ALTERATION OF MENSTRUAL CYCLE ASSOCIATED WITH TYPE 2 DIABETES MELLITUS IN WOMEN OF WEST BENGAL

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ABSTRACT:

Diabetes mellitus (DM) is a chronic metabolic disorder affecting almost all major systems of our body. However the effects of DM on menstrual cycle are not well established. Tracing back the signs and symptoms in patients with diabetes mellitus, particularly related to menstruation the intention of this study was to find out whether there is any relation between hypoinsulinaemia and serum level of sex steroid like estrogen and testosterone and its clinical effect on menstruation. This is a cross sectional study with 225 female diabetic who were attending diabetic clinic at Institute of Post Graduate Medical Education & Research (IPGME&R), Kolkata. Sample of blood was collected in the early follicular phase of the cycle, in empty stomach for measurement of serum insulin, free testosterone, estradiol, LH and FSH levels. The result showed that abnormalities in the level of LH, FSH are believed to be responsible for the irregular menstruation like oligomenorrhoea and amenorrhea that occur in diabetic women. Diabetic female who had irregular, heavy and scanty period showed high level of blood FSH and LH than normal females. In case of heavy period patients showed slightly less estradiol level and scanty period revealed less estradiol than control. Diabetic patients showed significantly low free testosterone level than normal. Diabetic patients with high insulin level showed incidence of scanty period than normal and less insulin revealed incidence of irregular period. This study was aimed to formulate a hypothesis regarding effect of diabetes mellitus on sex steroids and its clinical manifestation in diabetic women.

KEY WORDS: Diabetes Mellitus, Irregular Menstrual Cycle, Sex Steroid

INTRODUCTION:

Tracing back the signs and symptoms in patients with diabetes Mellitus, particularly related to menstruation the intention of this
study was to find out whether there is any relation between diabetes and serum level of sex steroid like estrogen and testosterone. Our aims and objectives were to analyze the prevalence of menstruation in female diabetic compared to non-diabetic population and the relation of insulin level and sex steroid level in clinical presentation with menstruation problem in selected group.

MATERIALS AND METHODOLOGY:

Collection of study samples:
This is a cross sectional study with 225 female diabetic who are attending diabetic clinic at IPGME & R, Kolkata. Particularly the female diabetic of reproductive age group and post-menopausal women with diabetes mellitus had been included. Age matched non-diabetic female controls were taken from the patients attending Uluberia, S. D. Hospital, Howrah who fulfilled the inclusion criteria. As there is no medical or surgical intervention, this study is completely safe for the participating ladies and there is no risk involved for any of them. Clinical data was collected from Diabetic Clinic of IPGME & R. The work has been approved by the Institutional ethical committee of IPGME & R, Kolkata (Ref. No. Inst/IEC/35, dated, 3rd January, 2007).

Subject inclusion criteria:
Female diabetic of reproductive age group was included, provided they were not taking oral contraceptive pill or injectable or oral steroid hormone for any other clinical reason. Post menopausal patients not taking hormone replacement therapy were also included. Normal sample was taken from volunteers without diabetes having similar menstrual disturbances.

Subject exclusion criteria:
Diabetic teenagers who have not attended menarche were not included. Diabetic female of reproductive age group taking injectable or oral hormone was excluded. Insulin dependent diabetic females were not considered for estimation of blood insulin level. After selection of the patients, information was collected by personal interview.

Hormone assay:
Sample of blood was collected in the early follicular phase of the cycle. Hormone estimation was done at the laboratory of Endocrine Department at IPGME & R by ELISA Chemo luminescence method. Particularly free testosterone and estrogen, LH, FSH levels were measured from blood sample taken within first 10 days of menstruation of diabetic ladies in reproductive age group, in case of post menopausal diabetic female, blood was collected on any date with informed consent of patient. Blood was collected for serum insulin estimation 48 hours after stoppage of anti diabetic medicine and insulin injection only if the clinical situations permit.

Grouping of diabetic females:
Diabetic females were grouped according to following clinical parameter like duration of overt diabetes more than five year or less than five year, diabetes controlled with insulin or oral medicine or both, whether she is obese, overweight, or underweight, other complication like ketoacidosis, nephropathy, retinopathy or neuropathy present or not and whether she was hypertensive or normotensive. As per menstrual history is concerned all participants were grouped into three categories like postmenopausal, with normal menstrual pattern and with abnormal menstrual history like oligomenorrhoea or amenorrhoea.
RESULTS:

Age and periodicity:

8 diabetic female patients of 31-40 yrs age and 7 patients of 41-60 yrs old age showed heavy period (Fig1: A). 45 diabetic female patients of 31-40 yrs age and 90 patients of 41-60 yrs old age showed scanty period (Fig1: B). 23 diabetic female patients of 20-30 yrs age, 13 patients of 31-40 yrs old age and 7 patients of 41-60 yrs old age showed irregular period (Fig1: C).

Irregular menstrual cycle and steroid hormone level

Diabetic female who had irregular, heavy and scanty period showed high level of blood FSH and LH than normal females (Fig2: A and B). In case of heavy period patients showed slightly less estradiol level and scanty period revealed less estradiol than control (Fig2: C). Diabetic patients showed significantly low testosterone level than normal (Fig2: D).

Insulin and irregular menstrual cycle

Diabetic patients with high insulin level showed scanty period than normal and less insulin revealed irregular period (Fig3: A).

DISCUSSION:

The population in India has an increased susceptibility to diabetes mellitus. The prevalence of disease in adults was found to be 2.4% in rural and 4 – 11.6% in urban dwellers, high frequencies of impaired G.T.T. ranging from 3.6 – 9.1% indicate the potential for further rise in prevalence of this disease in the coming decade (WHO 1998 prevention and control of Diabetes Mellitus report of an inter country workshop – Dhaka – Bangladesh – 27 – 30April 1998, SEA/NCD/40). In our study population diabetic female who had irregular, heavy and scanty period showed high level of blood FSH and LH than normal females (Fig2: A and B). In case of heavy period patients showed slightly less estradiol level and scanty period revealed less estradiol than control (Fig2: C). Diabetic patients showed significantly low testosterone level than normal (Fig2: D). Diabetic patients with high insulin level showed scanty period than normal and less insulin revealed irregular period (Fig3: A).

About 90% of female diabetics are of Type 2, resulting from insulin resistance. There is a well known co-relation between insulin resistance and hyper androgenemia however, it is seen that young woman with polycystic ovarian disease has increased risk of developing Type 2 Diabetes Mellitus in future (Kuhl C 1975 & 1998). Consequently, it will be pertinent to study, whether in established diabetes the hormonal changes (hyper androgenemia) still persists or not (Kuhl C 1975 & 1998). From our study it has been established that our patients with diabetes mellitus, particularly related to menstruation there is relation between hypoinsulinaemia and serum level of sex steroid like estrogen and testosterone. Now a day most type 1 diabetic women are fertile, although menarche is often delayed when diabetes develop before puberty and menstrual dysfunction is common (Solomon CG et al 2001). Abnormalities in the level of LH, FSH are believed to be responsible for the oligomenorrhoea and amenorrhea that occur in young diabetic women (Solomon CG et al 2001). Menstruation and ovulatory disturbances have been long recognized in poorly controlled diabetic women. Secondary amenorrhea has a prevalence of 8.2% in diabetic women, as compared with 2.8% in a normal population (Kiear K 1992). Amenorrhic diabetic women have fewer LH pulses and secretary episodes than do non-diabetic women. Their responses of LH to GnRH have been reported as normal or increased or decreased. It has been suggested that the LH, FSH pulse generator in pituitary being responsible for the
menstrual dysfunction (Djursing H 1982 and Francis O 1959 and Rosenthal MS 2006). Our results showed that there is significant association of fasting sugar and different hormonal levels (testosterone, LH, FSH and insulin) of diabetic patient who showed irregular period (Table 1).

Finally it is well known that ovarian hormone influence insulin sensitivity across the menstrual cycle, and in the menopausal transition. Therefore, specific cause of menstrual disorder may be formulated taking into consideration that estrogen and testosterone has effects on glucoregulation and vice-versa. This knowledge is important to individual for making life style choices and medical providers counselling patients who are considering hormone use for contraception or as replacement therapy.

**CONFLICT OF INTERESTS:**

The authors declare that there is no conflict of interests regarding the publication of this paper.

**REFERENCE:**


Tables and Figures:

Figure 1: Age and irregular periodicity in diabetic female patients

Figure 2 A: Relation of FSH (IU/L) with altered periodicity in diabetic and control female
Figure 2 B: Relation of LH (IU/L) with altered periodicity in diabetic and control female

Figure 2 C: Relation of estradiol (pg/ml) with altered periodicity in diabetic and control female
Fig2: D

Figure 2D: Relation of testosterone (pg/ml) with altered periodicity in diabetic and control female

Fig3: A

Figure 3A: Relation of insulin (IU/L) with altered periodicity in diabetic and control female
### Table 1: Association of fasting sugar and different hormonal levels of diabetic patient who showed irregular period.

All the data were presented as mean ±SEM. The data were analyzed by *t*-test. Results with *P* < 0.05 were considered statistically significant.

<table>
<thead>
<tr>
<th>Fasting Sugar</th>
<th>Hormone</th>
<th>Hormonal Level</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±SEM</td>
<td>Mean ±SEM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>(pg/ml)</td>
<td></td>
<td></td>
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<tr>
<td>230.8 ± 26.5</td>
<td>Estradiol</td>
<td>194.33 ± 17.5</td>
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<tr>
<td>Testosterone</td>
<td>0.54 ± 0.17</td>
<td>&lt;0.0001</td>
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<tr>
<td>FSH</td>
<td>11.23 ± 1.01</td>
<td>&lt;0.0001</td>
<td></td>
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<tr>
<td>LH</td>
<td>07.07 ± 1.007</td>
<td>&lt;0.0001</td>
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<tr>
<td>Insulin</td>
<td>3.04 ± 0.855</td>
<td>&lt;0.0001</td>
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