

## RESEARCH ARTICLE

### MORPHOPATHOLOGY OF PANCREAS IN DIABETES MELLITUS- A PROSPECTIVE STUDY DONE IN 50 AUTOPSY CASES

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**ABSTRACT:** The pancreas comprises exocrine and endocrine compartments, with the latter comprising the pancreatic islet with its endocrine cells. In both type 1 and type 2 diabetes, several morphological changes occur in the pancreas, but the predominant feature of beta cell loss. Our aim of this study is to find out of histopathological changes in pancreas due to diabetes and correlate it with clinical findings. Methods: A prospective study was done on 50 autopsy specimens of pancreas. Specimens were fixed in formalin and tissue was adequately processed. The sections were stained with routine haematoxyline and eosin stain. Results: In our study 86% cases were of T1DM and 14% of T2DM. Most common age group was between 40-60 years (62% cases). 68% cases had duration of DM of 10-20 years. On histopathological examination, 85% Cases of T1DM revealed cytolysis and inflammation in exocrine pancreas. In cases of T2DM cytolysis was seen in 32% cases, inflammation in 25% and fibrosis in 16% cases.. Fibrosis was present in 14% cases of T1DM and 25% cases of T2DM in endocrine pancreas. Insulinitis in endocrine pancreas was seen in 85% cases of T1DM and 34% cases of T2DM. Thus, the most common finding was reduced beta cell mass in T2DM and insulinitis in T1DM. Findings were correlated with age, sex and duration of diabetes. Conclusion: With increasing incidence of diabetes knowledge of pathogenesis of changes due to diabetes in pancreas may lead to research of further targeted therapy in better management of diabetes in future. Changes that occur in pancreas due to diabetes are more evident in long standing diabetes and early changes are not evident in routine histopathological sections.

**KEY WORDS:** diabetes mellitus, endocrine pancreas, exocrine pancreas, beta cell mass, insulinitis, fibrosis.

### INTRODUCTION:

Diabetes mellitus (DM) is defined by hyperglycemia with mainly two broad categories -type 1 and type 2. Type 1 DM is the result of complete or near total insulin deficiency. Type 2 DM is a heterogeneous group of disorders characterized by variable degrees

of insulin resistance, impaired secretion and increased glucose production. Insulin is secreted by beta cells in islets of Langerhans of endocrine pancreas. Islets comprise 1-2% of pancreatic mass.<sup>1</sup> These are too small to be seen by gross examination

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having an average size in the range of 100-150  $\mu$ m in humans.<sup>2</sup> There is strong association between beta cell loss and occurrence of amyloidosis in pancreas with the pathogenesis of DM.<sup>3</sup>

## **MATERIAL AND METHODS**

The present study was conducted on 50 gross autopsy specimens received in Department of Pathology, Government Medical College, Patiala. Specimens were received through police officials of concerned area with histopathology request form, police paper with brief history about the probable cause of death with history of any chronic illness like DM. The study proposal and procedure were approved by ethical committee of government medical college Patiala. All autopsy cases with natural and unnatural death with history of DM were included in the study. Crushed injury, poisoning cases and decomposed pancreas were excluded from this study. Specimens were fixed in 10% formalin. After gross examination of the specimens, these were processed as routine tissue processing and stained with H&E stain. Congo red stain was also used wherever required. The clinical data and histopathological findings were recorded. Frequency of various changes and their correlation with age and severity of disease was done. Chi-square test was used to determine the statistical significance. A p-value of <0.05 was considered statistically significant. Limitation of the present study was lack of immunohistochemical facility.

## **RESULTS**

In the present study, on gross examination weight of the pancreatic tissue received varied between 70 to 100 gm with mean value of 80 $\pm$  15 gm. (figure 1) Among 50 cases, 43 Cases were of T2DM and 7 cases were of T1DM. Distribution of cases according to age and sex is shown in Table 1.

**Table- 1 Age wise distribution of 50 cases**

Age (in years)	Males		Females		Total	
	No. of cases	Percentage (%)	No. of cases	Percentage (%)	No. of cases	Percentage (%)
<=40	5	14	5	25	10	18
40-60	21	62	10	62.5	31	62
>60	8	24	2	12.5	10	20
Total	34	68	16	32	50	100

Maximum number of cases (62%) were between age group of 40-60 years and 80% cases were in the age group of less than 60 years. 68% Of the total cases were males and 32% were females. 34/50(68%) had duration of DM of 11-20 years, 8/50 (16%) cases were with duration <10years and rest 8/50(16%) cases were with duration >20 years.

Histopathological examination of H& E stained sections of pancreas revealed cytolysis, inflammation and fibrosis (Table 2). 85% Cases of T1DM in exocrine pancreas revealed cytolysis and inflammation in exocrine pancreas while fibrosis was not seen in T1DM. In cases of T2DM cytolysis was seen in 32% cases, inflammation in 25% and fibrosis in 16% cases. (figure 2) Fibrosis was present in 14% cases of T1DM and 25% cases of T2DM in endocrine pancreas.(Table3). Insulitis (presence of inflammation) (figure 3) in endocrine pancreas was seen in 85% cases of T1DM and 34% cases of T2DM (Table 4).

**Table- 2. Histopathological findings in exocrine and endocrine pancreas**

FINDINGS	T1DM			T2DM	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
Exocrine pancreas	Cytolysis	6	85	14	32
	Inflammation	6	85	11	25
	Fibrosis	0	0	7	16
Endocrine pancreas	Insulinitis	6	85	15	34
	Fibrosis	1	14	11	25

Morphological changes that were seen in islets of Langerhans of endocrine pancreas included reduced number and small size of islets. Islets looked atrophic as compared to normal islets of pancreas. These changes were more evident in T2DM seen in 63% cases. (Table 3) (figure 4, 5)

**Table- 3 histopathological changes in islets cells of langerhans**

Islet cells	T1DM		T2DM		Total	
	No. of cases	Percentage (%)	No. of cases	Percentage (%)		
Normal	6	85	16	37.2	22	46
Reduced	1	15	27	62.8	28	54
TOTAL	7	14	43	86	50	100

There is significant correlation between type of diabetes and reduced and atrophic islets of langerhans cells with p value is <0.05

**Table 4. Correlation of presence of inflammation in endocrine pancreas with type of dm**

Inflammation	Type of DM				TOTAL	
	T1DM		T2DM			
	No. of cases	Percentage (%)	No. of cases	Percentage (%)	No. of cases	Percentage (%)
Present	6	85	15	35	23	44
Absent	1	15	28	65	28	54
TOTAL	7	14	43	86	50	100

Six cases (85%) of T1DM showed inflammation in islets and 35% (15) cases of T2DM showed inflammation in their islets.

Since p value is <0.05 so there is highly significant correlation between type of diabetes and presence or absence of inflammation in pancreas. Congo red positive cases were seen in 34% (17) cases. All cases were T2DM.





Figure-1 cut surface of pancreas with peri pancreatic fat attachment ( arrow)

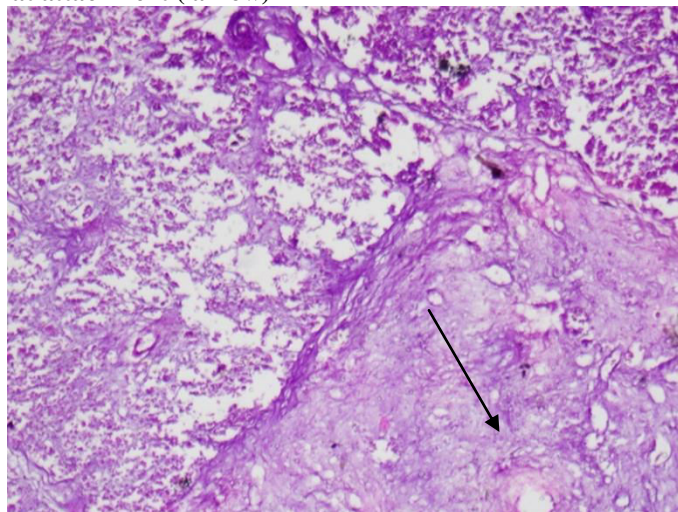


Figure-2 photomicrograph showing presence of fibrosis ( arrow) in the exocrine pancreas (400x H& E)

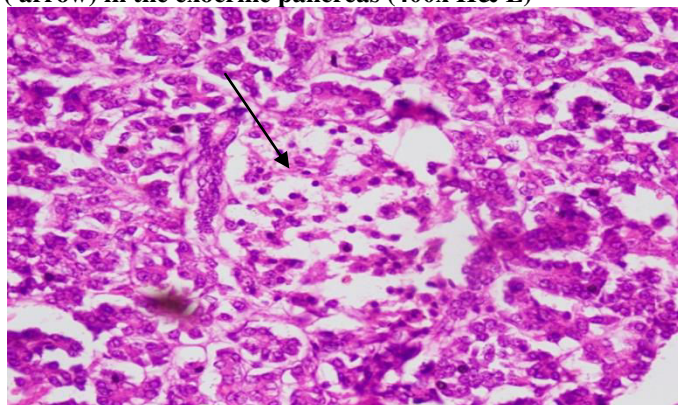


Figure-3 photomicrograph showing presence of inflammatory cells and reduced number of cells in islet of pancreas of T1DM (400x H&E)

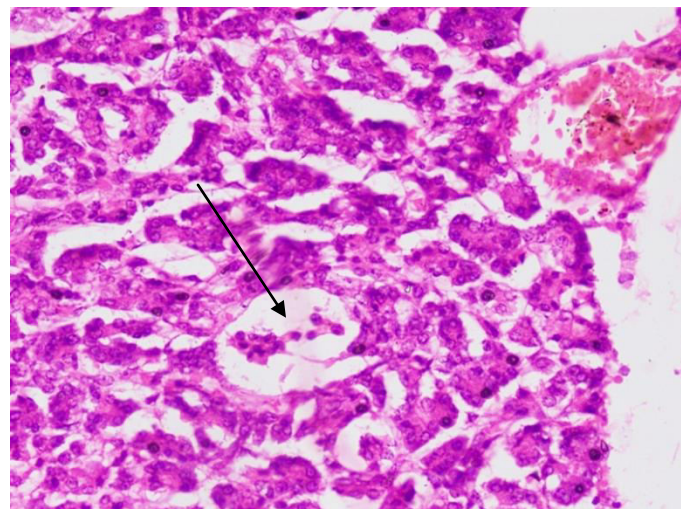
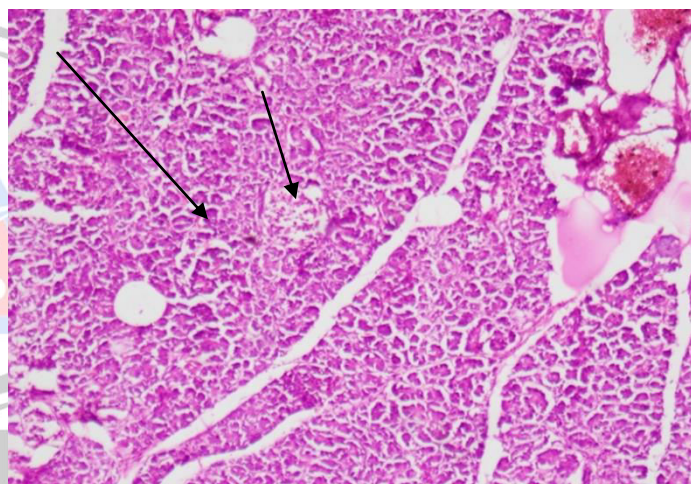


Figure -4 photomicrograph of pancreas of t2dm showing small, atrophic islet. There are very few cells in this islet. (400x H&E)

Figure-5 photomicrograph showing atrophic islet in



pancreas of T2DM (Arrow) 100x H&E

### DISCUSSION:

In the present study mean pancreatic weight of pancreas in 50 studied cases was  $80 \pm 15$ g. This finding was comparable with Gepts et al study and Rahier et al. (table 5). The difference between finding of present study and studies conducted by Lohe et al and Deng et al was due to difference between the region and race of the studying subjects.

**Table 5. Comparison on the basis of weight of pancreas with maximum no. Of cases**

Authors Name	Year	Mean weight of pancreas	No. of cases studied
Gepts <sup>[4]</sup>	1965	80±10g	54
Lohe et al <sup>[5]</sup>	1987	56.3g	26
Deng et al <sup>[6]</sup>	2004	104±34g	14
Rahier et al <sup>[7]</sup>	2008	73.5 ± 26.0g	57
Present study	2016	80±15g	50

In present study presence of insulinitis in 85% in T1DM cases. These finding were comparable with the findings of Botazzo et al and others.(table 6)

**Table 6. Comparison on the basis of presence of insulinitis in T1DM on the basis of maximum cases**

Author Name	Year	Presence of insulinitis	No. of cases
Foulis et al <sup>[8]</sup>	1986	78%	60
Botazzo et al <sup>[9]</sup>	1985	78%	10
Krogvold et al <sup>[10]</sup>	2016	82%	6
Present study	2016	85%	7

In present study beta cell mass is reduced in 27% of T2DM cases. These findings were comparable with studies conducted by Sakuraba et al and Rahier et al (Table 7)

Butler et al. in 2003 showed 60% reduction in beta cell mass and Deng S et al showed reduction in beta cell mass in 67% cases. Difference in findings of these studies with present study was mainly due to difference in method of study. Present study had used H& E staining method for evaluation of specimens while these studies had used Immunohistochemistry (IHC) method for evaluation of cases. IHC method is more specific method than routine H&E method.

**Table -7. Comparison on the basis of reduced beta cell mass in T2DM in different studies**

Author name	Year	% of Reduced beta cell mass	Total number of cases
Sakuraba et al <sup>[11]</sup>	2002	30%	14
Butler et al <sup>[12]</sup>	2003	60%	124
Deng et al <sup>[6]</sup>	2004	67%	14
Rahier et al <sup>[7]</sup>	2008	35%	57
Present study	2016	27%	43

## **CONCLUSION:**

Incidence of diabetes is increasing in many folds not only in developed countries but also in developing countries. Factors which influence the increase in incidence of DM probably are due to environmental factors, genetic factors, dietary changes and change in life style. . Pancreatic biopsy in humans is not recommended for diagnosis of DM because of inaccessibility of organ and its complications. But, from the studies of postmortem specimens we concluded that beta cell destruction is key element in pathogenesis of both T1DM and T2DM either by lymphocytic infiltration, apoptosis, amyloidogenesis or other mechanisms. Study of pathogenetic sequences in DM in pancreas can help in finding of better treatment options for diabetic patients and can reduce related morbidity and mortality.

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