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PREVALENCE OF HYPOTHYROIDISM IN RECURRENT PREGNANCY LOSS

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ABSTRACT

Background:

Aims: The aim of this study is to determine the frequency of hypothyroidism in females with recurrent pregnancy loss in Indian population and to determine the association between thyroid antibodies and miscarriage. **Material and methods**: The study is cross sectional, which included 103 females with recurrent pregnancy loss (RPL) and the control group consisting of 100 healthy pregnant women without history of abortion. All pregnant and non-pregnant women with a history of two or more consecutive miscarriages verified by a pregnancy test or ultrasonography, in the age group of 21–35 years were included in the study. Blood samples was collected in plain vials from patients with RPL and controls. Each blood sample was analysed for thyroid hormones T3, T4, TSH and anti-TPO Data collected and analysed. **Results**: In present study hypothyroidism was detected in 21 of females with recurrent pregnancy loss. In the control group 9 patients had hypothyroidism while 91 were euthyroid.TPO antibodies were positive in 18 patients in RPL patients and 10 controls. In the RPL group 3 patients were euthyroid with positive antibodies while 15 hypothyroid patients showed TPO positivity. In control group 4 patients were euthyroid with positive antibodies while 6 were hypothyroid with positive antibodies. The prevalence of thyroid autoimmunity was 17% in RPL patients and 10% in the the control group. **Conclusion**: The prevalence of

hypothyroidism in females with recurrent pregnancy loss is more than that found in healthy pregnant females.

KEYWORDS: In the RPL group 3 patients were euthyroid with positive antibodies while 15 hypothyroid patients showed TPO positivity.

INTRODUCTION

Spontaneous pregnancy loss occurs in about 15-20 % of all recognized pregnancies, and usually occurs before the 13th week of pregnancy. The actual percentage of miscarriages is estimated to be as high as 50% of all pregnancies, since many miscarriages occur without the woman ever having known she was pregnant .[1] Recurrent spontaneous miscarriage (RSM) is defined classically as three or more consecutive pregnancy losses prior to the 20th week of gestation.[2,3] Various causes known to contribute to recurrent miscarriage including: chromosomal anomalies, endocrine and autoimmune disorderss and pelvic anatomic abnormalities.[4] Autoimmune thyroid disease is by far the most frequent cause of hypothyroidism in women of reproductive age. The prevalence of hypothyroidism in the general population of reproductive age is 2–3%.[5,6] Euthyroid women with thyroid autoimmunity are twice as likely to experience spontaneous miscarriages.[7] Over the past decade, many reports have linked thyroid autoimmunity (TA) with recurrent abortions and it has been suggested that thyroid autoantibodies may serve as a marker for at-risk pregnancies.

AIMS

The aim of this study is to determine the frequency of hypothyroidism in females with recurrent pregnancy loss in Indian population and to determine the association between thyroid antibodies and miscarriage.

MATERIAL AND METHODS

The study is cross sectional case-control study in which patients attending the obstetrics and gynecology OPD of IMS, BHU were enrolled and tests were conducted in department of pathology and endocrinology. The target group was composed of 103 patients with recurrent pregnancy loss and the control group consisting of100 healthy pregnant women without history of abortion. All pregnant and non-pregnant women with a history of two or more consecutive miscarriages verified by a pregnancy test or ultrasonography, in the age group of 21–35 years were included in the study. Women with known autoimmune disorders, already on treatment for thyroid dysfunction, and a history of cervical incompetence or any other

uterine pathology were excluded. Detailed history was taken followed by a thorough physical examination. 3 ml volume of venous blood sample was collected in plain vials from patients with RPL and controls. Each blood sample was analysed for thyroid hormones T3, T4, TSH and anti-TPO by Immulite 2000. The reference range for the above hormones are as follows: T3 T4 TSH anti-TPO. Normal T3 70-200ng/ml T4 5-12.5 ug/dl TSH0.3-5uIU/mlTPO <35 nomal Various tests were done whever required which included VDRL, TORCH, Karyotyping, Prolactin, LH, FSH, diabetes, anatomical abnormalities septate/bicornuate, autoimmune LA, ACLA, SLE.

RESULTS

The study included 103 patients with recurrent pregnancy loss and 100 contol pregnant females with no abortions.hypothyroidism was detected in 21 of these patients while 82 were euthyroid in this group.in the control group 9 patients had hypothyroidism while 91 were euthyroid.TPO antibodies were positive in 18 patients in RPL patients and 10 controls.In the RPL group 3 patients were euthyroid with positive antibodies while 15 hypothyroid patients showed TPO positivity.In control group 4 patients were euthyroid with positive antibodies while 6 were hypothyroid with positive antibodies. The prevalence of thyroid autoimmunity was 17% in RPL patients and 10% in the the control group.

Table-1 Age-wise patient distribution

Age group	Patients with RPL	Control group
21-25	13(12.62%)	10(10%)
26-30	44(42.71%)	53(53%0
31-35	49(47.57%)	37(37%)

In present study most patients (47.57%) with RPL belonged to age group 31-35 yrs which was followed by 42.71% patients falling in age range 26-30 yrs.In the control group maximum patients (53%) were of age between 26-30 yrs.

The mean maternal age of RPL patient was 28.45 ± 6.28 and control group was 29.01 ±4.1

Table-2 Distribution of patients with RPL

No of RPL	No of patients	Percentage
2 RPL	81	(78.64%)
≥ 3RPL	22	(21.35%)

In present study 81 patients (78.64%) had two consecutive pregnancy losses while 21.355 patients had three or more pregnancy losses.

Table-3 Mean T3,T4,TSH levels

Type of thyroidism	No of pts.	Mean T3 levels (ng/dl)	Mean T4 levels(ug/dl)	Mean TSH levels(uIU/ml)
Pt with RPL	**103**			
Euthyroid	82(79.61%)	122.49 ± 24.38	8.72 ± 0.88	2.29 ± 1.21
Hypothyroid	21(20.38%)	59.24±15	4.29 ±22	32.16 ±42.12
Control Group	**100**			
Euthyroid	91	131.45 ± 30.07	9.214 ± 0.81	2.54 ± 1.46
Hypothyroid	9	63 .26 ±37	3.76 ±21	13.52 ±25

As shown in Table-3 mean T3,T4 levels were lower in the patients with RPL when compared to the levels in control patients. the mean TSH levels in RPL group were lower in the euthyoid patients but higher in the hypothyroid patients in comparison to the control.

Table -4 TPO positive patients.

	TPO Positive in RPL group(103)	TPO Positive in control group(100)
No of Patients	18	10
Age	28.03	27. 31
T3	120.38	127
T4	11.5	13.1
TSH	1.96	1.35

DISCUSSION

During pregnancy there is increased physiological demand of the body. At times reduced adaptation to the physiological changes of pregnancy occur due to reduction in the functional reserve of the thyroid gland which can contribute to minor changes in circulating thyroid hormone concentrations within the reference range. The high prevalence of thyroid autoantibodies in women of reproductive age group, raises concern due to increases in miscarriage rate and preterm birth in females at the individual as well as the population level. The increase in miscarriage rates in women positive for thyroid autoantibodies cannot merely be accounted to factors such as age[8] The presence of thyroid autoantibodies might be a marker of underlying subtle alteration in thyroid reserve. In this study, the prevalence of thyroid autoimmunity was higher in pregnant women with a history of recurrent abortion compared with the healthy pregnant control population. The TSH value was higher in the TPO Ab positive group than in the TPO Ab negative group, However the prevalence of hypothyroidism was also increased in this group compared to controls. In present study hypothyroidsm was seen in 9% healthy pregnant females and 20.38% females with RPL. Most studies in literatue have reported prevalence of 10–16%.[9] In study by Lata K et al, the

prevalence of subclinical hypothyroidism was 24% in healthy pregnant women without miscarriage, and 27% in pregnant women with a history of recurrent miscarriage.[10] The pathogenesis of thyroid autoimmunity is still not clearly understood. Recently, Twig et al.[11] described the pathogenesis that underlies infertility and increased pregnancy loss among women with autoimmune thyroid disease. Thyroid autoantibodies exert their effect in both a TSH-dependent and TSH-independent manner. The latter involves quantitative and qualitative changes in the profile of endometrial T cells, which results in the reduced secretion of IL-4 and IL-10 together with the hypersecretion of interferon-g. Polyclonal B-cell activation is two to three times more frequent in thyroid autoimmunity. The hyperactivity and increased migration of cytotoxic natural killer cells which alter the immune and hormonal response of the uterus has been found to be upto 40% more common in women with thyroid autoimmunity. Vitamin D deficiency is also linked to infertility and pregnancy loss,suggesting a potential interplay with thyroid autoimmunity in the context of infertility.[11] The prevalence of the thyroid autoantibodies in different studies varies between 5.4% and 31%.[12]

In most studies as also seen in present study euthyroid women with TPO antibodies show slightly higher TSH values than those without antibodies; this may indicate less thyroidal reserve in times of greater demand for thyroid hormones, such as in pregnancy.[13] Hypothyroidism is associated with infertility, but also with a higher miscarriage rate.[14] Muller et al.[15] found no difference between antibody negative and antibody positive women regarding miscarriage rate. Dendrinos et al,[16] found that 37% of women with recurrent abortions had positive thyroid autoantibodies compared with 13% of controls.It has been proposed in certain studies that selenium supplementation, a trace element essential in thyroid hormone synthesis may decrease thyroid autoantibodies. Selenium substitution decreased TPO antibody levels in euthyroid subjects in a double-blind randomized clinical trial. It also decreased TPO antibody levels in hypothyroid patients treated with T4 substitution in another trial.[17]

CONCLUSION

The prevalence of hypothyroidism in females with recurrent pregnancy loss is more than that found in healthy pregnant females.

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