Introduction

Breast cancer is the most common cancer in women and its impact on mortality and morbidity is significant and well documented *(**Ahmedin et al .,2008).***

Epidemiological studies have revealed several risk factors associated with increased susceptibility to breast cancer. Among these, familial history is one of the most important. Five to ten percent of breast cancers are believed to be hereditary ***(James et al., 2009***).

Nearly all cancers are caused by abnormalities in the genetic material of the cancer cells. These abnormalities typically affect two general classes of genes; Cancer-promoting oncogenes are often activated,while tumor suppressor genes are often inactivated in cancer cells ***(Tannock et al.,2005*).**

Normally DNA damage lead to the activation of tumor suppressor genes which arrest the progression of the cell cycle in order to carry out DNA repair, preventing mutations from being passed on to daughter cells. However, a mutation can damage the tumor suppressor gene itself, or the signal pathway which activates it, ***"switching it off",***leading to inhibition of DNA repair **.** DNA damage accumulates without repair, inevitably leading to cancer***(Kleinsmith, 2006).***

Both alleles of the tumor suppressor gene must be affected before an effect is manifested. This is due to the fact that if only one allele for the gene is damaged, the second can still produce the correct protein***(Parkin et al .,2002***).

Mutations of tumor suppressor genes that occur in germline cells are passed along to offspring, particularly in high-risk families(***Feinberg,2004).***

One of the most important tumor suppressor genes associated with breast cancer is BRCA1 gene ***(Easton et al.,2007).***

The BRCA1 gene is located on the long (q) arm of chromosome 17 at band 21 organized in 24 exons The BRCA1 protein interacts with the RAD51 protein to mend breaks in DNA ***(Boulton ,2006).*** By repairing the DNA, these two proteins play a role in maintaining the stability of the human genome**.** BRCA1 protein also interacts with many other proteins, including tumor suppressors and regulators of cell division cycle ***(Deng,2006).***

Germline mutations of BRCA1 gene are transmitted in the autosomal dominant fashion and predispose the carriers to the development of ovarian and/or breast cancers. Women who carry BRCA1 mutations have a probability of about 80% for developing breast cancer, during their lifetime **(*Laura et al.,2009***).

In a study of polish population , three important mutations in BRCA1 gene were detected including 5382insC, 185delAG and C61G on exons 11, 2and 5 respectively ***(Grzybowska et al., 2002).***

In addition , exons 2 and 5 of BRCA1 gene were found to have a significant role in protein function and exon 11 was found to cover a large segment of the gene. Also other significant studies showed that exons 2 , 5 and 11 are most likely to habour germ line BRCA1 mutations ***(Yassaee et al. ,2002***).

The aim of the work

The aim of this study is to detect 5382insC ,185delAG and C61G mutations in BRCA1 gene in female patients in Qalubia Governorate and correlate them with the presence or absence of family history of breast or ovarian cancer to allow identification of individuals at high risk.