

To Predict the Risk of Abortion in Pregnancy by Studying the Relation between Different Biochemical Markers (T₃, T₄, TSH and Blood Sugar)

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Abstract: World Health Organization defines an “abortion” as “pregnancy termination before 20 weeks gestation or foetus born weighing <500g”. There could be various fetal, paternal and maternal factors accounting for abortion. Maternal endocrine disorders like thyroid and diabetes are commonly encountered. Proper maternal thyroid function is important for both mother and fetus. Elevated maternal thyroid-stimulating hormone has been associated with an increased risk of abortion, pre-term birth, placental abruption and impaired neurological development in the child. Several studies showed that early miscarriage is associated with poor glycemic control but present study failed to show any correlation between the two. Euthyroxinemia is primarily important in early pregnancy to avoid abortions and to maintain normal placental development.

Keywords: Abortion, fetus, thyroid, placental abruption

1. Introduction

Pregnancy loss is an emotionally traumatic experience, similar to that associated with still birth or neonatal death. World Health Organization defines an “abortion” as “pregnancy termination before 20 weeks gestation or fetus born weighing <500 g”. Spontaneous abortion is the most common complication of early pregnancy. More than 80 percent of the spontaneous abortions occur within the first 12 weeks of gestation.¹ There could be various fetal, paternal and maternal factors accounting for abortion.

During pregnancy proper maternal thyroid function is important for both mother and fetus.² Elevated maternal thyroid-stimulating hormone (TSH) has been associated with an increased risk of pre-term birth, placental abruption, fetal death and impaired neurological development in the child.³ Thyroid dysfunction is common in women of reproductive age with the prevalence of elevated TSH ranging from 4 to 9%.⁴

Gestational diabetes is a common metabolic disorder in pregnancy. Several studies showed that early miscarriage is associated with poor glycemic control.⁵

Hence the present study is proposed to investigate these novel biochemical markers in the diagnosis and management of pregnancy complications. The ability to estimate the likelihood of final outcome would allow us to counsel and treat the patients appropriately.

2. Aims and Objectives

To predict the risk of abortion in pregnancy by studying the relation between different biochemical markers (T₃, T₄, TSH and blood sugar).

3. Material and Methods

This prospective observational study was carried out on 100 pregnant women with singleton pregnancy of 6-12 weeks of gestation admitted in labour room under emergency condition and attending the Out Patient Department of Obstetrics and Gynaecology, Pt. B. D. Sharma, PGIMS Rohtak for routine antenatal examination.

Exclusion Criteria

Women not sure of dates, known case of diabetes mellitus, hypertension, thyroid disorder, renal or liver disease, autoimmune disorder and multiple pregnancy.

All women were fully explained about the study and a written consent was taken for their inclusion in the study.

They were divided into three groups.

- Group 1- included 30 normal pregnant women with no history of abortion (control group)
- Group 2- included 35 pregnant females with history of previous abortion
- Group 3- comprised of 35 pregnant women were coming with chief complaint of bleeding per vaginum.

A sonography was performed in all the women at first antenatal visit to confirm gestational age, fetal maturity and was repeated at 18 weeks of gestation.

Following biochemical markers were analysed in antenatal women fulfilling the recruitment criteria: T₃ (triiodothyronine), T₄ (thyroxine), TSH (thyroid stimulating hormone) and blood sugar (fasting). Estimation of T₃, T₄ and TSH were carried out by chemiluminiscence while blood glucose was estimated by enzymatic method.

All patients were followed every four weekly till 20 weeks and the outcome was noted in terms of anembryonic pregnancy, missed abortion, spontaneous abortion or continuation of pregnancy.

Statistical Analysis

SPSS/ANOVA was applied to test for the differences in the mean values between different groups for various quantitative parameters. Statistical significance was considered as p value < 0.05.

4. Observations

Outcome of pregnancy

In group 1- out of total, 3.33% patients ended up with anembryonic and spontaneous abortion each and rest continued with pregnancy successfully.

Similarly, in group 2-88.58% patients continued with pregnancy while 5.71% cases resulted in anembryonic and missed abortion each.

In group 3-only 80.01% cases continued with pregnancy while 2.85% cases had anembryonic pregnancy, while missed and spontaneous abortion occurred in 8.57% cases each. The difference between all three groups in terms of outcome of pregnancy was statistically insignificant (p value >0.5).

Table 1: Final outcome of pregnancy in three groups

Outcome	Group I (n=30) n(%)	Group II (n=35) n(%)	Group III (n=35) n(%)	Statistical significance
Anembryonic pregnancy	1(3.33%)	2(5.71%)	1(2.85%)	0.809
Missed abortion	0	2(5.71%)	3(8.57%)	0.278
Spontaneous abortion	1(3.33%)	0	3(8.57%)	0.182
Continuation of pregnancy	28(93.34%)	31(92.58%)	28(80.01%)	>0.05

T3, T4 and Thyroid Stimulating Hormone (TSH)

The reference range for total T3 and T4 was 1.1-2.9 nmol/L and 85-150 nmol/L respectively in first trimester of pregnancy. Normal range for TSH was 0.1-2.5 mIU/ml in first trimester and 0.3-3 mIU/ml in second and third trimester.

Table 2: Distribution of patients according to thyroid profile in three groups

Thyroid profile	Group I (n=30) n(%)	Group II (n=35) n(%)	Group III (n=35) n(%)	Statistical significance
T3 (nmol/L)	1.94±0.57	1.72±0.48	1.89±0.64	0.280
T4 (nmol/L)	119.6±23.52	106.3±27.28	115.14±27.86	0.125
TSH (mIU/L)	1.58±0.76	1.92±0.77	1.79±0.90	0.238

Mean T₃ value in Group 1, Group 2 and Group 3 were 1.94 ± 0.57 nmol/L, 1.72 ± 0.48 nmol/L and 1.89±0.64 nmol/L respectively while mean value of T₄ in Group 1, Group 2 and Group 3 were 119.6 ± 23.52 nmol/L, 106.3 ± 27.28 nmol/L and 115.14±27.86 nmol/L respectively; the difference was not statistically significant (p value 0.125).

Mean TSH levels in group 1 was 1.58±0.76 mIU/L; in group 2 and 3 were 1.92±0.77 mIU/L and 1.79±0.90 mIU/L respectively.

Correlation of T3 and T4 with TSH

In all the three groups, TSH was negatively correlated with T3(r value -0.951 in both group 1 and 2; -0.563 in group 3) and T4 (r value -0.563, -0.950 and -0.927 in group 1, 2 and 3 respectively).

Table 3: Correlation coefficient (r value) between T3 and TSH

Group	r value	p value	Significance
Group 1	-0.951	<0.01	Significant
Group 2	-0.951	<0.01	Significant
Group 3	-0.563	<0.01	Significant

Table 4: Correlation coefficient (r value) of between T4 and TSH

Group	r value	p value	Significance
Group 1	-0.563	<0.01	Significant
Group 2	-0.950	<0.01	Significant
Group 3	-0.927	<0.01	Significant

Correlation of TSH with abortion

In group 1, 90% euthyroid patients had normal pregnancy. From the total 9.99% hypothyroid patients, 6.66% aborted and only 3.33% continued with pregnancy. This showed the strong association of TSH with abortion (p value <0.001).

In group 2 and group 3, 88.57% and 80% euthyroid patients had normal pregnancy respectively while 2.85% euthyroid female from group 3 aborted. Thus TSH was significantly associated with abortion in the present study (p value<0.05).

Table 5: Correlation of TSH with Abortion

TSH	Group I (n=30) n(%)	Group II (n=35) n(%)	Group III (n=35) n(%)	Statistical significance
< 2.5 (mIU/L)				
Abortion	0	0(0%)	1(2.85%)	0.363
Continuation	27(90%)	31(88.57%)	28(80%)	
>2.5 (mIU/L)				
Abortion	2(6.66%)	1(2.85%)	2(5.71%)	0.501
Continuation	1(3.33%)	3(8.57%)	4(11.42%)	
Statistical significance	<0.001 HS	<0.01 S	< 0.05 S	

Correlation of fasting blood sugar with abortion

In group 1, from 79.99% euglycemic patients, 73.33% had normal pregnancy while 6.66% patients aborted. 20% patients were hyperglycemic and all of them had normal pregnancy.

Also, in group 2, from 88.57% euglycemic patients, 80% had normal pregnancy while 8.57% patients aborted. 11.42% patients were hyperglycemic; from which 8.57% had normal pregnancy while 2.85% resulted in abortion.

Similarly, in group 3, from 88.56% euglycemic patients, 71.42% had normal pregnancy while 17.14% patients aborted. 11.42% patients were hyperglycemic; from which 8.57% had normal pregnancy while 2.85% resulted in abortion. Thus in all of the three groups FBS was found to be insignificantly associated with abortion (p value>0.05).

Table 6: Correlation of fasting blood sugar with Abortion

FBS	Group I (n=30) n(%)	Group II (n=35) n(%)	Group III (n=35) n(%)	Statistical significance
< 92 mg/dl				
Abortion	2(6.66%)	3(8.57%)	6(17.14%)	0.387
Continuation	22(73.33%)	28(80%)	25(71.42%)	
>92 mg/dl				
Abortion	0	1(2.85%)	1(2.85%)	0.416
Continuation	6(20%)	3(8.57%)	3(8.57%)	
Statistical significance	0.464	0.364	0.790	

5. Discussion

Spontaneous abortion is the most common complication of early pregnancy.¹ The incidence of spontaneous abortion in clinically recognized pregnancies upto twenty gestational weeks is 8 to 20 percent.⁶ Maternal factors accounting for abortion could be infections, medications, uterine defects, immunological factors, inherited thrombophilia, hormonal insufficiency, endocrine disorders mainly diabetes mellitus and thyroid disorders etc.¹

Thyroid hormone levels

Total triiodothyronine (T₃) and abortion

Mean T₃ in Group 1, Group 2 and Group 3 were 1.94 ± 0.57 nmol/L, 1.72 ± 0.48 nmol/L and 1.89 ± 0.64 nmol/L respectively and the difference between the mean values in three groups was not statistically significant (p value 0.28).

Thyroxine (T₄)

The reference range for normal T₄ was 85-150 nmol/L. In our study mean value of T₄ in Group 1, Group 2 and Group 3 were 119.6 ± 23.52 nmol/L, 106.3 ± 27.28 nmol/L and 115.14 ± 27.86 nmol/L respectively; the difference was not statistically significant (p value 0.125).

Donmez et al⁷ and Rao et al⁸ compared thyroid hormone levels in recurrent aborters with normal pregnant females and found significantly lower levels of T₃ and T₄ in study group. In the present study Group 2, showed lowest mean value (1.72 ± 0.48 nmol/L) which was statistically not significant in comparison to other groups (p value 0.28). This might be due to reason that in present study we included patients with history of abortion in group 2 instead of recurrent aborters.

Thyroid Stimulating Hormone (TSH)

Mean TSH levels in first trimester in group 1 was 1.58 ± 0.76 mIU/L; in group 2 and 3 were 1.92 ± 0.77 mIU/L and 1.79 ± 0.90 mIU/L respectively. The difference in the mean TSH value in the three groups was found to be statistically insignificant (p value 0.238).

Correlation of TSH with abortion

In group 1, 90% euthyroid patients had normal pregnancy. From the total 9.99% hypothyroid patients, 6.66% aborted and only 3.33% continued with pregnancy. This showed the strong association of TSH with abortion (p value <0.001).

In group 2 and group 3, 88.57% and 80% euthyroid patients had normal pregnancy respectively while 2.85% euthyroid

female from group 3 aborted. Thus TSH was significantly associated with abortion in the present study (p value <0.05).

Abalovich et al have reported that when treatment with levothyroxine was adequate, there was no abortion, when it was inadequate in subclinically hypothyroid group, abortion rate was 71.4%. In euthyroid group, abortion rate was 4%.⁹

Correlation of TSH levels with T₃ and T₄ levels

In the present study, mean TSH in first trimester was negatively correlated with mean T₃ (r value -0.951, -0.951 and -0.972) and mean T₄ values (r value -0.563, -0.950 and -0.927) in all the three groups respectively (p value <0.01). Benhadi et al described inverse relationship between TSH and FT₄.¹⁰

Fasting blood sugar and abortion

Mean value of FBS in group 1 was 90.16 ± 11.23 gm/dl, in group 2 and group 3 were 87.6 ± 15.59 gm/dl and 85.54 ± 6.73 gm/dl respectively. The difference between the mean value of FBS of patients in three groups was statistically insignificant (p-value 2.93). In group 1, 20% patients were hyperglycemic and all of them had normal pregnancy. While in group 2, 11.42% patients were hyperglycemic; from which 8.57% had normal pregnancy while 2.85% aborted. Similarly, in group 3, from 11.42% hyperglycemic patients, 8.57% had normal pregnancy while 2.85% resulted in abortion. Thus in all of the three groups FBS was found to be insignificantly associated with abortion (p value >0.05).

Wang et al reported no significant difference in levels of fasting plasma glucose, fasting plasma insulin, homeostasis model assessment of insulin resistance index, and homeostasis model assessment β function between recurrent aborters and the control group.¹¹

Outcome of pregnancy

In the present study, 6.66% patients in group 1, 11.42% in group 2 and 19.99% patients in group 3 end up in abortion. Similar incidence of pregnancy loss was also reported by Wilcox et al.⁶ In group 3, that is, threatened group patients had highest abortion rate (19.99%). It can be inferred that euthyroxinemia is primarily important in early pregnancy to avoid abortions and to maintain normal placental development.

6. Conclusion

Thyroid stimulating hormone levels were significantly higher in first trimester in women who aborted as compared to pregnant women who had successful continuation of pregnancy. TSH was negatively correlated with T₃ and T₄ levels. Thyroid screening is must at first antenatal visit. Adequate thyroxinere placement therapy should be given in cases of hypothyroidism for good perinatal outcome.

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