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MGF (IGF-1) GG GENE (RS6220) AND LOW-RISK IN AA ASSOCIATED TO BREAST CANCER RISK

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Abstract. Genetic factors and also as polymorphisms be associated to breast cancer. Breast cancer (BC) first of among death in women. This current study was determined the frequency MGF (IGF-1) Gene polymorphism in patients with breast cancer. The Mast cell growth factor gene polymorphism were associated with risk breast cancer. MGF is regulate to cell apoptosis, prolife, and differentiation. Present study to finds that MGF gene polymorphism has a relation with the risk of breast cancer. Two polymorphic variants (rs6220 and rs7136446) are associated to breast cancer. First time, we evaluated these study of 126 breast cancer and 160 controls Iranian women of peripheral blood, and then did extracted DNA using the genotyping technique by sequencing. In present study, MGF GG gene (rs6220) had significant association with breast cancer (37.3% frequency, Odd Retio;2.359, CI 0.208-3.621, P value; 0.001).

Keywords: MGF gene, polymorphism, breast cancer.

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1. INTRODUCTION

Breast cancer is most worldwide cancer rates in more developed regions (Ferlay, Soerjomataram, Dikshit, 2012) and also a multifactorial disease and genetic factor is the main risk factor (Mersch, Jackson & Park, 2015).

many authors discovered a high association between MGF gene polymorphism and breast cancer, however need for further study upon other population (Sarkissyan, Mishra & Wu, 2011) (Sarfstein & Pasmanik-Chor, 2012) (Christopoulos, Msaouel & Koutsilieris, 2015) .MGF is express by liver and stimulated by growth factor (GH) (Philippou, Maridaki, Pneumaticos, 2014).

Mast cell growth factor and IGF-2, are family of peptidyl hormones. MGF is a polypeptide, that located on chromosome 12 and contains 6 exons (Yu, Li & Smith, (2001) (Pavelić, Matijević & Knezevic, 2007) (Lelbach, Muzes & Feher, 2005) (Renehan, Zwahlen & Minder, 2004). MGF gene for expression need to transcriptional and post-translational (Denley, Cosgrove, Booker, 2005).On the other hands MGF is found also in normal mammary glands (Macias & Hinck, 2012). MGF is a main regulator growth, differentiation and apoptosis in combination with GH, insulin and sex hormones in cells. It acts with estrogen to promote tumor growth , so activated mitogen and anti-apoptotic in breast cancer cells (Cleveland, Gammon & Edmiston, 2006) (Philippou, Maridaki, & Pneumaticos, 2014) (Gunter, 2009).

levels of MGF depended to the age and increase maturation (Philippou, Halapas & Maridaki, 2007) (Yu, & Rohan, 2000) (Gennigens, Menetrier-Caux & Droz, 2006). Although among of MGF may be affected by environmental factors, but may be to expression by genetic polymorphisms (Guntur & Rosen, 2013).single nucleotide polymorphisms (SNPs) and variations lead to susceptibility to breast cancer (Kang, Ahn & Mishra, 2014). MGF is peptide growth hormones that induce epithelial cell proliferation in the normal and malignant breast (Sachdev, & Yee, 2001).It is known that MGF is associated with an increased risk of an other cancers (Tsuchiya, 2013) (Cao, 2014) (Ong, Salomon & Morsche, 2014) (Khorasani, & Almasifard, 2017)

this is the first study to funded association between the polymorphisms of MGF gene and risk of Breast cancer in Iranian population.

2. MATERIAL AND METHODS

2.1. Patients data:

In this study 126 patients Carcinoma Breast Cancer in grade 4 and 160 controls of the *Medical Center KHAS, Tehran, Iran* were conducted in ages 30-55 years.

This study ethically was approved by the local Ethical Committee of Islamic Azad University from samples rights.

The blood samples were collected from patients and then using DNA Extracted method upon peripheral blood lymphocytes. DNA was isolated by using FelxiGene DNA extraction kit (Qiagen Germany).

2.2.Genotyping

The polymorphisms were detected by sequencing method. The primers of the MGF (rs7136446) were forward 5′- CCTCCATGAGCAGTCAGTCA -3′ and reverse 5′- TCATTTGGCTCTTGAGTGGA -3′, also MGF (rs6220) forward 5′- TGCCTTTCAACTGGAAACTCT -3′ and reverse 5′- GCTATCCAAATAACTGGCCAAC -3′.

The cycling conditions were 94°C, 30 sec; 57°C, 30 sec; 72°C, 60 sec (35 cycles). we designed PCR primers by Primer3 online software and were direct sequencing. The genotypes of MGF polymorphisms in 2 groups were analyses by $\chi 2$, Frequency and odd ratio tests.

3. RESULTS

The point of our study, association MGF and breast cancer, Because It study do not upon our population.

There was a significant between MGF GG (37.3) polymorphism and breast cancer risk

In Table 1, 2 and Graph Showed that P value of Our results showed that the Genotype MGF GG in rs 6220 most risk factor was in our population compared to CT in rs 6136446: OR= 2.359, 95% CI= 0.208 - 3.621, p=0.001*** ; and OR= 0.12, 95% CI= 0.031-0.32, p=0.05 (Table 1, 2)

In our study were significant analyze and a relationship between presences of MGF and increasing of breast cancer.

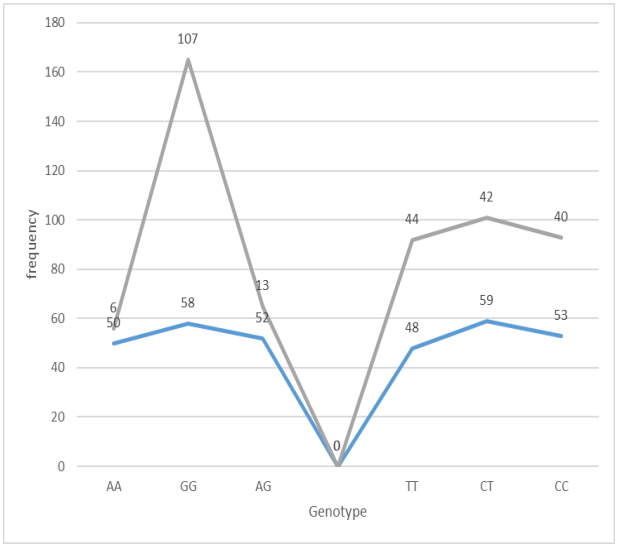
3.1.Tables, Graphs

Table 1: MGF genotype frequencies [n (%)] for cases and control

SNP	Genotype	OR	95% CL	P value
rs6220				
	AA	**1.412**	**0.082 - 0.547**	**0.078**
	GG	**2.359**	**0.208 - 3.621**	**0.001*** **
	AG	**1.076**	**0.030 - 0.189**	**0.026**
rs6136446				
	TT	**0.042**	**0.021-0.092**	**0.17**
	CT	**0.12**	**0.031-0.32**	**0.05**
	CC	**0.09**	**0.027-0.192**	**0.32**

*Table 2: Comparison between genotypes, odds ratio and p value, showed that P ***=P<=0.001, **=P<=0.05*

SNP	Genotype	Controls (n=160)	%	Cases, (n=126)	%
rs6220					
	AA	**50**	**(17.44%)**	**6**	**(2.1%)**
	GG	**58**	**(20.3%)**	**107**	**(37.3%)**
	AG	**52**	**(18.15%)**	**13**	**(4.53%)**
rs6136446					
	TT	**48**	**(15.44%)**	**44**	**(15.4%)**
	CT	**59**	**(23.3%)**	**42**	**(14.6%)**
	CC	**53**	**(18.45%)**	**40**	**(13.93%)**



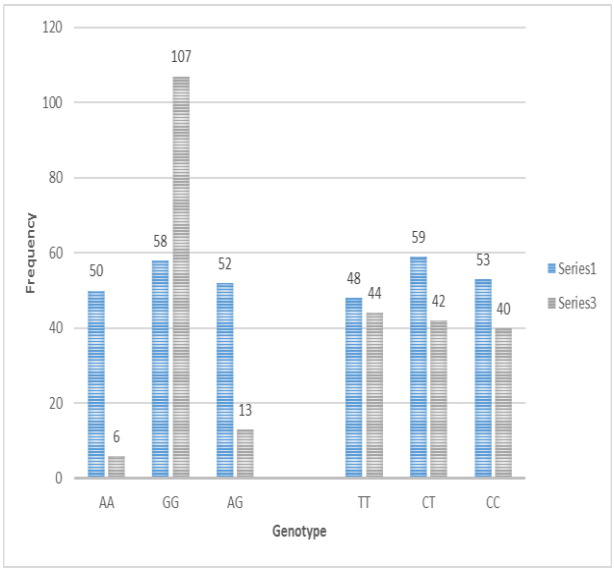


Figure 1,2: Line (up) and Column Chart(down), MGF genotype frequencies [n (%)] for cases and control: Analyses of 126 affected women and 160 controls: SNP rs6220(AA, GG and AG), SNP rs6136446 (TT, CT and CC).

4. DISCUSSION

Some Genome-Wide recognized in susceptibility loci with increased risk of breast cancer (Wang,

Liu, Li & Mccullough, 2014) (Chang, Low & Qiu, 2012) (Bastani, Ahmadi, & Damircheli, 2013) (Stacey, 2007) (Stacey, 2008) (Easton, 2007).

In the last years, increased to interest study MGF and other gene (Dai, Hu & Jiang, 2012) (Harlid, 2012) (Hosseini, 2013) that, involved in formation tumor, spatially in breast carcinoma. Two of the most widely studied genetic alterations of MGF gene is C and A genotype (Çiftçioğlu, & Almasifard, 2015).

Polymorphic CA make of 10 to 24 repeats in length, that this repeating is located region of upstream transcription so is thus similar a promoter polymorphism that to regulation of MGF protein levels (Costa-Silva D.R., da Conceição Barros-Oliveira M & Borges, R.S. (2017).

Gu (Gu, et al. 2010) by study upon Caucasian Women was observed No significant association between 302 SNPs of the MGF gene and breast cancer. Muendlein (2013) in Austrian Women find a significant association in MGF gene (rs 2946834) and over expression of HER2-positive in breast cancer.

Qian (2011) resulted a significant association between the MGF gene (rs7965399) and breast cancer with highly association in premenopausal women and also ER negative tumors.

Canzian (2010) observed in Caucasian population, any association of MGF gene and risk of breast cancer. Henningson (Canzian, 2010) No founded any associate with MGF, and develop breast cancer in Swedish Women. But opposite result was seen by Sarkissyan (Sarkissyan, Mishra, & Wu, 2011), that it was a significant association between the MGF gene and the risk of breast cancer in African-American and Hispanic Women.

A study in Norwegian postmenopausal women (Almasifard, 2013) (Almasifard, & Khorasani, 2017) and Swedish women (Canzian, 2010) also were a relation between to MGF levels and the risk of breast carcinoma.

In Another study that used of Caucasian women, no any observe of association with breast cancer risk (Qian, Zheng & Yu, 2011).

Although most of studies founded an association between MGF gene polymorphism and breast cancer risk, but in few studies have relations these polymorphisms to disease develop.

results of studies are still unknown but a possible explanation be in the ethnic populations (Biong, 2010) (Bastani, Ahmadi, & Damircheli, 2013) Therefore, expression of MGF gene may allow of women in high-risk for breast cancer, as well as the development of for early diagnosis and better treatment against the disease.

Finally, in our study show that MGF AA gene (rs6220), in low risk allele induced to significant association to Breast Cancer.

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