

## Histogenesis Of Pancreatic Acini In 50 Human Fetuses

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### Abstract:

*The pancreas derives its name from the Greek 'pan means all' and 'creas means flesh'. It is an organ containing two distinct population of cells. Endocrine cells are Islets of Langerhans that secrete hormones insulin and glucagon which together regulate blood glucose levels and also secretes somatostatin<sup>[1]</sup>.*

*The exocrine cells pancreatic acini secrete enzymes amylase, salts and alpha fetoproteina major serum protein during development. Pancreatic alpha fetoprotein has found to change the expression level during development and has been suggested to influence the pancreatic development.<sup>[2]</sup>*

*The purpose of this paper is to focus on histogenesis of Pancreas in fresh human aborted foetuses without gross abnormality from 12 to 40 weeks of gestational age. The foetuses were preserved in formalin and they were of both the sexes. And they were obtained from the department of obstetrics and gynaecology, KIMS Narkatpally, Nalgonda (Dt), Telangana, (INDIA).*

*Five stages of development of pancreatic acini were screened by haematoxylin and eosin staining and were observed under light microscope. The developmental study of pancreatic acini were discussed with the findings from the available literature.*

*The gaps of knowledge is necessary to understand the histogenesis of pancreas at various gestational ages which helps in planning new therapeutic strategies in reducing mortality and curing either or both diseases, pancreatic cancer and diabetes mellitus . Majority of studies focus on foetal pancreatic islets, but few studies were focus on the foetal pancreatic acini. Literature of development of human foetal pancreatic acini were few in number so that the present study was conducted to know the normal development of exocrine part of human foetal pancreas and its clinical correlation.*

**Keywords:** Pancreas, Serous acini, Gestational period, Islets of Langerhans, Histogenesis, Ducts, Alpha fetoprotein (AFP)

### Introduction:

Pancreas is one of the largest digestive gland in human, retort flask shape, occupying epigastrium and left hypochondrium. In adult it measures about 12 to 15 cm long and weighs 80 to 90 grams<sup>[3]</sup>. It is the target of two major diseases like pancreatic cancer and diabetes mellitus.

It develops at the foregut/ midgut junction and generates two pancreatic buds (dorsal and ventral

endoderm) which will fuse to form single pancreas at around 7<sup>th</sup> week IUL. Main and accessory pancreatic ducts develop at around 6<sup>th</sup> week. Pancreatic acini and Islets of Langerhans start developing from 12<sup>th</sup> week of foetal life<sup>[4,5]</sup>

The exocrine are secretory serous acini derived from the repeated sprouting of the ducts at 12 weeks IUL arranged in the form of lobules surrounded by thin intra lobular and interlobular

connective tissue septa with blood vessels, ducts and nerves.

The acinar cells or the duct system give rise to endocrine part, Islets of Langerhans which later gets detached and forms independent colonies scattered throughout the substance and they are more in density in tail of the pancreas<sup>[6,7,8]</sup>.

Many studies inferred that transition from Islets to acini or vice-versa can occur and developmentally they are not independent structures<sup>[7]</sup>

Alpha foeto protein which is the most abundant serum protein in foetus produced by distinct cell types during embryogenesis, but is transiently seen in foetal pancreatic acini during development. It was first identified in the sera of human foetuses by Bergstrand and Czar in 1956<sup>[9]</sup>

The knowledge of normal pancreatic growth and differentiation during development will inform ongoing studies of pancreatic regeneration following surgical pancreatectomy<sup>[6]</sup>. Islets are extremely difficult to isolate from adult human pancreas therefore isolated islets of foetal pancreas forms suitable transplantation in type 1 diabetes mellitus.

#### **Materials and methods:**

The material consists of 50 aborted human foetuses of gestational age between 12 to 40 weeks were obtained from the department of obstetrics and gynaecology KIMS, Narkatpally. Permission was obtained from institutional ethical committee.

The age of the foetuses was calculated by crown-rump length, bi-parietal diameter, head circumference and abdominal circumference. Foetuses were arranged in five gestational groups of 6 weeks interval.

After opening of the abdomen, pancreas was dissected out from the foetuses and fixed in 10% formalin. The tissues were subjected to routine histological preparation and paraffin blocks were

prepared. Sections of 3- 5 microns thickness were cut and stained with haematoxylin and eosin.

Microphotography of sections were studied under the trinocular microscope having close circuit camera and an adaptor.

#### **Histological Observations:**

##### **Group 1 (12 to 18weeks) Figure 1**

1. Mesenchymal tissue showed branched tubules with wide lumen.
2. Budding was observed at the end of the tubules forming primitive acini.
3. Undifferentiated cells were also seen within the mesenchyme.
4. Small islets having an ill-defined capsule without capillaries were seen.
5. Parenchyma begun to organise into lobes and lobules.

##### **Group 2 (18 to 24 weeks) Figure 2**

1. Mesenchymal tissue was reduced and proliferation of acinar cells
2. Establishment of small lobes and lobules.
3. Intra lobular ducts lined by cuboidal cells were adjacent to the duct.
4. Increased in size of the islet entrapped within the acinar cells.

##### **Group 3 (24 to 30 weeks) Figure 3**

1. Further acinar development was seen with well-formed lobes and lobules.
2. Clumps of undifferentiated cells from the intra lobular duct lined by Cuboidal epithelium was also observed.

Note: undifferentiated cells either form pancreatic acini or Islets or small ducts(REFE)

##### **Group 4 (30 to 36 weeks) Figure 4**

1. Well differentiated Islets with a thin capsule with capillaries were observed.
2. Lobes and lobules packed with serous acini.
3. Well-developed duct system with thick Interlobular septa was seen.

#### .Group 5 (Full term) Figure 5

The adult format of the microscopic appearance of pancreas was seen at 40<sup>th</sup> week. Lobes and lobules of mature acini surrounding large, vascular islets with thin interlobar septa were seen in all term fetuses. No further developmental changes were seen.

#### Discussion:

Development includes three fundamental processes: these are growth, differentiation and metabolism. Growth is increase in spatial dimensions and in weight. Differentiation is increase in complexity and organisation. This differentiation may not be apparent at first, but when apparent it is known as 'Histogenesis' [10]

Mammals, birds, reptiles and amphibians have a pancreas with similar histology and mode of development, while in some fish, the islet cells are segregated as Brockmann bodies. Invertebrates do not have a pancreas, but comparable endocrine cells may be found in the gut or in the brain [1]

Various studies in literature showed that expression of pancreas and duodenal home box gene for assessing reduced pancreatic function is correlated to alterations in the pancreatic parenchymal tissue.

Immunohistochemically investigated pancreatic enzymes alpha amylase, trypsinogen and lipase expression initially in foetal livers (9- 25 weeks) but disappeared thereafter. Beard [11] found that substances (digestive enzymes trypsin) secreted by the pancreas would inhibit the growth of cancers before they develop.

The alpha fetoprotein a major serum protein during development is one of the earliest protein to be

synthesised by the embryonic liver. It is subsequently expressed in the developing exocrine part of pancreas. AFP expression in Human embryos can catabolise amino acids which provide an important supply of metabolic energy for the embryo. [9] AFP is used as a serological marker for germ cell tumors and prenatal screening of neural tube defects and Down's syndrome. (Abelev & Erais, 1999)

The synthesis of AFP decreases dramatically after birth.

The selection of an appropriate developmental stage of foetal pancreas is of paramount importance for the successful transplant of pancreas in patients of insulin dependent diabetes mellitus.

In the present study in **group 1 (figure 1)** it was noted between 12 to 18 weeks of gestation, Mesenchymal budding at the end of the tubules forming primitive acini without central lumen. Parenchyma begun to organise into lobes and lobules. Small islets with ill-defined capsule without capillaries appeared and are connected to the ducts. Intralobular and interlobular ducts lined by cuboidal epithelium were also seen. These observations were supported by J. Conklin, Gupta. V et al, P. Robb and Achaya Anand [12, 13, 14, 15].

**Group 2 observations (figure 2)** between 18 to 24 weeks shows lobes and lobules with thin septa. Increased number of acini in the lobule and Islets with distinct capsule and capillaries seen. A similar architecture was reported by J. Conklin, Gupta. V et al, P. Robb and Achaya Anand. [12, 13, 14, 15]

**In Group 3 (figure 3)** According to J. Conklin and Gupta [12, 13] the current study between 24 – 30 weeks had similar features. It had widely distribution of acinar cells throughout the lobules and progressive increase in the size and number of Islets with capillaries. The marked feature at this stage also showed clumps of undifferentiated cells arising from intra lobular ducts.

**Group 4 (figure 4)** 30 – 36 weeks showed the Lobes and lobules were packed with serous acini with well differentiated colonies of Islets surrounded by thin capsule and capillaries. The duct system lined by cuboidal epithelium seen in the interlobular septa. These observations are in agreement with previous reports [12,13]

**In Group 5 (figure 5)** full term pancreatic architecture showed the adult format of the microscopic appearance. Few undifferentiated clusters of cells were seen in the interlobular septa. This suggested that the development and formation of new acini and islets. Acini and ductal system were well formed and Islets were large and prominent at this stage the acinar epithelium demonstrated great change. The cytoplasm of the cells became more basophilic.

Brown et al<sup>[13]</sup> 1980 reported human foetal pancreas between 20- 24 weeks may be a suitable donor material. The success of pancreatic transplant requires the knowledge of development, morphology, and islet genesis.

#### **Conclusion:**

Major exocrine part of human foetal pancreas assumed maturity only after 24 – 30 weeks of gestation. Development of new acini were seen throughout foetal life.

Destruction of acinar tissue by duct ligation followed by rapid regeneration but surgical removal of parts of pancreas is followed by incomplete regeneration of both acini and islets.

The pancreas produces the enzyme trypsin<sup>[11]</sup> which prevents germ cells from becoming malignant. Stomach, colon and rectal cancer are all common but small intestine cancer is rare.

Our observational studies suggest that both exocrine and endocrine components arising from same endodermal rudiment and concluding that pancreas is a single integrated organ from the biological point of view.

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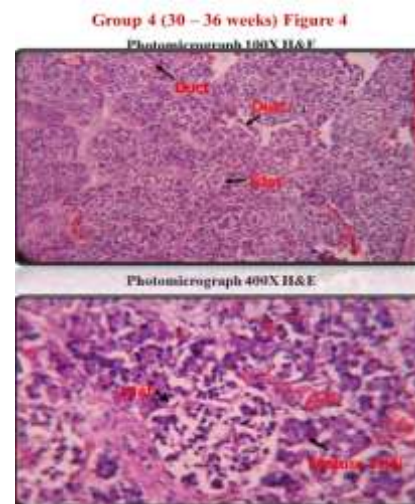
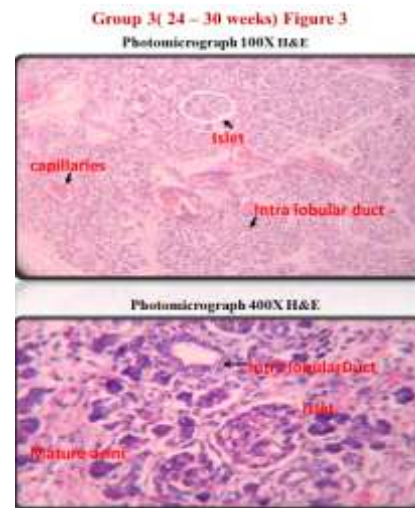
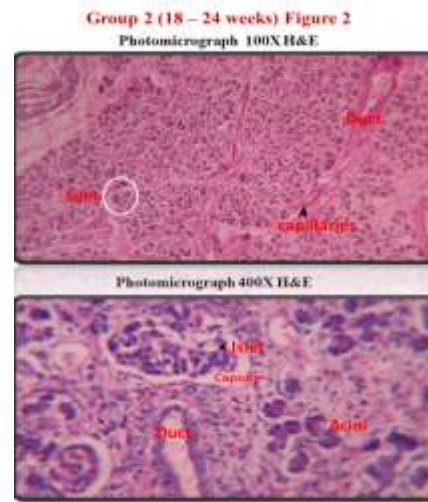
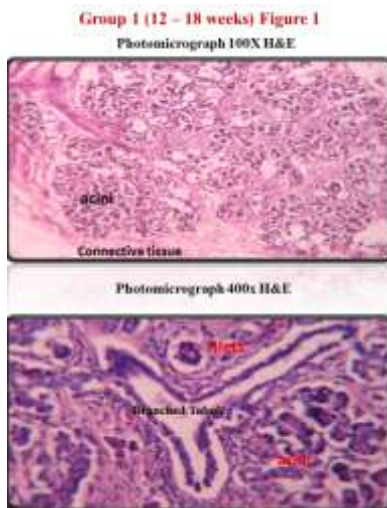
**Conflict of interest:** Nil.

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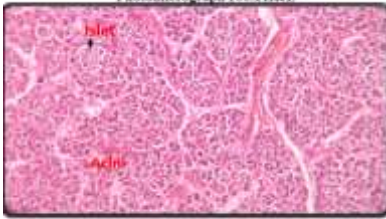
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### Histological Observations



Group 5 (36 weeks- term) Figure 5

Photomicrograph 100X H&E



Photomicrograph 400X H&E

