Association of TTTA polymorphism in *CYP19* gene with endometrial and ovarian cancers risk in Basrah

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A B S T R A C T

This study involved 62 patients and 60 healthy controls, genomic DNA was extracted from blood and *CYP19* gene amplified by PCR. The results showed The distribution of TTTA repeat polymorphism of the *CYP19* gene among the controls and endometrial cancer(EC), showed that the risk for EC was increased about two fold in the women which have (TTTA)9, (TTTA)11 and (TTTA)12 repeats OR = 1.56, 2.16, 1.56 respectively. The risk to develop Ovarian Cancer(OC) patients have increased about two fold in the women having (TTTA)11, OR = 2.087 and about four fold in the women with (TTTA)12, OR = 3.868.Asignificant effect in (7–11) heterozygote allele between control and EC patients the risk increased about eleven fold, OR = 10.5 and a significant effect in (7–10), (7–12) and (11−11) heterozygote alleles between control and Ovarian Cancer patients the risk increased about two fold, OR = 2.111,2.111,2.462 respectively, and about six fold in (7–11) heterozygote allele OR = 5.981. The (TTTA)n repeat lengths of ≤9 were classified as short (S), and those ≥10 were classified as long (L) the result showed the risk factor increased about six fold with S/L alleles of *CYP19* gene in EC. OR = 5.625 and about two fold with L/L alleles OR = 1..Alsothe risk factor increased about two fold with long allele of *CYP19* gene in OC. OR = 2.216, four fold with S/L alleles OR = 3.666 and about three fold with L/L alleles OR = 3.3. In conclusion, this study showed an association between *CYP19* polymorphisms, with Endometrial and Ovarian Cancer especially the long Alleles and the haplotype and genotypes frequencies of *CYP19* maybe an indicator for susceptibility for Endometrial and Ovarian Cancer.

1. Introduction

Endometrial cancer (EC) is cancer develops from the endometrium layer, it most common in developed countries, and its prevalence is increasing (Burke et al., 2014; Ferlay et al., 2015). As well as the fourth most common form of cancer overall, about 3% of mortality from cancer is attributable to EC (Murali et al., 2014).

Endometrial cancer has steadily increased, and annual incidence is currently estimated at 19–24 cases per 100,000 women in Sweden (Murali et al., 2014). Mean age at diagnosis is about 60 years (Murali et al., 2014; Sorosky, 2012) and fewer than 10–15% of cases are diagnosedbefore age 50 (Burke et al., 2014; Sorosky, 2012).

Classical risk factors include obesity, chronically anovulatory cycles, nulliparity, diabetes, and polycystic ovarian syndrome (PCOS) (Bansal et al., 2009; Haidopoulos et al., 2010) but also prolonged tamoxifen use and unopposed menopausal hormone treatment; all stimulating growth of the endometrium.

Ovarian Cancer (OC)is sixth cancer most commonly in the world that diagnosed in women (Muralikrishnan et al., 2016).The ovarian cancer incidence increases with old age. Wherever the elderly patients that infected by ovarian cancer have bad prognosis when it compared

with younger patients (Pignata et al., 2009). Genes of the hormones biosynthesis are considered accused because several studies indicate to the correlation between ovarian cancer and endocrine-related tumor (Parazzini et al., 1991).

Cytochrome P450 In humans, are drug- metabolizing enzymes. They are responsible for oxidation of drugs, fatty acids, carcinogens, toxins and steroids (Shimada et al., 1994; Badyal and Dadhich, 2001; Hamdy et al., 2002), and contribute to the metabolism of 90% of all drugs (Lewis and Ito, 2008). CYP proteins have a role in mediating the oxidation in phase (Burke et al., 2014) of the drug metabolism, that done in the liver, (70) % of the drugs are metabolized in these methods (Austin and Groves, 2011).

CYP19 gene is encoding enzymatic proteins called aromatase that are considered the primary enzyme for the final step of estrogen biosynthesis by transition 19-carbon steroids (androstenedione and testosterone) to 18-carbon estrogen (estradiol and estrone).The aromatase enzyme is working more in placental, ovarian, adipose, testicular, brain tissues and bone (Sebastian and Bulun, 2001). Aromatase enzymes are a member of the family of the cytochrome P450,and encoded by the *CYP19* gene (Bulun et al., 2004; Kitawaki et al., 1999).

CYP19 gene is located in the chromosome 15q21.2 contains ten