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Association of RAD51 (rs1801320) with Increased Risk of Ovarian Cancer

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ABSTRACT—*Ovarian cancers are heterogeneous group of neoplasm with varying clinical, histopathological molecular and biological behavior. There is significant increase in incidence rate of ovarian cancer in India, as it was 6% in 2005 which increased upto 7% in 2015. (Consolidated cancer registry report ICMR – NCRP. 2015). Various genes are involved in the progression of ovarian cancer. The RAD51 gene plays important role in repair of damaged DNA. In the present study, the association of RAD51-135G>C polymorphisms with ovarian cancer was analyzed in 86 ovarian cancer patients. The RAD51–135G>C is a promoter SNP located at 5' untranslated region (5'UTR) which rises due to transversion of G to C nucleotide. The SNP rs1801320 in RAD51 gene was genotyped using Taqman allelic discrimination assay and all genotypes were determined by endpoint reading on step one™ real time PCR using the SDS software. The minor allele frequency (MAF) in cases and controls were 0.12 and 0.02. RAD51-135CC (rare homozygous) genotype frequency was elevated in ovarian cancer as compared to controls (OR=9.05, p=0.01). However, RAD51 heterozygous genotype (GC) had two fold increased ratio (OR= 2.60, 95% CI; 1.06-6.36, p= 0.03). The allele frequency of RAD51 gene SNP rs1801320 revealed that C allele was more frequent in ovarian cancer patients compared to controls (OR- 3.46, 95% CI; 1.66- 7.22, p <0.005). The results from this study suggested that RAD51-135G>C polymorphisms might confer the risk to develop ovarian cancer due to increased error prone repair in RAD51-135CC genotype.*

1. INTRODUCTION

Ovarian cancer is the one of the most common cause of cancer death associated with gynaecological malignancy. Ovarian cancer is mostly a disease of postmenopausal women (4). Worldwide, there were 239000 new cases diagnosed and approximately 152000 deaths due to ovarian cancer annually (3). Ovarian cancer accounts for 2.5% of all female cancer cases, but 5% of cancer deaths is because of the disease's low survival. Eastern and Central Europe accounts 11.4 per 100000 and 6.0 per 100000 respectively while China reports 4.1 per 100000 (2). In India, the age adjusted incidence rate accounts for 8 per 100,000 and the age adjusted mortality accounts for 6 per 100,000.

Various genes are involved in the progression of ovarian cancer. The *RAD51* gene plays important role in repair of damaged DNA. The *RAD51*- 135G>C (rs1801320) polymorphism was assesed by different genotyping platforms (1). The aim of the present study was to analyse the association of *RAD51*-135G>C polymorphisms with ovarian cancer in patients from PGIMS, Rohtak.

2. MATERIALS AND METHODS

Eighty six patients of ovarian cancer diagnosed from the Department of pathology, Pt. B.D Sharma university of Health sciences, Rohtak were studied. A written informed consent was obtained from patients before study entry which was approved by Institutional Human Ethical Committee. Out of 86 patients diagnosed, there were 73 cases of epithelial tumor, 7 cases of Sex chord stromal tumor and 6 cases of Germ cell tumor. The healthy control group consisted of 57 healthy female without cancer or other disease.

These patients were analysed for age, histological type and tumor stage. Two ml blood was taken in EDTA vacutainer from patients as well as from healthy controls, and DNA was isolated using Qiagen blood mini kit. The DNA was stored at -20ºc for further molecular genetic analysis. . The *RAD51*(RS1801320) was genotyped using taqman genotyping assay.

Results

Mean age at diagnosis of patients was 58.93± 14.15 (Range, 31-79). Mean age of the control samples was 62.67± 12.81 (Range, 33-79). (Table 1) The SNP rs1801320 in *RAD51* gene was genotyped using Taqman allelic discrimination assay and allelic discrimination plot was generated . Genotype frequencies differed significantly between ovarian cancer patients and controls.

Among 86 ovarian cancer patients, there were 53 GG (62%), 23 GC (26%) and 10 CC (12%), whereas in controls 48 GG (84%), 8 GC (14%) and 1 CC (2%) respectively. (Fig 1).

Table 1: Mean age and their differences among ovarian cancer patients and Controls.

S. no	Groups	Mean Age ± SD	Range	Max	Min
1	**Ovarian cancer patients**	58.93±14.15	48	79	31
2	**Controls**	62.67±12.81	46	79	33

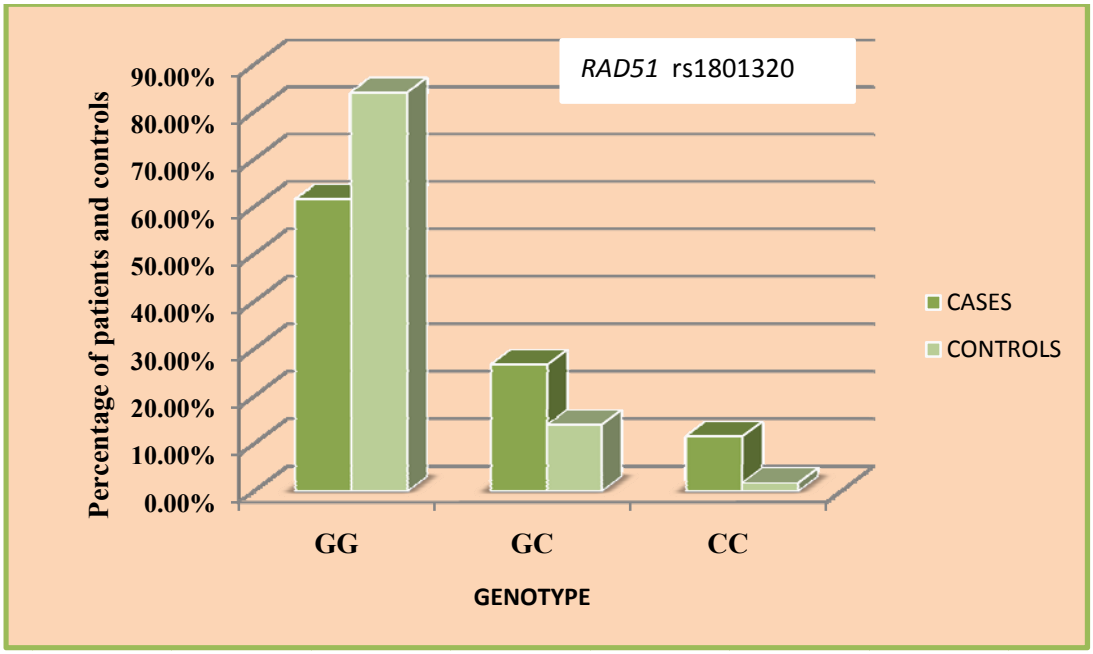

Fig. 1: Genotype frequency of G135G, G135C, and C135C Single nucleotide polymorphisms in Ovarian Cancer Patients and controls.

The G allele frequency of *RAD51* gene SNP rs1801320 was more in patients compared to controls. The C allele was more frequent in ovarian cancer patients compared with controls (OR- 3.46, 95% CI; 1.66-7.25, p =0.005) (Fig 2).

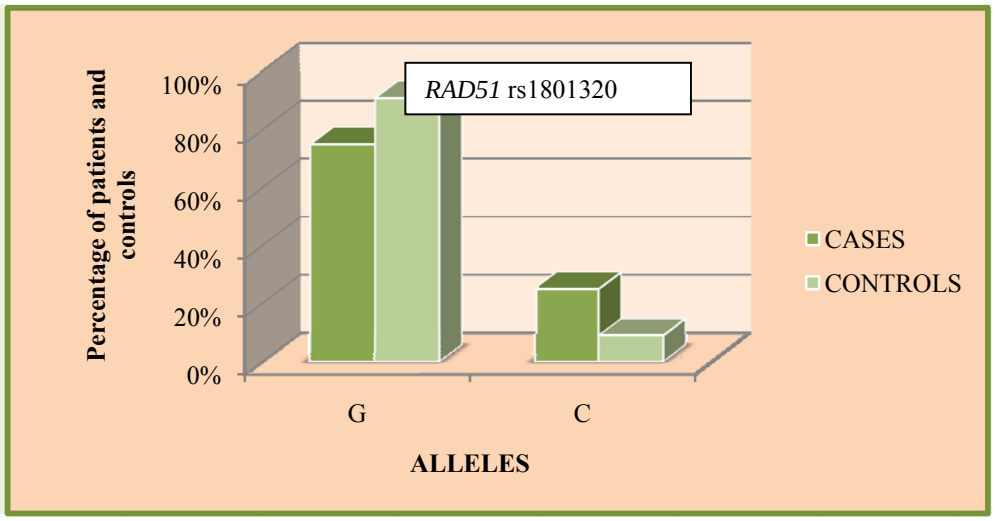

Fig 2: Percentage frequency of allele G and C in ovarian cancer patients and controls.

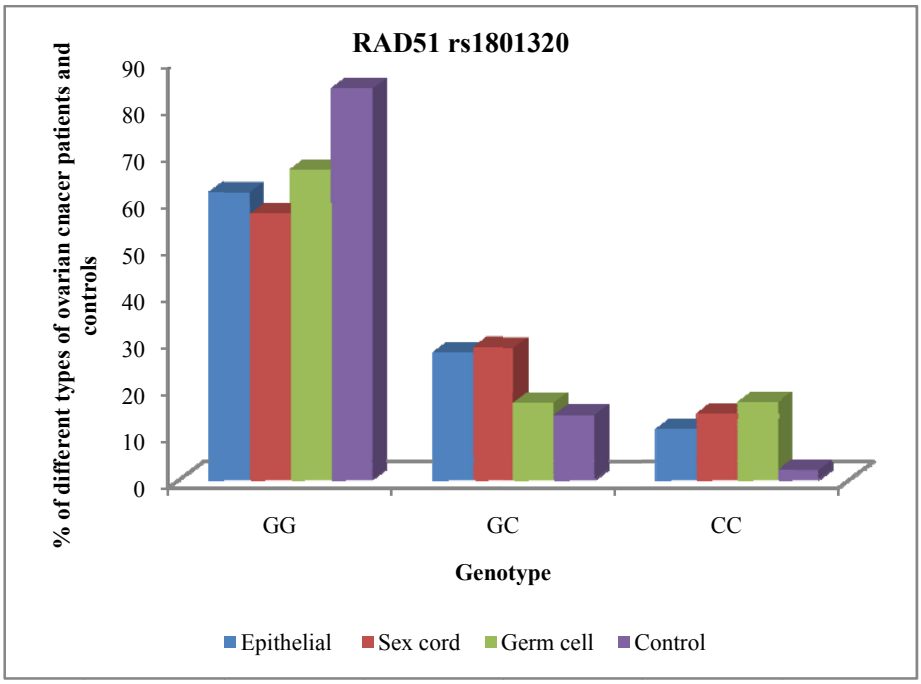

Fig 3: Percentage of G135G, G135C and C135C single nucleotide polymorphism in different typs of ovarian cancer patients and control group.

Among 73 epithelial ovarian cancer patients, there were 45 (61.7%) GG, 20 (27.3%) CG and 8 (10.9%) CC genotype, in germ cell patients 4 (57.1%) GG, 2 (28.5%) GC and 1 (14.2%) CC genotype, in sex cord stromal patients 4 (66.6%) GG, 1 (16.6%) GC and 1 (16.6%) CC genotype and in controls 48 (84%) GG, 8 (14%) GC and 1 (2%) CC genotype. (Fig 3).

DISCUSSION

Age has a strong correlation to ovarian cancer risk and 80% cases are diagnosed after 50 years of age (6). In the present study majority of the patients (81%) were above 50 years of age.

RAD51- 135G>C rs1801320 polymorphism was assesed by different genotyping platforms (1). The frequency of heterozygous GC genotype ranged from 4.7% in Iceland and 21.7% in Poland (ILUH and IHCC). Higher frequency (21.7%, 16.3% and 16.1%) of heterozygous GC genotype was observed in Poland (IHCC, CNIO, Spain, United States and Mayo clinic). A lower frequency of heterozygous GC genotype was observed in Iceland, Netherlands and Israel (ILUH, Leiden University medical centre and NICCC). In the present study frequency of heterozygous GC genotype was 26%. (1).

The present study revealed the frequencies of G and C allele were 0.75 and 0.25 in ovarian cancer patients whereas in case of controls it was 0.91 and 0.09. In Poland 19 studies were done in different types of cancer, the frequency of G allele ranged from 0.90 to 0.42 and the frequency of C allele ranged from 0.58 to 0.10 (7; 8 and 5). Higher frequency of G allele 0.93 and lower frequency of C allele 0.07 reported in Australia in ovarian cancer patients (9). Higher frequency of G allele was reported in UK, USA, Australia, multiple countries, korea, Russia, Chile, Portugal, Italy, America, Belgium, Egypt, China and Serbia in breast, glioma, AML, gastric, ovarian, HNC, endometrial , liver, prostate, colorectal and cervical cancer patients (8) The results from this study suggested that *RAD51*-135G>C polymorphisms might confer the risk to develop ovarian cancer due to increased error prone repair in *RAD51*-135CC genotype.

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REFERENCES

[1] Antoniou, C., Antoniou, Olga., Sinilnikova,M., Jacques, Simard, Mélanie Léoné., Martine, Dumont., Susan, L., Neuhausen, Jeffery., Struewing. (2007). RAD51 135G→C Modifies Breast Cancer Risk among BRCA2 Mutation Carriers: Results from a Combined Analysis of 19 Studies. *Am J Hum Genet,* 81(6), 1186–1200.

[2] Chen W (2016). Cancer statistics in China, 2015. *CA Cancer J Clin*, 66(2),115–32.

[3] Ferlay, J., Steliarova-Foucher, E., Lortet-Tieulent, A., Rosso, S., Coebergh., W, Comber,H.,. (2013) Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. *European Journal of Cancer,* 49, 1374– 1403.

[4] Hunn, J., Rodriguez, GC., (2012). Ovarian cancer: Etiology, risk factors, and epidemiology. *Clin. Obstet Gynecol*, 55, 3–23.

[5] **Krupa, R., Tomasz, S., Maria, W., Jan, CM, Wasylecka., L., Dziki., & Janusz, B., (2011). Polymorphisms in *RAD51, XRCC2 and XRCC3* genes of the homologous recombination repair in colorectal cancer—a case control study. *Mol Biol Rep,* 38(4), 2849–2854**

[6] Murthy, N., Srinivasa, S., Suman, G., Srekantaiah, P., Aleyamma, M., (2009). Changing Trends in Incidence of Ovarian Cancer - the Indian Scenario. *Asian Pacific J Cancer Prev*, 10, 1025-1030.

[7] **Romanowicz-Makowska, H., Smolarz, B., Zadrozny, M., Kulig, A., (2006). Analysis of RAD51 polymorphism and BRCA1 mutations in Polish women with breast cancer. *Exp Oncol,*28, 156-159.**

[8] Synowiec, E., Stefanska, J., Morawiec, Z., Blasiak, J., Wozniak, K., (2008). Association between DNA damage, DNA repair genes variability and clinical characteristics in breast cancer patients. Mutat Res, 648(1-2):65–72.

[9] Webb, PM., Hopper JL., Newman, B., Chen, X., Kelemen, L., Giles, GG., Southey, MC., Chenevix-Trench, G., Spurdle, AB., (2005) Double-strand break repair gene polymorphisms and risk of breast or ovarian cancer. *Cancer Epidemiol Biomarkers Prev* 14, 319–323.