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Research Article

**NFKBIA PROMOTER POLYMORPHISMS CONTRIBUTE TO
A DECREASED RISK OF OVARIAN CANCER**Dr. Muhammad Fasih Tariq¹, Dr. Hafiza Mahnoor Fatima², Dr. Mariyam Khalid¹¹District Headquarter Hospital, Khanewal²Bahawal Victoria Hospital, Bahawalpur**Article Received:** June 2020**Accepted:** July 2020**Published:** August 2020**Abstract:**

Introduction: Ovarian cancer is one of the leading forms of cancer, in worldwide. Each year, there is an estimated 225,500 new incidences of ovarian cancer cases globally. The lack of effective screening methods causes >70% of ovarian cancer patients to be diagnosed at late stages, which leads to the low 5-year survival rate and high mortality rate of the disease. **Objectives of the study:** The basic objective of the study is to find the NFKBIA promoter polymorphisms which contribute towards the decreased risk of ovarian cancer in females. **Materials and methods:** This cross sectional study was conducted in Bahawal Victoria Hospital, Bahawalpur during June 2019 to March 2020. The genomic DNA obtained was then used in polymerase chain reaction (PCR). **Result:** The association of the inflammatory gene polymorphisms with ovarian cancer risk was measured in OR units, with the wild type genotype served as the reference. **Conclusion:** It is concluded that there is no association found in NFKB1A genetic polymorphism and ovarian cancer in local population of Pakistan.

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INTRODUCTION:

Ovarian cancer is one of the leading forms of cancer, in worldwide. Each year, there is an estimated 225,500 new incidences of ovarian cancer cases globally. The lack of effective screening methods causes >70% of ovarian cancer patients to be diagnosed at late stages, which leads to the low 5-year survival rate and high mortality rate of the disease¹. Worldwide, ovarian cancer contributes to 114,000 deaths annually. A method for the identification of individuals at a higher risk of the cancer is therefore necessary for improving ovarian cancer screening strategy².

The principal risk factors for the occurrence of ovarian cancer are germ line mutations in the *BRCA1* or *BRCA2* genes. However, the carriers of such mutations account for only a small portion of total ovarian cancer cases, and a substantial proportion of ovarian cancer risk among sporadic cases remained unexplained³. It has been suggested that common low penetrance genetic variations could confer moderate risk to ovarian cancer cases without a heritable basis. Single nucleotide polymorphisms of genes involved in cancer-related pathways represent the candidates of such genetic variations⁴.

Cancer cells are characterized by the attainment of several characteristics that enable them to become tumorigenic¹. Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells⁵. If the spread is not controlled, it can result in death. Cancer is initiated by both external factors (tobacco, infectious organisms, chemicals, and radiation) and internal factors (inherited mutations, hormones, immune conditions, and mutations that occur from metabolism). These contributory factors may act collectively or in sequence to initiate or promote carcinogenesis⁶.

In Pakistan, ovarian disease is the fourth most regular danger in ladies. It is the most well-known disease of gynecologic origin. No data, in any case,

is accessible on the clinico-obsessive highlights and biologic conduct of this growth or if any distinctions exist amongst Pakistani and U.S. or then again European patients⁷.

Objectives of the study

The basic objective of the study is to find the NFKB1A promoter polymorphisms which contribute towards the decreased risk of ovarian cancer in females.

MATERIALS AND METHODS:

This cross-sectional study was conducted in Bahawal Victoria Hospital, Bahawalpur during June 2019 to March 2020. For this study we select the 20 female patients who was suffering from ovarian cancer. The blood was drawn for further analysis of micronutrients. Genomic DNA was extracted from the blood samples obtained using Blood Genomic DNA Kit according to the manufacturer's protocol. The genomic DNA obtained was then used in polymerase chain reaction (PCR). The genetic polymorphisms were detected by the PCR-restriction fragment length polymorphism (RFLP) method. Researchers were blinded to the identity and the case-control status of the samples. For all polymorphisms, ~10% of the samples were chosen at random and sequenced to confirm the genotypes.

Statistical analysis

Two-way ANOVA was performed to study the contributions. A chi-square test was used to examine the difference in the distribution of the fracture modes (SPSS 19.0 for Windows, SPSS Inc., USA).

RESULT:

The association of the inflammatory gene polymorphisms with ovarian cancer risk was measured in OR units, with the wild type genotype served as the reference. The risk association was summarized in table 01. There is no significant risk association was observed for the GC genotype of the NFKB1A polymorphism.

Table 01: Analysis of risk association of the polymorphisms with ovarian cancer.

Genotype	Patients	Controls	OR (95% CI)	p
PPARG				
Pro/Pro	624	643	Reference	—
Pro/Ala	62	42	1.52 (1.01–2.29)	0.04
Ala/Ala	1	2	0.52 (0.05–5.70)	0.59
IL6				
GG	683	676	Reference	—
GC	4	11	0.36 (0.11–1.14)	0.08
CC	0	0	—	—
E-selectin				
AA	662	644	Reference	—
AC	25	43	1.77 (1.07–2.93)	0.03
CC	0	0	—	—
NFKB1				
Del/Del	221	253	Reference	—
Del/Ins	351	339	1.19 (0.94–1.50)	0.15
Ins/Ins	115	95	1.39 (1.00–1.92)	0.05
NFKBIA				
CC	486	478	Reference	—
CT	181	190	0.94 (0.74–1.19)	0.59
TT	20	19	1.04 (0.55–1.96)	0.92
ICAM-1				
KK	209	180	Reference	—
KE	322	362	0.77 (0.60–0.98)	0.04
EE	156	145	0.93 (0.69–1.25)	0.62

DISCUSSION:

Important intracellular signal transduction pathways that are necessary for the action of some antineoplastic agents can also be affected by oxidative stress. There are two major pathways of drug-induced apoptosis following cellular damage by anti-neoplastic agents: (1) The mitochondrial pathway, initiated by release of cytochrome c; and (2) the CD95 death receptor pathway, initiated by CD95L binding to its death receptor⁸.

Unlike several other Asian countries, ovarian cancer is the most common cancer of gynecologic origin in Pakistani women. This study is probably the first detailed account of clinico-pathologic features of these patients. Such information is rarely forthcoming from other developing countries making it difficult to compare the results⁹.

The link between inflammation and cancer development has been well established.⁶ However, studies investigating the relationship between inflammatory gene polymorphisms and cancer risk have generated contradictory findings¹⁰. The allelic distributions of various polymorphisms could vary geographically and ethnically, thus leading to the discordant findings between these polymorphisms and cancer risk. In this study, we reported the association between six inflammatory gene polymorphisms and ovarian cancer risk in a

Chinese population. Our analysis showed that three of the polymorphisms were associated with an increased ovarian cancer risk, and one polymorphism was associated with a decreased ovarian cancer risk¹¹.

PPARG encodes for PPAR- γ , a member of the nuclear hormone receptor super family which has been shown to play a pivotal role in regulating cell differentiation, cell growth, glucose, and lipid metabolism, and several other processes known to be important in carcinogenesis¹². Activation of PPAR- γ causes a series of reactions that regulates the production of proinflammatory cytokines, including interleukin(IL)-6¹³. The variant allele of the *PPARG* Pro12Ala polymorphism has been shown to be associated with a reduced transcriptional activity of PPAR- γ . As such, this polymorphism has been hypothesized to contribute to an increased cancer risk. Our findings indicate that the Pro/Ala genotype of the *PPARG* Pro12Ala polymorphism was associated with an increased ovarian cancer risk¹⁴.

CONCLUSION:

It is concluded that there is no association found in NFKB1A genetic polymorphism and ovarian cancer in local population of Pakistan.

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