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KEY WORDS:

# A STUDY OF BODY COMPOSITION AND INSULIN RESISTANCE IN PATIENTS OF CHRONIC PANCREATITIS

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ABSTRACT

Diabetes secondary to pancreatic diseases is commonly referred to as pancreatogenic diabetes or type 3c diabetes mellitus. The failure to correctly diagnose type 3 diabetes mellitus leads to a failure to implement an appropriate medical therapy.

**Aim:** To evaluate the body composition and insulin re-sistance in patients of chronic pancreatitis with & without diabetes.

**Methodolgy:** A cross sectional study at a tertiary Hospital of North India of 50 cases diagnosed of chronic pancreatitis based on CT scan and USG was done. They were divided into two groups depending on presence (28 cases) or ab-sence(22cases) of diabetes. Various physiological and biochemical parameters of these groups were compared and analysed.

**Results:** HBA1c,ALKP, Total cholesterol, Body Fat, Physiological Age, and Fat % showed higher values in the diabetic group Vs non diabetic group. Statistically significant lower values of mean weight, mean abdominal circumference, hip circumference,BMC, RMR,FAT MASS and visceral fat in the diabetic group was seen.

**Conclusion:** There is significant correlation between body parameters indicating insulin resistance which can form a part of diagnostic and follow up evaluation of chronic pancreatitis cases for development of diabetes mellitus.

## INTRODUCTION

Pancreatitis and diabetes are known to be connected in at least two common ways. The pancreas is responsible for the production of insulin in the body and any damage to the organ results in lowered insulin production.Glucose intolerance and diabetes mellitus (DM) are the most frequent metabolic dysfunctions observed secondary to chronic pancreatitis. (1,2)

Type 1 and Type 2 Diabetes mellitus are the most common types of diabetes, people are more aware of and most of the studies are focused. However, diabetes mellitus caused secondary to pancreatic diseases, which constitutes Type3c of diabetes classification, is a clinically relevant condition rarely considered in everyday practice. However, recent data on T3cDM propose that it might be more common than counted so far and most often this important condition is under and/or misdiagnosed. (2-6)

Diabetes secondary to pancreatic diseases is commonly referred to as pancreatogenic diabetes or type 3c diabetes mellitus. In nearly 80% of all type 3c diabetes mellitus cases, chronic pancreatitis seem to be the underlying disease(7-12). The prevalence and clinical importance of diabetes second-ary to chronic pancreatitis has certainly been underestimated so far. In contrast to the management of type 1 or type 2 diabetes mellitus, the endocrinopathy in type 3c is very complex. The course of the disease is complicated by comorbidities such as maldigestion and malnutrition.However, in a patient first presenting with diabetes mellitus, chronic pancreatitis as a potential causative condition is sel-dom considered causing misdiagnosis. The failure to correctly diagnose type 3 diabetes mellitus leads to a failure to implement an appropriate medical therapy. In patients with type 3c diabetes mellitus treating exocrine pancreatic insufficiency, preventing or treating a lack of fat-soluble vitamins (espe-cially vitamin D) and restoring impaired fat hydrolysis and incretin secretion are key-features of med-ical therapy.(13, 14)

## AIM

To evaluate the body composition and insulin resistance in patients of chronic pancreatitis with & without diabetes.

## MATERIALS AND METHODS

It is a cross sectional study at a Tertiary Hospital of North India involving patients of chronic pancreati-tis for a period of one year. All patients diagnosed of chronic pancreatitis based on CT scan report, and USG within the age group 18-65 year were included.

**Exclusion Criteria:** (I) Presence of type1 diabetes
(ii) other endocrine disorders

**Diagnostic Criteria.**
Diabetes Mellitus. as per the ADA:
(I) HBA1c>6.5%
(ii) FPG>126mg/dl
(iii) 2 hr pg> 200 mg/dl during OGTT(75gm)
(iv) random pg>200mg/dl(11.1mmol/l)()

**Chronic pancreatitis.** Based on the CT Scan/ USG findings :-
(I) Inflammation
(ii) Fibrotic tissue replacing normal tissue
(iii) Destruction of pancreatic tissue (necrosis)
(iv) Injury or changes to the pancreatic duct, such as dilatation and calcifica-tions.

Correlation analyses done by the spearman's correlation and p value of < 0.05 considered sig-nificant for the statistical tests.

## RESULTS

Total patients of Chronic Pancreatitis during the study period were 50. Among them, 41(82%) were males and 9 (18%) were females. The mean age of patients was 43.44. Mean ht was 167 cm , wt was 63.83, abdominal circumference was 86.92, hip circumference was 91.7 , Waist Hip Ratio was .947, BMI was 22, body fat was 25.762,Resting Metabolic Rate was1398.42, visceral fat .061, physiologic age was 44.02. (Fig 1, Tab 1)

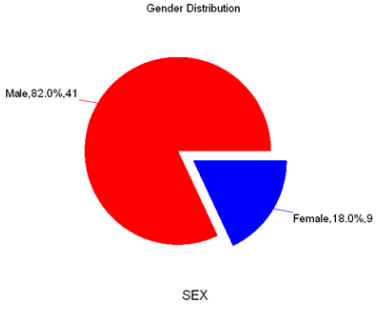


**Fig 1**

**TABLE 1: Descriptive statistics of Biological Parameters**

| Variable | N | Minimum | Maximum | Arithmetic Mean | Standard Deviation |
|---|---|---|---|---|---|
| ABDOMINAL CIRCUMFERENCE | 50 | 72 | 108 | 86.92 | 8.623 |
| HIP CIRCUMFERENCE | 50 | 78 | 107 | 91.7 | 7.316 |
| WAIST HIP RATIO | 50 | 0.847 | 1.059 | 0.947 | 0.045 |
| BMI/ KG/ M2 | 50 | 16 | 29.6 | 22.876 | 3.458 |

| | | | | | |
|---|---|---|---|---|---|
| BODY FAT | 50 | 0.32 | 41.3 | 25.762 | 8.156 |
| RESTING METABOLIC RATE/KG/M2 | 50 | 994 | 1,769.00 | 1,398.42 | 190.32 |
| VISCERAL FAT | 50 | 0.01 | 0.21 | 0.061 | 0.043 |
| PHYSIOLOGICAL AGE | 50 | 18 | 80 | 44.02 | 14.378 |

**TABLE 2: Descriptive statistics of Biochemistry Parameters**

| Variable | N | Minimum | Maximum | Arithmetic Mean | Standard Deviation |
|---|---|---|---|---|---|
| CALCIUM_MG/DL | 50 | 0.9 | 10.1 | 8.292 | 2.337 |
| PHOSPHORUS MG/DL | 50 | 1.26 | 132 | 6.195 | 18.181 |
| ALKPIU/LT | 50 | 34 | 232 | 102.94 | 34.843 |
| VIT_D_NMOL/LT | 50 | 8.13 | 81.24 | 25.8 | 15.602 |
| PTHPG/ML | 50 | 1.8 | 190 | 52.273 | 40.428 |

| Variable | N | Minimum | Maximum | Arithmetic Mean | Standard Deviation |
|---|---|---|---|---|---|
| HB_A1C | 50 | 0.049 | 0.119 | 0.067 | 0.015 |
| STIMULATED_C_PEPTIDE_NG/ML | 50 | 0.26 | 6.5 | 1.416 | 1.47 |
| FASTING_SERUM_INSULINE_MU/ML | 50 | 0.86 | 109 | 10.44 | 20.511 |
| TOTAL_CHOLESTR/L | 50 | 17 | 298 | 173.6 | 50.013 |
| LDL_CHOLESTREL | 50 | 38 | 621 | 121.762 | 77.674 |
| S_TRIGLYCERIDE | 50 | 45 | 406 | 136.68 | 73.853 |
| FASTING_BLOOD GLUCOSE_MG_DL | 50 | 58 | 191 | 103.42 | 27.858 |

The mean value of Calcium was 8.292, phosphorus was 6.195, VIT D was 25.8, PTH was 52.273, HBA1C was .067, C peptide was 1.416, fasting serum insulin 10.44, total cholesterol173.6, LDL cholesterol was 121.6, serum triglyceride was 136.68, fasting blood glucose level was 103.42.

The patients were divided into two groups as:
Group – I. Diabetic (28 cases). Group –II.Non - Diabetic (22 cases).

Various body measurements studied were height, weight, abdomen circumference, hip circumfer-ence and Body Mass Index (table 3).

**TABLE 3:**

| Body Measurements | Diabetes Mellitus | | | P-value |
|---|---|---|---|---|
| | Positive (n= 28) | Negative (n=22) | Total (n=50) | |
| 1.Height (cm) Mean +/- SD (CI)* | 166.66 +/- 7.78 (163.6 – 169.7) | 168.64+/- 8.45 (164.8 – 172.4) | 167.5+/- 8.0 (165.2 – 169.8) | 0.395 |
| 2.Weight (kg) Mean +/- SD (CI) | 60.15 +/- 9.71 (56.4 – 63.9) | 68.61+/-9.88 (64.2 – 72.9) | 63.8+/- 10.5 (60.9 – 66.9) | 0.004 |
| 3.Abdo Circ (cm) Mean +/- SD(CI) | 84.14 +/- 7.41 (81.3 – 87) | 90.45+/-8.92 (86.5 – 94.4) | 86.9+/- 8.6 (84.5 – 89.4) | 0.009 |
| 4.Hip Circ (cm) Mean +/- SD (CI) | 89.60 +/- 6.85 (87.0 – 92.2) | 94.36+/- 7.16 (91.2 – 97.5) | 91.7+/- 7.3 (89.6 – 93.8) | 0.021 |
| 5.BMI(kg/m$^2$) Mean +/- SD (CI) | 21.81 +/- 3.33 (20.5 – 23.0) | 24.24+/-3.2 (22.8 – 25.7) | 22.8+/- 3.4 (21.9 – 23.9) | 0.012 |

(*95% Confidence Interval for the true mean)
Various observations based on statistical comparisons between the groups were:

1. The duration of chronic pancreatitis was found to be much higher in the group with diabetes mellitus compared to without diabetes (P value = 0.145).
2. Most of the other body measurements were lower among chronic pancreatitis with diabe-tes mellitus compared to non-diabetic group particularly for weight, abdominal circumfer-ence, Hip Cir and BMI. these differences were statistically significant.
3. Amongst the biochemical parameters, HBA1c,ALKP, Total cholesterol, Body Fat, Physiologi-cal Age, and Fat % were showing higher values in the diabetic group vis-a vis non diabetic group. Rest of the parameters were less in the diabetic subset.
4. Parameters of BMC, RMR, S. triglyceride and fat mass were lesser in diabetic group. This can be explained by Malnutrition, lack of fat soluble vitamins, steatorroea and long duration of chronic pancreatitis in this subset. Much smaller values were reported in case of visceral Fat (%), Vitamin D PTH , and fasting serum insulin. However, these differences were not found to be statistically significant except for visceral fat and Simulated C Peptide. (Table 4)

**TABLE 4:**

| Parameters | Diabetes Mellitus | | | P-value |
|---|---|---|---|---|
| | Positive (n= 28) | Negative (n=22) | Total (n=50) | |
| 1. Calcium (mg/dl) Mean +/- SD (CI)* | 7.76+/-2.95 (6.6 – 8.9) | 7.75+/- 2.99 (6.4 -9.0) | 7.7+/- 2.9 (6.9 – 8.6) | 0.988 |
| 2. ALP (iu/lt) Mean +/- SD (CI) | 104.71+/- 39.92 (89.2 – 120.2) | 100.68+/- 27.82 (88.3 – 113) | 102.9+/- 34.8 (93.0 – 112.8) | 0.689 |
| 3. BMC (gm) Mean +/- SD (CI) | 2323.74+/- 453.13 (2148.0 – 2499.4) | 2557.37+/- 600.11 (2276.5 – 2838.2) | 2421.0+/- 526.3 (2268.2-2573.9) | 0.131 |
| 4. RMR (Kcal/day) Mean +/-SD (CI) | 1333.71+/- 166.23 (1269.3 – 1398.1) | 1480.77+/- 190.53 (1396.3 – 1565.2) | 1398+/- 190.3 (1344.3 - 1452.5) | 0.005 |
| 5. FBS (mg/dl) Mean +/- SD (CI) | 109.61+/- 33.86 (96.5 – 122.7) | 95.55+/- 14.85 (89.0 – 102.1) | 103.4+/- 27.8 (95.5 – 111.3) | 0.076 |
| 6. HB A1c (%) Mean +/- SD (CI) | 7.4+/-1.71 (6.7 -8.1) | 5.84+/- 0.62 (5.6 – 6.1) | 6.7+/- 1.5 (6.3 – 7.2) | 0.00 |
| 7. Tl. Chol. (mg/dl) Mean +/- SD (CI) | 177.79+/- 49.52 (158.6 – 197) | 168.27+/- 51.29 (145.5 – 191) | 173.6+/- 50.0 (159.4 – 187.8) | 0.51 |
| 8.S Triglcy. (mg/dl) Mean +/- SD (CI) | 122.07+/- 67.29 (96.0 – 148.0) | 155.27+/- 79.11 (120.0-190.0) | 136.6+/- 73.8 (115.7 – 157.7) | 0.115 |
| 9.Fat Mass (gm) Mean +/- SD (CI) | 16374.0+/- 6267.91 (13943.6 –188804.4) | 20019.52+ /5995.92 (17361.0 - 22678.0) | 17978.0+/63 55.8 (16171.7 – 19784.3) | 0.043 |

*95% Confidence interval for mean

**DISCUSSION**

Pancreatogenic diabetes is a form of secondary diabetes,

specifically that associated with disease of the exocrine pancreas. The most common disease of the exocrine pancreas associated with the devel-opment of diabetes is chronic pancreatitis. The pathogenesis of T3cDM is due to decreased insulin secretion caused by both a reduction in the number of islets and their functional capacity as a conse-quence of extensive fibrosis and sclerosis. (18,19) Chronic pancreatitis, however, must be seen as a progressive disorder and many patients will eventually require insulin therapy (20,21).

In our study we have included 50 patients of chronic pancreatitis over a period of 1 year. They were divided into two groups depending on presence (28 cases) or absence(22cases) of diabetes. The mean duration of chronic pancreatitis was 36 months in diabetic patients which was much higher than the mean duration without DM (24 months). However, this difference was not found to be statistically significant (p>0.05) . However it may indicate long duration of chronic pancreatitis can lead to diabe-tes.

The mean weight, mean abdominal and hip circumferences, BMI, BMC , mean RMR of patients with DM was found to be much lower (60.2 Kg, 84.1 cm, 89.6cm, 21.8, 2323.7 gm , 1333.7 Kcal/day re-spectively ), as compared to non- diabetic group (68.6 Kg, 90.5cms ,94.4 cm, 24.4 ,2557.4 gm ,1480.8 Kcal/day). This difference was found to be significant (P<0.05).

The mean value of HBA1C with diabetes mellitus positive was much higher (7.4% ) as compared to the cases with diabetes mellitus negative (5.8%) and this difference was found to be statistically signifi-cant(P<0.05).

The mean fat mass (16374.0 gm vs (20019.0 gm), visceral fat % (4%Vs 8.5%), Simulated c Peptide (SCP- 0.6 ng/ml Vs 1.2 ng/ml ) were considerably lower in the diabetic group as compared to cases without diabetes. This difference was found to be statistically significant (p<0.05).

Also, statistically significant lower value of mean weight, mean abdominal circumference, hip cir-cumference,BMC, RMR,FAT MASS and visceral fat in the diabetic group was seen. A possible explana-tion for this could be malnutrition ,lack of fat soluble vitamins and inverse correlation between stool fat and BMC. Malnutrition leads to decreased lean body mass, decreased functional mass, and de-creased weight . We also noticed that long duration of chronic pancreatitis associated with increased incidence of diabetes though not statistically significant, can lead to low value of these parameters. Weight loss is strongly associated with maldigestion of fat, and low BMC is due to increase stool fat. There was an inverse correlation between stool fat and BMC (r = -0.47; P = .03) in patients with chron-ic pancreatitis and steatorrhea in other studies also. (15)

Studies have shown that in long standing chronic pancreatitis due to maldigestion and steatorrea , de-creased BMI due to decrease pancreatic lipase is noted. (16, 17).In our study we also found that body fat, visceral fat, physiological age, stimulated c peptide, fasting serum insulin had association with age. Resting metabolic rate ,HbA1C ,LDL cholesterol had association with height. Weight had linear association with body fat, resting metabolic rate , visceral fat , physiological age , LDL cholesterol . Abdominal circumference had linear association with body fat , RMR, visc fat, physio age, stimulated c peptide total cholesterol. Hip circumference had linear association between body fat, resting metabol-ic rate, visc fat , physiological age. WHR had linear association between body fat, resting metabolic rate, visc fat and physiological age and stimulated c- peptide etc. BMI has linear association between body fat RMR, visc fat, physio age. In our study we also found that diabetic group had association with visceral adipose tissue and BMI had no association with visceral adipose tissue.

## CONCLUSION

In nearly 80% of all type 3C diabetes mellitus, Chronic Pancreatitis seems to be underlying cause. Hence, early detection of the same in case of long standing pancreatitis, is recommended. There is significant correlation between body parameters indicating insulin resistance which can form a part of diagnostic and follow up evaluation of Chronic Pancreatitis cases for development of Diabetes Melli-tus.

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