795 and interleukin-1A rs1800587 genotypes in the different stages of endometrial carcinoma patients**

| Gene/genotypes | Early, n (%) | Advanced, n (%) | OR (95% CI) | p |
|---|---|---|---|---|
| n | 85 | 15 | | |
| IL-6 rs1800795 | | | | |
| GG | 42 (49.4) | 5 (33.3) | R | |
| GC | 36 (42.4) | 5 (33.3) | 1.167 (0.31–4.35) | 0.819 |
| CC | 7 (8.2)* | 5 (33.3)* | 6 (1.37–26.2) | 0.017* |
| IL-1A rs1800587 | | | | |
| CC | 28 (32.9) | 6 (40 ) | R | |
| CT | 53 (62.4) | 8 (53.3) | 0.704 (0.22–2.23) | 0.552 |
| TT | 4 (4.7) | 1 (6.7) | 1.167 (0.11–12.4) | 0.898 |

Comparisons of column proportions with Bonferroni adjustment, data expression: n (%). p value of OR by simple binary logistic regression. *p value is significant if ≤ 0.05. OR: Odds ratio, CI: Confidence interval, R: Reference category, IL: Interleukin.

Table 6 shows that there were no significant differences in the distribution of all studied genotypes of IL-6 rs1800795 and IL-1A rs1800587 polymorphisms among the different tumor grades (p = 0.118 and p = 0.456, respectively) and histotypes (p = 0.233 and p = 0.539, respectively).

## Discussion

Endometrial carcinoma (EC) is one of the most common malignant tumors in the female reproductive system. Early detection is critical to improve the prognosis of EC [4], [23]. Novel and sensitive biomarkers could be used to enhance EC patients' early diagnosis [3]. Interleukins and other cytokines are crucial immunoregulatory biomarkers that can also impact the proliferation, maturation, adhesion, and metastasis of many types of cells, including endometrium tumor cells [4]. Due to the critical role of diagnosis and prognosis in EC, the present study aimed to explore the association of IL-6 rs1800795 and IL-1A rs1800587 polymorphisms along with their serum levels with the EC occurrence and to relate their genotypes with clinicopathological parameters (stage, grade, and histotype) in Egyptian EC patients.

Inteleukin-6 (IL-6) rs1800795 polymorphism is a SNP in the IL-6 gene promoter at −174 position that was found to increase the risk of gynecological malignancies; including EC [24]. IL-6 rs1800795 was postulated to affect the transcription and expression of IL-6 gene, making it a common target in tumor research [25]. Our results showed a statistically significant difference in the distribution of C allele, homozygous CC genotype, and heterozygous GC genotype of IL-6 rs1800795 in EC patients, which came in agreement with a previous genetic study which reported that −174 C allele and −174 CC genotype of IL-6 rs1800795 were significantly more prevalent in EC patients than in healthy control subjects in Chinese population [10]. Another study found that the frequency distribution of IL-6 (rs1800795) GC genotype was significantly associated with a type of cancer in comparison to healthy controls [26].

In recent years, various studies have investigated the function of IL-6 in the formation and progression of malignant tumors, indicating that this cytokine has been involved in a variety of tumor tissues [25]. In agreement, the EC patients in the current study had significantly higher serum levels of IL-6 than the control group. This complied with the previous studies [27], [28]. The explanation for the correlation of IL-6 levels with susceptibility to gynecological cancer could be that the expression of IL-6 contributes to the tumor cells' escape from immune surveillance and the promotion of oncogenesis [29].

Furthermore, our study did not find any significant difference in the association between IL-6 serum levels and different genotypes of rs1800795 (GG, GC, and CC) in both EC patients' group and control group. Our findings were consistent with recent studies on ovarian cancer in Egypt [30], cervical cancer in India [31], and many disorders in the United States and Egypt [32], [33].

**Table 6: Distribution of the interleukin-6 rs1800795 and interleukin-1A rs1800587 genotypes in the different grades and types of endometrial carcinoma patients**

| Gene/genotypes | Grade | | OR (95% CI) | p | Type | | OR (95% CI) | p |
|---|---|---|---|---|---|---|---|---|
| | Low grade, n (%) | High grade, n (%) | | | Type 1, n (%) | Type 2, n (%) | | |
| n | 83 | 17 | | | 80 | 20 | | |
| IL-6 rs1800795 | | | | | | | | |
| GG | 42 (50.6) | 5 (29.4) | R | | 40 (50) | 7 (35) | R | |
| CC-GC | 41 (49.4) | 12 (70.6) | 0.4 (0.1–1.2) | 0.118 | 40 (50) | 13 (65) | 1.9 (0.7–5.1) | 0.233 |
| IL-1A rs1800587 | | | | | | | | |
| CT | 52 (62.6) | 9 (52.9) | R | | 50 (62.5) | 11 (55) | R | |
| CC-TT | 31 (37.3) | 8 (47.1) | 0.7 (0.2–1.9) | 0.456 | 30 (37.5) | 9 (45) | 1.4 (0.506–3.7) | 0.539 |

Comparisons of column proportions with Bonferroni adjustment, data expression: n (%). p value of OR by simple binary logistic regression. OR: Odds ratio, CI: Confidence interval, R: Reference category, IL: Interleukin.

Moreover, our results detected a significant increase in the occurrence of the IL-6 (rs1800795) CC genotype at the advanced stage versus early stage, indicating that this polymorphism might have a useful prognostic value for EC. The same finding was found in cervical cancer [31] and in breast cancer [34].

In addition, our results did not detect any significant relation of the IL-6 rs1800795 genotypes with grade and histotype of EC in the patients. A number of factors could have contributed to these findings whereas the genotypes of IL-6 rs1800795 influenced by medication, psychological factors such as depression [35], diet, and nutritional status [36].

In terms of IL- 1A (rs1800587), we detected no significant difference in the proportion of alleles (C vs. T) and genotypes (CC and CT vs. TT) among EC patients. In the Chinese population, a meta-analysis study found no significant association between the risk of C allele, and the genotypes (CT and TT) of IL-1A (rs1800587) and cancer susceptibility [19].

Our results revealed that there were significantly higher IL-1A serum levels in the EC group relative to the control group. Litmanovich *et al*. confirmed this result [37]. As well, Daley-Brown *et al*. verified the prior finding among African-American and Chinese patients [38]. Different reasons may account for increased IL-1A levels in EC patients. IL-1A in the tumor microenvironment can stimulate the development, invasion, and metastases of cancer cells [37], [19]. On the other hand, some reports have indicated that the immune response mediated by IL-1A builds up immunological memory for tumor cells, allowing it to continue to play antitumor roles by directing the immune system to destroy tumor cells [19]. As a result, IL-1A could have both cancer-causing and anticancer effects; and more research into this interesting and potent point is needed.

In addition, we observed that there was no significant difference/association between IL-1A serum levels and rs1800587 polymorphisms' genotypes in both EC patients and control groups. Eser *et al*. detected the same result in gynecologic disease [39].

Our study did not find any significant relation of IL-1A rs1800587 polymorphism with the clinical prognostic parameters such as FIGO stage, grade, and histotype of EC. A similar finding was observed by Ioana *et al*. who clarified no correlations between the distribution of the IL-1A (rs1800587) alleles and the same parameters of ovarian cancer [40].

Cancer development is a complex process. Therefore, it is recommended to validate the results in larger and various ethnicities and to investigate them as predictors and therapeutic targets in EC.

This study is limited by the small sample size of the patient population. Further, the studied polymorphisms may vary ethnically and this study examined these polymorphisms in the Egyptian population only.

## Conclusions

The present study manifested that the C allele, homozygous CC genotype, and heterozygous GC genotype of IL-6 rs1800795 are associated with the risk of EC and exhibit a correlation between CC genotype of IL-6 rs1800795 with the advanced stage of EC. Consequently, IL-6 rs1800795 polymorphism and its genotype (CC) help in the prognosis of EC. Furthermore, there were higher serum levels of both IL-6 and IL- 1A cytokines in the EC group. Accordingly, they may serve as diagnostic and prognostic markers predicting the development of EC.

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