Endocrine Dysfunction in Recurrent Pregnancy Loss

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ABSTRACT

Introduction: Miscarriage is the spontaneous loss of the conceptus before 20 weeks of gestation. Several disorders are known to contribute to recurrent miscarriage including: chromosomal anomalies; anti-cardiolipin antibodies; endocrine disorders such as poorly controlled diabetes mellitus; hyperprolactinaemia and thyroid diseases; and pelvic anatomic abnormalities. Study aimed to investigate the endocrine dysfunction in recurrent pregnancy loss

Material and Methods: A prospective study comprising 70 subjects was carried out. Fifty cases of recurrent abortions constituted the study group. Twenty healthy multipara females of same reproductive age group constituted the control group. Venous blood samples were collected, and serum was analyzed for hormone analysis (T_3, T_4, TSH, LH, FSH, PRL, Testosterone) by ELISA method.

Results: The mean prolactin level in cases of recurrent abortions was 19.96 ng/ml, while in controls was 11.77 ng/ml. The p value was 0.006 which was found to be statistically highly significant. The mean TSH level in recurrent abortions cases was 5.81 mIU/L, while in controls was 1.95 mIU/L. The p value was 0.004 which was found to be statistically highly significant.

Conclusion: The patients with recurrent abortions had significantly raised levels of TSH and Prolactin. The prevalence of thyroid disorder and hyperprolactinemia were higher in pregnant women with a history of recurrent abortion compared with healthy pregnant control population. Universal screening of pregnant females for endocrine profile can improve the foetal outcome as well as social well-being of females.

Keywords: Triiodothyronine (T_3), Tetraiodothyronine (T_4), Thyroid Stimulating Hormone, (TSH), Leutinizing Hormone (LH), Follicular Stimulating Hormone (FSH)

INTRODUCTION

Recurrent pregnancy loss (RPL), also referred to as *recurrent miscarriage or habitual abortion,* is historically defined as 3 consecutive pregnancy losses prior to 20 weeks from the last menstrual period. It is estimated that approximately 8% to 12% of all cases of recurrent pregnancy loss (RPL) are caused by endocrine diseases.[1] RPL is a multifactorial disorder resulting from genetic factors, anatomic factors, autoimmune disorders, endocrine dysfunction, thrombophilia, life style factors, and maternal infections. However, the underlying cause remains undetermined in up to 50% of cases.[2,3] Maternal hypothyroidism has been associated with increased foetal and neonatal losses and mental retardation with living euthyroid offsprings.[4,5] RPL evaluation would result in substantial health-cost savings while ensuring that women with a higher risk of further euploid miscarriage would be appropriately evaluated. Physiologic changes during early pregnancy can dramatically impact thyroid function. Rapidly increasing beta human chorionic gonadotropin (b-hCG) in early pregnancy stimulates the thyroid gland directly by binding to the thyroid-stimulating hormone (TSH) receptor, resulting in slightly higher production of thyroxine (T4) transiently.[6] Induced hyperprolactinemia impaired ovarian follicular development, especially during the recruitment period which is supposed to lead to a luteal phase defect and implantation failure.[7] Present study aimed to investigate the endocrine dysfunction in recurrent pregnancy loss.

MATERIAL AND METHODS

The present study was conducted in Department of Biochemistry on 70 cases reporting in the Department of Radiodiagnosis of a Tertiary Care Center in North India.

These cases were divided into following groups:

Study group: included 50 clinical cases of recurrent abortions.

Control group: included 20 healthy multipara females of same reproductive age group.

A written consent and a detailed history was taken from all selected patients and approval of Institutional Ethics Committee was procured.

The cases of three consecutive recurrent abortions were included. Those females with previous history of Tuberculosis, Diabetes mellitus**,** Cardiovascular disorder, Thyroid disorder,Polycystic ovarian disease, Abnormal hormonal assay, Infection (TORCH, HIV) and Abnormal sonographic studies were excluded. None of the patients or controls was pregnant at the time of the study, and none was taking any medication likely to affect results (e.g. oestrogens, progesterones, dopamine antagonists and glucocorticoids).

Fasting blood samples were taken routinely between 8.00 and 10.00 a.m. after a resting period of 30 min during the early follicular phase. Hormonal analyses were performed by ELISA technique[8] by commercially available ELISA Kits for follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, testosterone, and T3,T4. Thyroid stimulating hormone (TSH).

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	Recurrent abortions (Mean value ± SD)	Controls (Mean value ± SD)	P	S
LH (N.V:0.5-10.5) mIU/mL	7.70±2.17	7.41±1.60	0.859	NS
FSH (N.V: 3-12) mIU/mL	8.49±2.63	8.59±2.01	0.987	NS
PRL (N.V:1.2-19.5 ng/ml	19.96±13.47	11.77±3.23	0.006	Highly Significant (HS)
SD Standard Deviation NS Non Significant PRL Prolactin				

Table-1: Comaprison of LH, FSH and prolactin levels in study and control groups

	Recurrent abortions (Mean value ± SD)	Controls (Mean value ± SD)	p	S
T_3 (N.V:0.49-2.02) ng/ml	1.41±0.47	1.31±0.51	0.480	NS
T_4 (N.V:4.7-12.8) µg/dl)	8.66±1.82	8.63±1.70	0.998	NS
TSH(N.V:0.44-3.45 mIU/L	5.81±6.05	1.95±0.77	0.004	Highly Significant (HS)

Table-2: Comaprison of T3, T4 and TSH levels in study and control groups

	Recurrent abortions (Mean value ± SD)	Controls (Mean value ± SD)	p	S
Testosterone (N.V: 0.2-0.8 ng/mL)	0.44±0.16	0.53±0.15	0.181	NS

Table-3: Comaprison of serum testosterone levels in study and control groups

Name of author	TSH (mIU/ml) Mean ±SD		p value	Significance
	Study group	Control group		
Ia Marca[11] (1998)	1.72±0.84	1.01±0.41	<0.001	HS
Dal Lago et al[12] (2011)	–	–	<0.001	HS
Present study	5.81±6.05	1.95±0.77	0.004	HS

Table showing thyroid stimulating hormone levels in various studies

STATISTICAL ANALYSIS

Statistical analysis was performed and the results of laboratory tests in the study and control groups were compared using Student's *t*-test.

RESULTS

The mean LH level in recurrent abortions was 7.70 mIU/mL, while in controls was 7.41 mIU/mL. The p value was 0.859 which was found to be statistically non significant.

The mean FSH level in recurrent abortions was 8.49 mIU/mL, while in controls was 8.59 mIU/mL. The p value was 0.987 which was found to be statistically non significant (table-1).

The mean prolactin level in recurrent abortions was 19.96 ng/ml, while in controls was 11.77 ng/ml. the p value was 0.006 which was found to be statistically highly significant.

The mean T_3 level in recurrent abortions cases was 1.41 ng/ml while in controls was 1.31 ng/ml. The p value was 0.480 which was found to be statistically non significant

The mean T_4 level in recurrent abortions cases was 8.66 µg/dl while in controls was 8.63 µg/dl. The p value was 0.998 which was found to be statistically non significant

The mean TSH level in recurrent abortions was 5.81 mIU/L, while in controls was 1.95 mIU/L. the p value was 0.004 which was found to be statistically highly significant (table-2).

The mean testosterone level in recurrent abortions was 0.44 ng/mL, while in controls was 0.53 ng/mL. the p value was 0.181 which was found to be statistically non significant (table-3).

DISCUSSION

In the present study serum TSH and prolactin levels were significantly raised in cases of recurrent abortions. Hypothyroidism and hyperprolactinemia may contribute to luteal phase defect leading on to decreased progesterone levels in the luteal phase of menstrual cycle bringing on the menstrual bleeding and thus causing early miscarriages. Subclinical hypothyroidism may be associated with ovulatory dysfunction and adverse pregnancy outcome Even minimal hypothyroidism can increase rates of miscarriage and foetal death and may also have adverse effects on later cognitive development of the offspring. Hyperthyroidism during pregnancy may also have adverse consequences. Rapidly increasing beta human chorionic gonadotropin (b-hCG) in early pregnancy stimulates the thyroid gland directly by binding to the thyroid-stimulating hormone (TSH) receptor, resulting in slightly higher production of thyroxine (T4) transiently. Iodine concentrations decline in early pregnancy as a result of an increased glomerular filtration rate starting in early pregnancy. In addition, the early pregnancy rise in estrogen leads to increased production of thyroid binding globulin, which in turn binds circulating thyroxine[9] Along with an increased maternal blood volume, the thyroid gland must increase its production of thyroid hormones to maintain homeostasis.[10]

Fumiki Hirahara et al[13] (1998) observed serum prolactin levels (31.8–55.3 ng/mL) during early pregnancy (5–10 weeks of gestation) were significantly higher in patients who had miscarriage than in patients whose pregnancies were

successful (4.6–15.5 ng/mL, p <0.01 or p<0.05).

S Bussen[14](1999) in his study observed the mean prolactin level in study group was 14.2±6.7 ng/ml and in control group was 10.5±3.5 ng/ml. The p value was found to be 0.015 which was highly significant.

In the present study mean prolactin levels in recurrent abortions study group was 19.96±13.47 ng/ml and in controls was 11.77±3.23 ng/ml. The p value was (p=0.006) which was also found to be highly significant.

So the present study is comparable to the above mentioned studies with respect to prolactin levels and thyroid levels in cases of recurrent abortions.

CONCLUSION

The prevalence of thyroid disorder and hyperprolactinemia were higher in pregnant women with a history of recurrent abortion compared with healthy pregnant control population. Factors responsible for recurrent pregnancy loss are multiple, and endocrine dysfunction is one of them. Universal screening for thyroid hormone abnormalities is not routinely recommended at present, but thyroid function must be examined in female with foetal loss or menstrual disturbances. Altered endocrine profile results in loss of pregnancy, especially in the early stages of gestation. There is need of the hour that women expecting a pregnancy must be screened to assess the endocrine profile even before conception to ensure a healthy pregnancy outcome and to improve the health and social well-being of the females.

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