

Relationship of SNPs (rs3212227) in IL-12 with Gynecological and Breast Cancer

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Abstract

Cancer refers to any disease among a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissues. Cancer often has the ability to spread throughout the body. Cancer is the second leading cause of death in the world, Cancers can occur in any part of the female reproductive system — the vulva, vagina, cervix, uterus, fallopian tubes, or ovaries. These cancers are called gynecologic cancers.

Gynecological cancers can invade directly nearby tissues and organs, or spread (metastasize) through the lymph vessels, lymph nodes (lymph system), or the bloodstream to distant parts of the body. Breast cancer occurs when some breast cells begin to grow in an abnormal way. These cells divide more rapidly than healthy cells and continue to accumulate, forming a lump or tumor. The cells may spread (metastasize) through the breast to the lymph nodes or to other parts of the body.

Interleukin-12 (IL-12) is an anti-inflammatory cytokine that links innate and adaptive immune responses against cancer cells. Single nucleotide polymorphisms (SNPs) in the IL-12 genes have been associated with cancer risk. The role of IL-12 in breast cancer and gynecological risk overall, association of the IL-12 signaling pathway and BC risk in women, The current study aims to evaluate the role of Interleukin-12 gene polymorphism among patients who have breast and gynecological cancer ,Interleukin-12 SNPs detection from patients and control DNA. , 199 samples were taken and divided into (120) patient blood samples and (79) samples as a control group, Women enrolled in the present study complain of the following types of cancer: breast cancer was seen in 50 patients out of 120, uterine cancer was seen in 50 patients out of 120, ovarian cancer was seen in 10 patients and cervical cancer was seen in 10 patients out of 120. SNP rs3212227 (IL 12 gene) was determined by: PCR RFLP

PCR RFLP was performed for identification of IL-12 (rs3212227) gene polymorphism in cancer patients and in healthy control blood samples. This method was carried out according to described by (Jafarzadeh , 2015) ,The statistical analysis and presentation of data in the current study showed that (120) women with cancer (uterus, breast, ovaries, and cervix) were included as a study group, while the control group consisted of (79) healthy women.

The prevalence of the homozygous (A / A) wild genotype, associated with IL-12, was 75.9% (60 of 79) in the control group and 56.7% (68 of 120) in the study group. In addition, the prevalence of the wild and recessive genotype (A / C), associated with IL-12, was 21.5% (17 of 79) in the control group and 33.3% (40 of 120) in the study group. Moreover, the prevalence of a homozygous recessive genotype (C / C) was associated with IL-12, 2.5% (2 of 79) in the control group and 10.0% (12 of 120) in the study group. The difference in these rates was significant (P = 0.012).

A significant proportion (9.2 %) of women were younger than 40. This mean that in our community risk factors associated with these malignancies need to be searched for and studied thoroughly in order to identify reasons behind acquisition of such malignant tumors by women in their fourth decade of life .Individual harboring IL-12 A allele is less likely to get cancer by 0.58% that individual lacking this allele; whereas an individual harboring IL-12 C allele is at 2.37 fold risk to develop cancer in comparison with an individual who lacks this allele .We conclude from that Wild IL-12 (A) allele may play a protective role against cancer. Whereas the recessive IL-12 allele (C) may play a carcinogenic role.

Keywords: Gynecological cancer , Breast cancer, Interleukin-12, SNP.

Introduction

Cancer is a group of diseases involving the abnormal growth of cells with the potential to invade or spread to other parts of the body. Changes may result from an interaction between an individual's genetic factors and three classes of external factors, including: biological, chemical, and physical carcinogens, such as infection from certain viruses, bacteria, or parasites (1).

Cancer that begins in a woman's reproductive system is called gynecological carcinomas (cervical, ovarian, uterine, vaginal and vulvar cancer). When gynecological cancers are caught early, treatment is very effective (2).

Breast cancer is the most common type of malignancy among women, and its incidence is increasing all over the world. It has the highest mortality rate of any type of cancer in women. It is well known that breast cancer is the most feared type of cancer for females; it is the most common malignant neoplasm and the second leading cause of cancer death in women (3).

Cytokines are molecules that cells secrete in response to certain stimuli that change the behavior of the cells themselves or other cells. Cytokines are important molecules that work in the defense of the organism against viral infection. Several genetic studies have attempted to link cytokine polymorphisms to human diseases, including cancer. The importance of the IL12 polymorphism to cancer is that it has both immunosuppressive and antiangiogenic properties (4).

IL-12B gene coding is located in the chromosome (5q 31-33) in humans. (rs3212227) is located in the untranslated region 3 of the cytokine gene. (5). Rs3212227 has been demonstrated to be functionally important as it alters IL-12 production and is associated with cancer. (6)

This study was performed among patients with breast cancer to assess serum level of IL-12 in Iran in addition to its association with tumor stages and SNP rs3212227 (7).

As for cancer research, the focus has been on nucleotides that alter gene function or gene expression, as this allows researchers to try to explain the observed links to a mechanism of pathogen. Indeed, gene polymorphisms in functionally important genes have been proposed as risk factors for the development of a variety of cancers, including endometrial cancer. Candidate SNPs may be involved in DNA damage repair, steroid metabolism, carcinogen metabolism, cell cycle control, programmed cell death and steroid receptor activation pathways over the past few decades, and extensive efforts have been made in identifying sources of genetic susceptibility to cancer (8).

The role of the immune system in shaping cancer development and prognosis has recently become an intense area of focus in the industry. Harnessing the immune adaptive arm for tumor resection has shown promising results in a variety of tumor types. Therefore, as the differences between tissues require a greater understanding of the adaptive immune programs active within each tumor type. In breast cancer, adaptive immune programs play diverse roles depending on the cell infiltration present in each tumor. Cytotoxic T lymphocytes and type 1 helper T cells can induce tumor resection, while regulatory T cells and helper T cells type 2 have been known to participate in immunosuppressive responses to tumor booster (9).

IL-12 consists of P35 and P40 (encoded by the IL-12A and IL-12B genes, respectively), linking innate and adaptive immunity. IL-12 is expressed in a number of leukocytes such as natural killer cells, T and B lymphocytes (10).

The important functions of IL-12 are: increased IFN production from NK and CD4 + T cells, induction of cytotoxicity to natural killer cells and CD8 + T cells, induction of Th1 immune response. IL-12 has been shown to be able to suppress tumorigenesis and induce stable tumor regression by enhancing the adaptive immunity associated with Th1 along with the cytotoxic response (11).

Materials and Methods

Subjects:

1. Study design and dating of the study:

This is the design of a case control study conducted for a period of (January 2018 - January 2019) for genetic studies.

Ethical Issues:

All of the patients and the healthy control subjects were counseled and vocally agreed on the inclusion in the study before participation in the study.

This study was performed & being facilitated with permission from Babylon university, College of Medicine and the General Health Directorate of Babil governorate.

Diagnosis of breast and gynecological cancer:

All the patients were diagnosed as having gynecological cancer by histopathology. All the 79 control subjects consisted of apparently healthy individuals who had no health problem at time of this study.

Inclusion criteria:

The inclusion criteria for the patients group included any patient who had recently diagnosed with gynecological cancer both clinically and histologically. The healthy subject were apparently seemed healthy and otherwise had no acute nor chronic health problem.

Exclusion criteria:

Exclusion criteria included any patient who had normal histological results after suspicion of cancer, any patient who took therapy, any patient with chronic health problem or had a condition associated with suppressed immune system, any patient with cancer other than gynecological cancer, any patients with history of any autoimmune disease.

2. No. of samples: A total of 199 subjects in this study included 120 women with gynecological cancer distributed as follows (50 breast, 50 uterine, 10 ovarian, and 10 cervical samples), serving as a study group and 79 apparently healthy women working as a control group. All patients were engaged from those patients referred to the Babylon Hospital for Maternal and Children also Al-Hillah General Teaching

Results and Discussion

Statistical analysis and data presentation showed. In the current study, 120 women with cancer (uterus, breast, ovaries, and cervix) were

included as the study group and 79 apparently healthy women working as a control group. The importance of discussing issues about these types of malignancies in women comes from the fact

Extraction of DNA:

Blood samples were taken from all the participants for genetic study.

Five milliliters of whole venous blood with EDTA, as an anticoagulant, is collected from each woman for DNA extraction, Every detail of working method and quantity DNA is explained depending on the method of work followed in the gSYAN DNA mini extraction kit.

Polymorphism-Genotyping:

PCR-RFLP method was used to determine IL-12 at rs3212227 .

RFLP master mix was for IL-12 (rs3212227) gene polymorphism was prepared by using TaqI restriction enzyme (New England Biolabs. UK (PCR RFLP method -:

PCR RFLP was performed for identification of IL-12 (rs3212227) gene polymorphism in cancer patients and in healthy control blood samples. This method was carried out according to described by (7).

Statistical Analysis:

Data were summarized, analyzed and present using two software programs, these were the statistical package of social sciences (SPSS version 23) and Microsoft Office Excel 2010. Categorical variable were presented as number and percentage whereas numeric variables were expressed as mean, median, standard deviation inter-quartile range. Independent samples t-test was used to compare means between two groups in case of normally distributed data whereas Mann Whitney U test was used in case of not normally distributed data and One way ANOVA followed by post hoc test was done for normally distributed data among more than two groups, whereas Kruskal Wallis test was used instead when data were not normally distributed. Chi-square test was used to study association between categorical variables. Risk was estimated using odds ratio, etiologic fraction (EF) and preventive fraction (PF). The level of significance was considered significant at $P < 0.05$ and highly significant at $P < 0.01$.

included as the study group and 79 apparently healthy women working as a control group. The importance of discussing issues about these types of malignancies in women comes from the fact

that these disorders are fairly common worldwide. For instance, breast cancer is the most frequent malignant tumor affecting women globally (12). Malignancies affecting female

Comparison of mean age between control and study groups

The age range of women with Gynecologic carcinoma was from 35 to 76 years with a wide range of 41 years. Whereas, the age range of apparently healthy women (control group) was from 43 to 64 years with a relatively narrow range of 21 years. However, in terms of mean age and standard deviation, there was no significant difference ($P = 130$), despite the fact that the mean age of study group was slightly greater than that of control group, 54.12 ± 9.76 years versus 52.54 ± 4.65 years, as shown in table 3.1. Indeed, such finding that is the lack of significant difference in mean age is mandatory for such case-control study to avoid any possible bias in the results when age variable is taken into consideration.

The frequency distribution of women with Gynecologic carcinoma in terms of number of cases and percentage out of total is shown in

genital tracts are also common in clinical practice and represent a big proportion in terms of morbidity and mortality targeting women worldwide (13).

figure 1. Women younger than 40 years of age accounted for 11 out of 120 cases (9.2 %), women between 40 and 49 years of age accounted for 35 out of 120 cases (29.2 %), women between 50 and 59 years of age accounted for 36 of cases (30.0 %), women between 60 and 69 years of age accounted for 32 out of 120 case (26.7 %) and women older than 70 years of age accounted for 6 (5 %).

Indeed, finding women with cancer despite being younger than 50 years old is a horrible fact. However, reports all over the world exist that these malignant tumors can affect women younger than 50 years (14), but in the present study a significant proportion (9.2 %) of women were younger than 40. This mean that in our community risk factors associated with these malignancies need to be searched for and studies thoroughly in order to identify reasons behind acquisition of such malignant tumors by women in their fourth decade of life.

Table .1: mean age and age range in control and study groups

Characteristic	Control group <i>n</i> = 79	Study group <i>n</i> = 120
Mean age (years) ±SD	52.54 ±4.65	54.12 ±9.76
Age range (min.-max.)	21 (43-64)	41 (35-76)
<i>T</i>	-1.522	
<i>P</i> *	0.130	
	NS	

N: number of cases; SD: standard deviation; *: Independent samples t-test (equal variance is not assumed); NS: not significant at $P \leq 0.05$.

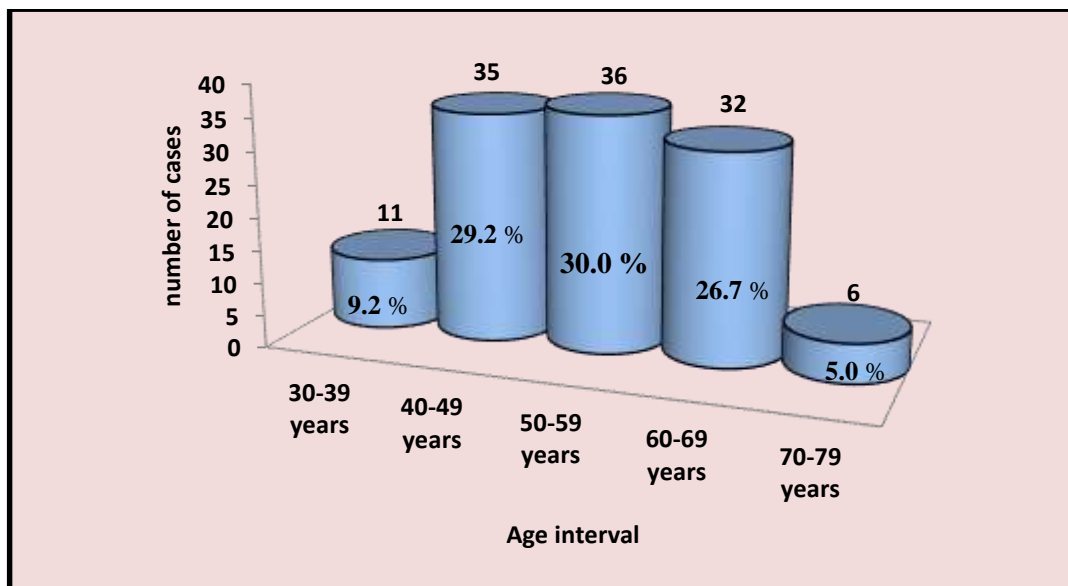


Figure .1: Histogram showing the number and percentage of patients with cancer according to 10 years age intervals

Women enrolled in the present study complain of the following types of cancer: breast cancer was seen in 50 patients out of 120 (41.7 %), uterine cancer was seen in 50 patients out of 120 (41.7 %), uterine cancer was seen in 10 patients out of 120 (8.3 %) and cervical cancer was seen in 10 patients (8.3 %), as shown in figure (2). The highest mean age was possessed by women with uterine cancer (61.90 ± 6.50 years) followed by women with cervical cancer (56.40 ± 6.83 years) then women with ovarian cancer (53.50 ± 7.17 years) and lastly by women with breast cancer

(46.00 ± 6.37 years), as shown in figure (3). the difference in mean age according to one way ANOVA was highly significant ($P < 0.001$) and individual differences as assessed by post hoc Benferoni test revealed the following: Mean age of women with uterine cancer was significantly the highest; no significant difference was found between women with ovarian cancer and women with cervical cancer; however, the mean age of women with breast cancer was significantly the lowest among all women with cancer.

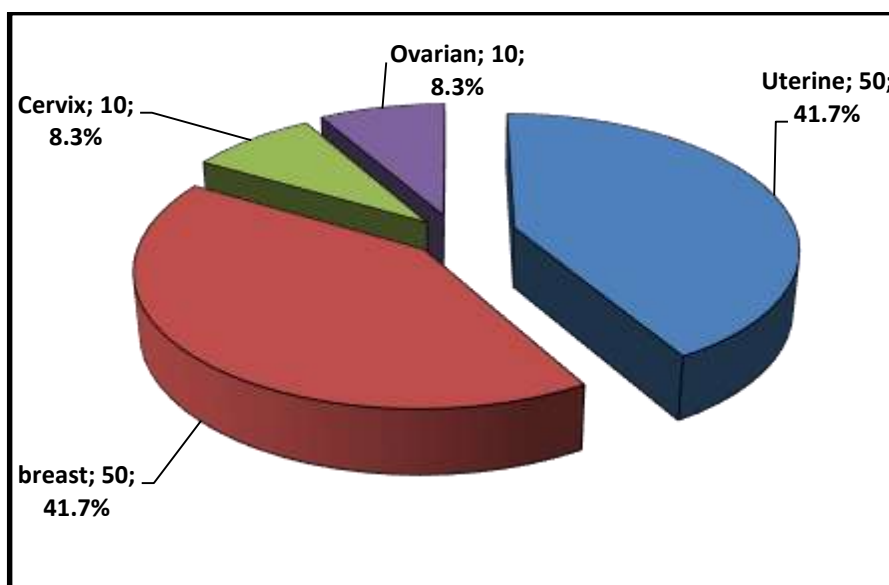


Figure 2: Pie chart showing the number of percentage of women according to histological type of cancer

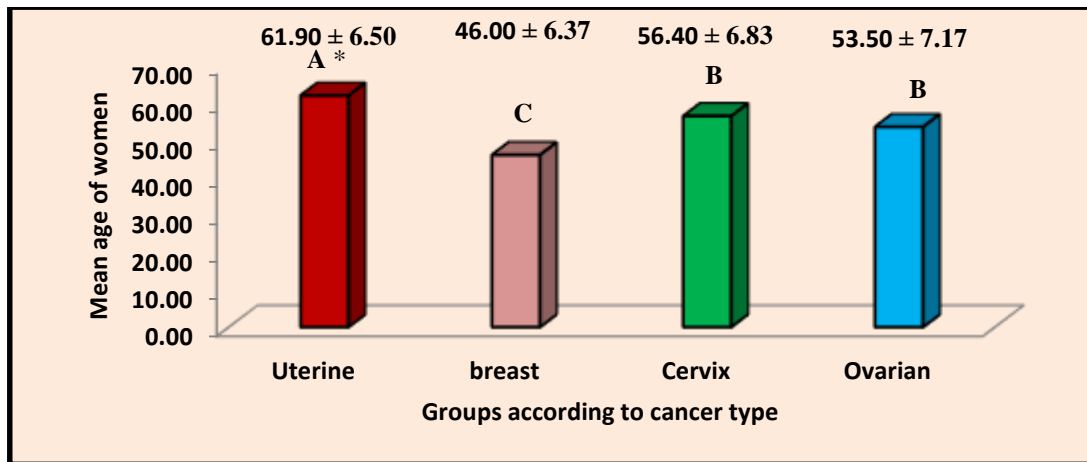


Figure 3: Three dimensional bar chart showing mean age of women according to histological type of cancer

*: Uppercase to indicate level of significance according to Benferoni's subsequent test; Similar letters indicate no significant difference at P 0.05, while different

letters indicate no significant difference at * P 0.05; A takes the highest value followed by B, then C.

Interleukin 12 genotype and its association with type of cancer

Single nucleotide polymorphism related to IL-12 was based on PCR analysis and accordingly patients and control subjects were labeled as one of three genotype combinations: Homozygous for the wild allele (A / A), Heterozygous for the wild and recessive alleles (A / C) and Homozygous for the recessive allele (C / C), as shown in figure

(4). In order to know whether control sample was representative to the population, in terms of frequency of single nucleotide polymorphism (SNP) of IL-12, Hardy Weinberg equilibrium was assessed and the results are shown in table (2). The difference between observed and expected counts was not significant (P = 0.555); for that reason, the sample was considered representative to the population.

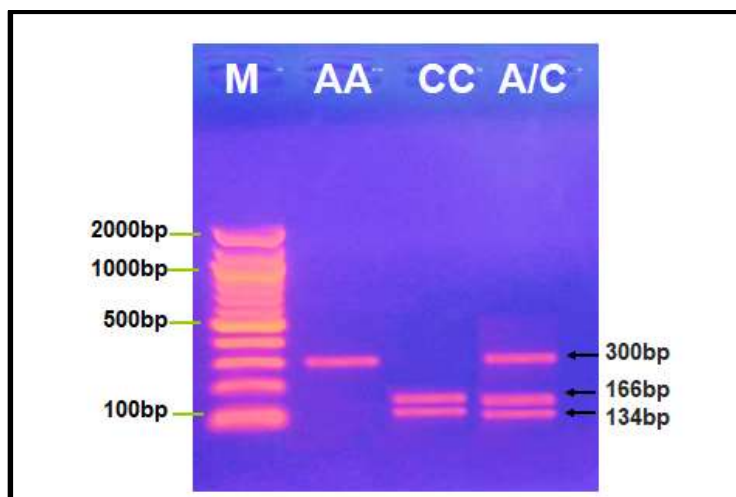


Figure 4: The RFLP-PCR product analysis of IL-12 gene polymorphism (rs 3212227) using TaqI restriction enzyme in (2 %) agarose, lane (AA) of the homozygous wild-type that appear undigested by the restriction enzyme in the range of 300 dpi, and lane (CC) of the homozygous mutant type, the product digested by Restriction enzyme 166bp and 134 bp domain, and the heterozygous (A / C) pathway, product digested by restriction enzyme to ranges of 300 bp, 166 bp, and 134 bp.

Table 2: Hardy Weinberg equilibrium of IL-12 alleles (control groups)

Genotypes	Observed count	Expected count	χ^2	P *
Homozygote reference (A / A)	60	59.40	0.348	0.555 NS
Heterozygote (A / C)	17	18.21		
Homozygote variant (C / C)	2	1.40		

A: wild IL-12 allele; C: recessive IL-12 allele; *: chi-square test; NS: not significant at $P \leq 0.05$.

The prevalence (A / A), associated with IL-12, was 75.9% (60 out of 79) in the control group and 56.7% (68 out of 120) in the study group, as shown in Table (3). In addition, the prevalence of the wild and recessive genotype heterozygous (A / C), associated with IL-12, was 21.5% (17 of 79) in the control group and 33.3% (40 of 120) in the study group, as shown. In table (3). Moreover, the prevalence rate (C / C), associated with IL-12, was 2.5% (2 out of 79) in the control group and 10.0% (12 out of 120) in the study group, as shown in the table (3). The difference in these rates was significant ($P = 0.012$). Whereas, women with cancer expressed a homozygous recessive allele (C / C) of IL-12 at a higher rate than control women, 10.0% versus 2.5%; It was also evident that the cancer women expressed the homozygous wild allele (A / A) of IL-12 at a lower rate than the control women, 56.7% versus 75.9%, as shown in Table (3). Table (4) shows the wild IL-12 allele was less common in the study group than in the control group, 73.3% versus 86.7% ($P = 0.001$), while the recessive IL-12 allele (C) was more common in the study

group than in the control group. Studying Control group. . 26.7% versus 13.3% ($P = 0.001$).

The current results demonstrate the protective role of wild IL-12 (A) allele against cancer and this was proven after calculating the odds ratio for allele A, which was 0.42. (being less than one indicates a protective role) with a 95 % confidence interval of 0.25 - 0.72. On the other hand, these findings implies that the recessive IL-12 (C) allele may play an etiologic role for cancer and this was proved following calculation of Odds ratio for allele C which was 2.37 (being more than one indicates a causative role) with a 95 % confidence interval of 1.38 - 4.08. In summary, one can conclude that an individual harboring IL-12 A allele is less likely to get cancer by 0.58% that individual lacking this allele; whereas an individual harboring IL-12 C allele is at 2.37 fold risk to develop cancer in comparison with an individual who lacks this allele. The preventive fraction of IL-12 A allele, in statistical terms, was calculated to be 0.44; while the etiologic fraction (EF) of IL-12 C allele, in statistical terms, was calculated to be 0.44, as shown in table (4).

Table 3: IL-12 genotype frequency distribution in control and study groups

IL-12 genotype	Control group <i>n</i> = 79	Study group <i>n</i> = 120	χ^2	P *
AA, <i>n</i> (%)	60 (75.9 %)	68 (56.7 %)	8.852	0.012 S
AC, <i>n</i> (%)	17 (21.5 %)	40 (33.3 %)		
CC, <i>n</i> (%)	2 (2.5 %)	12 (10.0 %)		

A: wild IL-12 allele; C: recessive IL-12 allele; *n*: number of cases; *: chi-square test; S: significant at $P \leq 0.05$.

Table 4: IL-12 allele frequency distribution in control and study groups

IL-12 allele	Control n = 158	Study n = 240	χ^2	P	OR	95% CI	EF	PF
Wild (A)	137 (86.7 %)	176 (73.3 %)	10.149	0.001 HS	0.42	0.25 - 0.72	---	0.44
Recessive (C)	21 (13.3 %)	64 (26.7 %)			2.37	1.38 - 4.08	0.44	---

n: number of alleles; HS: highly significant at $P \leq 0.01$; OR: Odds ratio; CI: confidence interval; EF: etiologic fraction; PF: preventive fraction.

The Kårvatn, *etl.* (15) found an association between risk of breast cancer and IL-12 gene polymorphism; in support for our findings, they stated that women who were homozygous for minor alleles and those who were homozygous for the wild allele expressed significant variation in rate of breast in cancer so that IL-12 gene polymorphism may either protect against breast cancer with an odds ratio of 0.22 or enhances the development of breast cancer with an odds ratio of 1.68. (16) Demonstrated that gene and allele polymorphism in relation to IL-12 can be a risk factor for cervical cancer in women and that the association was significant and the odds ratio of the protective allele was 0.38 and that of the risk allele was 1.20. (17) Also were able to show significant association between risk of cervical cancer in women and IL-12 gene polymorphism. The protective allele exhibited an odds ratio of 0.63 and the risk allele showed an odds ratio of 1.56. (18), found that IL-12 genetic polymorphism was associated significantly with cervical cancer. (19) were able to demonstrate that genetic polymorphism of IL-12 gene was significantly associated with increased risk of ovarian cancer and that the odds ratio expressed by the blamed risky allele in comparison with wild allele was 2.47. So far, our study agrees with the previously mentioned studies that allelic polymorphism in IL-12 gene leads to significantly greater risk of developing breast cancers and cancers related to women genital tract such as uterine, cervical and ovarian cancer. In accordance with our finding, risk of cervical cancer and that the odds ratio was relatively high (2.83) and this value (20) have shown that IL-12 CC genotype was associated with significant increase in approximately similar to that of the present study. In addition, (21) have also demonstrated that women with IL-12 rs3212227 CC genotypes possess a 6.00-fold (95% CI, 2.86-

12.56) elevated cervical cancer risks; also supporting the finding of the present study.

These studies showed odds ratio for the risky allele in the range of 1.2 up to 6; the present study brought about a value of 2.37 which is comparable to these studies; in addition these studies disclosed that the odds ratio for the protective allele ranged from 0.63 to 0.22; our results suggested an odds ratio of 0.42 for the protective allele, That lies somewhere between the values expressed by previous studies.

To explain this association it is important first to highlight the immunological role of IL-12. IL-12 is principally synthesized by antigen-presenting cells at time of activation, including dendritic cells, macrophages and monocytes. IL-12 is a heterodimeric cytokine protein which is formed by two polypeptide chains (p40 and p35) that are linked by disulfide bonds. These chains are encoded by IL-12B and IL-12A genes, independently. The location of these genes has been shown to be associated with chromosomes 5q31-33 and 3p12-q13.2 (22). IL-12 has the ability to promote the activity of cytotoxic T lymphocyte and natural killer cells as well as the induction of differentiation of immature CD4+ T cell to become Th1 cells and also the production of IFN-gamma (23). These immune responses are essential both for elimination of invading pathogens including virus and possibly limitation of the acquisition and or replication of HPV inside epithelial cells and also essential in identification and elimination of cell clones that are genetically damaged and limit their future transformation in tumor mass (24).

In addition, IL-12 may delay the mechanism of new blood vessel formation in cancers by acting as an antagonist to the pro-angiogenic molecules. Studies on experimental animals substantially provided evidences that both specific and nonspecific and antitumor immune reactions were

stimulated following transfecting the gene of IL-12 into neoplastic cells (25). Moreover, clinical trials showed that serum concentration of IL-12 was correlated to the prognosis of patients with cancer (26), and also shared some effect relating to the progression of other forms of cancer (27).

Macrophages have been isolated from the microenvironment of solid neoplasms, and despite being able to impart antitumor activities; they can also share an important contribution in tumor progression. "Tumor-associated macrophages (TAMs)" can enhance proliferation of cells and formation of new blood vessels and can retard immune responses (28). These variables contributions may be attributed to the recognition of 2 macrophage subtypes: the proinflammatory M1 phenotype and the immunomodulatory M2 phenotype. In order to make tissue repair effective, M2 macrophages acquire a profile that produce an enhance synthesis of matrix metalloproteinase 9 (MMP9) and vascular endothelial growth factor (VEGF).

Nevertheless, when enhanced by neoplasms, M2 macrophages may enhance disruption of basement membrane, growth of neoplasm and hence metastasis (29). M2 subtype is associated with to pro-neoplastic reaction in a number of ways. The antitumor characteristics of M1 macrophages are principally a reflection of the dominant activity of interleukin 12 (IL-12), a cytokine that is produced by M1 phenotype. Therefore, the acquisition of M2 phenotype by macrophages renders them unable to produce IL-12 that is essential for the enhancement of the antitumor activity mediated by Th1 cells, natural killer cells and cytotoxic T cells. On the contrary, M2 phenotype synthesizes interleukin 10 (IL-10), that enhances Th2 cell polarization, hence leading a positive feedback loop maintained by interleukin 4 (IL-4) release which favors M2 macrophage polarization. In addition, the cytokine "transforming growth factor beta (TGF- β)", with immune regulatory properties, is associated with Th2 response (27).

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علاقة تعدد الاشكال الوراثية (rs3212227) للانترلوكين 12 وسرطان الجهاز التناسلي الانثوي و الثدي

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الخلاصة

يشير السرطان إلى أي مرض من بين عدد كبير من الأمراض التي تتميز بتطور خلايا غير طبيعية تنقسم بشكل لا يمكن السيطرة عليه ولديها القدرة على التسلل إلى أنسجة الجسم الطبيعية وتدميرها. غالبًا ما يكون للسرطان القدرة على الانتشار في جميع أنحاء الجسم. السرطان هو السبب الرئيسي الثاني للوفاة في العالم. يمكن أن تحدث السرطانات في أي جزء من الجهاز التناسلي الأنثوي - الفرج أو المهبل أو عنق الرحم أو الرحم أو قناة فالوب أو المبيض. تسمى هذه السرطانات بسرطان الجهاز التناسلي الأنثوي يمكن أيضا ان تغزو الأنسجة والأعضاء المجاورة مباشرة ، أو تنتشر (تنتقل) عبر الأوعية الليمفاوية أو الغدد الليمفاوية (الجهاز الليمفاوي) أو مجرى الدم إلى أجزاء بعيدة من الجسم. يحدث سرطان الثدي عندما تبدأ بعض خلايا الثدي في النمو بشكل غير طبيعي طريق. تنقسم هذه الخلايا بسرعة أكبر من الخلايا السليمة وتستمر في التراكم وتشكل كتلة او ورماً. قد تنتشر الخلايا (تنتقل) عبر الثدي إلى العقد الليمفاوية أو إلى أجزاء أخرى من الجسم.

Interleukin-12 (IL-12) هو سيتوكين مضاد للالتهابات يربط بين الاستجابات المناعية الفطرية والتكيفية ضد الخلايا السرطانية. ارتبطت أشكال النوكليوتيدات المفردة (SNPs) في جينات IL-12 بمخاطر الإصابة بالسرطان. دور IL-12 في سرطان الثدي والجهاز التناسلي الأنثوي بشكل عام ، تهدف الدراسة الحالية إلى تقييم دور تعدد الأشكال الجيني Interleukin-12 بين المرضى المصابين بسرطان الثدي وسرطان الجهاز التناسلي الأنثوي.

الكشف عن تعدد الاشكال الوراثي لساييتوكين 12 من المرضى ومجموعة السيطرة في الحمض النووي، تم أخذ 199 عينة وقسمت إلى (120) عينة دم مريض و (79) عينة كمجموعة ضابطة.

تشكو النساء المسجلات في الدراسة الحالية من الأنواع التالية من السرطان: سرطان الثدي شوهد في 50 مريضا من أصل 120 ، وسرطان الرحم شوهد في 50 مريضا من أصل 120 ، وسرطان المبيض شوهد في 10 مرضى وسرطان عنق الرحم شوهد في 10

المرضى من أصل 120. NP rs3212227 (جين IL 12) تم تحديده بواسطة: PCR RFLP تم إجراء PCR RFLP لتحديد تعدد الأشكال الجيني (rs3212227) IL-12 في مرضى السرطان وفي عينات الدم، أظهر التحليل الإحصائي وعرض البيانات في الدراسة الحالية أن (120) امرأة مصابة بالسرطان (الرحم والثدي والمبيض وعنق الرحم) تم ضمهن كمجموعة دراسية ، بينما تكونت المجموعة الضابطة من (79) امرأة سليمة.

كان انتشار النمط الجيني البري متمائل (A / A) ، المرتبط بـ IL-12، 75.9% (60 من 79) في المجموعة الضابطة و 56.7% (68 من 120) في مجموعة الدراسة. بالإضافة إلى ذلك ، كان انتشار النمط الجيني البري والمتنحي (A / C) ، المرتبط بـ IL-12، 21.5% (17 من 79) في المجموعة الضابطة و 33.3% (40 من 120) في مجموعة الدراسة. علاوة على ذلك ، ارتبط انتشار النمط الوراثي المتنحي متمائل (C / C) بـ IL-12، 2.5% (2 من 79) في المجموعة الضابطة و 10.0% (12 من 120) في مجموعة الدراسة. كان الاختلاف في هذه المعدلات معنويا (P = 0.012). كانت نسبة كبيرة (9.2%) من النساء تقل أعمارهن عن 40 عامًا. وهذا يعني أنه في مجتمعنا ، يجب البحث عن عوامل الخطر المرتبطة بهذه الأورام الخبيثة ودراستها بدقة من أجل تحديد الأسباب الكامنة وراء اكتساب النساء لهذه الأورام الخبيثة في الرابعة. عقد من الحياة. الفرد الذي يوزي IL-12 أليل هو أقل عرضة للإصابة بالسرطان بنسبة 0.58% من الفرد الذي يفتر إلى هذا الأليل ؛ في حين أن الفرد الذي يحتوي على أليل IL-12 C معرض لخطر الإصابة بالسرطان بمقدار 2.37 ضعف مقارنة بالفرد الذي يفتر إلى هذا الأليل. نستنتج من أن أليل (A Wild IL-12) قد يلعب دورًا وقائيًا ضد السرطان. في حين أن أليل IL-12 المتنحي (C) قد يلعب دورًا مسرطنًا.

الكلمات المفتاحية: سرطان الجهاز التناسلي للأنثى ، سرطان الثدي ، ساييتوكين 12 ، تعدد اشكال النوكليوتيدات المفردة.