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Original Research Article Clinical Effect of Estradiol and Lipid Profile Status in Type-2 Diabetes of Male and Female in West Bengal, India

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Abstract: Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. With increased oxidative stress there is a chance of hyperglycemia or DM. A total 360 subjects were involved in the study. Of which 90 were male diabetics, 90 were female diabetics (case) and 90 male non diabetics, 90 females non diabetics (control). The mean and sd values of Estradiol, Cholesterol, Triglycerides, LDL, HDL were calculated for all cases and control of both sexes. Diabetic females had lower estradiol level as compared to controls but the diabetic males had higher estradiol level as compared to controls. Triglycerides and LDL were significantly higher among cases for different age group for both sexes compared to control (p≤0.05). The HDL level were significantly lower (p≤0.05) among cases in comparison to control for different age group of both the sexes.
Key Words: Diabetes, Estradiol, Hyperlipidemia

I. INTRODUCTION

Estradiol (E2) is the most potent natural estrogen, produced mainly by the ovary, placenta, in smaller amount by the adrenal gland and the male testes. Estradiol is a steroid hormone which is derived from cholesterol. During the metabolism of cholesterol, androstenedione is a key intermediary which is formed due to the cleavage of the side chain of the steroid hormone. Aromatase is an enzyme which helps to convert androstenedione to estrone which is then converted to estradiol.(1)

Estradiol has various functions such as growth of female reproductive organ (Estradiol acts as a growth hormone for the reproductive organ of females). Estradiol maintains eggs in the ovary and triggers a series of events that causes ovaluation. Estradiol 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 follow a cyclic, biphasic pattern with the highest concentration found just before the ovaluation. During pregnancy level of estradiol increases above pre-ovulatory peak levels and high level are sustained throughout pregnancy.(3)

Type 2 diabetes insulin resistances and in a male patient occur due to the loss of estrogen function. Estrogen acts directly on beta-cells 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 overstimulation.(5)

II. MATERIALS AND METHODS

The study was carried out at 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. One hundred and eighty (180) apparently healthy and non diabetic were used as control and one hundred and eighty (180) diabetes used to test subjects. A total one hundred and eighty (180) males and one hundred and eighty (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 are collected in between 1-4 days of menstrual cycle. The research protocol was approved by ethics committee of the Institution. Proper vein puncture technique was employed in the collection of the 5ml of blood sample from the subjects. Sample collected aseptically from cases and control was subjected to serum analysis. Blood samples was centrifuged at 3000rpm for 10 minutes

Serum Cholesterol was measured by CHOD/PAP method, Serum Triglycerides was measured by GPO/PAP method, Serum LDL was measured by Direct Enzymatic method, and Serum HDL was measured by PEG/CHOD-PAP method, all Elisa Kit Provided by Coral Clinical System.

Serum Estradiol was measured by Enzyme linked immunosorbant assay (Elisa, Callbiotech).

Data generated were analyzed using statistical package for social science (SPSS) version 20.00 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 95% confidence interval ($p<0.05$).

III. RESULT

Table 1: Comparison between Age And Sex related levels for Estradiol and Lipid profile among cases and controls of males.

Age group (years)	18 to 26		27 to 35		36 to 45	
Male	Case (Mean ± SD)	Control (Mean ± SD)	Case (Mean ± SD)	Control (Mean ± SD)	Case (Mean ± SD)	Control (Mean ± SD)
Estradiol(pg/ml)	25.39±2.60	20.15±1.69	27.32±1.85	21.44±1.02	38.03±1.65	28.32±2.30
Cholesterol(mg/dl)	247±33.16	155±9.99	198±14.90	161±4.58	259±28.89	167±7.81
Triglycerides(mg/dl)	249±20.93	128±9.41	219±31.64	132±7.28	212±34.76	140±9.67
LDL(mg/dl)	187±28.20	101.10±8.28	122±7.44	105±5.29	124±10.81	98±11.14
HDL(mg/dl)	35±3.76	49±5.88	38±4.88	43±4.0	37±8.96	42±7.79
P value	≤0.05	≤0.05	≤0.05	≤0.05	≤0.05	≤0.05

Table 2: Comparison between Age And Sex related levels for Estradiol and Lipid profile among cases and controls of females

Age group (years)	18 to 26		27 to 35		36 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)
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
Cholesterol(mg/dl)	212.43±30.09	164.76±6.96	188±31.84	163.72±9.83	270.50±10.26	160.93±7.42
Triglycerides(mg/dl)	249±41.75	127.46 ±9.67	230.83±22.69	134.27±15.89	234.96±9.07	147.70±7.26
LDL(mg/dl)	135.03±17.86	97.90±17.59	137.76±8.23	103.48±10.81	114.33±7.38	103.40±6.95
HDL(mg/dl)	37.56±8.10	51.93±6.64	36.46±5.11	45.24±5.08	34.5±4.75	39.90±7.02
P value	≤0.05	≤0.05	≤0.05	≤0.05	≤0.05	≤0.05

IV. DISCUSSION

In this study the mean values of Estradiol and lipid profile were estimated for all cases and control of both sexes. The mean and sd values of Cholesterol, Triglycerides and LDL were significantly higher among cases for different age group for both sexes compared to control ($p\leq0.05$). The mean and sd values of HDL were significantly lower ($p\leq0.05$) among cases in comparison to control for different age group of both the sexes. The mean and sd values of Estradiol in case of females were significantly lower

($p \leq 0.05$) among cases compared to controls. It was found from the study that estradiol level in female gradually decreases with increasing age. On the other hand the mean and sd values of estradiol in case of males were significantly higher ($p \leq 0.05$) among cases compare to control. Estrogens play a significant role in metabolic regulation. Gradual decrease in circulating levels of estrogen, 17β-estradiol (E2), due to either natural or surgical menopause has effects beyond reproductive health. E2-deficiency and impairment of its cellular action lead to an abrupt reduction in metabolic rate, increase in central adiposity, dyslipidemia, and progression of metabolic syndrome (MetS). Together these changes increase the risk of developing type 2 diabetes, and cardiovascular disease and related complications.(6) Since the E2 levels of female cases were lower than controls, they are thought to be more prone to develop type 2 diabetes. Estrogen plays a vital role in the pathogenesis of type-2 diabetes. Estrogen reduces the level of plasma insulin and hyperglycemia by some mechanism which helps to inhibit diabetes. Our results are in concordance with a study conducted by Yadav, et .al.(7). The decrease in insulin sensitivity with menopause suggests that E2 plays a protective role against insulin resistance in women. E2 may regulate insulin action directly via actions on insulin-sensitive tissues or indirectly by regulating factors like oxidative stress, which contribute to insulin resistance. In skeletal muscle, E2 receptor α (ERα) is thought to have a positive effect on insulin signaling and GLUT4 expression whereas ERβ may be prodiabetogenic and cause reduced GLUT4 expression (8,9).Moreover, loss of estrogen function has been shown to cause insulin resistance and type 2 diabetes in a male patient .Dyslipidemia is one of the major risk factors for major cardiovascular disease (CVD) in T2DM. The characteristic features of dyslipidemia are high plasma triglyceride concentration, reduced high density lipoprotein cholesterol (HDL-c) concentration, and increased concentration of small dense LDL particles. These changes are caused by an increased inflammatory adipokines and excess flow of free fatty acid in circulation as a result of insulin resistance are associated (10) .Results from various cross-sectional and prospective studies revealed relation between T2DM and E2 levels in both men and postmenopausal women.

The male hormone testosterone may regulate much of the metabolism in males, but HFD-fed liver-specific ERα knockout male mice have greater impairment of hepatic insulin sensitivity and increased liver triglycerides and diacylglycerides than the wild type floxed controls (11) Further, the E2-testosterone balance may be crucial in metabolic regulation since progressive testosterone predominance, particularly bioavailable testosterone (ratio of testosterone to sex hormone-binding globulin) in women without HRT or preexisting diabetes and MetS, was independently associated with increased visceral fat and risk of MetS after menopause (12,13)They found that estrogen replacement therapy on postmenopausal women reduces the level of glycosylated heamoglobin. Our results are in concordance with a study of Koh and associates (14). They found estrogen lowers LDL cholesterol whereas increase HDL cholesterol and triglyceride level.

Women tend to acquire fat primarily in the subcutaneous regions whereas men tend to have visceral adiposity which is positively correlated with risk for CVD and MetS. The incidence of CVD and MetS increases in women after menopause because adiposity shifts from subcutaneous to the visceral area . Two main mechanisms have been suggested to explain the shift in fat distribution with menopause. Firstly, alteration of the lipid storage characteristics of the fat depots occurs due to the influence of E2 on adrenergic receptors. The balance between lipolytic β1-2 receptors and antilipolytic α2 adrenergic receptors between the subcutaneous and visceral depots can be shifted by E2 (15). Secondly, altered distribution of ERα and ERβ in adipose depots allows E2 to modulate distribution of fat between the depots. Males have lower ERα in their visceral depots and are therefore readily store more fat viscerally (16). The effect of E2 on diabetes is a combination of many factors, including direct effects on insulin signaling in insulin-sensitive tissue, effects on pancreatic beta cells regulating insulin release, its role in adipose tissue metabolism and energy expenditure, its effects in hepatic glucose production and on the hypothalamus to regulate food intake, and its effects on energetics and metabolism.

V. CONCLUSION

Serum estradiol levels were significantly lower in diabetic females as compared to controls. Patients with type-2 diabetes have abnormality in estradiol level. These associations should be kept in mind during the treatment of type-2 diabetes patients. From a clinical prospective it is suggested that possible clinical application of sex hormone biomarkers should be investigated to define the risk level better. The hormone therapy plays a vital role but there is always a risk factor of hormone replacement therapy associated with diabetes for women.

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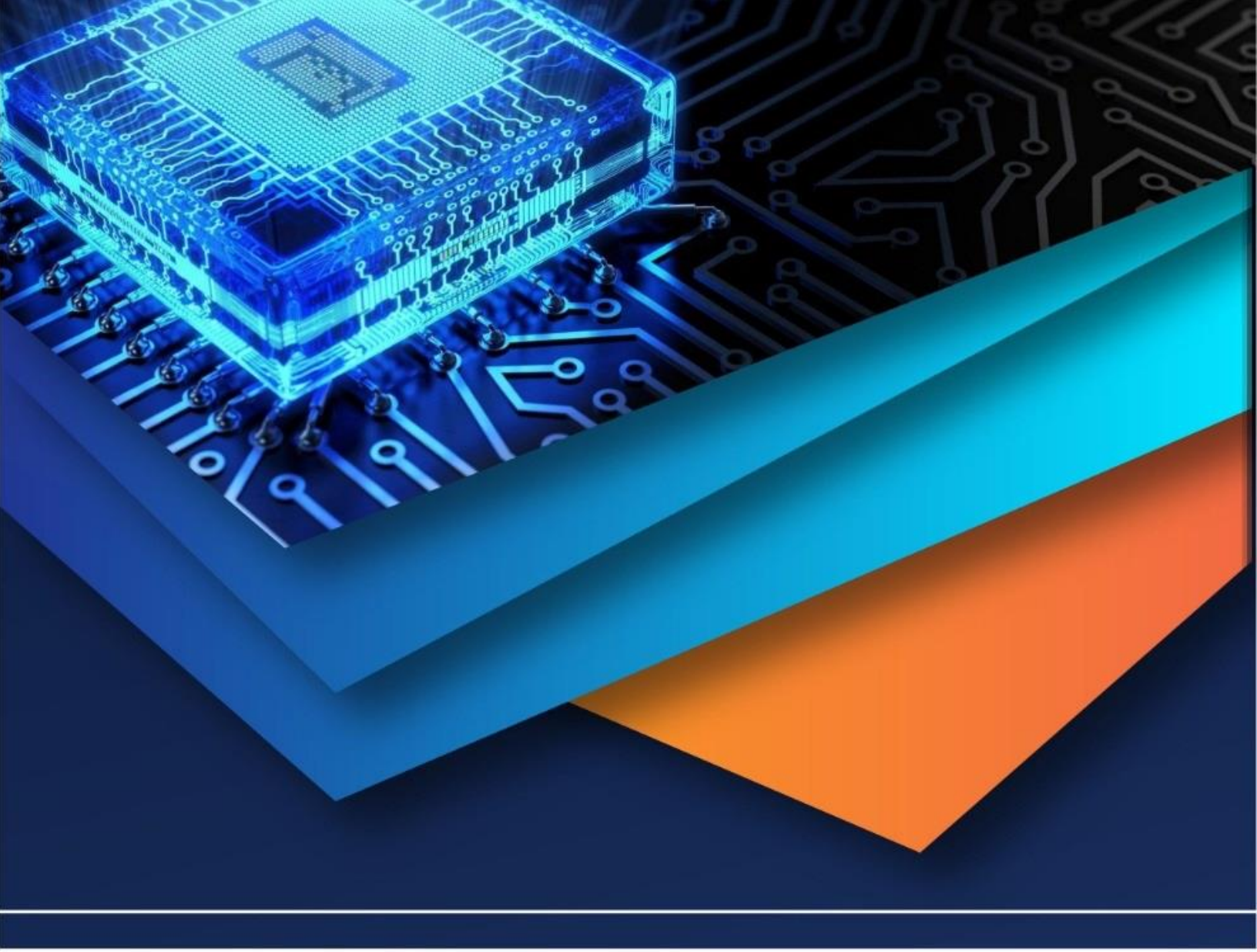

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