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FREE RADICAL AND ANTIOXIDANTS IN OBESE DIABETICS AND NORMAL BMI DIABETICS

KEYWORDS: Type-2 Diabetes Mellitus, Free Radical And Antioxidants, Obese and Normal BMI Diabetics

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ABSTRACT *India has a high prevalence of diabetes mellitus and the numbers are increasing at an alarming rate. In India alone, diabetes is expected to increase from 40.6 million in 2006 to 79.4 million by 2030. The problems of obesity and impaired glucose tolerance are not confined to adults alone but children are also increasingly getting affected. Most long standing macro and micro vascular complications are also more common among Indian diabetics as compared to other races and ethnic groups.*

Aim:- To study free radical and antioxidant status in type 2 diabetes mellitus with respect to obesity.

Meterial and Methods:- Present study was prospective, carried out in the Department of Biochemistry, MGM Medical College and Diabetology clinics of MGM Group of Hospitals, Vashi, Belapur & Kamothe, Navi Mumbai. 80 type-2 diabetic patients of both genders aged between 35 to 65 years were divided into two groups. Group-1 comprised of 40 obese diabetes, Group-2 40 nomal BMI diabetics and 40 healthy individuals acted as control Group-3. Oxidative stress markers MDA, NO and antioxidants SOD and Catalase were estimated.

Results:- Oxidative stress makes MDA (3.04 ± 0.54) (nmol/ml) and NO (42.26 ± 12.25) (µmol/L) were highest while antioxidants SOD (1.29 ± 0.31) (U/ml) and catalase (16.75 ± 0.11) (U/mg) were least in obese diabetics.

Conclusion:- Obesity and diabetes plays an important role in the development of increased oxidative stress and associated complications leading to easier membrane lipoperoxidability and membrane damage. Obesity increases oxidative stress synergistically in type-2 diabetes mellitus.

Introduction:-
Diabetes Mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of different organs, especially eyes, kidneys, nerves, heart and blood vessels.[1] It is the most prevalent metabolic condition and one amongst major health and socio economic problem worldwide. [2]

Diabetes is pandemic in both developed and developing countries. By the year 2030, over 85 percent of the world's diabetic patients will be in developing countries. In India alone, the prevalence of diabetes is expected to increase from 31.7 million in the year 2000 to 79.4 million in 2030. These estimates are valid only if the prevalence of obesity remains the same. The prevalence of T2DM parallels the increasing prevalence of obesity; since the incidence of obesity is rising at an alarming rate in developed and developing countries. [3]

Obesity is a condition of increased adipose tissue mass. It has been defined as an increased in body weight beyond the limits of physical requirement as a result of an excessive accumulation of triacylglycerol in fatty tissue that is the net result of excessive energy intake compared to energy usage.[4] Obesity can be seen as the first wave of a defined cluster of non-communicable diseases called "New World Syndrome", creating an enormous socioeconomic and public health burden in poorer countries.[5] Type-2 diabetes and obesity are clearly connected; Overweight and obesity (having a body mass index (BMI) over 25 have been estimated to account for around 65 to 80 % of new cases of type-2 diabetes. A report published by Diabetes UK suggests that obese people are up to 80 times more likely to develop type-2 diabetes than those with a BMI of less than 22. [6]

Oxidative stress in diabetes mellitus causes several adverse effects on the cellular physiology. This is particularly relevant and dangerous for the β-cell of islet pancreas, which is among the tissues that have the lowest levels of intrinsic antioxidant defence mechanism. Multiple biochemical pathways and mechanisms of action have been implicated in the deleterious effects of chronic hyperglycemia and oxidative stress on the function of vascular, retinal and renal tissues. [7]

Type-2 diabetes is associated with multiple metabolic derangements that result in the excessive production of reactive oxygen species and oxidative stress. ROS are the by product in type 2 diabetes, generated during protein glycation and as a consequence of advanced glycation end products receptor binding; they impair insulin signalling pathways and induce cytotoxicity in pancreatic beta cells. [8]

Antioxidants are the first line of defence against free radical damage, and are critical for maintaining optimum health and wellbeing. The need for antioxidants becomes

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even more critical with increased exposure to free radicals. Pollution, cigarette smoke, drugs, illness, stress, and even exercise can increase free radical exposure. The intensity of this oxidative stress depends on the rate of generation of free radicals and other active oxygen and nitrogen oxidative species, and on antioxidant defences. [9]

Material and Methods:-
The present study was the prospective study, carried out in the Department of Biochemistry, MGM Medical College, Kamothe and Diabetology clinics of MGM Group of Hospitals, Vashi, Belapur & Kamothe, Navi Mumbai.

Study Design:-
The subject were groupized as follows. Group1 included 40 Type 2 diabetic patients with BMI (18.5 to 24.9), Group 2 included 40 Type 2 Diabetic patients with BMI ≥ 30 and Group 3 included 40 Healthy control individuals. Written consent was taken from patients and healthy individuals. Fasting and postprandial blood samples were collected in fluoride bulb for Glucose estimation and in EDTA bulb for glycosylated Hb estimation. Lipid profile, oxidative stress and total antioxidant capacity were estimated in serum.

MDA was estimated by K Satoch method, NO was estimated by Najwa Cortas and Nabil Wakid method, Catalase by Sinha K. method & Superoxide Dismutase (SOD) by Marklund and Marklund method. Patients on lipid lowering drugs and Diabetic patients with complications other than obesity were excluded.

Statistical analysis:-
Statistical analysis of the data was carried out with SPSS, version 16; The data was reported as mean ± SD. The comparisons between two groups was be tested by student t-test and Correlation was studied by Pearson's correlation.

Results:-
The characteristics of the subjects are shown in the Table. The levels of FPG, PPPG, HbA1c, cholesterol, triglycerides and MDA were significantly higher in the diabetics. So ($p \leq 0.001$). The plasma MDA levels were significantly elevated.

We correlated the different parameters by the Pearson Correlation Coefficient and find r- value.

Table. No. 1: The biochemical parameters of control group, diabetic groups and obese diabetic groups.

S.No.	Parameters	**Control** mean± SD (n=40)	**Diabetic** mean ± SD (n=40)	**Obese Diabetics** mean ± SD (n=40)
1.	BMI(Kg/m^2)	22.4 ± 0.5	24.5 ± 2.1	35.3 ± 3.3*
2.	HbA1C	5.0 ± 0.5	7.1 ± 1.1	9.0 ± 2.1
3.	FBS (mg/dl)	91.8 ± 23.4	172.6±22.1	183.0 ± 40.1
4.	PPBS (mg/dl)	126.1 ± 24.4	218.2±81.1	223.4 ± 88.3
5.	T G (mg/dl)	147.8 ± 48.5	184.1±27.5	187.5 ± 57.4
6.	T.Cholesterol (mg/dl)	165.5 ± 33.5	223.3±15.0	242.5 ± 29.6
7.	HDL(mg/dl)	48.5 ± 12.5	42.6 ± 7.5	36.8 ± 6.1
8.	LDL(mg/dl)	85.2 ± 31.0	88.5 ± 46.8	107.0 ± 79.0
9.	NO (µmol/L)	32.3 ± 9.1	39.7 ±10.6	42.2 ± 12.2
10.	Catalase (U/mg)	21.0 ± 26.2	17.0 ± 0.6	16.7 ± 0.1
11.	SOD (U/ml)	1.79 ± 0.48	1.62 ± 0.39	1.29 ± 0.31
12.	MDA (nmol/ml)	1.66 ± 0.27	2.62 ± 0.43	3.04 ± 0.54

P- Value $p \leq 0.01$* for all parameters biochemical parameters of control group, diabetic groups and obese diabetic groups.

Table No. 2 : Shows Correlation between biochemical parameters.

	HbA1C	T. Chol.	HDL
MDA	0.56	0.61	- 0.38
SOD	0.43	- 0.59	0.18

Figure No. 1 : Correlation between HbA_1C and MDA in control group and study groups.

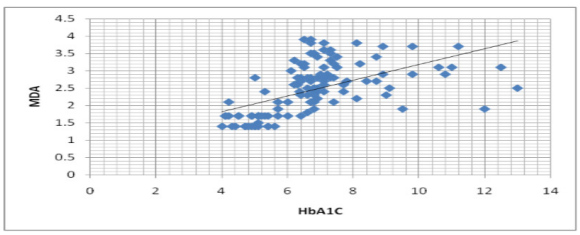


Figure No. 2 : Correlation between HbA1C and SOD in control group and study groups.

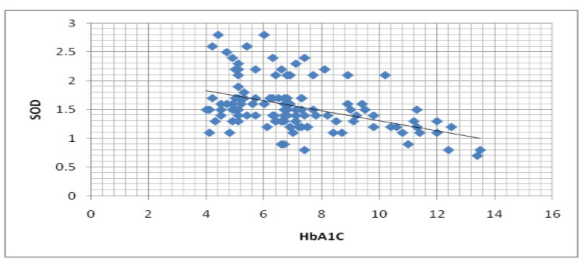
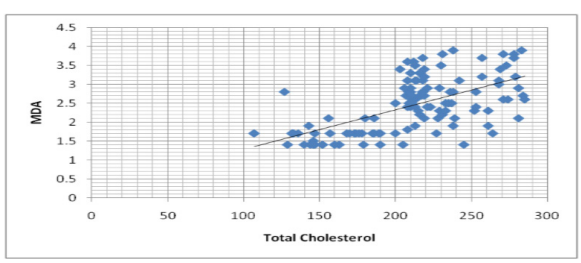


Figure No. 3 : Correlation between Total Cholesterol and MDA in control group and study groups.



Discussion:-
Obesity and type-2 diabetes (T2DM) are public health problems, with health consequences and economic costs that have raised concern world-wide. The increase in the prevalence of diabetes parallels that of obesity. Some experts call this dual epidemic ***"diabesity"***. Both are major public health problems throughout the world and are associated with significant, potentially life threatening co morbidities and enormous economic costs. There is a strong association between obesity and type 2 diabetes.

In our study we found that mean BMI, HbA1C, Lipid profile, MDA, NO, SOD and Catalase in control group, diabetic group and obese diabetic group significantely elevated in the diabetic and obese diabetic groups respectively. The values are above in the Table.1

We correlated the levels of BMI and MDA in all groups (n = 120) and found a significant positive correlation (r = 0.60). Suryawanshi N.P, observed a significant increase in the lipid peroxide (MDA) and lipid profile. In their study

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they concluded that high level of cholesterol, triglyceride, LDL-cholesterol and low HDL-cholesterol may be due to the obesity, increase calorie intake and lack of muscular exercise in the patients of diabetes mellitus .[10]

We correlated the levels of HbA_1C and MDA in all groups (n = 120) and found a significant positive correlation (r = 0.56). Mohammed Naji Kassim reported statistically positive correlation between HbA1c with MDA ($p< 0.01$). [11] The values are above in the Table.2 and Figure no. 1.

Desai Vidya et al., in their study showed a positive correlation between plasma MDA and HbA1c .Their results suggested that increased lipid peroxidation and a decline in the antioxidant defense mechanisms plays a very important role in the initiation and progression of micro-vascular complications.[12]

We correlated the levels of HbA_1C and SOD in all groups (n=120) and found a significant negative correlation (r = -0.43) Our results are similar to that obtained by M Indran, who reported negative correlation between SOD with HbAlc (r = -0.374), ($p<0.05$). Decline in the level of SOD in diabetic tissue and blood has been reported in many studies. Recently Kim (2013) reported that diabetic skin tissues express a relatively small amount of extracellular protein and concluded that extracellular SOD is related to the altered metabolic state in diabetic skin, which elevates ROS production. Study performed by Lucchesi and colleagues to observe the oxidative balance of diabetic rats reported diminished activity of SOD and other antioxidant enzymes in the liver tissue.[13] The values are above in the Table.2 and Figure no. 2.

The levels of Total cholesterol and MDA in all groups (n = 120) and found a significant positive correlation (r = 0.61) When we correlated the levels of HDL and MDA in all groups (n = 120) we observed a significant negative correlation (r = - 0.38). Our findings are similar that obtained by Matsuda et al. who reported that MDA-LDL level was significantly correlated with TG and HDL cholesterol levels. [15] The values are above in the Table.2 and Figure no. 3.

Conclusion:-

As diabetes is a disease of self management, appropriate nutrition (low calories, low carbohydrates, and low fat with high fiber diet) regular physical activity and proper medication to achieve good glycaemic control have to be followed. Patients of diabetes with obesity-weight management are a key factor. It is established that reducing total cholesterol and LDL cholesterol levels can significantly reduce the risk of CHD morbidity and mortality. Aggressive therapy of hyperlipidaemia / dyslipidaemia can help to reduce the epidemic of premature coronary artery disease seen in Indians and people from other countries. Life style modifications like regular exercise, quitting smoking and alcohol along with yoga will help the diabetic patients to live a better life.

Obesity and diabetes plays an important role in the development of increased oxidative stress and associated complications leading to easier membrane lipoperoxidability and membrane damage. Further studies using antioxidant enzymes, vitamin supplementation, lifestyle, dietary habit and other lipid peroxidation parameters in diabetic animal model are recommended to evaluate the effect of oxidative stress on obese individuals with diabetes.

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