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Microantomic study of human pancreatic islets in correlate with diabetes mellitus

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Abstract
Back ground & aim: The islets of Langershans is an important endocrine gland which regulate the blood glucose level. The rise in blood glucose level results in diabetes- mellitus, an age old disease which affects all the systems of our body, Nowadays an increase in the incidence of diabetes is noticed in younger age group also. The increased intake of alcohol in our state also affects the gland.
Materials & methods: Fifty five autopsied specimens of pancreas an age range from 10 weeks old fetus to 80 yrs old adult were collected for analysis from the department of pathology and mortuary of Government Medical College Trivandrum, Kerala. Histological examinations of the glands were done in the histology laboratory of department of Anatomy Government Medical College, Trivandrum, Kerala.
Results: According to the present study, both acini & islets were developed from the endodermal secretary tubules. Acini and islets were appeared by 12th weeks and beta cells by 14th weeks and beta cell granules by 32nd week in fetuses of non diabetic mothers. The beta cells appeared by 12th weeks and their granules by 28th weeks in fetuses of Diabetic mothers. Well defined islet groups appeared in full term fetuses of non diabetic mothers but well defined islets groups with staining characteristic similar to adult appeared by 36th weeks in fetuses of diabetic mothers.
Conclusion: In fetuses of non diabetic mothers, the islets and acini appeared by 12th week and beta cells by 14th week and their granules by 32nd week. But in fetuses of diabetic mothers the beta cells appeared by 12th weeks and their granules by 28th week. In non diabetic adults the number of beta cells decreased after the age of 40 yrs, but in diabetic on insulin treatment the size and number of beta cells increased. The beta cell destruction may be due to chemicals, diet, genetic factors and autoimmune diseases.

Keywords: Fetal pancreatic islets, adult pancreatic islets, beta cells and diabetic mellitus

Introduction
The role of maternal insulin in the development of fetal pancreatic islets and its cells were significant in fetal period. The insulin level in fetuses has a role in maturation of fetal organs and induction of abortions and premature labour without any other apparent cause. The microscopic study of fetal islets could prove to be useful for radiologists, neonatologists and diabetologists alike. Diabetes mellitus is an age old problem for which there is no complete cure. Recently the incidence of diabetes mellitus increased and it affect the younger age groups also. In the present study, the microscopic change of islets and its cells were studied in corralate with diabetes mellitus.
In recent studies five types of cells were identified in the islets. Researchers have also observed that autoimmune diseases, blood cholestrol levels, HbA1C viruses and chemicals also have a role in blood glucose level. Hence this study will be useful to both endocrinologists and gastroenterologists.
The aim of the present study is to find out the microscopic changes in fetal islets of non diabetic and diabetic mothers and also in non diabetic adults and diabetic adults on insulin treatment and correlate with each other.
Most of the microscopical studies were limited to the pancreas of animals like sheep, rat etc. very few studies were done on human fetal and adult pancreas and also in diabetic patient.

Materials and methods

17 fetal autopsy specimens were collected from the department of pathology (gestational age range from 10 weeks-40 weeks) and 38 adult specimens were (age 40-80yrs) collected from the mortuary of Government Medical College Trivandrum, Kerala. The tissue samples were taken from the tail end of the pancreas where islets are concentrated more.

Inclusion criteria

Since autolysis of pancreas is rapid, samples were collected only from autopsies performed within 6 hrs after death.

Exclusion criteria

1. Autopsies performed 6 hrs after death
2. Crush injuries of abdomen,
3. Fetuses with congenital abnormalities of abdominal viscera

The age of the fetuses were taken from the hospital record and crown- rump length.

During autopsy after opening the abdomen found out the pinkish gray coloured gland lying transversally across the posterior abdominal wall retroperitoneally extending from the concavity of duodenum to the hilum of spleen.

The bits were taken from the gland and fixed in Bouins fluid for 24 hrs. After fixation the specimens were subjected to routine histological processing, as per the standard procedure described by Mac Manus and Moury (1960). The paraffin blocks were serially sectioned at a thickness of five microns using a rotary microtome. After incubating for one hour the sections were stained with standard haematoxylin and eosin (H &E) stain.

Microscopic evaluation of the islet cells with special stains like Masson's trichrome, chromealumhaematoxylin, PAS etc. The mounted specimens were observed under low power and oil immersion objectives of a binocular microscope. The sections were observed under oilimmersion objective to study the characteristic of different types of cells and measurements were taken with a horizonatal eye piece micrometer called the graticule, which is calibrated with a stage micrometre.

Results

The 55 samples collected for the present study were grouped as per their age (Fetuses 10 -40 weeks and adults 40-80 yrs) (Table I). The beta cells appeared early and more in number is a feature of fetuses of diabetic mothers than a non diabetic mothers. The size of islets and diameter and number of beta cells increased in diabetic adult on insulin treatment when correlate with non diabetic adults (Table-II).

In standard H&E staining the islets appeared as more or less speherical masses of pale staining areas in which the cells were arranged as irregular anastomotic cords and surrounded by pancreatic acini. (Fig:-9)

The islets were separated from the acinar groups by a thin capsule made up of reticular fibres clearly distinguished by Mallory trichromestain. (Fig:-10)

According to the present study both acini and islets were developed from the secretary tubules (Fig:-5). 10 weeks old fetus contain only connective tissue and duct system (Fig:-1). In a 12^{th} week old fetus of diabetic mother, both acini and islets with beta cells were appeared (Fig:-3) but no cells in fetus of no diabetic mother (Fig:-2). But in a fetus of non diabetic mother beta cells were first appeared by 14^{th} week (Fig:-4). In a fetus of diabetics mother at 28^{th} week the acini were grouped, into well defined lobules by interlobular connective tissue and the beta cells shows granules in their cytoplasm (Fig:-5). But these changes will appeared by 32^{nd} week in fetus of non diabetic mother (Fig:-6).

In a 36^{th} week old fetus of diabetic mother, two third of pancreatic tissue is filled with islet cells and the staining characteristic of islet cells were similar to that of adults (Fig:- 7). But in a fetus of non diabetic mother all these features appeared by full term (Fig:-8).

In a full term baby of diabetic mother the islet cells were arranged in a cord like form similar to that of a child and the islets occupied a major portion of the pancreatic tissue (Fig:-9).

Above 40 yrs, in diabetic patients on insulin treatment the diameter of islets and the diameter and number of beta cells were increased, when correlate to non diabetic persons of similar age group (Fig:-10,11). As age advances the number of beta cells decreased in an islet as seen in an 80 year old non diabetic patient (Fig:-16). But in an 80 year old diabetic patient on insulin the islet showed more number of beta cells. (Fig:-16).

In a 48 yrs old chronic alcoholic diabetic patient on insulin, treatment the changes were segmental, one segment showed hyperplasia of islets (Fig:-12) while in another segment a large islet group with more number of beta cells were appeared (Fig:-14) and in a third segment amyloid deposits were observed (Fig:-13).

Table 1

Sl. No.	Age Group (Fetuses)	No of Specimens
1	10-20 weeks	7
2	21-40 weeks	10
(Adults)		
3	41-60 years	20
4	61- 80 yrs	18
Total		55

Table 2

Age Group	Mean dimeter of islets (μ)		Average number of beta cells	
	Non Dibetic	Dibetic on insulin	Non Dibetic	Dibetic on insulin
41-60 yrs	170	182	72	76
61-80 yrs	180	194	58	66

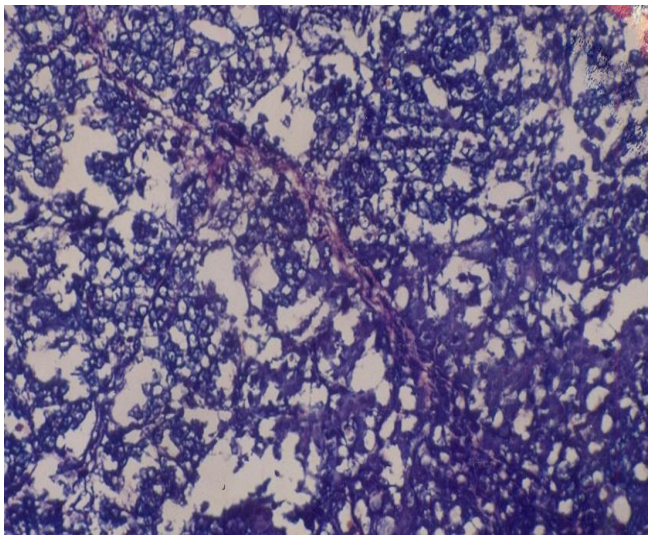

Fig 1: 10 weeks old fetus, Fuchsinblue stain shows only connective tissue (C) and ducts (D)

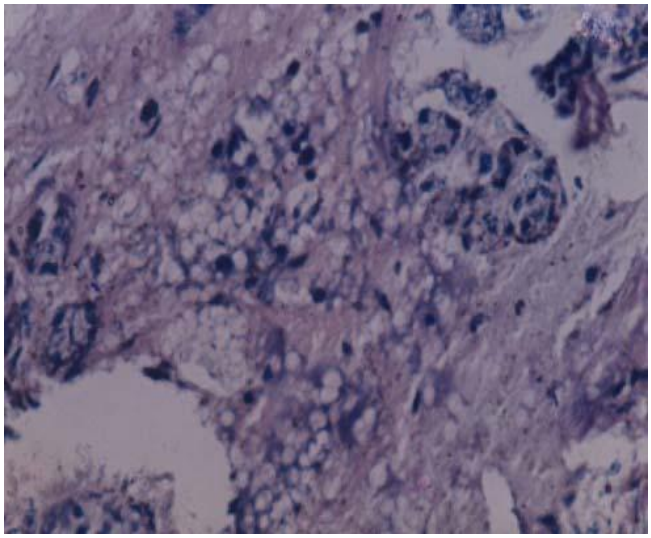

Fig 2: 12 weeks old fetus of non diabetic mother, chromealum hamatoxylin stain shows acinar groups (A) and islets without any cells (I).

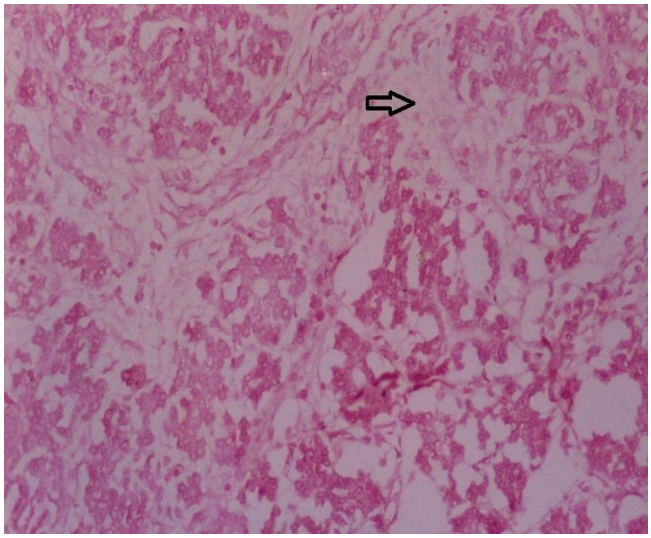

Fig 3: 12 weeks old fetus of diabetic mother, PAS stain islets shows few beta cells (⇨)

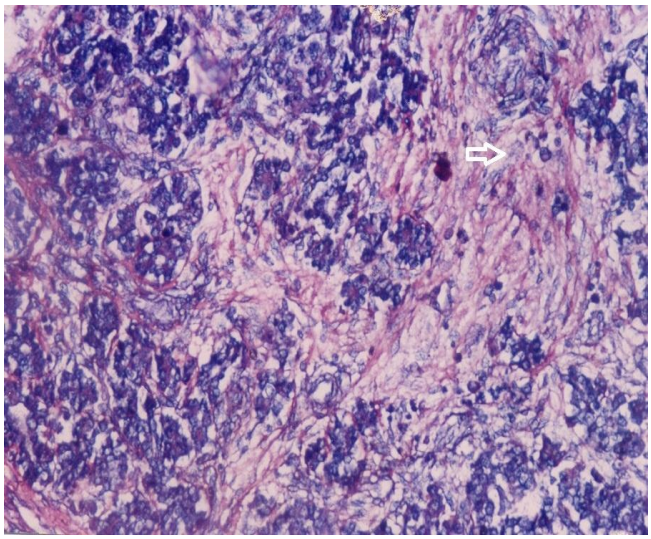

Fig 4: 14 weeks old fetus of non diabetic mother, stain chromealum haematoxylin phloxin stain, islets shows beta cells without granules (⇨)

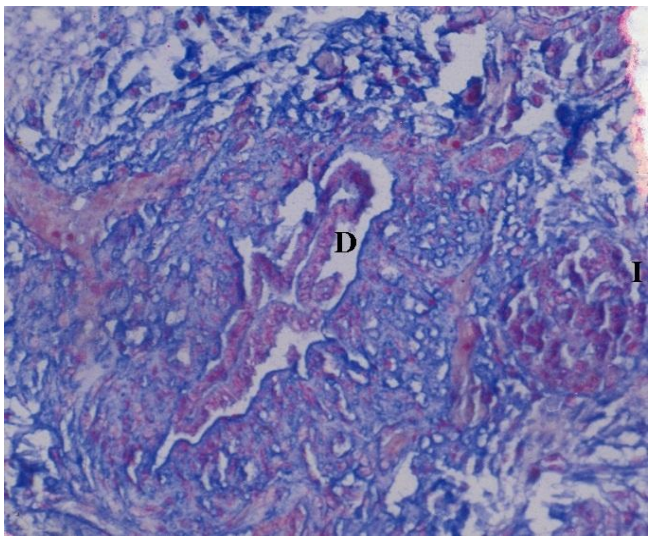

Fig 5: 28 week old fetus of diabetic mother chromealum haematoxylin phloxin stain secretory tubule (D). Islet with alpha and beta cells (I).

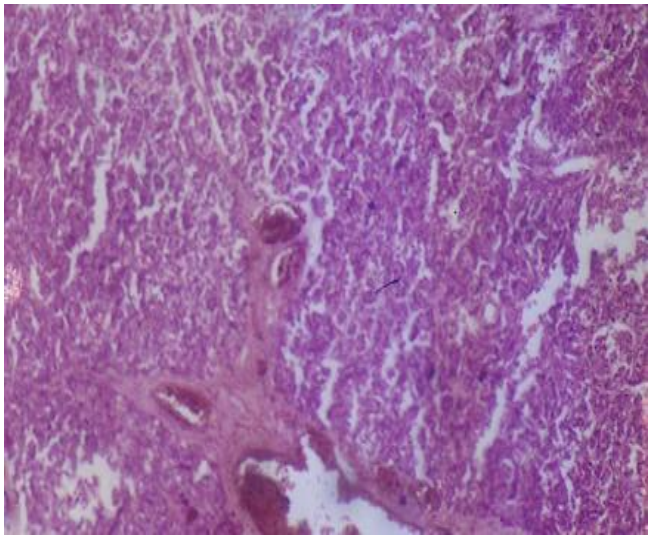

Fig 6: 32 week old fetus of non diabetic mother, PAS stain. Islet with few cells (I).

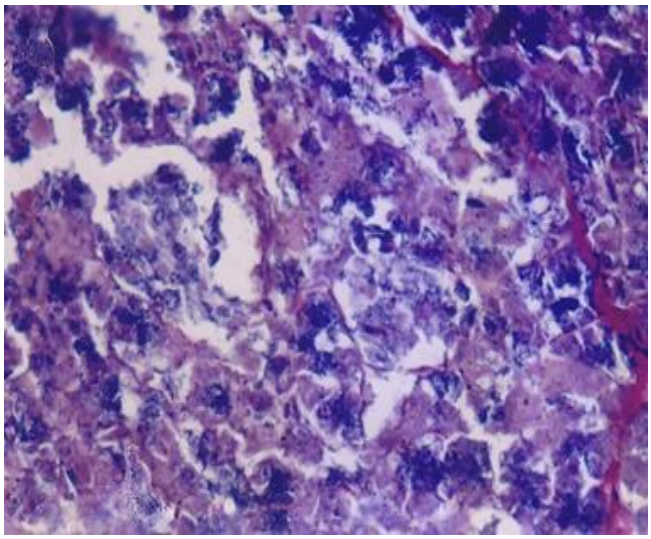

Fig 7: 36 week old fetus of diabetic mother chromealum hematoxylin stain. Islet with beta cell granules (I).

(D- duct), (I- islets shows beta cells with granules and alpha cells.)

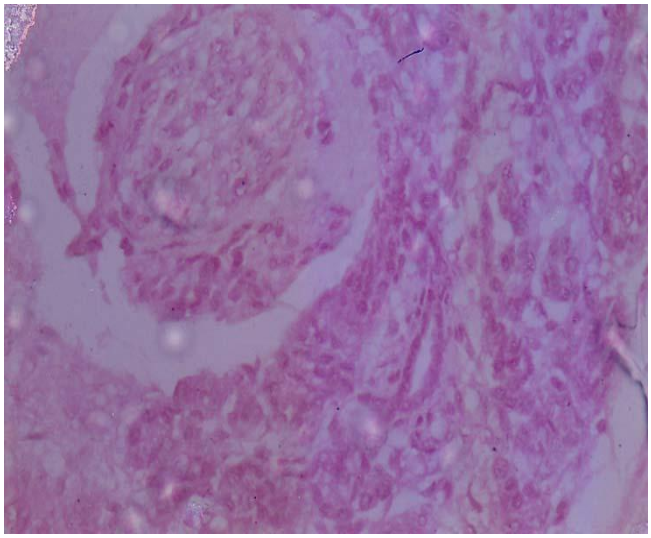

Fig 8: Full term fetus of non diabetic Mother PAS stain, islets shows Groups of cells (I).

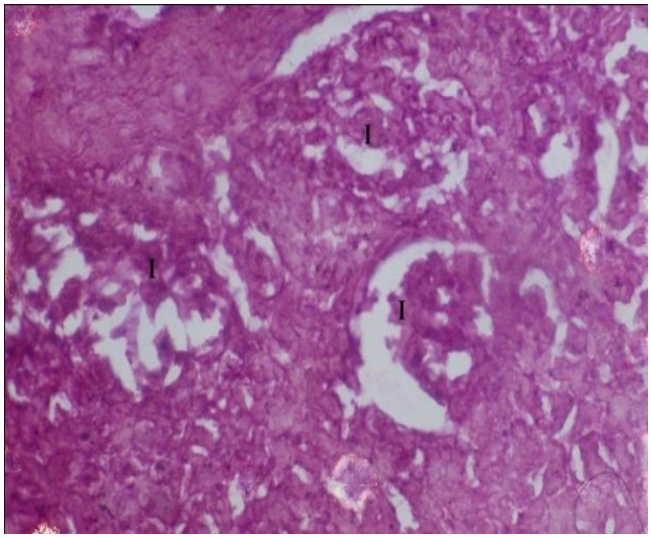

Fig 9: full term fetus of diabetic mother, azocarmine stain islets shows cords of cells (I).

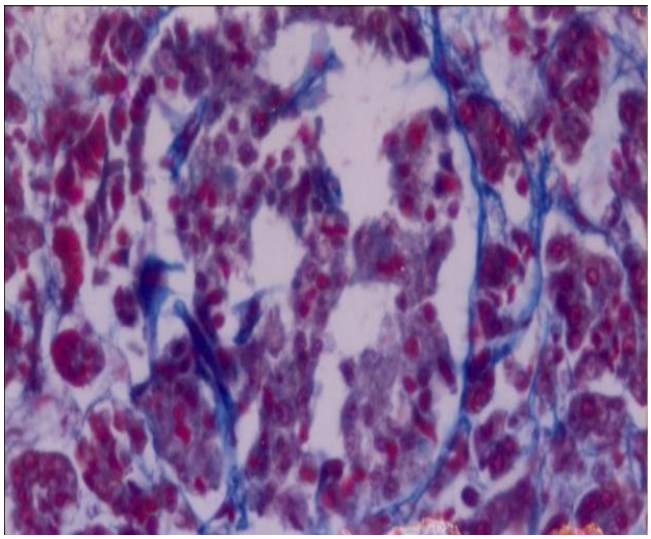

Fig 10: 48 year old non diabetic, massosn's Trichrome stain, a large islet (I) surrounded by blue colured capule (C)

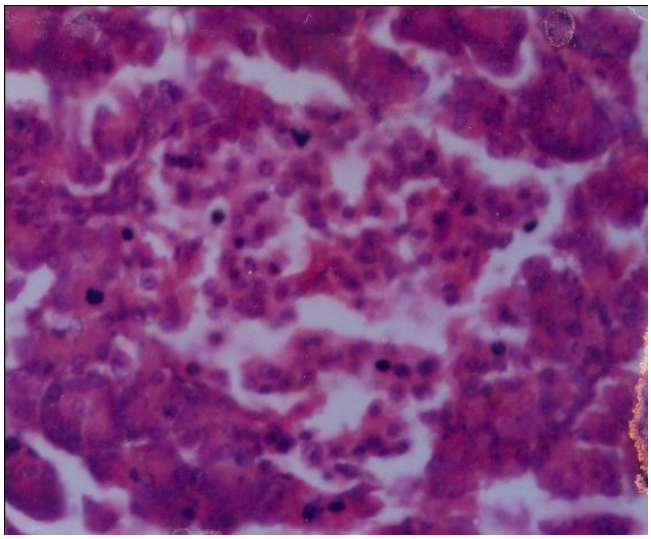

Fig 11: 48 year old diabetic on insulin, islet shows more number of beta cells (I). Azocarmine stain

48 year old chronic alcoholic diabetic patient on insulin

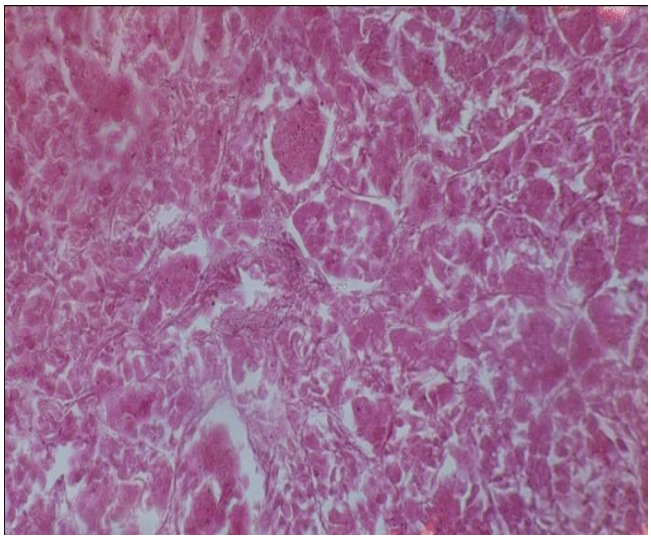

Fig 12: H & E stain, pancreatic tissue shows multiple islets groups (I)

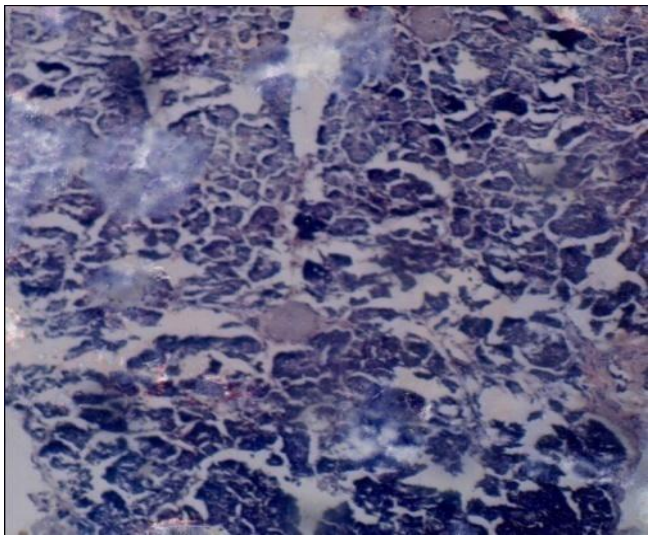

Fig 13: Congored stain, amyloid deposit in islet (A)

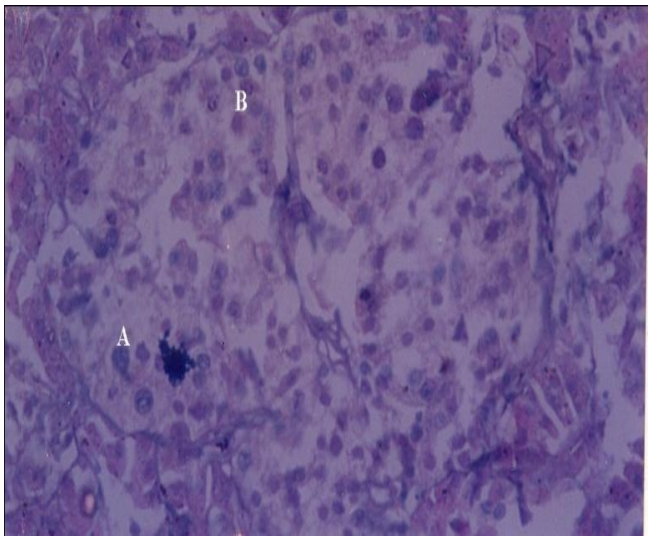

Fig 14: Chromealum haematoxylin stain

A large islet group with more number of beta cells (B) and alpha cells (A)

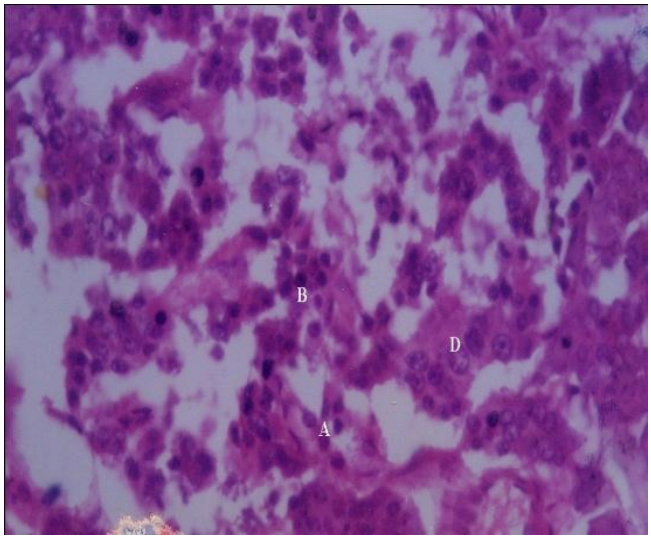

Fig 15: 80 year old non diabetic, azocarmine phloxin stain. A large islet group with few alpha and beta cells (I).

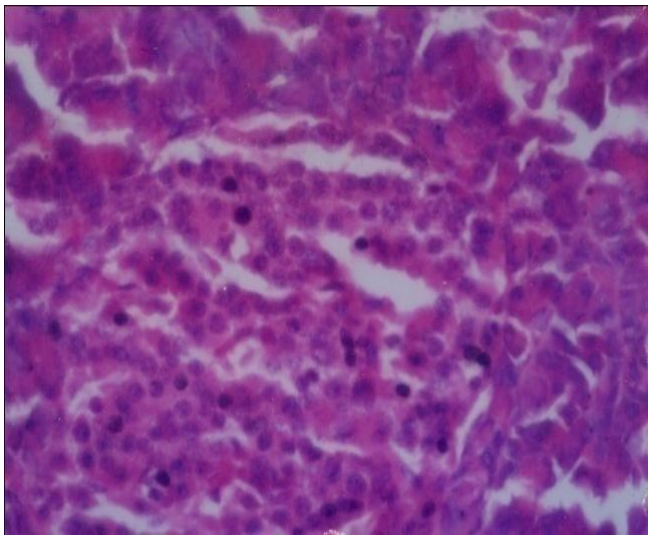

Fig 16: 80 year old diabetic on insulin azocarmine phloxin stain. A large islet group with more number of alpha and beta cells (I).

Discussion

The present work provide an opportunity to understand the normal microscopic appearance of fetal pancreatic islets of diabetic mothers and non diabetic mothers as well as the adult pancreatic islets in a diabetic patients on insulin treatment and non diabetic persons and correlate with each other [5-8].

In the present study both islets and acini had a common origin the secretary tubules, studies have shown that islets and acini take origin from duct system and centro acinar cells [2]. Acinar cells were thought to be capable of transforming into islet cells and islet cells into acinar cells [1]. The relative proportion of each being governed by functional requirements [11].

In a 10th week old fetal pancreas only connective tissue and duct system were observed [13]. In a 12th week old fetuses of non diabetic mother round or oval light stained areas of islet with out any cells could be observed, but in a 12th week old fetus of diabetic mother islets with beta cells could be observed [12].

In a fetus of diabetic mother at 28th weeks, the alpha cells, beta cell granules and well defined acinar groups could be seen. All the above changes were, observed only at 32nd week in fetuses of non diabetic mothers. In a fetus of diabetic mothers at 36nd week, the volume of islets more compare to acini and the staining characteristic of islets is similar to that of adult islets. All these changes occurred only at full term in a fetus of non diabetic mother [6, 14].

In a full term fetus of diabetic mothers the major portion of pancreatic segment was composed of islets and the islet cells were arranged is a cord like form [4]. When correlate with the full term fetuses of non diabetic mothers.

In adults known diabetic patients on insulin treatment after the age of 40 yrs, the diameter of islets and the number and diameter of beta cells were increased when correlate with the non diabetic of similar age group. This finding is in conformity with the study of Hellman [8]. Giddings and Mordian also observed that the number of beta cells were more is diabetic patients on insulin treatment [5]. The insulin stimulate the multiplication of beta cells. In a 48 yrs old chronic alcoholic diabetic patients on insulin treatment, in one segment there were hyperplasia of islets, in another segment amyloid deposits and in a third segment, showed large islet with more number of beta cells [8, 9].

Insulin secretions diminished in response to glucose as age advances [8]. It was also observed that diabetes can be prevented and the incidence of diabetes can be substantially reduced by neonatal stimulation of pancreatic beta cells [10]. It was also studied that children of diabetic fathers developed diabetes at an earlier age and the incidence was 6.1%whears children of diabetic mothers the incidence was only 2.15% and at a later age [13, 14].

The microscopic changes in the pancreatic islets of fetuses of diabetic and non diabetic mothers and its correlative study attracted the attention of many researchers working on gestationel diabetes.

In diabetic patients, the insulin intake multiplied the beta cells in order to secrete more insulin [3]. As a result the islet showed more number of beta cells and their size also increased [9]. In this study I could not make out any sexual differences in diabetic patients on insulin, since only three cases of female specimens were obtained. pancreatitis could be triggered during pregnancy due to CYP24A1 mutation. Association between 1gE mediated allergic conditions and diabetes mellitus was also detected. Recently the expression of transient receptor potential channels in the purified human pancreatic beta cells were reported [13].

Conclusion

1. In fetuses of known diabetic mothers the islet cells and their granules were appeared 2-4 weeks earlier than fetuses of non diabetic mothers.
2. Diabetic mothers can protect their children from diabetes when compared to diabetic fathers to some extent by the neonatal stimulation of pancreatic beta cells.
3. In a diabetic patient on insulin treatment, the size of islets, the number and size of beta cells were more when correlate with the non diabetic persons of similar age group.
4. In a chronic alcoholic patient on insulin treatment, there were hyperplasia of islets, amyloid deposits and increase in number of beta cells were observed.

The present micro anatomic study attracted the attention of many researchers, due to the increased incidence of diabetes mellitus from younger age onwards and the increased incidence of gestational diabetes, so the present study correlate between the micro anatomy of pancreatic islets in non diabetic and diabetic patients over consumption of alcohol, produces increased level of glucose in blood by gluconeogenesis, to counteract this islets multiples and the size and number of beta cells increased, and the person may develop alcoholic diabetes mellitus.

This is only a preliminary study as this is done on autopsy specimens. This study can serve as a base for further researchers pertaining to the role of diabetic -mothers in fetal pancreatic islet cells as well as in adults diabetic patients on insulin treatment.

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