CHAPTER - 6

DISCUSSION
Chapter 6: Discussion

Considering the epidemic proportion of diabetes, present study is an attempt to find those individuals who are potentially inclined to become diabetics and those are subjects who require special attention. In this regard, the most potential group of individuals is first degree relatives of established patients of type-2 diabetes mellitus. This study had thus focused on the cohort of population who after being identified may further on be subjected to different regimes of primary prevention.

This study is specific in regard that it covers various facts of abnormalities related to carbohydrate and lipid abnormalities in addition to measurement of insulin resistance, its correlation with various modalities and also measurement of obesity and its correlation with leptin and adiponectin levels. Thus the study opens a wide perspective of various modalities which we hope will be of immense importance while dealing with preventive strategies.

With the incidence of diabetes mellitus rising alarmingly, various studies around the globe are being directed on the line of prevention of diabetes mellitus and are conducted to identify the population at risk of developing diabetes mellitus. In the present study we have made maximum efforts to find the risk of developing diabetes mellitus and insulin resistance in first degree relatives of type-2 diabetes mellitus. A total of 450 first degree relatives of type-2 diabetes mellitus and a total of 450 controls were selected as per the criteria described above from the diabetic clinic, CSM Medical University and from the Medicine Department, CSM Medical University. Socioeconomic status, activity and level of education of participants have not been included as parameters of the study, so these were not studied.
PREVALENCE OF IFG, IGT & DM IN CONTROLS AND CASES

![Bar chart showing the prevalence of IFG, IGT, and DM in controls and cases.](image)

Fig.-1
1. **PREVALENCE OF IFG, IGT AND DIABETES MELLITUS IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS**

According to Third National Health and Nutrition Examination Survey (NHANES -III) in USA population aged 40 -74 years, the prevalence of diabetes in those without a medical history of diabetes was 4.35% and in those with a medical history was12.27%.

According to Momin, Robert and Dana, the prevalence of IFG was 5%, that of IGT was 15% and that of DM 12.5% in asymptomatic subjects aged ≥15 years.\(^{56}\)

Costa and Rios reported that the prevalence of IGT was 20.5% and that DM was 10.2 %.\(^{57}\)

According to Kohler and co-worker the prevalence of IFG was 27.1%, that of IGT was 26.2% and that of DM was 15.1% in first degree relatives of type-2 diabetic patients.\(^{59}\)

Zargar, Khan and Masoodi from India reported that the subjects with family history of diabetes had a significantly higher prevalence of abnormal glucose tolerance test.\(^{60}\)

Lindahl reported that the prevalence of IGT in first degree relatives of Type-2 diabetes patients was 52.8% (24.5% in males and 38.3% in females).\(^{181}\)

In our study, the prevalence of IFG was 22.67%, that of IGT was 26.67% and that of diabetes mellitus was 20.44% in first degree relatives of type-2 diabetes mellitus patients (Table -2).

2. **PREVALENCE OF IGT IN SUBJECTS HAVING IFG AND THAT OF IFG IN SUBJECTS HAVING IGT IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS**

According to Bernt Lindahl, 32% of subjects with IFG had associated IGT in a study conducted in general population.\(^{181}\) Another study by Tripathy and co-workers from Sweden reported that 36% of subjects with IFG had associated IGT, whereas 38% of subjects with IGT had associated IFG in their study conducted in the general population.\(^{58}\)
In our study, 40.20% (41 out of 102) of first degree relatives with IFG had associated IGT, whereas 34.17% (41 out of 120) of first degree relatives with IGT had associated IFG (Table -2).

The associated higher prevalence rate (40.20%) of IGT found in subjects with IFG in our study could be due to that the previous studies had been conducted in the general population, whereas our study was conducted in specifically at risk population for developing type-2 diabetes mellitus.

3. PREVALENCE OF IFG, IGT AND DIABETES MELLITUS AMONG MALES AND FEMALES IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS

According to Lindahl, the prevalence rate of IGT was 5.5% in women and 3.6% in men in their study conducted in the general population.\(^{(181)}\)

Zargar and co-workers reported that females were 1.49 times at risk of developing abnormal glucose tolerance as compared to males.\(^{(60)}\)

In our study conducted only in first degree relatives of type-2 diabetic patients, the prevalence, in males and females, of IFG was 21.88% & 24.07%; of IGT was 28.13% & 23.46%; and of diabetes was 22.57% & 16.67%. Of course, these values of IFG, IGT & DM in males and females were significantly higher than those found in general population (Table-3&4).

4. DISTRIBUTION OF IFG, IGT AND DIABETES MELLITUS IN DIFFERENT AGE GROUPS OF FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS

According to Lindahl, the prevalence of IGT was increasing with increasing age (in males, from 0.5% in 30 years old men to 9.3% in 60 years old men; in females from 1.71% to 12.4% in similar age groups).\(^{(181)}\)

Zargar and co-workers from India had reported that subjects with higher age (\(\geq 50\) years) had 1.87 times of developing abnormal glucose tolerance test.\(^{(60)}\)

In our study conducted in first degree relatives of type-2 diabetes patients, the prevalence rate of IFG, IGT and DM, in a particular age group, was higher in first degree relatives than in general population. Moreover, the highest rate of prevalence
of IFG was found in age group of 40-50 years whereas highest rate of prevalence of IGT & DM was fond in 50-60 years of age group (Table-5&6).

5. PREVALENCE OF IFG, IGT AND DIABETES MELLITUS IN OBESE FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS

Lindahl, reported that the prevalence of IGT and diabetes mellitus in obese (BMI ≥27Kg/m²) first degree relatives increased with increasing age; that of IGT being 8 to 22% and that of diabetes mellitus being 3 to 5% in men of 40-60 years of age and that of IGT in females from 12-46% and that of diabetes mellitus in females from 1 to 13% in 40-60 years of age.\(^{(181)}\)

Zargar, Khan and Masoodi reported that in obese subjects there was 2.3 times risk if developing abnormal glucose tolerance.\(^{(60)}\)

In our study, the prevalence rate of IFG, IGT and diabetes mellitus was more in obese first degree relatives than in general population. Moreover, in our study, the prevalence rate of IFG, IGT and diabetes mellitus in obese first degree relatives was 25.69%, 29.36% and 33.95% respectively, when obesity was considered according to BMI; and 30.27%, 38.31% and 29.50% respectively, when obesity was considered according to WHR (Table-7-9). The higher prevalence rate found in our study could be due to geographical and racial variations, different dietary habits and lack of physical exercise in specific population in our study.

6. PREVALENCE OF OBESITY IN SUBJECTS HAVING NGT, IFG, IGT AND DIABETES MELLITUS AMONG MALES AND FEMALES IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS

Isomaa, Peter and Lathi reported that 76% of men and 36% of women with normal glucose tolerance (NGT) were obese, when obesity was considered as per WHR; and 10% of men and 14% of women with NGT were obese, when obesity was considered as per BMI.\(^{(87)}\)

According to Lindahl, only 25% of IGT subjects were obese (obesity as per BMI) in the general population.\(^{(181)}\)
Fig-2

Prevalence of obesity (as per BMI) in controls and cases having IFG, IGT and DM

Fig-3

Prevalence of obesity (as per WHR) in controls and cases having IFG, IGT and DM
In our study, prevalence of obesity in subjects having IFG, IGT and diabetes Mellitus was 37.84%, 26.67% and 40.22% (as per BMI) and was 77.45%, 83.33%, 83.79% (as per WHR) with statistically significant p values (Table-10&11).

Our study showed that 15.38% of men and 16.44% of women with NGT were obese (obesity as per BMI); and 25.96% of men and 14.29% of women with NGT were obese (obesity as per WHR) (Table-12&13).

28.57% of men and 25.64% of women with IFG were obese (obesity as per BMI); and 79.37% of men and 74.37% of women with IFG were obese (obesity as per WHR) (Table-12&13).

27.16% of men and 26.32% of women with IGT were obese (as per BMI); and 76.54% of men and 100% of women were obese (as per WHR) (Table-12&13).

41.54% of men and 37.04% of women with diabetes mellitus were obese (as per BMI); and 83.08% of men and 85.19% of women with diabetes mellitus were obese (as per WHR) (Table-12&13).

So, it was concluded from our study in first degree relatives that the prevalence of obesity in first degree relatives having IFG, IGT and diabetes mellitus was more common as compared to controls.

Again, it was found that the first degree relatives having IFG, IGT and diabetes mellitus were abdominally more obese (79.37%, 76.54%, 83.08% respectively in males; 74.36%, 100% and 85.19% respectively in females) than when obesity was considered as per BMI (28.57%, 27.16% and 41.54% respectively in males; 25.64%, 26.32% and 37.04% respectively in females).

It was also observed that the prevalence rate of obesity in first degree relatives having NGT & IFG was higher in males than in females. However, in first degree relatives with IGT & diabetes mellitus, the prevalence rate of obesity was higher in females than in males.

7. **ASSOCIATION OF IFG, IGT AND DIABETES MELLITUS WITH DYSLIPIDEMIAS IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS**

Previous data from literatures suggested that type-2 diabetes mellitus was associated with hypertriglyceridemia and ↓HDL cholesterol.
**Fig-4**

Association of IFG, IGT and DM with Hypertriglyceridemia controls and cases

**Fig-5**

Prevalence of decrease in HDL in controls and cases having IFG, IGT and DM
In our study, we found similar observations in first degree relatives of type-2 diabetes mellitus patients.

It was observed that hypertriglyceridemia was significantly prevalent in first degree relatives having NGT, IFG, IGT and DM (15.25%, 68.63%, 57.67% and 79.35% respectively) than in general population (1.56%, 3.45%, 2.38% and 18.52% respectively).

Prevalence rate of elevation in LDL levels was higher in first degree relatives i.e. 14.69%, 42.16%, 34.17%, 33.70% as compared to 7.19%, 24.14%, 17.86% and 14.81% of controls having NGT, IFG, IGT and DM respectively.

Decreased HDL levels were also observed in our study. These levels in first degree relatives having NGT, IFG, IGT & DM were 25.99%, 63.73%, 52.50% & 85.87% as compared to controls which showed 15.31%, 37.93%, 28.57% & 33.33% respectively.

Again, it was observed that the prevalence rate of rise in serum triglyceride level (15.25% → 57.67% → 68.63% → 79.35%) & decrease in serum HDL levels (25.99% → 52.5% → 63.73% → 85.87%) followed the natural pathway of the disease i.e.; NGT → IGT → IFG → DM (Table-14).

8. RELATIONSHIP OF MEAN VALUES OF FASTING SERUM INSULIN IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS AND IN GENERAL POPULATION

McAuley, Shelia and Nick described in their study that the mean level of fasting insulin was 10.0±9.5 (µU/L) in the general population.\(^{(91)}\)

Kwame Osci and co-workers also demonstrated that there was significantly higher fasting serum insulin (P<0.05) in African-American first degree relatives (16±3.0 µU/L) when compared with healthy control subjects (6.3±1.0µU/L).\(^{(57)}\)

In our study, the mean level of fasting serum insulin in first degree relatives was significantly higher (28.97±11.28µU/ml) than that in general population (21.30±10.88µU/ml) (Table -1).
9. **RELATIONSHIP OF MEAN VALUES OF FASTING SERUM INSULIN IN OBESE FIRST DEGREE RELATIVES HAVING NGT, IFG, IGT AND DM**

(a) According to Isomaa, Peterand and Lathi, the mean fasting insulin level rises from 7.5±4.5 μU/L in NGT subjects to 10.4±6.0 μU/L in IFG/IGT subjects to 15.2±11.2 μU/L in DM subjects.\(^{(87)}\)

In our study, the rise in mean fasting insulin level in obese subjects also followed the natural history of the disease i.e. it progressively raises from NGT → IGT → IFG (Table- 15&16). However, the mean level of fasting insulin level was slightly lower in obese first degree relatives with DM than in obese first degree relatives with. This could be due to early β-cell failure in them.

(b) Manbucci and Bardini demonstrated that subjects with IFG had shown higher insulin values as compared to IGT subjects.\(^{(90)}\)

Tripathy and co-workers also reported that subjects with IFG had higher insulin level than those with IGT and DM.\(^{(58)}\)

Similar observation was found in our study also (40.30±11.90 μU/ml in cases vs. 32.86±11.22 μU/ml in controls) (Table -16).

(c) According to Costa and Rios, basal insulin level was higher in NGT first degree relatives of type-2 DM than controls without having family history.\(^{(57)}\)

Similar observation was found in obese NGT subjects in our study (21.58±6.74 μU/ml in cases vs. 17.89±6.71 μU/ml in controls) (Table - 15).

---

10. **SENSITIVITY AND SPECIFICITY OF VARIOUS METHODS FOR MEASUREMENTS OF INSULIN RESISTANCE IN OUR STUDY**

Mc Auley and co-workers reported that Insulin Sensitivity Index (McFarland Index) was the most sensitive and specific for determination of insulin resistance.\(^{(91)}\)

According to Haffner Miettinen and Stern, HOMA\(_{IR}\) in NIDDM subjects was very strongly correlated with fasting insulin (r=0.98).\(^{(83)}\)

According to Masonori and Yoshiki and Matthews and co-workers there was strong correlation between HOMA\(_{IR}\) and clamp-IR in type-2 diabetic subjects.\(^{(79,80)}\)
Matsuda and DeFronzo reported that fasting plasma insulin and HOMA\textsubscript IR were the most simple and repeatable indices in epidemiological studies.\textsuperscript{(77)}

In various studies being conducted presently all over the globe, HOMA\textsubscript IR is taken as gold standard for measurement of insulin resistance. Comparing with HOMA\textsubscript IR, it was observed that QUICKI index maintained highest sensitivity (100%) and specificity (98.23%) whereas fasting plasma insulin showed sensitivity 98.80% and specificity 90.25%. Bennett Index also maintained high sensitivity (96.73%) and specificity (95.21%). Insulinogenic index showed 90.48% sensitivity and 83.33% specificity whereas McFarland Index showed least sensitivity (79.76%) and (79.43%) (Table-17).

In our study, the maximum value of the co-efficient of correlation was of fasting insulin with HOMA\textsubscript IR was 1.471 whereas, Bennett Index showed the value of this co-efficient 0.541 which signified that there was strong positive correlation between fasting insulin and HOMA\textsubscript IR. All other indices were negatively correlated with HOMA\textsubscript IR (Table -18&19).

11. PREVALENCE OF INSULIN RESISTANCE IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETIC PATIENTS

According to Camps and co-workers insulin sensitivity was lower in first degree relatives of type-2 diabetes mellitus as compared to healthy controls (36.3% vs. 51.8%, \(P=0.0001\)).\textsuperscript{(88)}

Volk and Ronn reported that the prevalence of insulin resistance in first degree relatives was 40%.\textsuperscript{(89)}

In our study, the prevalence of insulin resistance in first degree relatives of type-2 diabetes patients was found to be significantly higher as compared to controls by all the indices of measuring insulin resistance.

The prevalence rate in first degree relatives was 49.78% as compared to controls (24.89%), with \(P<0.001\), when insulin resistance was measured by HOMA\textsubscript IR. The prevalence rate was 50.44% vs. 26.44% by QUICKI (\(p<0.001\)); 58.44% vs. 27.56% by fasting plasma insulin (\(p<0.001\)); 61.56% vs. 26.89% by Insulinogenic Index (\(p<0.001\)); 60.67% vs. 24.67 \%(\(p<0.001\)) by McFarland Index and 50.44% vs. 27.78 \(p<0.001\) by Bennett Index in case vs. control respectively (Table-20).
Prevalence of insulin resistance in controls & cases as measured by different indices

Fig-6
12. PREVALENCE OF INSULIN RESISTANCE IN FIRST DEGREE RELATIVES HAVING NGT, IFG, IGT AND DIABETES MELLITUS

(a) According to Costa and Rios, basal insulin levels were higher in NGT first degree relatives of type-2 diabetes mellitus patients than controls without having family history of Type-2 diabetes mellitus (3.6±0.4% vs. 3.9±0.4%, p=0.000).\(^{(57)}\)

Osei and co-workers reported that glucose tolerant first degree relatives of type-2 diabetes mellitus patients were having both fasting hyperinsulinemia and insulin resistance as compared to healthy control subjects.\(^{(84)}\)

Similarly, in our study, the insulin resistance in first degree relatives with NGT was 23.73% as compared to controls 15.63%, when insulin resistance was measured by fasting insulin level; and was 17.51% as compared to 13.13% in controls, when IR was measured by HOMA\(_{IR}\) method. This prevalence was 12.43% vs. 15.31(p=0.379) by QUICKI, 29.38% vs.15.63 % (p=0.001) by Insulinogenic Index, 37.29% vs. 15.94% (P<0.001) by McFarland Index, 14.69%vs. 16.25 %(p=0.647) by Bennett Index (Table -21-26).

(b) According to Tripathy and co-workers from Sweden, compared with NGT subjects, subjects with IFG were more insulin resistance (HOMA\(_{IR}\) values 2.64±0.08 vs. 1.73±0.03, p<0.0005).\(^{(58)}\)

Isomaa and co-workers reported that the prevalence of insulin resistance was increased two folds in subjects with IFG/IGT (2.83±1.69) and three folds in patients with type-2 diabetes mellitus (6.58±1.87) as compared with subjects with normal glucose tolerance. They also reported that the prevalence rate of insulin resistance was 59% in IFG/IGT and 88% in type-2 diabetes mellitus.\(^{(87)}\)

Bonora, Kiechl and Willleit showed that the prevalence of insulin resistance was 66% in subjects with IGT and 84% in subjects with type-2 diabetes mellitus.\(^{(92)}\)

In our study, the prevalence rate of insulin resistance (HOMA\(_{IR}\)) was higher in first degree relatives having IFG (98.04%), IGT (52.50%) and DM (75%) as compared to controls (82.76%, 40.48% and 77.78% respectively); the highest rate being shown by IFG subjects (Table-21).
The prevalence of insulin resistance was not higher in first degree relatives having diabetes mellitus as compared to controls having diabetes mellitus (p=0.768) i.e., the data was not significant.

The prevalence rate of insulin resistance (either by HOMAIR or, by fasting insulin) in first degree relatives with IFG and IGT was significantly higher (97.06% and 72.50% respectively) as compared to 82.76% and 45.24% controls respectively (Table-22). But, such type of association was not statistically significantly seen in subject with diabetes mellitus.

13. PREVALENCE OF INSULIN RESISTANCE AMONG MALES AND FEMALES IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS

Our study showed that the prevalence of insulin resistance (by either criteria) was found to be more common in males (51.39% by HOMAIR, 59.38% by FPI, 52.08% by QUICKI, 66.67% by Insulinogenic index, 64.24% by McFarland Index and 53.13% by Bennett Index) than in females (46.91% by HOMAIR, 56.79% by FPI, 47.53% by QUICKI, 52.47% by Insulinogenic index, 54.32% by McFarland Index and 45.68% by Bennett Index) (Table -27).

14. PREVALENCE OF INSULIN RESISTANCE IN OBESE FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS

(a) According to Osei, Cottrell and Harris obesity had been strongly associated with insulin resistance in first degree relatives of type-2 diabetes mellitus in African-Americans.\(^{(86)}\)

Similarly, in our study, the prevalence of insulin resistance (by HOMAIR) in obese first degree relatives was 55.88% as compared to obese controls (37.31%) with p<0.001 (Table-28).

(b) According to Kirsten and co-workers BMI would not have been as important in predicting insulin resistance as WHR.\(^{(91)}\) Isomaa, Peter and Lathi reported that the relative risk of developing insulin resistance was higher in obese with high WHR than in obese with high BMI.\(^{(87)}\)
Similarly, our study also showed that obesity measured by WHR was a strong predictor of insulin resistance than obesity measured by BMI. The risk of developing insulin resistance was 1.46 times in obese first degree relatives as compared to non-obese controls, when obesity was measured by BMI (p<0.088) (Table-29) and was 2.14 times in obese first degree relatives as compared to non-obese controls, when obesity was measured by BMI (p<0.001) (Table-30).

15. **REVALENCE OF METABOLIC SYNDROME IN FIRST DEGREE RELATIVES HAVING NGT, IFG, IGT AND DIABETES MELLITUS**

According to Isomaa, Peter and Lathi, the prevalence rate of metabolic syndrome was present in 10% of subjects with NGT, 50% of subjects with IFG/IGT and 80% of subjects with type-2 diabetes mellitus.\(^{(87)}\)

Our study conducted only in first degree relatives of type-2 diabetes mellitus showed that the prevalence of metabolic syndrome (hypertriglyceridemia + obesity + HOMA\(_{IR}\)) having NGT was 8.5% and 0.31% in controls. The prevalence of metabolic syndrome (hypertriglyceridemia + obesity + HOMA\(_{IR}\)) in first degree relatives having IFG was 20.60% and none in controls. The prevalence of metabolic syndrome (hypertriglyceridemia + obesity + HOMA\(_{IR}\)) in first degree relatives having IGT was 18.30% and none in controls. The prevalence of metabolic syndrome (hypertriglyceridemia + obesity + HOMA\(_{IR}\)) in first degree relatives having DM was 35.87% and 3.7% in controls (Table-33). The prevalence rate of metabolic syndrome (hypertriglyceridemia + obesity + HOMA\(_{IR}\)) in first degree relatives was seen to rise gradually from NGT→IGT→IFG→DM.

The prevalence rate of metabolic syndrome (hypertriglyceridemia + obesity) in first degree relatives having NGT was 9.6% and 0.31% in controls (p<0.001) (Table-32).

The prevalence rate of metabolic syndrome (hypertriglyceridemia + obesity) in first degree relatives having IFG was 25.49% and none in controls (p<0.001) (Table-32).
Plasma leptin levels in controls and cases

Fig. 9
The prevalence rate of metabolic syndrome (hypertriglyceridemia + obesity) in first degree relatives having IGT was 24.17% and none in controls (p<0.001) (Table-32).

The prevalence rate of metabolic syndrome (hypertriglyceridemia + obesity) in first degree relatives having diabetes mellitus was 43.48% and 3.70% in controls (p<0.001) (Table-32). The prevalence rate of metabolic syndrome (hypertriglyceridemia + obesity) in first degree relatives was seen to rise gradually from NGT→IGT→IFG→DM.

16. SERUM LEPTIN CONCENTRATIONS IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS AND GENERAL POPULATION

According to Nyholm and co-workers, the increased concentrations of serum leptin in the first degree relatives of type-2 DM patients were associated with the insulin resistance, but not with a family history of NIDDM(213). However in our study, concentrations of fasting serum leptin in first degree relatives of type-2 DM patients was significantly higher (11.302 ± 6.455ng/ml) than that in general population (5.386±2.558ng/ml) (Table -1).

17. MEAN VALUES OF LEPTIN IN FIRST DEGREE RELATIVES HAVING NGT, IFG, IGT AND DM

According to Vauhkonen, Niskanen, Haffner, Kainulainen, Uusitupa and Laakso, in the non-diabetic offsprings of type-2 DM patients with insulin resistant phenotype, the higher serum leptin levels was markedly explained by lower rates of whole body glucose uptake.(214)

The mean values of leptin were significantly higher in first degree relatives having NGT, IFG, IGT and diabetes as compared to general population. These values in first degree relatives having NGT, IFG, IGT and DM were 10.66 ng/ml, 12.63 ng/ml, 9.40 ng/ml and 13.61 ng/ml compared to 5.39 ng/ml, 3.81 ng/ml, 5.84 ng/ml and 5.70ng/ml in controls respectively (Table-34).
18. **SERUM LEPTIN CONCENTRATIONS IN INSULIN RESISTANT FIRST DEGREE RELATIVES OF TYPE-2 DM PATIENTS AND CONTROLS**

According to Nyholm and co-workers serum leptin is increased in insulin-resistant offspring of NIDDM patients.\(^{213}\) Similarly our study showed that leptin is increased in insulin resistant first degree relatives of type-2 DM patients as compared to controls (Table-38).

19. **SERUM LEPTIN CONCENTRATIONS IN OBESE FIRST DEGREE RELATIVES OF TYPE-2 DM PATIENTS AND CONTROLS**

According to Havel and co-workers, serum leptin concentrations are highly correlated with BMI in both obese and normal weight women.\(^{215}\) Our study, carried out in specific population, showed that leptin levels are increased in obese first degree relatives (13.39 ng/ml) as compared to controls (6.46 ng/ml)(Table-36).

20. **SERUM ADIPONECTIN LEVEL IN FIRST DEGREE RELATIVES OF TYPE-2 DIABETES MELLITUS PATIENTS AND CONTROLS**

Pellme and co-workers showed that circulating serum adiponectin levels were decreased in non-obese first degree relatives.\(^{216}\)

Lihn, Ostergard, Nyholm, Pedersen, Richelsen and Schmitz showed that there is a tendency of dysregulation of adiponectin gene expression in first degree relatives. The study concluded that first degree relatives have reduced adiponectin mRNA in subcutaneous adipose tissue but normal levels of circulating adiponectin. Adiponectin mRNA levels are positively correlated with insulin sensitivity in control subjects but not in first degree relatives.\(^{217}\)

In our study, the concentration of fasting serum adiponectin in all first degree relatives was significantly lower (10.046±1.694 mg/l) than that in general population (13.804±7.189 mg/l) (Table-1).

21. **MEAN VALUES OF ADIPONECTIN IN FIRST DEGREE RELATIVES HAVING NGT, IFG, IGT AND DM**

Ryan and co-workers, while studying correlation between adiponectin and glucose utilization in adult women, found adiponectin levels to be lower in pre-
Plasma adiponectin in insulin resistant controls and cases

Fig-12
Plasma adiponectin levels in non-obese & obese controls & cases

Adiponectin levels (mg/l)

non-obese     obese

Fig-13
diabetic women as compared to normal glucose tolerant women. They also concluded that adiponectin is positively associated with glucose utilization across the age span in studied women.\(^{(219)}\)

In our study, the mean values of adiponectin were significantly lower in first degree relatives having NGT, IFG, IGT and DM as compared to general population. These values in first degree relatives having NGT, IFG, IGT and DM were 9.68 mg/l vs. 14.26 mg/l, 10.15 mg/l vs. 12.47 mg/l, 10.10 mg/l vs. 13.46 mg/l and 10.61 mg/l vs. 9.96 mg/l in case vs. controls respectively (Table-35).

22. **SERUM ADIPONECTIN CONCENTRATIONS IN INSULIN RESISTANT FIRST DEGREE RELATIVES OF TYPE-2 DM PATIENTS AND CONTROLS**

According to Osei, Gaillard and Schuster, serum adiponectin levels were significantly lower in insulin-resistant, non-diabetic first degree relatives of African-American patients with type-2 diabetes and in those with newly diagnosed type-2 diabetes. Decreased serum adiponectin and insulin resistance coexist in a genetically prone subset of first degree African-American relatives before development of type-2 DM.\(^{(218)}\)

Pellme and co-workers showed that circulating serum adiponectin levels were decreased in non-obese but insulin-resistant first degree relatives and, in addition, related to several facets of the insulin resistance syndrome.\(^{(216)}\)

Similarly, we found in our study that circulating adiponectin levels were significantly decreased in all insulin resistant first degree relatives as compared to insulin resistant controls (Table-38).

23. **ADIPONECTIN LEVELS IN OBESE FIRST DEGREE RELATIVES OF TYPE-2 DM PATIENTS AND CONTROLS**

Ryan and co-workers showed that adiponectin levels are negatively associated with BMI in women.\(^{(219)}\)

Our study showed that adiponectin levels are significantly reduced in obese first degree relatives as compared to controls when obesity was measured as per WHR (Table-37).
24. **CORRELATION AMONG LEPTIN AND ADIPONECTIN**

According to Ryan and co-workers, adiponectin levels are negatively associated with leptin levels in women.$^{(219)}$

Matsubara, Maruoka and Katayose, adiponectin was negatively correlated with serum leptin concentration. They found an inverse correlation between adiponectin and leptin in vivo.$^{(220)}$

Similarly, in our study, bivariate regression analysis showed that in first degree relatives, leptin and adiponectin were inversely correlated with a statistically significant correlation co-efficient (-0.242)(Table-39).

25. **CORRELATION AMONG FASTING PLASMA INSULIN AND ADIPOCYTOKINES**

According to Ryan and co-workers, adiponectin levels are negatively associated with fasting plasma insulin and leptin levels in women.$^{(219)}$

In our study, multivariate regression model showed that fasting plasma insulin was positively associated with leptin (correlation coefficient $\beta=0.198185$) and negatively correlated with adiponectin (correlation coefficient $\beta=-0.01072$) (Table-40).

In addition, we also studied correlation between adipocytokines, insulin resistance and other parameters evaluated. Bivariate analysis showed that the coefficient of correlation of leptin with HOMA$_{IR}$ was 0.235 which signified that there was strong positive correlation between leptin and insulin resistance (HOMA$_{IR}$) whereas adiponectin is negatively correlated with insulin resistance (HOMA$_{IR}$) (correlation co-efficient= -0.174) (Table-41).

Among other correlations studied, adiponectin showed a statistically significant negative correlation with leptin, fasting plasma glucose, fasting plasma insulin, postprandial plasma glucose, triglycerides and VLDL; of which the significant correlations were with leptin and postprandial plasma glucose only. Adiponectin showed a significant positive correlation with HDL. However, leptin showed significantly positive correlation with all the parameters except for adiponectin and HDL (Table-42).
In conclusion, present study revealed statistically significant alterations in values of glucose uptake, levels of fasting plasma insulin, status of insulin resistance, lipid levels, degree of obesity and levels of adipocytokines. Inter correlation between these parameters have also been found to be statistically significant in the studied population which indicates that first degree relatives exhibit many of metabolic abnormalities related to type-2 DM which might be crucial in management of this pre-diabetic state and more importantly, in prevention of type-2 DM.