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Thyroid functions in early pregnancy loss

Jourwal S.*, Agarwal M., Rajoria L., Verma A.

Department of Obstetrics & Gynaecology, S. M. S. Medical College & Associated group of hospitals, Jaipur, Rajasthan, India.
Correspondence Address: * Dr. Sanjana Jourwal, 56, Kailashpuri, Jagatpura, Jaipur- 302017, Rajasthan, India.

Abstract

Objective: To evaluate the relation of timing of pregnancy loss with subclinical hypothyroidism and TPO antibodies (Thyroid autoimmunity).

Methods: 144 pregnant women with diagnosis of early pregnancy loss (<12 wks), coming to OPD were recruited for study after applying exclusion criteria. Miscarriages were classified as very early pregnancy loss (VEPL) (crown rump length ≤10 mm) and early pregnancy loss (crown rump length >10mm). Blood samples were taken for assays of T4, TSH, TPO antibodies, then women were subdivided into four groups: - Euthyroid (ET), Subclinical Hypothyroidism (SH), Overt Hypothyroidism (OH) and Thyroid Autoimmunity (TAI).

Results: 78.4% women had normal thyroid function, 16% cases had positive thyroid antibodies and 5.6% patients were found to had subclinical hypothyroidism. Serum TSH levels were found to be higher in the VEPL group (2.73 μIU/ml) than in the EPL group (1.78 μIU/ml) ($p<0.001$) and in patients affected by SH (4.5 μIU/ml) compared to ET (1.8 μIU/ml) and autoimmune women (1.8 μIU/ml) ($p<0.001$). In women with SH mean gestational age at abortion was 6.3 wks whereas in ET and TAI groups the mean gestational age at abortion was 7.97 wks and 8.47 wks respectively ($p<0.001$).

Conclusion: Both thyroid diseases subclinical hypothyroidism and autoimmune disorder are independently associated with early pregnancy loss, but women suffering from subclinical hypothyroidism have a lower gestational age at abortion.

Keywords: Subclinical hypothyroidism, Thyroid autoimmunity, Euthyroid

Introduction

Thyroid disease often manifests itself during the reproductive period of a woman's life and is the second most common endocrinopathy that affects women of childbearing age.[1] Fetal thyroid hormone is needed from earliest stages of pregnancy for the fetal brain development. Since the fetal thyroid gland become fully functional only after midgestation, maternal euthyroidism is necessary for the normal psycho-neurological development of the fetus. Thyroid dysfunction has been associated with obstetrical complications such as premature delivery, gestational hypertension, preeclampsia and placental abruption.

Materials and methods

This was a hospital based observational study conducted in Department of Obstetrics and Gynaecology, Zenana Hospital, SMS Medical College, Jaipur from April 2012 to April 2013. Sample size was calculated at 80% study power and α error of .05% assuming 10% abnormality in thyroid function in first trimester abortion at absolute allowable error of 5%. Minimum sample size came out to be 144 patients of diagnosed early pregnancy loss. 144 pregnant women with diagnosed early pregnancy loss (<12 wks) with no previous history of thyroid disease will be enrolled. Exclusion criteria were pregnant women with overt thyroid disease, diagnosed diabetes, PIH, renal disease, hypertension; pregnant women with consanguineous marriage; pregnant women with known anatomical cause like septate, subseptate and bicornuate uterus; pregnancy obtained after assisted reproduction technologies; pregnant women with other than thyroid autoimmune disorders; pregnant women with diagnosed early pregnancy loss (by USG) were enrolled and categories than into two groups on the basis of CRL - very early pregnancy loss (EPL) or embryo loss (crown rump length ≤ 10 mm) and EPL or fetal loss (crown rump length >10 mm). Blood samples were taken for assays of T_4, TSH and TPO antibodies and women were then subdivided into four groups - Euthyroid (ET), Subclinical hypothyroidism, Overt hypothyroidism and Thyroid autoimmunity group. In our study we took following values as normal - TSH (0.4-2.5 μIU/ml, fT4 (0.8 - 1.9 ng/dl) and TPO antibodies (upto 35 IU/ml). All these parameters were measured by IMMULITE 2000 System Analyser available in Central Lab of SMS Medical College, Jaipur. All datas were evaluated statistically by chi-square test, anova test and 't' test (Tukey's Post Hoc Test).

Results

The mean age of women was 25.6 yrs. 91.67% cases were diagnosed as missed abortion and 8.3% were diagnosed as blighted ovum on USG. 24 out of 144 pregnancies (16.67%) ended in VEPL, whereas the remaining 120 (83.3%) in EPL. Regarding the endocrinological pattern, 113 women had normal thyroid function (78.4%), 23 patients were found to had positive thyroid antibodies (16%) and in 8 cases (5.6%) SH was found. No case of OH was recorded. The mean overall level of serum TSH and fT_4 were 1.9 μIU/ml and 1.08 ηg/dl respectively. The difference in mean serum TSH in relation to gravidity was not significant (P = 0.557). Regarding TSH levels in relation to gestational age, a significant difference was found between VEPL (2.7 μIU/ml) and EPL group (1.78 μIU/ml) (P < 0.001). Mean serum TSH was 1.8 μIU/ml in the ET and TAI groups and 4.5 μIU/ml in the SH group (P < 0.001). In contrast, no difference was found for serum fT_4 levels (ET - 1.07 ng/dl, TAI - 1.1 ng/dl, SH - 1.17 ng/dl, P = 0.37). The mean gestational age at miscarriage was 7.97 wks in the ET group, 8.47 wks in the TAI group and 6.3 wks in the SH group. A significant difference was found between ET and SH group (P < 0.001) and between TAI and SH groups (P < 0.001). Maximum proportion of the cases with thyroid antibody positive had EPL (91.3%) and only 8.7% had VEPL.

Discussion

The aim of the study was to evaluate thyroid function in a wide sample of pregnant women in which pregnancy ended in early miscarriage. The prevalence of TAI in our study was 16%, probably because we include only pregnancies with diagnosed miscarriage. Ghalia et al., (2010)[2] reported in their study that prevalence of antithyroid antibody positive cases was 15.3% in fetal loss group. In our study, no case of OH was reported and this may be due to the low

prevalence of the disorder in pregnancy (0.3-0.5%). The most important finding in our study is the relation between TSH levels and gestational age at abortion. The SH group was characterized by a lower mean gestational age at miscarriage compared to the ET and TAI groups. Antonio De Vivo et al (2010)[3] reported in their study that mean gestational age at miscarriage was 8.2 ± 1.6 wks in ET group, 8.2 ± 2.1 wks in the TAI group and 6.5 ± .9 wks in the SH group. A significant difference was found between the ET and SH group (P = 0.016) and between TAI and SH group (P = 0.037) and no difference was found between ET and TAI group (P = 0.99). The association between TSH and gestational age at abortion was also confirmed by subdividing miscarriage into VEPL and EPL, since higher levels of TSH were found in the VEPL group. Antonio De Vivo et al (2010)[3] reported in their study that a significant difference in serum TSH levels between the VEPL (1.4 ± 1 mU/L) and the EPL group (1.1 ± .7 mIU/ml). These adverse effects are not directly caused by high serum levels of TSH but likely reflect a decreased capacity of the thyroid to meet the increased requirement due to pregnancy. Hence, maternal thyroid status is significant for trophoblast function and to maintain pregnancy since the earliest stages of gestation. Dhanwal et al (2013)[4] found in their study, mean serum TSH was 3.6 μIU/ml in SH. Roberto Negro et al (2010)[5] reported in their study that median S.TSH was 0.82 (.36 - 1.4) mIU/L in euthyroid group and 3.14 (2.79 - 3.44) mIU/L in subclinical hypothyroidism. The difference between these two groups was found significant (P < .001). Benhadi et al (2009)[6] reported in their study that mean TSH in women with child loss was 1.48 mU/L compared with 1.11 mU/L in women without child loss. Regarding the effect of thyroid antibodies on timing of abortion, no significant difference was found in the mean gestational age at miscarriage between autoimmune and ET women. Our findings reveal that the presence of autoantibodies may play a role in the early miscarriage and confirm that high incidence of TAI in women affected by abortion. In our study no difference was found in mean serum TSH between patients with or without thyroid antibodies. Patients with high autoantibody titers are more likely to be in an advanced stage of the disease and more likely to develop hypothyroidism.

Table 1: Comparison of Pregnancy Outcomes in Different Thyroid Status Groups

Groups	ET		SH		TAI		Total	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
VEPL	16	14.00	6	75.00	2	8.70	24	16.67
EPL	97	86.00	2	25.00	21	91.30	120	83.33
Total	**113**	**100.00**	**8**	**100.00**	**23**	**100.00**	**144**	**100.00**

Table 2: Distribution of Cases According to Mean S.TSH in VEPL and EPL Groups

Group (CRL)	N	Mean Serum TSH (μIU/ml)	SD	T-test P-value LS
EPL	120	1.78	.41	< 0.001 HS
VEPL	24	2.73	1.20	
Total	**144**	**1.94**	**.70**	

Table 3: Distribution of Thyroid Status Groups According to Mean Gestational Age at Miscarriage

Groups	N	Mean Gestational Age (in wks)	SD	ANOVA Test
ET	113	7.97	1.402	
SH	8	6.3	.862	P < 0.001
TAI	23	8.47	1.129	HS
Total	**144**	**7.96**	**1.403**	

Table 4: Comparison of Mean Serum TSH Level in Thyroid Status Groups

Groups	N	Mean Serum TSH (μIU/ml)	SD	ANOVA Test P-Value
ET	113	1.8	0.3	
SH	8	4.5	0.8	P < 0.001, HS
TAI	23	1.8	0.3	
Total	**144**	**1.9**	**0.7**	

Table 5: Distribution of Cases According to Thyroid Status in Pregnancy Outcome Groups

Groups	EPL		VEPL		Total	
	No.	**%**	**No.**	**%**	**No.**	**%**
ET	97	81.00	16	66.66	113	78.40
SH	2	1.60	6	25.00	8	5.60
TAI	21	17.40	2	8.34	23	16.00
Total	**120**	**100.00**	**24**	**100.00**	**144**	**100.00**
$\chi^2 = 21.164$		*d.f. = 2*	*P = 0.001*		*HS*	

Conclusion

Pregnancy influences thyroid functions and it may bring to light mild and latent disorders. Thyroid dysfunction has been related to obstetrical complications. Both thyroid diseases SH and autoimmune disorders are independently associated with early pregnancy loss, but women suffering from SH have a lower gestational age at abortion. Given these results, it could be useful to perform a preconceptional or early screening for thyroid disorders, to evaluate the need for hormonal supplementation.

Conflicts of interest and source of funding: None

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