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Original Research Article

Determining the Mechanism of Female Hypogonadism in Diabetic Population in Eastern India: An Original Article

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ABSTRACT

Hypogonadism in female is one of the causes of menstrual irregularities and infertility. This clinical syndrome is characterized by decreased sex steroid secretion either due to primary gonadal failure or secondarily due to central hypothalamic-pituitary causes. In our study, it is found that patients with diabetes have primary ovarian failure with low estradiol and high FSH, LH values.

Keywords: Hypogonadism, estradiol, FSH, LH, Diabetes.

INTRODUCTION

Female hypogonadism follows mainly 2 pathogenic pathways, primary and secondary. Primary or hypergonadotropic hypogonadism is due to primary ovarian failure and biochemically characterizes by low estradiol, high FSH and high LH levels, as occurs in post menopausal women. Secondary or hypogonadotropic hypogonadism occurs due to disrupted hypothalamic-pituitary-ovarian axis. It is characterized biochemically by decreased levels of all 3 of the above stated hormones.

Estradiol (E2) is the most potent natural estrogen, produced mainly by the ovary. It is a steroid hormone derived from cholesterol. [(1)] Estradiol has various functions such as growth of female reproductive organs, maintaining the egg in the ovary and triggering a series of events that cause ovulation. It also helps in the development of secondary sexual characteristics (normal breast development, skin changes, change in body shape and distribution of fat). [(2)] In non pregnant women with normal menstrual cycle, estradiol secretion follows a cyclic, biphasic pattern with the highest concentration found just before the ovulation. [(3)]

Estrogen acts directly on beta cells of the pancreas to make them resistant to apoptosis and increase production of insulin. [(4)] However inappropriate estrogen function, due to abnormal increases in estrogen or stimulation with estrogen-mimics like bisphenol-A, can actually provoke insulin resistance by exhausting beta-cells through over stimulation. [(5)]

Available literatures till date have mostly found an association between secondary hypogonadism with type 2 diabetes. Type 1 diabetes was shown to be much less associated with alterations in gonadal and gonadotropic hormones. The data from the study of Zyed et al showed serum FSH and LH levels were reduced in diabetic patients of both sexes. [(6)] Another study also showed similar findings where

low levels of gonadal hormones were found to be associated with low gonadotropic hormones. This study hypothesized that this effect may be the inhibitory actions of insulin resistance and high levels of inflammatory mediators in diabetes on the hypothalamic-pituitary axis. [(7)]

Much data are not available showing evidence of primary gonadal dysfunction caused by diabetes. Some literatures show that some primary ovarian failure syndromes may lead to insulin resistance and diabetes. One such literature mentions that 30-60% Turner syndrome adults have impaired glucose tolerance and 2-4 times higher risk of developing diabetes than normal women without this syndrome. [(8)]

It has been established for quite a long time that PCOS leads to insulin resistance and type 2 diabetes, where the risk of developing diabetes is 5-10 times higher than general population.

In all these studies showing association between primary ovarian failure and diabetes, the primary gonadal failure was diagnosed much earlier, which led to diabetes. Moreover, there is serious lack of such studies in India. We have tried in our study to determine the mechanism of female hypogonadism occurring in known cases of diabetes. Any significant deviation from the currently established facts are intended to be explored in terms of pathogenesis, impact on individual and public health and finding out therapeutic remedies by further researches.

MATERIALS AND METHODS

The study was carried out at the Department of Biochemistry, Calcutta National Medical College and Hospital, Kolkata, West Bengal. Total three hundred and sixty (360) subjects of age between 18 to 45 years constituted the study population. 180 diabetic patients constituted the 'case' group and 180 non diabetic healthy individuals constituted the 'control' group. A total 180 males and 180 females were involved in the study. These subjects of both the sexes were categorized under three age groups such as 18 to 26 years, 27 to 36 years and 37 to 45 years. In females, samples were collected in between 1st-4th days of menstrual cycle. The research protocol was approved by Ethics Committee of the institution. Proper venipuncture technique was applied to collect 5ml of blood sample from the subjects for biochemical analysis. Blood samples were centrifuged at 3000rpm for 10 minutes.

Fasting blood glucose and postprandial blood glucose were measured by GOD-POD method and HbA1c% was measured by ion exchange resin method by coral clinical system kit. LH was measured by LH ELISA kit (adapted solid phase direct sandwich ELISA). FSH was measured by FSH ELISA kit (solid phase assay using streptavidin/biotin method).Serum Estradiol was measured by ELISA method (Elisa, Calbiotech).

Data generated were analyzed using SPSS version 20.00 software and Microsoft Excel 2007. Comparison mean and standard deviation values were made for the various parameters for test and control subjects using student-t test. Results were considered statistically significant with 95% confidence interval ($p<0.05$)

RESULTS

Table 1:-Age based comparison between case& controls for LH, FSH, Estradiol, FBS, PPBS and HbA1C% parameters among females.

Age group (years)	18 to 26		27 to 36		37 to 45	
Female	Case (Mean and SD)	Control (Mean and SD)	Case (Mean and SD)	Control (Mean and SD)	Case (Mean and SD)	Control (Mean and SD)
LH(mIu/ml)	6.19±0.69	4.10±0.91	8.84±2.82	5.97±0.85	26.68±3.91	5.86±0.86
FSH(mIu/ml)	8.11±0.81	5.33±0.68	9.04±2.17	6.95±0.87	17.91±3.07	7.05±0.68
Estradiol(pg/ml)	18.78±3.35	25.09±1.64	14.71±3.08	22.88±5.71	10.84±2.72	20.96±3.14
FBS (mg/dl)	179.96±16.70	82.33±8.35	159.33±10.01	92.89±3.92	158.43±9.29	105.10±3.18
PPBS (mg/dl)	232.76±36.77	105.16±9.30	222.80±25.60	111.58±5.68	210.96±13.57	118±5.73
HbA1C%	9.64±1.00	4.67±0.67	8.13±0.77	4.54±0.49	7.53±0.26	5.17±0.32
P value	≤0.05	≤0.05	≤0.05	≤0.05	≤0.05	≤0.05

DISCUSSION

In our study, it is shown that, mean estradiol levels (pg/ml) in female cases in the age groups of 18-26 yrs, 27-36 yrs and 37-45 yrs were 18.78±3.35, 14.71±3.08 and 10.84±2.72 respectively. Mean estradiol levels (pg/ml) in control groups of the same age groups were 25.09±1.64, 22.88±5.71 and 20.96±3.14. In all the age groups, estradiol levels were significantly lower in case groups compared to the control populations with a p value of ≤0.05.

Similarly, the FSH levels (mIU/ml) in the above mentioned case groups were 8.11±0.81, 9.04±2.17 and 17.91±3.07 respectively in the respective control groups, the values of FSH (mIU/ml) were 5.33±0.68, 6.95±0.87 and 7.05±0.68. hence, the cases groups of all the age groups have significantly higher FSH levels of FSH with a p value of ≤0.05.

LH levels (mIU/ml) in the case groups of the above mentioned age groups were 6.19±0.69, 8.84±2.82 and 26.68±3.91 respectively. In the control populations of the respective age groups, the LH levels (mIU/ml) were 4.10±0.91, 5.97±0.85 and 5.86±0.86. So the case groups of all the age groups have significantly higher LH levels compared to the control populations of respective age groups with a p value of ≤0.05.

CONCLUSION

From our study, it is evident that female hypogonadism occurring in diabetes is due to primary ovarian failure rather than disruption of hypothalamic-pituitary-ovarian axis. This may be due to the effects of insulin resistance, inflammatory mediators and raised free radicals and reduced antioxidants found in diabetes, mainly type 2.

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