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Evaluation of Thyroid Hormones in Women Patients with Recurrent Miscarriage

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Annotation: Recurrent miscarriage is defined as the loss of two or more consecutive pregnancies before 20 weeks of gestation. This condition results from multiple factors, including genetic, hormonal, anatomical, immunological, and environmental influences. This study investigates the role of thyroid hormone levels (T3 and T4) and body mass index (BMI) in recurrent miscarriage women. A total of 190 women aged 20–44 years were studied. Participants were divided into two groups: 82 women with successful pregnancies (Standard group) and 108 women with three or more recurrent miscarriages (Recurrent miscarriage group). Results showed no significant difference in age between the groups ($p = 0.0896$). However, BMI was significantly higher in the recurrent miscarriage group (25.25 ± 0.360) than in the standard group (23.73 ± 0.423, $p = 0.0068$). T4 levels were lower in the recurrent miscarriage group (62.76 ± 2.487 nmol/L) compared to the standard group (70.66 ± 2.397 nmol/L, $p = 0.0267$). T3 levels did not significantly differ between groups ($p = 0.2587$).

These findings suggest that elevated BMI and reduced T4 levels may contribute to recurrent miscarriage risk. Addressing these factors may improve pregnancy outcomes.

Introduction:

A miscarriage also referred to as spontaneous pregnancy loss and occurs when a pregnancy ends before the fetus is capable of surviving outside the womb typically prior to 20 weeks of gestation

[1]. It is a situation with multiple contributing factors including immunological, genetic, anatomical, hormonal and environmental effects [2]. Miscarriage is the most frequent complication in early pregnancy, affecting an estimated 10–15% of pregnancies that have been clinically confirmed [3]. However, the actual rate may be higher as many losses happen before the pregnancy is officially recognized.

Miscarriages in clinical are classified into several types, such as threatened, inevitable, incomplete, complete, missed, and recurrent (which refers to three or more consecutive losses) [4]. Symptoms can vary widely, ranging from no noticeable signs detected during an ultrasound to vaginal-bleeding, abdominal cramping or the expulsion of fetal-tissue. Diagnosis typically involves transvaginal-ultrasound and measurement of "serum β-hCG" levels, with further investigations conducted in cases of recurrent miscarriage to uncover potential underlying causes [5]. The causes of miscarriage are multifaceted with chromosomal-abnormalities responsible for approximately "50–70%" of early pregnancy losses. Extra factors include structural issues in the uterus (septate uterus, fibroids) hormonal-disruptions, infections and autoimmune conditions like "antiphospholipid syndrome" [6]. Advanced maternal age, as well as lifestyle factors such as smoking, excessive alcohol consumption and obesity, also significantly increase the risk.

Thyroid hormones (T3 and T4) play a critical role in pregnancy, influencing maternal health, fetal development, and overall pregnancy outcomes. Proper thyroid function is essential for maintaining a healthy pregnancy, as thyroid hormones regulate metabolism, energy balance, and the development of the fetal nervous and skeletal systems [7]. This study aim to evaluate effect of levels of thyroid hormones (T3 and T4) on recurrent miscarriage in addition to other factor such as obesity and age.

Materials and Methods:

Subject:

This study including 190 participant women in age 20 - 44 years old. They are classified in two group when the first group (N=82) including women with history of successful pregnancy without miscarriage as standard women whereas second group (N= 108) women with three or more of miscarriage (recurrent miscarriage). Study including compared between them according to Thyroid hormone (T3, T4), Age and BMI. Women with polycystic ovarian syndrome, Diabetes mellitus or taking Levothyroxine as supplement were exclusion from study.

Sample collection:

Blood samples were taken from women participants by venuos puncture and 5 ml of blood collected in EDTA tube and centrifuged at 1500 RPM for 20 minutes. Plasma is separated and transferred in plane tube and kept in freeze until using in thyroid assay [8,9].

Thyroid assay:

T4 assay was determined using minivadis instrument deepening on combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA). The Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipetting device for the assay. Whereas the T3 assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA). The Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipetting device for the assay [10,11].

Statistical analysis:

Data were analysed using GraphPad prism program (Version 8) using t- test independing Coloumn statistiacal. All tables and figures are created using Microsoft Excel 2020 and GraphPad prism 8 Software.

Results and Discussion:

Recurrent miscarriage named also as "recurrent pregnancy loss" (RPL) refers to the occurrence

of two or more consecutive pregnancy losses before 20 weeks of gestation [12]. The precise cause of recurrent-miscarriage is often unknown. Diagnosing the state typically requires extensive testing, such as blood tests, genetic-analysis, imaging and occasionally, consultation with a fertility specialist. Although "recurrent miscarriage" can be emotionally devastating and many women experiencing this issue can achieve successful pregnancies with the right medical treatment and support [13].

Table 1: Results of participant women with normal and recurrent miscarriage, P value ≤ 0.05

Groups	N	Mean ± SEM	Range	Significantly different (P < 0.05)	95% confidence interval
According to Age samples					
Standard women	82	32.62 ± 0.688	20 - 44	0.0896 (NS)	-0.2616 to 3.610
Miscarriage women	108	34.30 ± 0.676	21 - 44		
According to BMI					
Standard women	82	23.73 ± 0.423	16- 30	0.0068 (S**)	0.4240 to 2.613
Miscarriage women	108	25.25 ± 0.360	18-31		
According to T4 hormones					
Standard women	82	70.66 ± 2.397	37-130	0.0267 (S*)	-14.88 to -0.9212
Miscarriage women	108	62.76 ± 2.487	22-148		
According to BMI					
Standard women	82	1.773 ± 0.093	0.19 – 3.3	0.2587 (NS)	-0.1029 to 0.3807
Miscarriage women	108	1.712 ± 0.084	0.23 – 3.7		

As shown in table 1 there is no significant difference in age between groups when mean of standard group 32.62 ± 0.688 years old. Whereas recurrent miscarriage women showed mean 34.30 ± 0.676 years old. As shown in Figure 1, age is an important factor in the risk of miscarriage. As women get older especially after the age of thirty-five, the chances of miscarriage increased [14]. This is mainly due to a decline in "egg quality" and a rise risk of "chromosomal abnormalities" in embryos. Older women are more likely to produce eggs with chromosomal-issues such as aneuploidy (an abnormal chromosome number), which can lead to miscarriage [15,16].

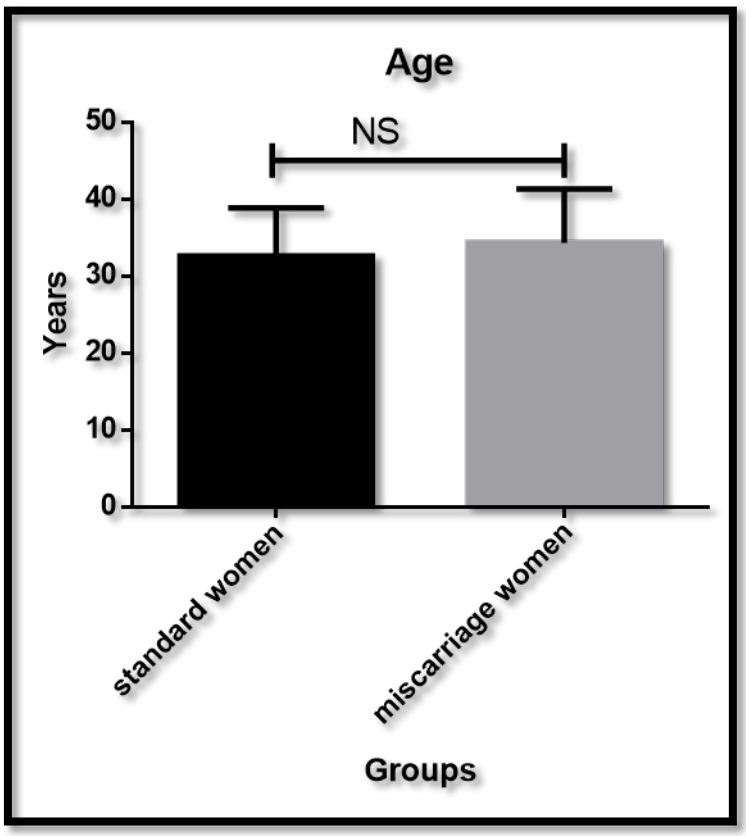

Figure 1: Comparison between groups according to age

As shown in table 1 and figure 2, there was a significant difference between the mean of BMI of the two groups with P value of 0.0068 (S**). Since the standard women showed a mean of BMI of 23.73 ± 0.423. Whereas, in the miscarriage women it was 25.25 ± 0.360 and groups.

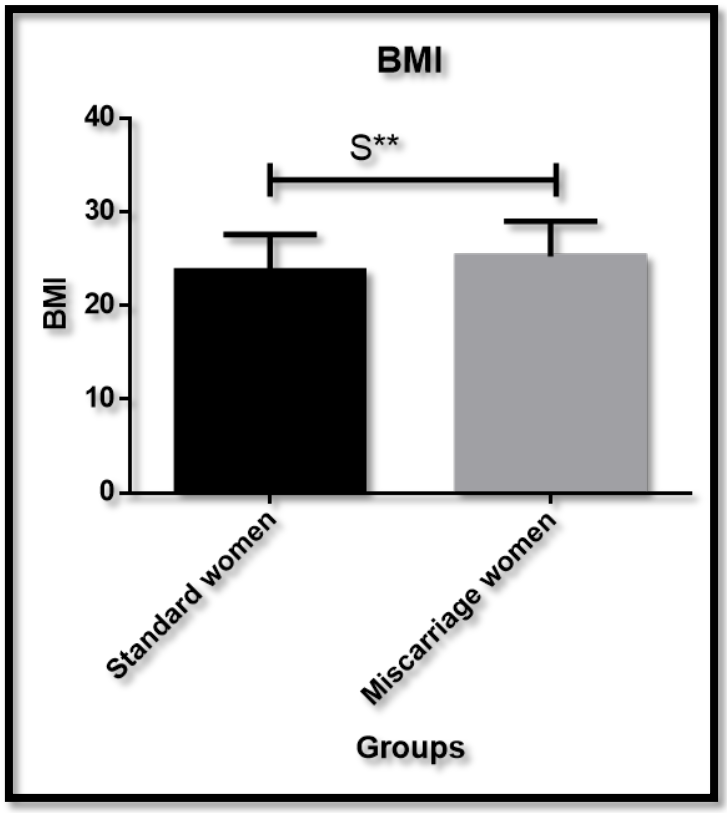

Figure 2: Comparison between groups according to BMI

Obesity is linked to a higher risk of miscarriage in women. Women with a body mass index (BMI) of 30 or above are more prone to pregnancy loss compared to those with a healthy weight [17]. Several factors contribute to this association between obesity and miscarriage such as hormonal factor, Inflammation and immune system response and Polycystic ovary syndrome.

Regarding the thyroxine hormones (T4) levels, table 1 showed low levels of T4 in women with recurrent miscarriage 62.76 ± 2.487 Nmole/L compared to the standard women group (70.66 ± 2.397 Nmole/L) with a significant difference and P value of 0.0267 (S*) (Figure 3).

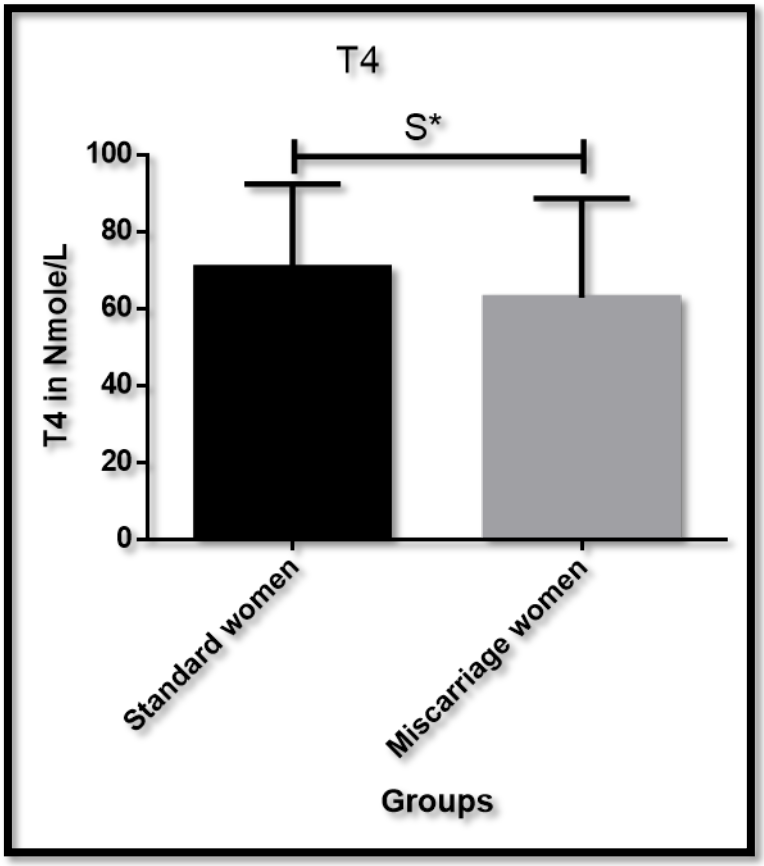

Figure 3: Comparison between groups according to T4 hormone

Thyroid dysfunction, whether it involves hypothyroidism "underactive thyroid" or hyperthyroidism "overactive thyroid" can have a profound impact on pregnancy-outcomes [18]. The thyroid gland is essential for regulating metabolism and producing hormones and any imbalance can disrupt the proper functioning of the reproductive system.

When the thyroid-gland produces insufficient thyroid hormones, it can result in infertility, challenges in conceiving and a heightened risk of miscarriage [19]. Low thyroid hormone levels "disrupt hormonal balance" potentially affecting embryo implantation and fetal development.

On the other hand, there was a non- significant difference in the levels of T3 hormone with a P value of 0.2587 (NS). Since the levels of T3 in standard women and miscarriage women group were 1.773 ± 0.093 Nmole/dl and 1.712 ± 0.084 Nmole/ dl, respectively (Figure 4).

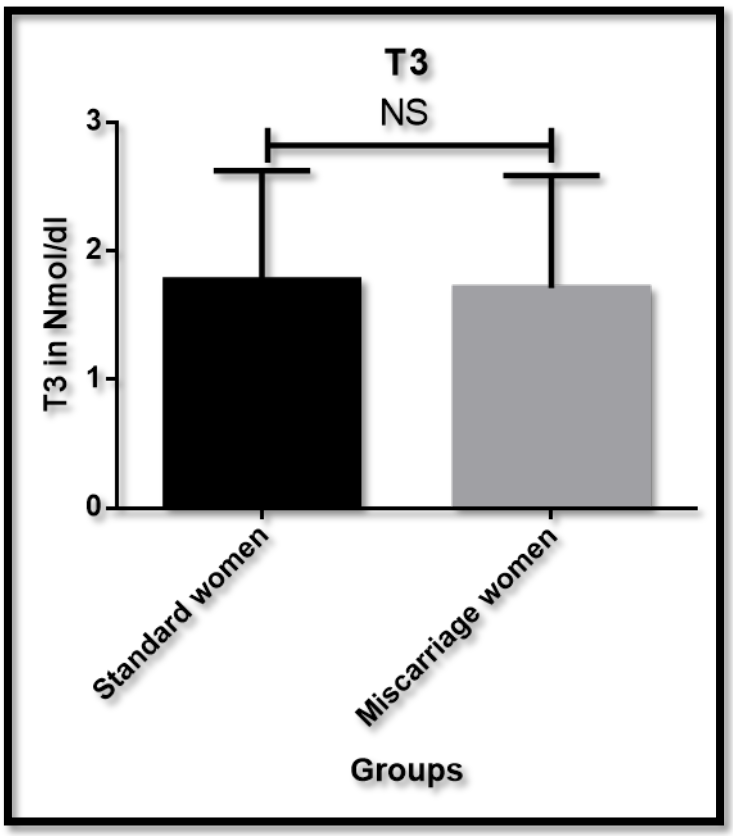

Figure 4: Comparison between groups according to T3 hormone.

When thyroid dysfunction and obesity occur together, they can compound each other's effects. Both hypothyroidism and obesity are associated with insulin resistance, which can further disrupt the hormonal environment necessary for pregnancy and increase miscarriage risk and increase inflammation in the body, which may negatively impact the uterus and affect embryo implantation and development [20]. For women with obesity and thyroid disorders it is important to address both conditions through appropriate medical care. Managing thyroid hormone levels and maintaining a healthy weight can improve the chances of a successful pregnancy and reduce the risk of miscarriage.

Conclusion

The conclusion of this study emphasize the significant role of increasing BMI and decreasing T4 levels in rise the risk of recurrent miscarriage. Targeted-management of obesity and thyroid hormones dysfunction can potentially enhance reproductive outcomes and support successful-pregnancies.

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