

Hypothyroidism In Women With Recurrent Spontaneous Abortion

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ABSTRACT

Recurrent miscarriage, defined as loss of two or more consecutive pregnancies, occurs in 1–2% of couples attempting to bear children. The major causes of recurrent pregnancy loss (RPL) based on the literature include parental structural chromosome rearrangement, immunologic factors (i.e. antiphospholipid syndrome), thrombophilic factors (both inherited and acquired), anatomic factors of uterine anomalies, and endocrinologic disorders. Luteal phase defect, polycystic ovarian syndrome (PCOS), diabetes mellitus, thyroid disease and hyperprolactinemia are among the endocrinologic disorders implicated in approximately 17% to 20% of RPL. The prevalence of hypothyroidism in the general population of reproductive age is about 2-3%. The aim of this study is to observe the benefit of screening for hypothyroidism amongst women with recurrent spontaneous abortion early in the first trimester. The study included one hundred and sixty (160) women, in the reproductive age of life, where their ages ranged from 20 – 33 years, and divided into two groups. Study group which included eighty (80), non pregnant women with a history of two or more consecutive spontaneous abortions early in the first trimester, with no living children and control group which included eighty (80), non pregnant women having one or more living children without any history of abortion. Hypothyroidism was noted in ten (10) cases (12.5%) in the study group and noted in two (2) cases (2.5%) in the control group with a statistically significant difference ($P < 0.01$). The mean levels of TSH in the study group was 22.71 ± 13.13 $\mu\text{IU/ml}$. Conclusion: Screening for hypothyroidism has clinical significance and would help to reduce miscarriage rate in women with recurrent spontaneous abortion.

Keywords: Hypothyroidism – Recurrent spontaneous abortion – TSH – Free T3 – Free T4.

INTRODUCTION

Recurrent miscarriage, defined as loss of two or more consecutive pregnancies, occurs in 1 – 3% of couples attempting to bear children⁽¹⁾. The major causes of recurrent pregnancy loss (RPL) based on the literature include parental structural chromosome rearrangement, immunologic factors (i.e. antiphospholipid syndrome), thrombophilic factors (both inherited and acquired), anatomic factors of uterine anomalies, and endocrinologic disorders. Nevertheless a definite cause of RPL is identified in only half of the couples⁽²⁾. More than 50% of couples have unexplained recurrent pregnancy loss (uRPL), in whom the cause and risk are not identifiable, and therefore are believed to mostly experience RPL attributable to chance alone⁽³⁾.

Luteal phase defect, polycystic ovarian syndrome (PCOS), diabetes mellitus, thyroid disease, and hyperprolactinemia are among the endocrinologic disorders implicated in approximately 17% to 20% of RPL⁽⁴⁾. The prevalence of hypothyroidism in the general population of reproductive age is about 2 – 3%⁽⁵⁾. Thyroid dysfunctions are common in women during reproductive age with the prevalence of elevated TSH ranging from 4% to 9% and the prevalence of thyroid peroxidase antibodies (TPO-Ab) ranging from 11.3% to 18% in the population⁽⁶⁾. The American college of Obstetrics and Gynecology characterized overt hypothyroidism as an elevated TSH and low circulating thyroid hormones (Free T4)⁽⁷⁾. Normal physiologic changes during early pregnancy, such as increased plasma blood volume, decreased iodine concentrations, and increased production of thyroid-binding globulin, which binds circulating thyroid hormones, all lead to an amplified demand placed on the thyroid during pregnancy to increase the production of thyroid hormones⁽⁸⁾. Effect of overt hypothyroidism include increased risk of miscarriage, low birth weight, premature delivery, placental abruption, hypertensive disorders of pregnancy, and lower intelligence quotient scores⁽⁹⁾.

Aim of the work

The aim of this study is to observe the benefit of screening for hypothyroidism amongst women with recurrent spontaneous abortion early in the first trimester.

SUBJECTS AND METHODS

This is a randomized controlled study, conducted at Benha Teaching Hospital in Egypt, during the period from June 2019, to July 2020.

The study included one hundred and sixty (160) women in the reproductive age of life where their ages ranged from 20 to 33 years, and divided into two groups:

1. Study group: this group included eighty (80), non pregnant women with a history of two or more consecutive spontaneous abortions early in the first trimester, with no living children.
2. Control group: this group included eighty (80), non pregnant women without any history of spontaneous abortion and having one or more living children.

ELIGIBLE CRITERIA

Women with known thyroid disorders, diabetes mellitus, history suggestive of polycystic ovarian syndrome (PCOS), known hyperprolactinemia or auto-immune disorders, history of cervical incompetence or any other uterine pathology were excluded.

All women underwent a comprehensive medical evaluation including detailed history taking and thorough physical examination.

All women in both groups were investigated for thyroid stimulating hormone (TSH), free tri-iodothyroxin (F-T3) and free thyroxine (F-T4) levels.

SAMPLE PREPARATION

1. Collect blood specimens and separate the serum immediately.
2. Specimens may be stored refrigerated at (2-8°C) for 5 days. If storage time exceeds 5 days, store frozen at (-20°C) for up to one month.
3. Avoid multiple freeze – thaw cycles.
4. Prior to assay, frozen sera should be completely thawed and mixed well.
5. Do not use grossly lipemic specimens.

PROCEDURE

Done through multiple steps starting by bringing all specimens and kit reagents to room temperature (18-26°C), gently mixing and lastly reading absorbance on ELISA reader at 450 nm within 15 minutes after adding the stopping solution.

Results were constructed through the standard curve, according to SIGMA ALDRICH COMPANY, 3050 PruG Street, St. Louis, M063703, USA, with expected values as follows:

TSH: Adult: 0.4 – 4.2 µIu/ml.

Free T4: Adult : 0.8 – 2.0 ng/dl.

Free T3: Adult : 2.3 – 4.2 pg/ml

RESULTS

Table (I): Shows that there were no significant statistical differences between the two groups for all demographic variables.

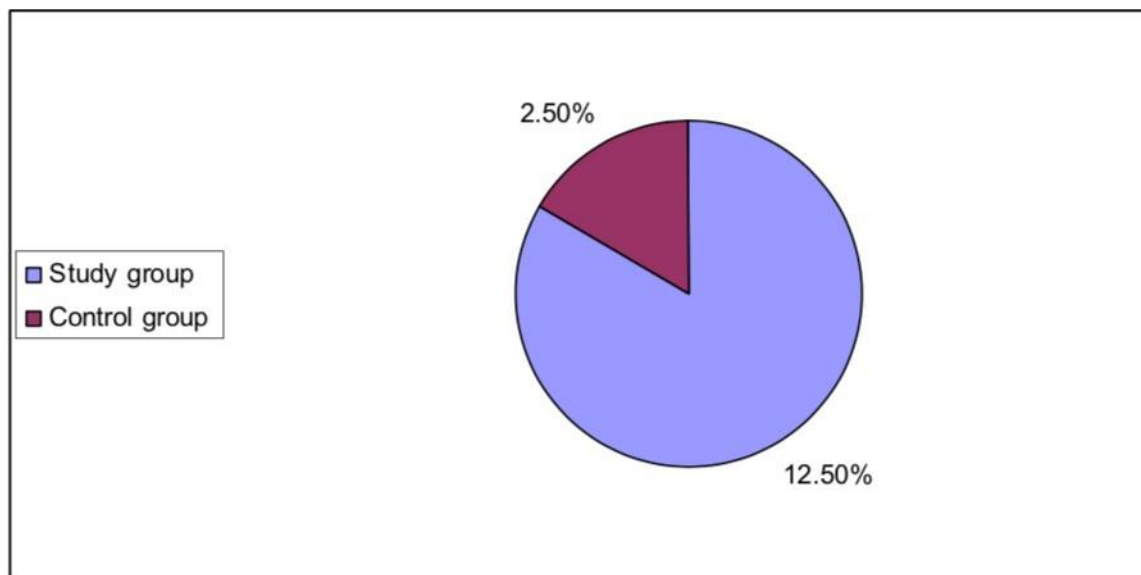
Variable	Study group Number = 80	Control group Number = 80	P - value
	Mean ± SD OR Number (%)	Mean ± SD OR Number (%)	
Age (Years)	26.8 ± 4.9	26.7±5.3	0.985
BMI (kg/m²)	24.99 ± 4.79	25.28 ± 4.87	0.933
Residence:			0.731
Rural	38(47.5%)	40 (50%)	
Urban	42(52.5%)	40 (50%)	

Table (II): Shows that there were no statistically significant difference in the number of pregnancy losses in the study group.

Study group Number = (80)	Number of pregnancy losses	Percent	P. value
38	Two	47.5%	0.731
42	Three or more	52.5%	

Table (III): Shows that, there was a statistically significant difference between the two groups as regarding the number of positive cases for hypothyroidism.

Group	Positive cases for hypothyroidism (Number)	Percent (%)	P - value
Study group Number = (80)	10 cases	12.5 (%)	< 0.01
Control group Number = (80)	2 cases	2.5%	

**Figure (I): Shows number of positive cases of hypothyroidism in both groups.****Table (IV): Levels of TSH, Free T3 and Free T4 as regarding hypothyroidism and euthyroid women, in both groups.**

Variable	Study group (Number = 80)		Control group (Number = 80)	
	Hypothyroidism	Euthyroid	Hypothyroidism	Euthyroid
	Number = 10 cases	Number = 70 cases	Number = 2 cases	Number = 78 cases
	% = 12.5%	% = 87.5%	% = 2.5%	% = 97.5%
TSH 0.4 – 4.2 μ Iu/mL	22.71 $\pm$ 13.13	1.87 $\pm$ 1.2	12.1	2.1 $\pm$ 1.54
Free T3 2.3 – 4.3 pg/ml	1.45 $\pm$ 0.72	2.91 $\pm$ 1.99	1.69	3.08 $\pm$ 1.28
Free T4 0.8 – 2.0 ng/dl	0.59 $\pm$ 0.20	1.22 $\pm$ 0.72	0.64	1.45 $\pm$ 0.45

DISCUSSION

During pregnancy proper maternal thyroid function is important for both mother and fetus⁽¹⁰⁾. The symptoms of thyroid disease are often less than obvious, many women with recurrent miscarriages wonder whether they might have an untreated thyroid condition. Furthermore, increased production of thyroid-binding globulin and the subsequent binding of circulating thyroxine result from the increased level of estrogen that occurs in early pregnancy⁽¹¹⁾. In pregnant women with limited thyroid reserves, hypothyroidism may be unmasked by these increased demands⁽¹²⁾. Dramatic changes in physiologic status occur during pregnancy, likewise, thyroid function is also affected.

For example direct stimulation of the thyroid by TSH receptor binding of β -human chorionic gonadotrophin, a hormone synthesized in rapidly increasing levels in early pregnancy, transiently increases T4 production. In addition the iodine concentration decreases as a result of the increased glomerular filtration rate⁽¹³⁾. Women with hypothyroidism have decreased fertility⁽¹⁴⁾, even if they conceive, the risk of miscarriage is increased⁽¹⁵⁾. Preconception or early pregnancy screening for thyroid dysfunction has been proposed but is not widely accepted. However, measurement of thyroid function should certainly be considered in those who are at high risk⁽¹⁶⁾.

In the present study, the prevalence of hypothyroidism in women with recurrent spontaneous abortion early in the first trimester is (12.5%), with a statistically significant difference. This agrees with the two studies done by *Dinesh et al.*⁽¹⁷⁾ and *Khalid et al.*⁽¹⁸⁾, where the prevalence rate of hypothyroidism was 14.3% and 11.45% respectively.

Sharma et al.⁽¹⁹⁾, found a significant association of thyroid function with an abortion rate of 14.63% in their study group i.e. pregnant women with hypothyroidism and 4.96% in their control group. In the study of *Rama et al.*⁽²⁰⁾; hypothyroidism was found in seven out of 163 (4.29%) women with recurrent pregnancy loss and one out of 170 (0.58%) as control group. The study demonstrates that hypothyroidism has a statically significant relationship with recurrent pregnancy loss in the first trimester and suggests that diagnosis of hypothyroidism could help couples with RPL to have a successful outcome in subsequent pregnancies.

In the study of *Masand and Patel*⁽²¹⁾, hypothyroidism was found in seven out of one hundred (7%) of women with recurrent pregnancy loss and in two out of one hundred (2%) as control group. The study demonstrates that hypothyroidism has a statistically significant relationship with recurrent pregnancy loss and concludes that screening for thyroid dysfunction should be done in all pregnant and non pregnant women who had recurrent pregnancy losses necessarily during first trimester itself soon after confirmation of pregnancy.

In the present study, the mean levels of TSH is 22.71 ± 13.13 μ lu/mL.

In the two studies done by *Alssandro et al.*⁽²²⁾ and *Verma et al.*⁽²³⁾, the mean levels of TSH were 17.8 ± 1.23 mlu/L and 29.8 ± 21.13 mlu/L respectively. A positive relationship was identified between higher TSH in early pregnancy and the risk of child loss, defined as spontaneous abortion, fetal death or neonatal death⁽²⁴⁾.

CONCLUSION

The prevalence of hypothyroidism is higher in non pregnant women with a history of recurrent spontaneous abortion, so screening for hypothyroidism has clinical significance and would help to reduce miscarriage rate in those women.

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