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Correlation Between Subclinical Hypothyroidism and Repeated Miscarriage in Pregnant Women

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Abstract

Background: Abortion is a minor complication of pregnancy, defined as the spontaneous loss of the fetus, which occurs in 15–20% of pregnant women. Recurrent miscarriages, which occur in ~1% of women of childbearing age are defined as miscarriages of two or more pregnancies in consecutive pregnancies.

Aim: To determine the association between subclinical hypothyroidism in pregnant women and recurrent miscarriage.

Patients and methods: This observational study was conducted in December 2021 and May 2022 on nine pregnant women at Assiut University's Al-Azhar Hospital. Patient groups who complained of recurrent miscarriages (at least two unexplained recurrent miscarriages) and control groups included pregnant women who had previously given birth to at least one child.

Result: Statistically significant differences between the two groups studied (case and control). The mean miscarriage rate in the case groups was ranged from 2.0 to 7.0. The mean factor in the control group was ranged from 1.0 to 7.0. The calculation was entered as statistically significant for the studied groups (cases and controls) with respect to free thyroxine (FT4), thyroid status, cholesterol, triglycerides, creatinine, urine, alanine transaminase (ALT), aspartate transaminase (AST) and albumin. It appears that there were not enough combinations (cases and controls) of free triiodothyronine (FT3) and thyroid stimulating hormone syntax to be statistically significant. Statistics show that the number of combinations (tilde and control) without anti-thyroid peroxidase (TPO) syntax has a significant impact.

Conclusion: There is a weak association between subclinical hypothyroidism and recurrent spontaneous abortion in pregnant women.

Keywords: Miscarriage, Pregnant, Reccurent, Subclinical hypothyroidism

1. Introduction

Autoimmune thyroid disease is the most common cause of hypothyroidism in women of childbearing age. It has long been suspected that thyroid disease can lead to premature pregnancy loss and other adverse pregnancy outcomes. While the worst hypothyroidism is rare in pregnancy, the incidence of subclinical hypothyroidism is 2–3%.¹

A miscarriage is the spontaneous termination of a pregnancy before the fetus can survive outside the uterus. Recurrent miscarriage, defined as the loss of two or more consecutive pregnancies, affects 1% of

couples trying to conceive. The etiology of recurrent miscarriage includes antiphospholipid antibody syndrome, genetic, anatomical, and endocrine factors. In contrast, ~50% of recurrent miscarriages remain unexplained.²

In women with thyroid autoimmunity, there is a double risk of miscarriage due to the presence of a systemic disease of immune activation which, in addition to the transplacental passage of antibodies blocking thyroid receptors, also leads to an increased clinical risk of pathological conditions. movement against the thyroid Thyroid disease. Subclinical hypothyroidism. Therefore, screening

for subclinical hypothyroidism with TPO3 antibodies may be necessary in cases with a documented history of recurrent miscarriage.³

For this reason, the study aims to show the association between subclinical hypothyroidism in pregnant women admitted to Al-Azhar-Assiut University Hospital and recurrent miscarriages.

2. Patients and methods

In this observational study, 90 pregnant women from the Department of Obstetrics and Gynecology, Al-Azhar University Assiut was divided into two groups in the period December 2021 to May 2022; A group of patients detailing intermittent unsuccessful labors (no less than two repetitive premature deliveries) and a benchmark group of pregnant ladies with no less than one living youngster. Pregnant ladies with intermittent unconstrained early terminations are characterized as at least two non-sequential fetus removals except if the condition is affirmed by pregnancy test, ultrasound, or both, before 20 weeks' incubation. An undiscovered myocardial localized necrosis is protected when there are liars that could be risk factors for creating myocardial dead tissue. Pregnant ladies with a background marked by thyroid sickness who have been treated with thyroxine or thyroid chemicals and have not gotten educated assent.

A written declaration of consent will be obtained from everyone before the start of the course and after the end of the course.

Complete patient medical history, including demographics, medical history, birth history and history of drug-related chronic diseases, free and low

T4 levels, complete blood count, liver function test, kidney function test and lipid profiles.

Data processing and statistical analysis was performed using SPSS Version 20. This information is continuously displayed and analyzed. *P* values below 0.05 (5%) were considered statistically significant.

3. Results

There was statistically significant difference between the two studied groups (cases and control) as regard age. The mean age in cases group was 29.93 ± 5.06 SD with range (18.0–42.0). The mean age in control group was 27.58 ± 5.44 SD with range (18.0–42.0) (Table 1).

There was no statistically significant difference between the two studied groups (cases and control) as regard DM, HTN and Mitral stenosis (Table 2).

There was no statistically significant difference between the two studied groups (cases and control) as regard trimester (Table 3).

The mean number of abortion in cases group was 3.13 ± 1.59 SD with range (2.0–7.0) (Table 4).

The mean number of delivery in control group was 2.49 ± 1.52 SD with range (1.0–7.0) (Table 5).

There was no statistically significant difference between the two studied groups (cases and control) as regard systolic blood pressure, diastolic blood pressure and pulse (Table 6).

There was statistically significant difference between the two studied groups (cases and control) as regard FT4. There was no statistically significant difference between the two studied groups (cases and control) as regard FT3 and TSH (Table 7).

Table 1. Comparison between the two studied groups according to age.

	Cases (n = 45)	Control (n = 45)	t	P
Age (y)				
Minimum–maximum	18.0–42.0	18.0–42.0	2.127*	0.036*
Mean \pm SD.	29.93 \pm 5.06	27.58 \pm 5.44		
Median (IQR)	30.0 (27.0–32.0)	27.0 (23.0–30.0)		

Table 2. Comparison between the two studied groups according to co-morbidity.

	Cases (n = 45) [n (%)]	Control (n = 45) [n (%)]	χ^2	FE _p
DM				
No	43 (95.6)	44 (97.8)	0.345	1.000
Yes	2 (4.4)	1 (2.2)		
HTN				
No	44 (97.8)	45 (100.0)	1.011	1.000
Yes	1 (2.2)	0		
Mitral stenosis				
No	44 (97.8)	44 (97.8)	0.001	1.000
Yes	1 (2.2)	1 (2.2)		

Table 3. Comparison between the two studied groups according to trimester.

	Cases (n = 45) [n (%)]	Control (n = 45) [n (%)]	χ^2	MC_p
Trimester				
1	9 (20.0)	17 (37.8)	4.700	0.109
2	3 (6.7)	5 (11.1)		
3	33 (73.3)	23 (51.1)		

Table 4. Descriptive analysis of the studied cases according to number of abortion in cases group (n = 45).

	Min. – Max.	Mean \pm SD.	Median (IQR)
Number of abortion	2.0–7.0	3.13 \pm 1.59	3.0 (2.0–3.0)

Table 5. Descriptive analysis of the studied cases according to number of delivery in control group (n = 45).

	Minimum–maximum	Mean \pm SD.	Median (IQR)
Number of delivery	1.0–7.0	2.49 \pm 1.52	2.0 (1.0–3.0)

Table 6. Comparison between the two studied groups according to clinical signs.

	Cases (n = 45)	Control (n = 45)	U	P
Systolic blood pressure (mmHg)				
Minimum–maximum	90.0–120.0	100.0–140.0	926.00	0.423
Mean \pm SD.	111.6 \pm 6.73	113.3 \pm 7.39		
Median (IQR)	110.0 (110.0–120.0)	110.0 (110.0–120.0)		
Diastolic blood pressure (mmHg)				
Minimum–maximum	60.0–80.0	60.0–90.0	984.50	0.793
Mean \pm SD.	72.44 \pm 5.70	72.89 \pm 6.26		
Median (IQR)	70.0 (70.0–80.0)	70.0 (70.0–80.0)		
Pulse				
Minimum–maximum	75.0–140.0	75.0–118.0	980.00	0.785
Mean \pm SD.	89.04 \pm 11.19	88.0 \pm 9.08		
Median (IQR)	90.0 (80.0–92.0)	90.0 (80.0–92.0)		

Table 7. Comparison between the two studied groups according to thyroid function.

Thyroid function	Cases (n = 45)	Control (n = 45)	U	P
FT3				
Minimum–maximum	1.90–5.20	2.0–9.90	932.50	0.515
Mean \pm SD.	3.68 \pm 0.68	3.86 \pm 1.10		
Median (IQR)	3.90 (3.10–4.20)	3.80 (3.40–4.30)		
FT4				
Minimum–maximum	0.20–1.80	0.01–1.80	673.0*	0.006*
Mean \pm SD.	1.12 \pm 0.39	0.82 \pm 0.48		
Median (IQR)	1.20 (1.10–1.30)	0.70 (0.50–1.30)		
TSH				
Minimum–maximum	0.70–9.90	0.10–8.20	872.50	0.258
Mean \pm SD.	3.36 \pm 2.13	2.92 \pm 2.09		
Median (IQR)	2.90 (1.8–4.3)	2.70 (1.2–4.1)		

FT3, free triiodothyronine; FT4, free thyroxine.

There was statistically significant difference between the two studied groups (cases and control) as regard thyroid status as we found in control group, 16 (35.6%) had Hypothyroidism, 1 (2.2%) had Hyperthyroidism, 0(0%) with Subclinical hypothyroidism and 28 (62.2%) had Euthyroidism. In study

group, 6 (13.3%) had Hypothyroidism, 1 (2.2%) had Hyperthyroidism, 2 (4.4%) with Subclinical hypothyroidism and 36 (80%) had Euthyroidism (Table 8).

There was highly statistically significant difference between the two studied groups (cases and control) as regard mean Anti TPO (Table 9).

Table 8. Comparison between the two studied groups according to thyroid status.

Thyroid status	Cases (N = 45) [n (%)]	Control (N = 45) [n (%)]	χ^2	^{MC}p
Hypothyroidism	6 (13.3)	16 (35.6)	7.374*	0.022*
Hyperthyroidism	1 (2.2)	1 (2.2)		
Subclinical hypothyroidism	2 (4.4)	0		
Euthyroidism	36 (80.0)	28 (62.2)		

Table 9. Comparison between the two studied groups according to Anti TPO.

Anti TPO	Cases (N = 45) [n (%)]	Control (N = 45) [n (%)]	Test of Significance	P
Negative	40 (88.9)	38 (84.4)	$\chi^2 = 0.618$	$^{MC}p = 0.802$
Positive	4 (8.9)	5 (11.1)		
Border line	1 (2.2)	2 (4.4)		
Minimum–maximum	4.50–730.5	1.70–2622.0	U = 641.50*	0.003*
Mean \pm SD.	38.69 \pm 112.6	94.47 \pm 393.3		
Median (IQR)	11.10 (8.8–14.9)	16.30 (12.2–21.6)		

TPO, thyroid peroxidase.

There was statistically significant difference between the two studied groups (cases and control) as regard Cholesterol, Triglycerides, Creatinine, Urea, ALT, AST and Albumin. There was no statistically significant difference between the two studied groups (cases and control) as regard RBCs, HB, MCV, RDW, WBCs and PLTs (Table 10).

There was no statistically significant difference between thyroid status as regard number of abortion (Table 11).

There was no statistically significant difference with positive correlation between thyroid function as regard number of abortion (Table 12).

There was no statistically significant difference between thyroid status as regard Anti TPO in cases group (Table 13).

There was no statistically significant difference between thyroid status as regard Anti TPO in control group (Table 14).

4. Discussion

Around 15% of all clinically noticed human pregnancies bring about an unnatural birth cycle. Discontinuous preterm birth (IM) is normal in 1–3% of couples who think about it. Ladies with uterine anomalies, endocrine problems, hyperhomocysteinemia and antiphospholipid disorder, and couples with parental chromosomal irregularities are bound to foster recurrent miscarriage (RM).⁴

Subclinical hypothyroidism is related with pregnancy difficulties, however its relationship with intermittent unsuccessful labor is obscure. Hence, in the review, we zeroed in on the relationship between subclinical hypothyroidism in pregnant

ladies. In this observational investigation of pregnant ladies owned up to the Al-Azhar School Clinical Center in Asyut between December 2021 and May 2022, we separated the individuals into two gatherings, gatherings of patients who grumbled of rehashed disappointments in labor and the benchmark group comprised of pregnant ladies with no less than one living kid. All agents went through lab trial of thyroid science including free T3, free T4, thyroid stimulating hormone (TSH) and against thyroid peroxidase (TPO)-BA. Moreover, all survey individuals went through complete blood count, liver function test, kidney function test, and lipid profile testing.

Genuinely tremendous contrasts between the two gatherings contemplated (case and control). The mean premature delivery rate for the situation bunches was range from 2.0 to 7.0. The mean consider the benchmark group was range from 1.0 to 7.0. The computation was placed as measurably huge for the concentrated on gatherings (cases and controls) concerning free thyroxine (FT4), thyroid status, cholesterol, fatty oils, creatinine, pee, alanine transaminase (ALT), aspartate transaminase (AST) and egg whites. Apparently there were insufficient mixes (cases and controls) of free triiodothyronine (FT3) and TSH punctuation to be measurably critical. Insights show that the quantity of blends (tilde and control) without hostile to TPO language structure has a huge effect.

In the genuine review and meta-survey by Dong *et al.*⁵ played out a meta-audit of five examinations and observed that the predominance of subclinical hypothyroidism in recurrent pregnancy loss (RPL) was 12.9% (certainty span [95% confidence interval

Table 10. Comparison between the two studied groups according to routine lab.

Routine lab	Cases (n = 45)	Control (n = 45)	Test of Significance	P
RBCs				
Minimum–maximum	2.50–5.30	2.80–5.40	U = 824.00	0.123
Mean ± SD.	3.89 ± 0.52	4.04 ± 0.49		
Median (IQR)	4.0 (3.5–4.1)	4.0 (3.8–4.4)		
HB				
Minimum–maximum	6.70–14.0	7.70–14.0	U = 957.50	0.652
Mean ± SD.	11.0 ± 1.26	11.01 ± 1.33		
Median (IQR)	11.0 (10.3–12.0)	11.0 (10.0–12.0)		
MCV				
Minimum–maximum	66.0–92.0	63.0–90.0	U = 866.50	0.234
Mean ± SD.	80.62 ± 5.70	80.84 ± 6.0		
Median (IQR)	80.0 (80.0–85.0)	82.0 (80.0–84.0)		
RDW				
Minimum–maximum	10.60–28.0	8.0–23.0	U = 939.50	0.551
Mean ± SD.	14.20 ± 2.97	13.79 ± 2.60		
Median (IQR)	14.0 (12.1–15.0)	13.0 (12.0–15.0)		
WBCs				
Minimum–maximum	4.0–15.0	4.0–19.0	t = 0.165	0.869
Mean ± SD.	8.58 ± 2.34	8.68 ± 3.43		
Median (IQR)	8.0 (7.0–10.0)	8.0 (6.0–10.0)		
PLTs				
Minimum–maximum	127.0–353.0	115.0–450.0	t = 0.706	0.483
Mean ± SD.	234.8 ± 50.23	244.4 ± 76.96		
Median (IQR)	237.0 (204.0–260.0)	237.0 (186.0–273.0)		
Cholesterol				
Minimum–maximum	90.0–255.0	79.0–230.0	t = 2.437*	0.017*
Mean ± SD.	161.8 ± 43.85	139.8 ± 41.68		
Median (IQR)	150.0 (130.0–200.0)	132.0 (114.0–145.0)		
Triglycerides				
Minimum–maximum	45.0–240.0	40.0–225.0	U = 423.50*	<0.001*
Mean ± SD.	110.6 ± 52.12	70.04 ± 36.93		
Median (IQR)	100.0 (70.0–150.0)	60.0 (45.0–79.0)		
Creatinine				
Minimum–maximum	0.10–0.90	0.30–1.10	706.00*	0.011*
Mean ± SD.	0.48 ± 0.15	0.60 ± 0.22		
Median (IQR)	0.50 (0.40–0.50)	0.50 (0.40–0.70)		
Urea				
Minimum–maximum	6.60–36.0	9.60–44.0	746.50*	0.031*
Mean ± SD.	16.95 ± 4.59	19.30 ± 5.86		
Median (IQR)	17.40 (15.0–18.0)	19.0 (15.0–23.0)		
ALT				
Minimum–maximum	4.0–46.0	3.0–119.0	U = 636.50*	0.002*
Mean ± SD.	17.67 ± 9.21	14.96 ± 17.01		
Median (IQR)	14.0 (12.0–22.0)	11.0 (9.0–14.0)		
AST				
Minimum–maximum	13.0–103.0	11.0–145.0	U = 527.00*	<0.001*
Mean ± SD.	25.29 ± 13.62	20.84 ± 19.78		
Median (IQR)	21.0 (19.0–30.0)	15.0 (15.0–21.0)		
Albumin				
Minimum–maximum	2.50–4.30	2.90–4.20	t = 2.690*	0.009*
Mean ± SD.	3.33 ± 0.53	3.58 ± 0.33		
Median (IQR)	3.30 (2.9–3.7)	3.60 (3.4–3.8)		

ALT, alanine transaminase; AST, aspartate transaminase.

(CI)], 0%–35.2). %). A meta-survey of 17 examinations tracked down areas of strength for a relationship among recurrent pregnancy loss (RPL) and thyroid autoimmunity (chances proportion 1.94, 95% CI 1.43–2.64). In any case, a randomized preliminary found that euthyroid ladies with thyroid

autoimmunity had no advantage from levothyroxine. They additionally found two mediation focuses at which levothyroxine did not further expand the quantity of live births in ladies with subclinical hypothyroidism, paying little mind to thyroid antibodies.

Table 11. Relation between thyroid status and number of abortion in cases group (n = 45).

Number of abortion	Thyroid status				s	P
	Hypothyroidism (n = 6)	Hyperthyroidim (n = 1)	Subclinical hypothyroidism (n = 2)	Euthyroidism (n = 36)		
Minimum–maximum	2.0–3.0		2.0–7.0	2.0–7.0	0.001	1.000
Mean ± SD.	2.67 ± 0.52	3.0#	4.50 ± 3.54	3.14 ± 1.62		
Median	3.0		4.50	2.50		

Table 12. Correlation between number of abortion and thyroid status in group cases (n = 45).

Thyroid function	Number of abortion	
	r _s	P
FT3	0.127	0.410
FT4	0.053	0.735
TSH	0.113	0.464

FT3, free triiodothyronine; FT4, free thyroxine.

Additionally, Sarkar⁶ showed that pregnant ladies with subclinical hypothyroidism or thyroid antibodies have an expanded gamble of intricacies like pre-eclampsia, perinatal demise, and preterm birth. At present, an exhaustive evaluation of thyroid science is not regularly suggested, be that as it may, thyroid limits ought to be surveyed in ladies with unfavorable fetal results or gynecologic intensifications.

As per our review, Benhadi *et al.*⁷ found 27 instances of youth disappointment. Mean TSH and FT4 levels in ladies with one despondent kid were 1.48 mU/l and 9.82 pmol/l versus 1.11 mU/l and 9.58 pmol/l in ladies without youngsters. The gamble of losing a youngster expanded with each 60% increment in TSH consumption, with an OR of

1.60 (95% certainty span (CI) 1.04–2.47). This affiliation persevered in the wake of controlling for smoking, age, orientation, diabetes mellitus, hypertension, history of preterm birth, and pattern of preterm birth and regular birth (change in chances proportion = 1.80 (95% CI: 1.07–3.03)). This was not the situation for FT4 hot blazes (OR = 1.41 (95% CI 0.21 to 9.40), P = 0.724). In a few pregnant ladies without a solitary thyroid crack, stroke risk has been stretched out to youngsters with higher maternal TSH levels. No affiliation was found between maternal FT4 levels and kid misfortune.

In the concentrate by Allan *et al.*⁸ ladies with a TSH greater than 6 mU/l (2.2% of the review populace) had an expanded basic gamble of still-birth (OR 4.40 (95% CI: 1.9–9, 5)). They could see no unmistakable hypothyroidism or subclinical hypothyroidism. Despite the fact that we avoid ladies with obvious thyroid brokenness and keep on examining the relationship between TSH levels and hazard of kid misfortune, our discoveries are by and large predictable with their discoveries.

Cleary-Goldman *et al.*⁹ examined whether maternal hypothyroidism is related with incoherence.

Table 13. Relation between thyroid status and Anti TPO in cases group (n = 45).

	Thyroid status				χ ²	MC _p
	Hypothyroidism (N = 6) [n (%)]	Hyperthyroidim (N = 1) [n (%)]	Subclinical hypothyroidism (N = 2) [n (%)]	Euthyroidism (N = 36) [n (%)]		
Anti TPO						
Negative	5 (83.3)	1 (100.0)	2 (100.0)	32 (88.9)	6.411	0.688
Positive	1 (16.7)	0	0	3 (8.3)		
Border line	1 (0.0)	0	0	1 (2.8)		

TPO, thyroid peroxidase.

Table 14. Relation between thyroid status and Anti TPO in control group (n = 45).

	Thyroid status				χ ²	MC _p
	Hypothyroidism (N = 16) [n (%)]	Hyperthyroidim (N = 1) [n (%)]	Subclinical hypothyroidism (N = 0) [n (%)]	Euthyroidism (N = 28) [n (%)]		
Anti TPO						
Negative	15 (93.8)	1 (100.0)	0	22 (78.6)	5.555	0.362
Positive	0	0	0	5 (17.9)		
Border line	1 (6.3)	0	0	1 (3.6)		

TPO, thyroid peroxidase.

Subclinical hypothyroidism happened in 2.2% (240 of 10 990) in the primary trimester and in 2.2% (243 of 10 990) in the subsequent trimester. Hypothyroxinemia was accounted for in 2.1% (232 of 10 990) in the principal trimester and in 2.3% (247 of 10 990) in the accompanying trimester. Subclinical hypothyroidism has not been related with clashing outcomes. During the principal trimester, hypothyroxemia was related with preterm birth (adjusted chances proportion [ORa] 1.62; 95% certainty span [CI]: 1.00–2.62) and macrosomia (ORa 1.97; 95% CI: 1.37–2.83). In the following trimester, it was related with gestational diabetes (aOR 1.7; 95% CI 1.02–2.84). 15% (1585 of 10 990) in the primary trimester and 14% (1491 of 10 990) in the accompanying trimester had thyroid antibodies. Since the two antibodies were positive in the two trimesters, the gamble of untimely diaper crack was higher ($P = 0.002$ and $P < 0.001$, independently). They found no proof of a distinction in the unnatural birth cycle between ladies with subclinical and euthyroid hypothyroidism. Which goes against our outcomes. As in our survey, Abramson and Stagnaro-Green¹⁰ as well as Negro and Mestman¹¹ and Prummel and Wiersinga¹² detailed that ladies with TPO abs have a higher gamble of birth disappointment (range ratio (RR) somewhere in the range of 1.9 and 4.4) than ladies without TPO abs.

4.1. Conclusion

There is a slight connection between subclinical hypothyroidism and rehashed unsuccessful labor in pregnant ladies.

Conflicts of interest

There are no conflicts of interest.

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