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# INVESTIGATION OF THE ENZYMATIC ROLE OF MTHFR ON METABOLIC PROFILE AND PHYSIOLOGICAL REPRODUCTIVE HORMONES IN WOMEN USING AN ORAL HORMONAL CONTRACEPTIVE

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## Abstract

Women's Health Initiative demonstrated heart diseases and cardiovascular risk correlated to the using of oral hormonal contraceptive (OHC) pills therefore the aim of this study is to find out the prevalence of metabolic profile and the effect of OHC on MTHFRA activity in a group of women of reproductive age in Iraqi women. This study enrolled 45 women with OHC and 45 women without consumption of OHC in their reproductive ages. MTHFR activity and TES were determine by ELISA methods, while FSH andLH, were estimated by Cobas C111 Analyzer, the metabolic profile were assessment by spectrophotometric methods with specific kits. The results of this study demonstrated that BMI of OHC group has been statistically increased (p-value<0.05) compare to control group. Results from a recent study indicate that statistical significant differences in MTHFR activity, FSH, and LH hormones levels of both OHC and control groups (p-value< 0.05). The metabolic profile that estimated in present study showing significant differences in both study groups OHC and control (p-value< 0.05). The results showing positive correlation between MTHFR and FSH levels in OHC group (r=0.342) while we suggested negative correlation between MTHFR and LH levels in OHC group (r=-0.123).

**Key words:** Oral hormonal contraceptives, metabolic profile, LH, FSH and MTHFR.

## 1. Introduction

Oral Hormonal Contraceptives (OHC) were created more than forty years prior as a compelling, quickly reversible prophylactic. Through this time, the portions of estrogen and progestin diminished, consequently decreasing the likely danger while looking after adequacy (Tayob *et al*., 2021). All the more as of late the contraceptives have been adjusted to abbreviate or dispense with fake treatment pills to reduce feminine side effects (Trego, 2007). Mix hormonal contraceptives are normally taken orally and estradiol is the significant estrogen delivered by the ovary however its utilization is restricted because of helpless ingestion when taken in a non-micronized structure. The expansion of an ethyl gathering to the 17 positions delivers the species orally dynamic and accordingly ethyl estradiol is the most well-known estrogen accessible in current OHC (Trussell, 2004). OHC is an old style to given in a cyclic way with 21 days of dynamic pills followed by seven days of a fake treatment (Sulak *et al*., 2002). Quite possibly the most financially savvy general wellbeing mediations is family arranging, which can altogether improve the strength of ladies and their families. Family arranging empowers ladies to decide the circumstance and dividing of their kids and offers moms and infants a chance to remain solid (Levesque and Lamarche, 2008; Olson, 2009). The past examinations indicating that utilizing

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OHC effects affect pulse, lipid profile, body weight, and serum glucose focuses (Yamada *et al.*, 2005). MTHFR activity may be inhibited by Dihydrofolate (DHF) and Sadenosyl methionine (SAM) and MTHFR can also be phosphorylated allows it to be more easily inhibited by SAM (Wan *et al.*, 2018). MTHFR is a vital protein of folate digestion during the time spent one-carbon digestion. MTHFR changes over 5,10-methylene tetrahydrofolate to 5-methyltetrahydrofolate and take an interest in folate and homocysteine transformation connected to DNA methylation (Tuttelmann *et al.*, 2007). Women's Health Initiative demonstrated metabolic disorders and other diseases risk correlated to the using of OHC pills, therefore the present work was initiated to explore to find out the prevalence of metabolic profile and the effect of OHC on MTHFRA activity in a group of women of reproductive age in Iraqi women.

## 2. Materials and Methods

### Study group

A case-control study was conducted in Babylon province/Iraq that starting from Nov 2019 till to Nov 2020 at Al-Qasim Green University. This study included 45 women have taken OHC at least two years as cases group, while other 45 of healthy women were not used any types of OHC in any time of their reproductive life as control group.

### Measurement of MTHFR and TES levels

The levels of serum MTHFR (ng/ml) and TES (ng/ml) were measured by Enzyme-linked immunosorbent assay (ELISA) depending to manufacture instructions. The levels of MTHFR and TES in the serum of OHC and control groups was assessed by comparing the absorbance of assays to the standard curves of both markers (Hamzah *et al.*, 2020; Ali, 2020), as shown in Figure – 1.

### Measurement of FSH, LH, TES hormones

Serum FSH and LH hormones were estimated by Cobas C111 analyzer using a commercial kit according to the manufacturer instructions.

### Measurement of Metabolic profile

FBG, TC, TG, LDL, and HDL were measured by spectrophotometric methods depending on protocols provided by the manufactures kits.

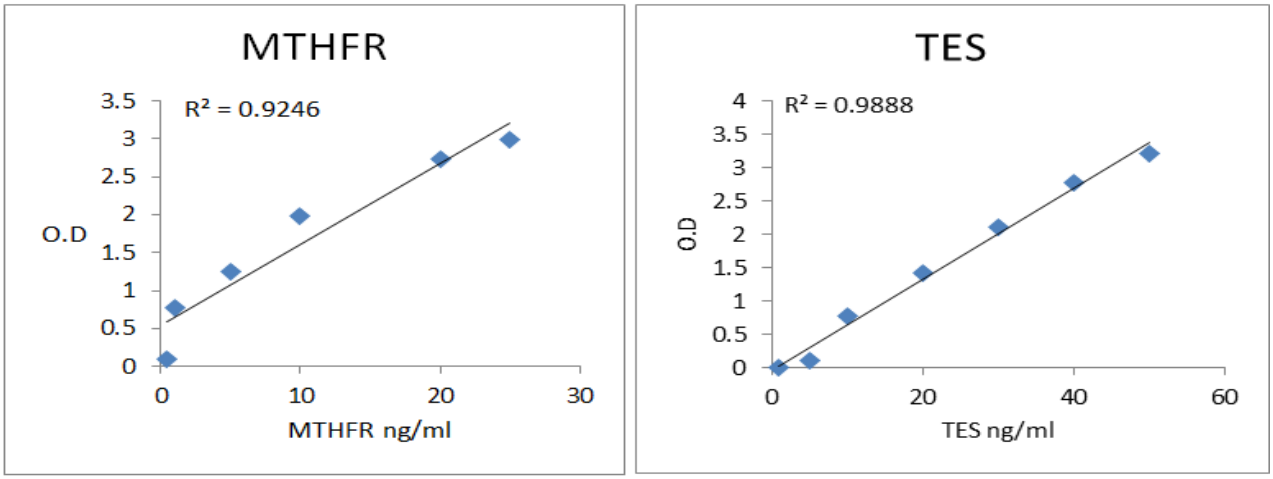


**Figure - 1: MTHFR and TES standard curves**

## 3. Results

The present study showing that Age and BMI of study groups were listed in Table – 1.

**Table - 1: Age and BMI in study groups**

| Parameter | OHC (N=45) | Control (N=45) | p-value |
|---|---|---|---|
| Age | 31±6.5 | 30±7.3 | 0.161 |
| BMI | 29±5.9 | 24±6.8 | 0.0001 |

The results of this study were showing statistical significant differences in MTHFR activity, FSH, and LH hormones levels of both OHC and control groups (p-value< 0.05) as listed in Table – 2.

**Table - 2: MTHFR levels (ng/ml) in study groups**

| Groups | MTHFR (ng/ml) mean±SD | FSH (IU/ml) mean±SD | LH (IU/ml) mean±SD | TES (ng/ml) mean±SD |
|---|---|---|---|---|
| OHC (N=45) | 14±4.89 | 2.987±0.19 | 6.342±0.71 | 26.32±5.71 |
| Control (N=45) | 22±0.89 | 7.543±0.34 | 3.006±0.29 | 23.87±7.59 |
| p- value | 0.0001 | 0.0001 | 0.0001 | 0.021 |

The metabolic profile that estimated in present study were listed in Table – 3.

**Table - 3: Metabolic profile levels (ng/ml) in study groups**

| Groups | FBG mg/dl | TG mg/dl | TC mg/dl | LDL mg/dl | HDL mg/dl |
|---|---|---|---|---|---|
| OHC (N=45) | 112±13 | 187±23 | 198±19 | 114±9 | 34±8 |
| Control (N=45) | 109±11 | 143±19 | 187±20 | 103±6 | 39±7 |
| p- value | 0.119 | 0.0001 | 0.034 | 0.001 | 0.003 |

The correlations between MTHFR with reproductive hormones FSH,LH, and TES in OHC group were depicted in Figure – 2.

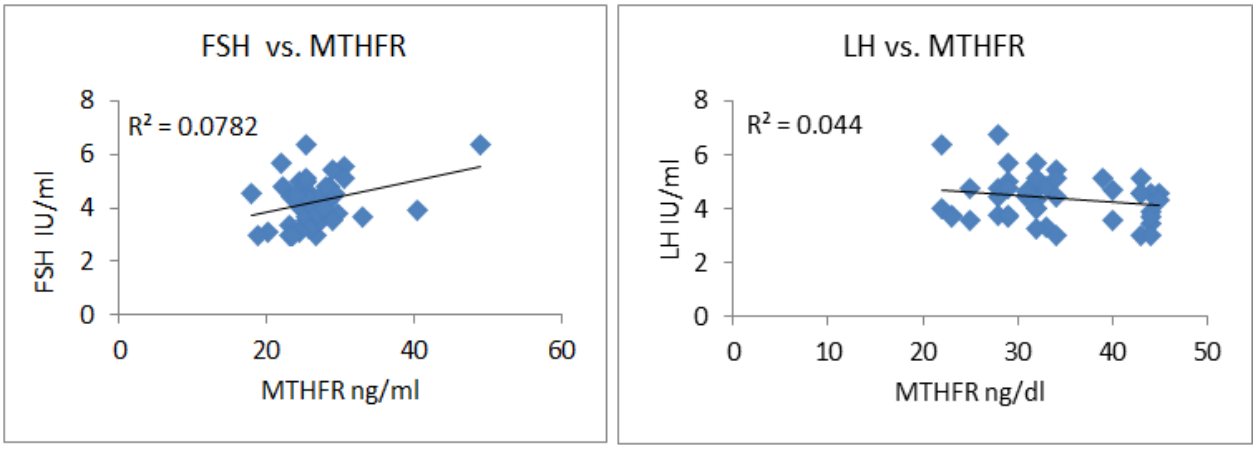


**Figure - 2: MTHFR correlation with FSH and LH levels**

## 4. Discussion

One of the well-known that MTHFR is a vital compound of folate digestion during the time spent one-carbon digestion. It has been found that MTHFR changes over 5,10-methylenetetrahydrofolate to 5-methyl tetrahydrofolate and partake in folate and homocysteine transformation related to DNA methylation (Kelly *et al*., 2005). MTHFR is one of the administrative compounds associated with folate digestion, DNA replication, and methylation of both DNA and protein and it is an antecedent of SAM that capacities as a methyl contributor for DNA and amino corrosive methylation in spermatogenesis (Brunner and Hogue, 2005). The results of this study were showing statistical significant differences in MTHFR activity, FSH, and LH hormones levels of both OHC and control groups (p-value< 0.05).

Fertility hormones, FSH, LH and TES were estimated for both groups to check the effect of OHC on their levels. It was shown from the Table - 2 that the elevation in LH hormone was more in the OHC group (6.342±0.71), compare to control group (3.006±0.29). In contrast, for the FSH hormone it was noticed that this hormone decreased significantly in the OHC group (2.987±0.19) compare to control group (7.543±0.34).The results showing positive correlation between MTHFR and FSH levels in OHC group (r=0.342) while we suggested negative correlation between MTHFR and LH levels in OHC group (r=-0.123). Table - 1 showing the effects of OHC on BMI of women whom using it for more than two years duration,29±5.9 vs. 24±6.8 of OHC and control group, respectively. Two retrospective cohort studies were completed by Brunner *et al*. (2005). This investigation sketched out that tallness and weight were accounted for by 2,064 ladies who were utilizing OHC, recommended no expanded danger of OHC disappointment was seen in unadjusted or adapted to (age, conjugal status, instructive level, neediness level, race/ nationality, equality, double strategy use, and fruitfulness status) models of ladies in the higher weight classes (171–190 lb and >190 lb) contrasted with ladies in the reference classification (111–130 lb). The unadjusted danger of disappointment was essentially higher [RR = 1.8 (1.01–3.20)] among ladies in the most elevated BMI gathering (≥30) than among ladies in the reference BMI gathering (20–24.9), however, the changed RR was not critical. In the subsequent examination, the example is 1,491 ladies utilizing OHC. In this study, OHC will increasing the BMI and this may be make a risk factor for obesity. The many studies and analysis completed by other researchers suggested that the genetic disorders and polymorphism is a risk factor for CAD, which is possibly and partly mediated by abnormal lipid levels (Kzar *et al*., 2020; Al-Hussainy *et al.,* 2020).

## 5. Conclusion

OHC have a risk factor for deficiency in MTHFR and elevation in lipid profile levels and make women more resettable to increasing of BMI and metabolic syndrome disorders.

## Conflict of interest

None

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