

Original Research Article

**Serum Leptin Level in Diabetes Mellitus : A Case Control Study in India****Dr. Amit Kumar Sagar<sup>1\*</sup>, Dr. Kishan Gopal Barupal<sup>2</sup>, Dr. C.P. Mathur<sup>3</sup>, Dr. Sandeep Tak<sup>4</sup>, Dr. Manju Lata Verma<sup>5</sup>**<sup>1,2</sup>Asst.Prof., Dept. of Medicine, Dr. Sampurnanand Govt. Medical College, Jodhpur -Raj<sup>3</sup>Sen.Prof., Dept. of Medicine, Dr. Sampurnanand Govt. Medical College, Jodhpur -Raj<sup>4</sup>Prof., Dept. of Medicine, Dr. Sampurnanand Govt. Medical College, Jodhpur -Raj<sup>5</sup>Senior Resident, Dr. Sampurnanand Govt. Medical College, Jodhpur -Raj**\*Corresponding author**

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**Abstract:** It is a universal endocrine disorder and both its incidence and prevalence are alarmingly increasing day by day. Leptin is a hormone communicating information on the body fat store or energy reserve to the brain, thus maintaining normal functions of several neuro endocrine axis. Obesity, eating disorder (Anorexia Nervosa and Bulimina Nervosa) is associated with altered serum leptin. Leptin level is higher in obese (highest in obese diabetics) reflecting leptin resistance (akin to hyperinsulinemia in type II DM) possibly caused by reduced transport into the cerebrospinal fluid or defective post receptor signaling. A close relationship of leptin concentration to insulin resistance has been reported emphasizing that the resistance to the action of leptin may be present in subject with insulin resistance. The main aim of the study to observed the relationship of leptin level in different anthropometric and metabolic covariates in various groups. Prospective study, of total 4 groups 20 in each group, total 80 different patients were included in our present study. In this we observed the leptin level. Obese had 9.5575 leptin levels and lean had 7.0725 leptin level. Obese diabetic had highest leptin level i.e. 10.965 and least was present in lean non-diabetic i.e. 6.315 group. Highest body mass index group had highest leptin level (obese diabetic group). The group which had lowest body mass index had lowest level of leptin. In this, we concluded that Leptin level higher in obese as compare to lean. Leptin level is highest in obese diabetics followed by obese non diabetic, lean diabetic and lean non-diabetic. Leptin level strongly correlated with body mass index, waist hip ratio and waist circumferences. There is inverse relationship- of leptin level with HDL cholesterol. There is no relationship of leptin with glycaemic control.**Keywords:** Diabetes, Obese, Leptin, BMI, Glycaemic Control

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**INTRODUCTION**

Diabetes mellitus is a syndrome characterized by chronic hyperglycemia with disturbances of carbohydrates, fat and protein metabolism resulting from either an absolute or relative deficiency of insulin secretion and/or action. It is a universal endocrine disorder and both its incidence and prevalence are alarmingly increasing day by day. WHO report the prevalence of diabetes in adults worldwide will rise from 4% in 1995 to 5.4% and the number will rise from 135 million in 1995 to 300 million by the year 2025 [1]. Leptin, the obese (Ob) gene product is a 16K Da (containing 167 amino acid proteins) peptide hormones secreted by adipocyte [2]. Leptin is a hormone communicating information on the body fat store or energy reserve to the brain [3, 4], thus

maintaining normal functions of several neuro endocrine axis [5]. Obesity, eating disorder (Anorexia Nervosa and Bulimina Nervosa) is associated with altered serum leptin. It could contribute to body weight regulation through modulation feeding behaviors or energy expenditure [6]. It suppresses appetite & increases energy expenditure [7, 8], thus proposed as a mediator in negative feedback loop that control body adiposity [6]. Leptin level is higher in obese (highest in obese diabetics) reflecting leptin resistance (akin to hyperinsulinemia in type II DM) possibly caused by reduced transport into the cerebrospinal fluid or defective post receptor signaling. Feeding and administration of CCK-8 decreased gastric leptin immunoreactivity and protein content and increased plasma leptin concentrations. Thus gastric-derived

leptin may act locally in the gastrointestinal tract and the brain to influence satiety [9]. Leptin is distributed to several organs, like in stomach, hypothalamus, pituitary, skeletal muscle, placenta & mammary gland and cleared mainly by the kidney [10, 11].

A close relationship of leptin concentration to insulin resistance has been reported emphasizing that the resistance to the action of leptin may be present in subject with insulin resistance [12]. In one of the study only a weak association between plasma insulin & leptin in Asian southern Indian area observed. Shimabukuro said that obese rat have fat over loading their insulin producing pancreatic islet beta cells which don't functions normally. Leptin action can reverse this & rid the islet of excess fat however the hormone had no effect on the cells of obese rats because they have defective leptin receptor which allow fat to forming faster & disabling the beta cell. Recently, SOCS-3 has been suggested to act as apotential mediator of central leptin resistance [13]. Low leptin levels mediate the hormonal response to fasting primarily by acting on neuronal targets in the hypothalamus and possibly through regulation of pituitary function [14]. Over the year some studies have done for detecting and assessing the relationship of plasma leptin to obesity and the level of leptin in different diabetic group. Hence present study was undertaken to assess relationship of plasma leptin to obesity.

#### Aims and Objectives

- Estimation of serum leptin level in diabetic patients
- To find out the relationship of serum leptin level to obesity.
- To find out the relationship of serum leptin with lipid profile.

#### MATERIAL AND METHODS

Diabetic subject are recruited from medical outdoor patients, diabetic clinics and indoor patients of MG Hospital attached to Dr. S. N. Medical College, Jodhpur (RaJ).

The following four groups were studied:-

- A. Lean Non Diabetic (n=20)
- B. Lean Diabetic (n=20)
- C. Obese Non Diabetic (n=20)
- D. Obese Diabetic (n=20)

In total 4 groups 20 in each group, total 80 different patients were included in our present study. In this we observed the leptin level. The main aim of the study to observed the relationship of leptin level in different anthropometric and metabolic covariates in all the four groups.

#### METABOLIC MEASUREMENTS-

The all groups except diagnosed diabetes were screen with OGT performed according to standard WHO criteria. Baseline sample were taken for leptin and lipid profile after a 12-hour overnight fast. In the diabetic patients fasting and postprandial samples were taken on medication and later analysed for blood glucose and glycosyleted hemoglobin level. Fasting serum with stored at -20°C for the analysis of leptin level. The leptin level estimated using solid phase double antibody RIA kit. The limit of detection for the RIA of leptin was 0.20ng/ml.

#### EXCLUSION CRITERIA

- Patients on Steroid ,Insulin & Eltroxin
- Pregnancy ,Diabetic Ketoacidosis
- B. Sugar F > 450 ,HbA<sub>1c</sub> > 11.3 & BMI > 45

#### METHOD OF QUANTITATIVE MEASUREMENT OF HUMAN LEPTIN IN SERUM

- BIOSOURCE LEPTIN EASIA KIT
- THE BIOSOURCE LEPTIN EASIA ASSAY:

#### STATISTICAL ANALYSIS

In the above study the following analytic statistical formulae were incorporated for various calculations-Unpaired t-Test & Chi-Square(X<sup>2</sup>) Test

#### OBSERVATIONS & RESULTS

Present study was conducted in Mahatma Gandhi Hospital attached to Dr. S. N. Medical College, Jodhpur (Rajasthan). Total 80 patients were included in the present study and they were divided in to four groups, which were:-GroupA-Obese Diabetic, Group B-Obese Non-Diabetic, Group C-Lean Diabetic, Group D-Lean Non-Diabetic.

Diabetic subject are recruited from MOPD/IPD patients & diabetic clinics. Following are the observation based on patients characteristics.

**Table 1: Clinical and Metabolic Characteristics**

Variables	Obese Diabetic	Obese Non-Diabetic	Lean Diabetic	Lean Non-Diabetic
Age (years)	53.4+8.51	46.95+8.47	49.75+8.78	30.65+5.49
Body Mass Index (Kg./m <sup>2</sup> )	32.63+4.25	29.81+3.18	24.11+0.62	21.35+2.38
Waist Circumference (cm)	112.78+18.42	105+9.92	88.8+8.35	78.45+15.54
Waist Hip Ratio	1.02+0.11	0.95+0.06	0.89+0.06	0.87+0.08
Triglycerides (mg%)	139+31.29	134.8+81.90	207.5+114.43	133.5+44.34
Total Cholesterol (mg%)	208+28.91	185.6+36.09	210.65+30.25	188+30.70
HDL-C (mg%)	35.55+3.81	41.55+1.84	44.3+5.53	48.55+6.98
LDL-C (mg%)	137.65+20.86	124.2+21.64	127.85+25.53	112.75+27.38
Leptin (ng/ml)	10.96+13.92	8.15+8.5	7.83+8.83	6.31+5.69
HbA1C	7.86+1.64	4.93+1.35	9.48+1.92	5.36+0.44

All Values in Mean +S.D

**Table 2: Age Distribution**

Age Group	Obese Diabetic	Obese Non-Diabetic	Lean Diabetic	Lean Non-Diabetic
0-20	0	0	0	0
21-40	2	4	4	19
41-60	14	16	14	1
<b>61-80</b>	4	0	2	0

Table 2 shows the age distribution of the patients in different age groups. The maximum number

of patients present between the group of 41-60 that is 45. There were no patients in age group of 0-20.

**Table 3: Sex Ratio**

Sex	Obese Diabetic	Obese Non-Diabetic	Lean Diabetic	Lean Non-Diabetic
Male	13	7	15	13
Female	7	13	5	7

Table 3 shows the sex ratio of the patients in different age groups. The numbers of male patients were 13, 7, 15 and 13 in obese diabetic, obese non-diabetic, and lean diabetic and lean non-diabetic

respectively. The numbers of female patients were 7, 13, 5 and 7 in obese diabetic, obese non-diabetic, and lean diabetic and lean non-diabetic respectively.

**Table 4: Presentation of Hypertension In Patients**

Hypertension	Number of Patients
Present	30
Absent	50

Table 4 shows the presentation of hypertension in total number of patients in all the four groups. Out of

80 patients 30 were hypertensive.

**Table-5: Presentation of Hypertension According To Sex Ratio**

Sex	Number of Patients
Male	17
Female	13

Table 5 shows the presentation of hypertensive patients in male and female. Out of 30 hypertensive

patients 17 were male and 13 were female.

**Table 6: presentation of hypertension according to different subject**

Hypertension	Obese Diabetic	Obese Non-Diabetic	Lean Diabetic	Lean Non-Diabetic
Present	14	7	9	0
Absent	6	13	11	20

Table 6 shows the presentation of hypertensive patients in different group. Out of 20 obese diabetic 14 were hypertensive, Out of 20 obese non-diabetic 7 were

hypertensive, Out of 20 lean diabetic 9 were hypertensive and there were no hypertensive in lean non-diabetic

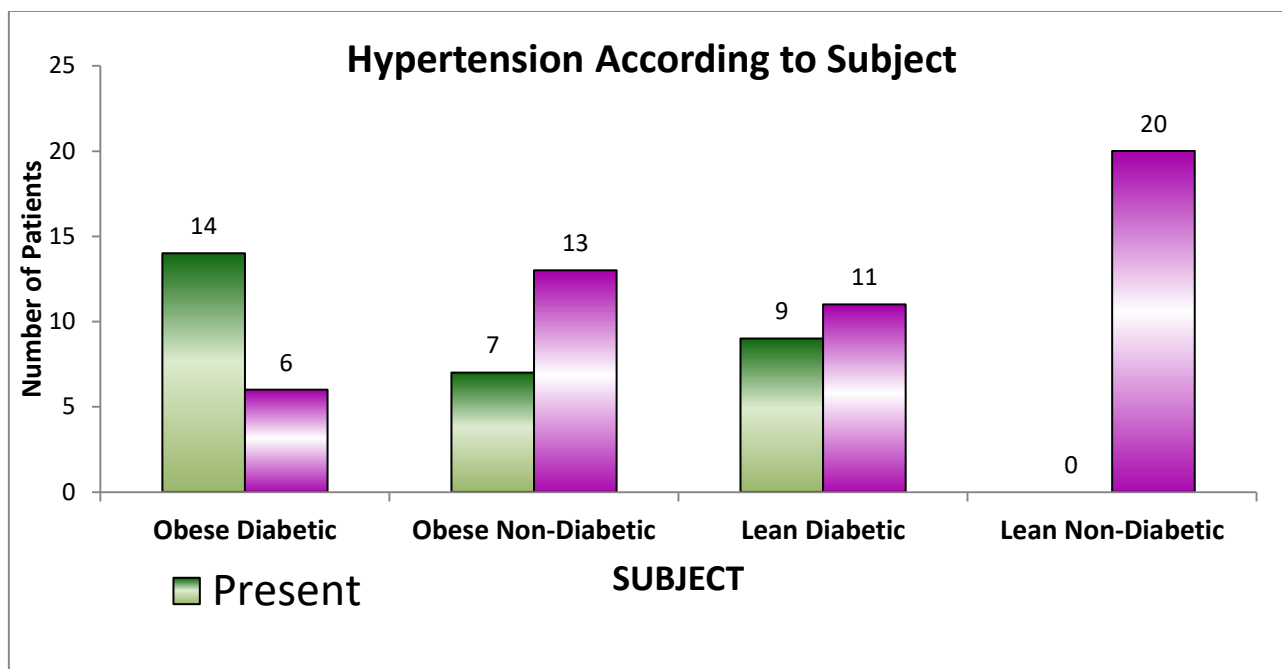


Fig-1: Hypertension According to Subject

Table 7: Leptin level in Obese And Lean Subjects

Subject	Leptin Level
Obese	9.5575
Lean	7.0725

Table 7 shows the leptin level in obese and lean subject. Obese had 9.5575 and lean had 7.0725

leptin level respectively.

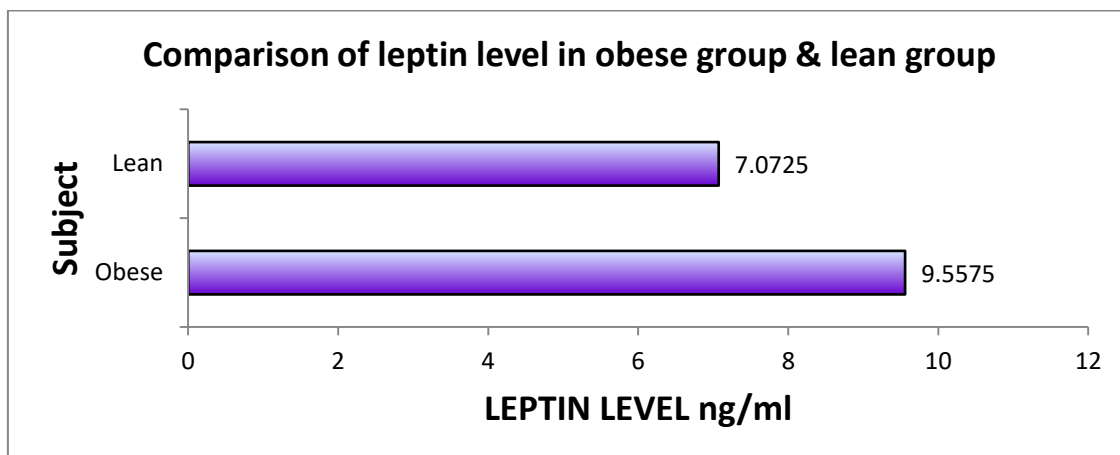


Fig-2: Comparison of leptin level in obese group & lean group

Table 8: Leptin Level in Different Subject

Subject	Leptin Level
Obese Diabetic	10.965
Obese Non-Diabetic	8.15
Lean Diabetic	7.83
Lean Non-Diabetic	6.315

Table 8 shows the leptin level in different subject. Obese diabetic had highest leptin level i.e. 10.965 and

least was present in lean non-diabetic i.e. 6.315.

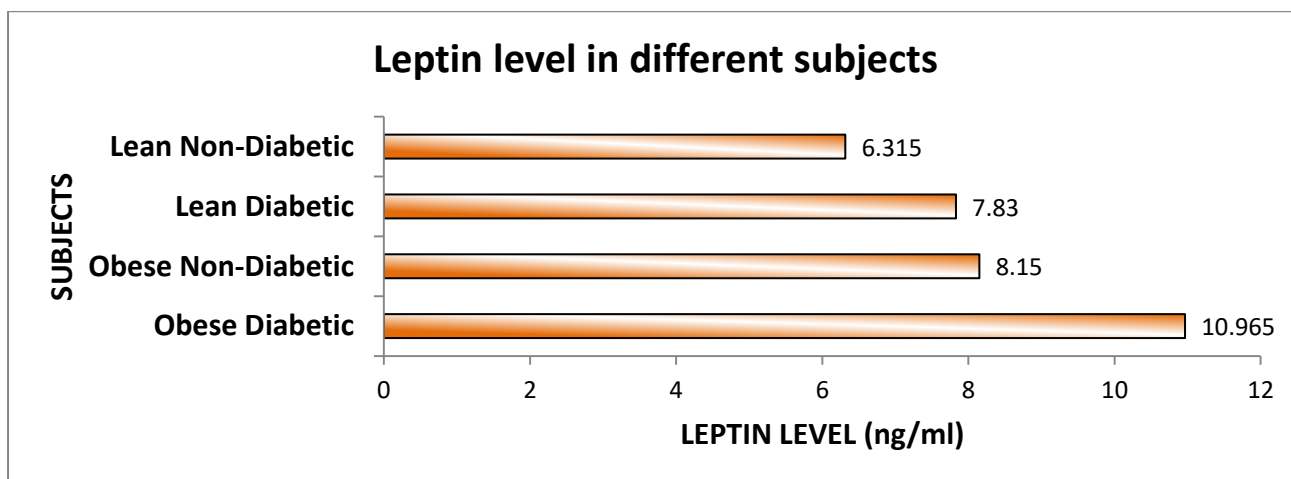


Fig-3: Leptin level in different subjects

Table 9: Co-Relation between Leptin Level With Waist Circumference

Covariates	Obese Diabetic	Obese Non-Diabetic	Lean Diabetic	Lean Non-Diabetic
Leptin Level	10.965	8.15	7.83	6.315
Waist Hip Ratio	112.785	105	88.8	78.45

Table 9 shows co-relation between leptin levels with waist circumference. The group which had highest waist circumference had highest leptin level

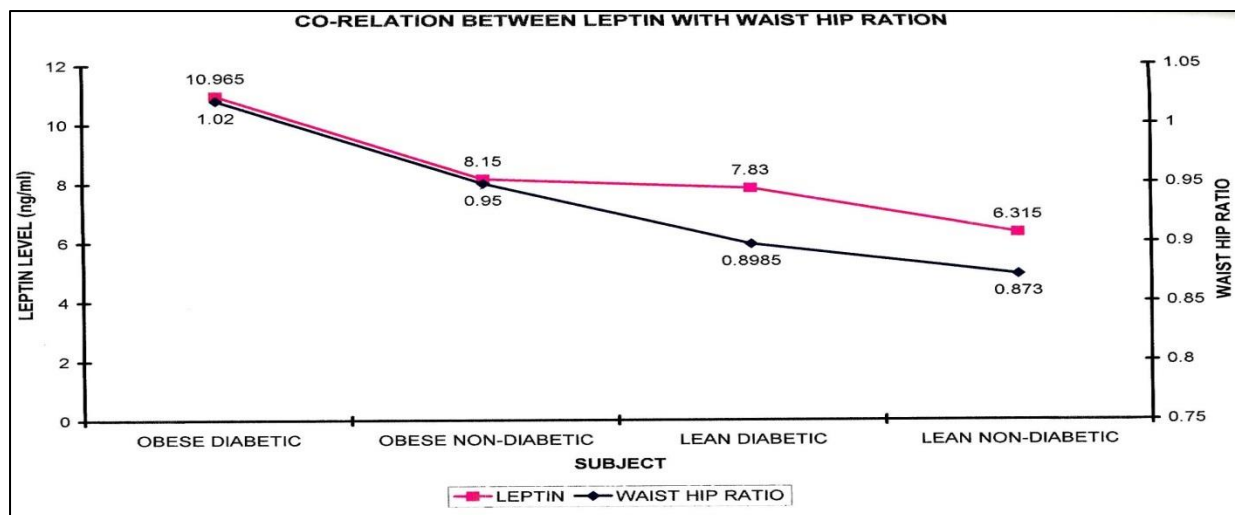
(obese diabetic group). The group which had lowest waist circumference had lowest level of leptin.

**Table 10: Co-Relation Between Leptin Level with Waist HIP Ratio**

Covariates	Obese Diabetic	Obese Non-Diabetic	Lean Diabetic	Lean Non-Diabetic
Leptin Level	10.965	8.15	7.83	6.315
Waist Hip Ratio	1.02	0.95	0.8985	0.873

Table 10 shows co-relation between leptin levels with waist hip ratio. The group which had highest

waist hip ratio had highest leptin level (obese diabetic group). The group which had lowest level of leptin.



**Fig-4: Co-Relation Between Leptin Level with Waist HIP Ratio**

**Table 11: co-Relation Between Leptin Level with Body Mass Index**

Covariates	Obese Diabetic	Obese Non-Diabetic	Lean Diabetic	Lean Non-Diabetic
Leptin Level	10.965	8.15	7.83	6.315
Body Mass Index	32.63	29.8135	24.115	21.35258

Table 11 shows the co-relation between leptin level with body mass index. The group which had highest body mass index had highest leptin level (obese

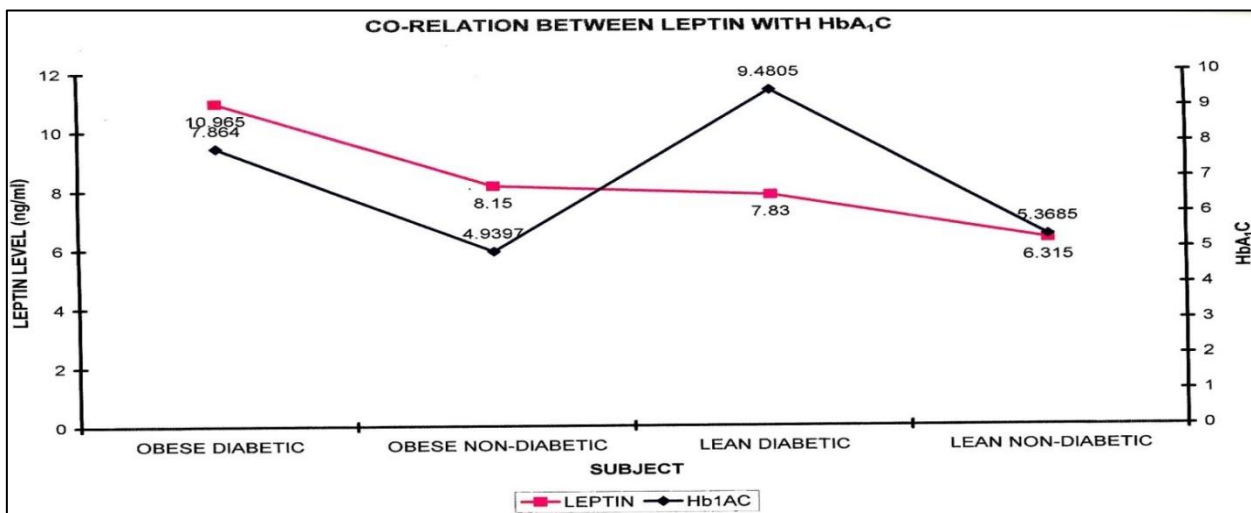
diabetic group). The group which had lowest body mass index had lowest level of leptin.

**Table 12: Co-relation Between Leptin Level with HbA1c**

Covariates	Obese Diabetic	Obese Non-Diabetic	Lean Diabetic	Lean Non-Diabetic
Leptin Level	10.965	8.15	7.83	6.315
Body Mass Index	7.864	4.9397	9.4805	5.3685

Table 12 shows the co-relation between leptin levels with HbA<sub>1c</sub>. There is no relation between leptin

level and HbA<sub>1c</sub>.



**Fig-5: Co-relation Between Leptin Level with HbA1c**

**Table 13: Co-Relation between Leptin Level with Serum HDL-C**

Subject	Leptin Level	S.HDL-C
Obese Diabetic	10.965	35.55
Obese Non-Diabetic	8.15	41.55
Lean Diabetic	7.83	44.3
Lean Non-Diabetic	6.315	48.55

Table 13 shows the co-relation between leptin levels with serum HDL-C. This table shows inverse relationship between leptin level and S.HDL-C. The obese diabetic had highest level of leptin but they had lowest level of S.HDL-C, while lean non-diabetic lowest level of leptin but had highest level of HDL-C.

**DISCUSSION**

The present study was conducted at M.G. Hospital attached to Dr. S.N. Medical College, Jodhpur (Rajasthan). A total number of 80 patients divided in to different group (20 in each) were studied. The patients divided as, Group A (Obese Diabetic), Group B (Obese Non-Diabetic), C (Lean Diabetic), Group D (Lean Non-Diabetic)

The male and female are randomly distributed in our study. Total 48 males and 32 female were included. Out of 80 subject maximum numbers of patients that is 70% were lying in 41-60 years of age, 20% in 60-80 years of age, and 10% in 21-40 years of age. Hypertension was present in 30 patients out of 80 patients. Out of 30 HTN, 17 were male and 13 were female. Obese diabetic has maximum number of hypertensive that is 14, lean diabetic has 9 hypertensive patients and obese non-diabetic has 7 hypertensive patients. There was no hypertensive in lean non-diabetic group.

In present study we observed that leptin level is higher in obese group (diabetic and non-diabetic) than lean group (diabetic and non-diabetic). The leptin level is highest in obese diabetic group, which is followed by obese non-diabetic, than lean diabetic and least in lean non-diabetic. This result is in close conformity with other studies. A. Mishra and N. Arora *et al.*; studied in 2001 that the relationship of plasma leptin level to obesity, which shows that leptin level is higher in obese group in comparison to lean group which were similar to our results (highest in obese diabetic). Hague Z and Rahaman *et al.*; in year 2003 observed the same results in there study. Al-Daghri N *et al.*; compared plasma leptin in type 2 and coronary artery disease with non-diabetic control and they concluded that leptin is increased in obese group.

In our present study we also observed that the level of leptin is strongly correlated with BMI. Leptin level is directly proportional to the BMI. It is highest in obese diabetic who have highest body mass index in there group. Leptin level is least in lean non-diabetic, who have lowest level of BMI. The observations are similar with studies done by A. Mishra *et al.*; and Hague Z *et al.*; Fischer *et al.*; studied that patient with type 2 diabetes mellitus have higher level serum leptin independently of body fat mass, but positively

correlated with the body mass index. Chen. Y *et al.*; studied relationship between bodyweight and level of leptin in *Cynomolgus* monkey and they observed that leptin level directly related to the body weight.

Asakawa H *et al.*; studied the relationship of leptin level with metabolic disorder. Patients with high body mass index had higher level of leptin which match with our study. Tatti P *et al.*; [15] studied the leptin level in diabetic and non-diabetic. They observed the leptin level appeared to be significantly related to the body mass index in the non-diabetic while no relationship reached the level of statistically significant among the diabetics which is different from our study. In present study we observed that leptin level is directly proportional to the waist circumference and waist hip ratio. The results were similar to the finding of A. Mishra *et al.*; [16]. In our study we also observed that there is no relationship between glycaemic controls with leptin level which is similar to A. Mishra study. In this study we also observed that HDL cholesterol is inversely proportional to the leptin level. The highest level of leptin present in obese diabetic group while HDL cholesterol is lowest in this group. This observation was similar to the Fischer *et al* who studied insulin resistance patient with type 2 diabetes have higher serum leptin level independent body fat mass while HDL cholesterol is inversely related to leptin level. Mishra *et al.*; studied that there is no significant correlation between plasma leptin concentration and level of HDL cholesterol which no matched to our study.

#### CONCLUSION

- Leptin level higher in obese as compare to lean
- Leptin level is highest in obese diabetics followed by obese non diabetic, lean diabetic and lean non-diabetic
- Leptin level strongly correlated with body mass index, waist hip ratio and waist circumferences.
- There is inverse relationship- of leptin level with HDL cholesterol.
- There is no relationship of leptin with glycaemic control.

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