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Original Research Article

Morphometry and Histogenesis of Human Foetal Pancreas

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ABSTRACT

BACKGROUND: From the medical Point of view pancreas is an important organ. It is the target of two major diseases like Diabetes mellitus and pancreatic cancer. Understanding the development of Pancreas helps in planning new therapeutic strategies that help in reducing mortality, morbidity, preventing and curing of either or both of these diseases. **OBJECTIVES:** The present study on human foetal panereas specimens of different gestational ages was conducted with the following objectives to observe variations in morphology and morphometry and to observe the histogenesis. **MATERIALS & METHODS:** This work was conducted on 17 formalin preserved dead fetuses and they are of both sexes between 6 weeks to 40 weeks gestational age and without any congenital anomalies. **RESULTS & CONCLUSIONS:** In the present study all the specimens were pink in colour. These findings on colour are in agreement with that reported in the literature. Minimum length of pancreas observed was 2.4cm and maximum was 4.0cm. The minimum and maximum width of the pancreas at the level of head was 1.0cm and 1.5cm whereas the same at the level of body of pancreas were 0.5 and 1.2cm. Thickness of pancreas at the level of head was ranging between 0.3 to 0.9cm and at the level of body it was 0.2 – 0.6cm. The weight of pancreas ranged from 1.1 grams to 2.5 grams.

KEY WORDS: Pancreas, Islets, Foetus, Histogenesis

INTRODUCTION

Functionally Pancreas is both an exocrine and an endocrine gland. It plays a vital role in nutrition due to the presence of distinct types of glandular tissue. Exocrine Pancreas secretes enzymes and salts into the gut. It consists of acini and duct system. These exocrine secretions play a major role in intraluminal digestion of all varieties of foods. The endocrine pancreas releases hormones into the blood stream that regulates blood glucose level. This is composed of Islets of Langerhans and some other cells in the walls of smaller pancreatic ducts.

Pancreas developed from ventral and dorsal pancreatic buds, these buds originate from the endodermal lining of the duodenum. In the 3rd month of foetal life, pancreatic islets develop from the parenchymatous pancreatic tissue and scatter throughout the pancreas. According to Potter

(1961) Islands of Langerhans are proportionately more numerous in fetuses and infants than in older individuals. Pancreas is a soft lobulated retroperitoneal gland, it extends nearly transversely across the posterior abdominal wall from the duodenum to the spleen behind the stomach, Grays. [1] Parts of pancreas from the right side to the left side head, neck, body and tail. The adult pancreas measures as follows Length 12 to 15 cm, Breadth 3 to 4 cm, Thickness 1.5 to 2 cm, Weight 80 to 90 gms. Pancreas has two ducts Main duct or Duct of Wirsung and Accessory Duct or Duct of Santorini.

Cytogenesis of human fetal pancreas:

The initial survey on pancreatic islet formation in the human fetus was reported by Pearce (1903) who described the development of the islet from the primitive pancreatic tubules. The islets were first identifiable in a 54 mm fetus as clusters of small eosinophilic cells attached to the tubule. Seyfarth (1920) and Nakanura (1924) confirmed the origin of the islets but differed from Pearce (1903) in that they found the first islet in 50 mm and 80 mm fetuses respectively. The occurrence of two cell types in the fetal islet was initially reported by Weich Selbaun and Kryle (1909), while Kardase (1927) described two cell types with in duct system of a 45 mm fetus. The first indication of islet development was noted by Kardasewitch (1927) in a 60 mm fetus. But typical islets were not observed until the 90 mm stage.

In a more recent study on the fetal pancreas Ferner and Stoeckenfus (1951) divided islet development in to three stages Single cell stage in the single cell stage observed in a 130 mm fetus, consisted of alpha cells within the walls and terminal processes of the duct system and beta cells within the walls of the intercalated ducts and terminal processes. Inselfeld stage - In the inselfeld stage single or small groups of cells had accumulated to form islet processes. Montelinsel – In this stage islet processes contained alpha and beta cells and also a rose colored cell with UN granulated cytoplasm.

MATERIALS AND METHODS

This work was conducted on 17 formalin preserved dead fetuses with relevant obstetric records available at the department of anatomy, S.V. Medical College, Tirupati, Andhra Pradesh, India. Two were embryos of less than 12 weeks, which were later subjected to serial sections. Others were from fetuses aged between 16 to 40 weeks. The fetuses were preserved by injecting 10% formalin solution in to the pleural, peritoneal and cranial cavities.

The Pancreas specimens (figure: 01) collected were weighed in simple balance and recorded in grams. The length, width and thickness of pancreas were recorded by using vernier calipers in centimeters. The morphometric parameters were recorded in the data sheet and The Crown-rump (CR) and Crown-heel (CH) lengths and weight of fetuses were also recorded. The pancreatic specimens were categorized into four groups based on gestational age into 0-12 wks, 12.1-24 wks, 24.1 -36 wks and more than 36 wks (table: 01).

Collection of specimens for gross and histological studies:

Two embryos of less than 12 weeks were preserved in formalin and were processed for serial sectioning. Fetuses of more than 12 weeks gestational age were dissected for obtaining pancreas specimen. Abdominal cavity of each fetus was opened and the position, relations, appearance, color and blood supply of the pancreas were observed in situ. The entire duodenum was separated from stomach and jejunum by applying ligatures at both ends to prevent

the spillage of contents. Pancreas along with duodenum and spleen were removed as one unit. Later the duodenum and spleen were separated from the pancreas.

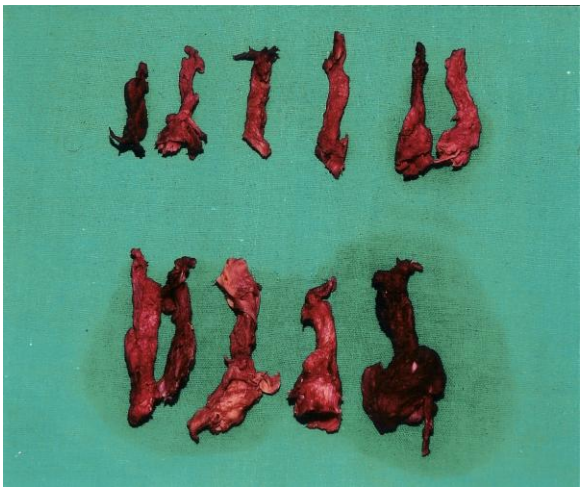

Figure: 01: Picture shows the collected foetal pancreases in different gestational ages.

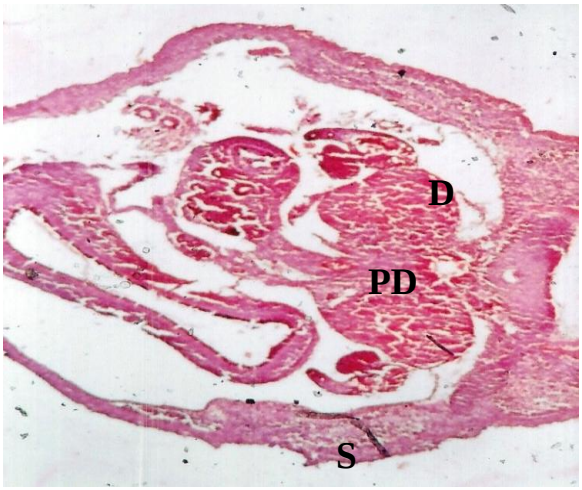

Figure: 02: Picture shows the section of 6-8 weeks embryo consists of developing pancreatic buds, pancreatic ducts (PD), stomach (S) and duodenum (D).

The pancreas specimens collected were categorized according to their gestational ages. One specimen of pancreas from each group was subjected to routine tissue processing method for formalin preserved tissue. The paraffin block of tissue was cut into 6-micrometer thickness and stained with haematoxyline and eosin stains. The sections thus obtained were observed for the microscopic appearance at different gestational ages. The histological sections were photographed by microphotography.

RESULTS

MORPHOMETRIC FEATURES

The collected specimens were measured for length, width and thickness by using the Vernier scale. Weight of the pancreas was measured in grams by using simple balance. The data on various morphometric characters viz. length, width thickness and weight of the pancreas were presented in (table: 02). The length, width and thickness of pancreas were measured in centimeters. The width and thickness were measured at two levels viz. one at the level of head and the other at the level of body of pancreas. In the present study minimum length of pancreas observed was 2.4cm and maximum was 4.0cm. The minimum and maximum width of the pancreas at the level of head was 1.0cm and 1.5cm whereas the same at the level of body of pancreas were 0.5 and 1.2cm. Thickness of pancreas at the level of head was ranging between 0.3 to 0.9cm and at the level of body it was 0.2 – 0.6cm. Average length, width and thickness of pancreas at different gestational ages were represented in (table: 03). There is gradual increase in length with the increase in gestational age excepting in one specimen of 28 weeks gestational age obtained from a female fetus where the length was more (4.0cm) than that observed in specimens of higher gestational age (3.5cm).

Group	Gestational age (wks)	CR length(s)	Number of specimen
1	<12	<3.0	2
2	12.1 -24.0	15 - 20	5
3	24.1 -36.0	20 - 26	6
4	>36	26 - 28	4
TOTAL			17

Table: 01: Distribution of Pancreas specimens According to Groups

S. No	Age/ Weeks	Sex	CR length in CM	CH length in CM	Weight of pancreas Grams	Measurements			Weight of foetus in grms
						Length cm	Width cm	Breath cm	
1	16	Male	15	16	1.2	3.3	Head-1.4 Body-0.9	Head-0.7 Body-0.4	400
2	16	Male	16	18	1.1	3.0	Head-1.3 Body-0.8	Head-0.7 Body-0.5	450
3	20	Female	32	36	2.5	3.5	Head-1.5 Body-0.9	Head-0.8 Body-0.5	1000
4	20-23	Male	24	28	2.2	2.6	Head-1.1 Body-0.7	Head-0.5 Body-0.2	1100
5	24	Male	20	24	2.4	2.8	Head-1.3 Body-0.8	Head-0.9 Body-0.6	1000
6	26	Female	18	20	0.9	2.7	Head-1 Body-0.5	Head-0.4 Body-0.2	700
7	28	Female	20	22	1.0	3.2	Head-1.4 Body-0.8	Head-0.6 Body-0.4	900
8	28	Female	24	32	1.2	3	Head-1 Body-0.5	Head-0.5 Body-0.3	850
9	28-30	Female	22	25	1.7	4	Head-1.5 Body-1	Head-0.8 Body-0.6	1500
10	30	Female	26	33	0.6	3.5	Head-1.5 Body-1.2	Head-0.3 Body-0.5	1100
11	32	Female	20	25	0.7	2.4	Head-1 Body-0.6	Head-0.7 Body-0.4	2600
12	38	Female	27	34	2.2	2.8	Head-1.2 Body-0.5	Head-0.5 Body-0.3	2000
13	38	Female	26	32	1.9	2.7	Head-1.2 Body-0.5	Head-0.5 Body-0.3	1600
14	38	Female	26	30	2.4	2.6	Head-1.2 Body-0.5	Head-0.6 Body-0.3	2000
15	full term	Female	23	29	2.4	3.0	Head-1.4 Body-0.7	Head-0.6 Body-0.3	2800

Table: 02: Morphometric parameters of Length, width, thickness and weight of the pancreas.

Group	Gestational ages	Length		Width		Thickness	
		Range	Average	Range	Average	Range	Average
1.	12.1-24.0	2.6-3.5	3.04 (n=5)	H 1.1-1.5 B 0.7-0.9	H 1.32 B 0.8	H 0.5-0.9 B 0.2-0.6	H 0.7 B 0.4
2.	24.1-36.0	2.4 - 4.0	3.1 (n=6)	H 1.0-1.5 B 0.5-1.2	H 1.2 B 0.6	H 0.3-0.8 B 0.6	H 0.2-06 B 0.6
3.	36.1-fultern	2.6-3.00	2.7 (n=4)	H 1.2-1.4 B 0.5-0.7	H 1.2 B 0.7	H 0.5-0.6 B 0.3-0.6	H 0.5 B 0.3

Table: 03: Averages of Length, Width and Thickness of pancreas Specimens

Sl. No.	Gestational age in Weeks	Average weight of the foetus in gms	Average weight of the pancreas in gms	Ratio	Percentage
1.	16 Weeks (2)	450	1.15	1:391	0.25%
2.	20 Weeks (2)	1050	2.2	1:477	0.20%
3.	24 Weeks (1)	1000	2.4	1:416	0.24%
4.	26 Weeks (1)	700	0.9	1:777	0.12%
5.	28 Weeks (2)	850	1.1	1:772	0.12%
6.	30 Weeks (2)	1300	1.2	1:1083	0.09%
7.	32 Weeks (1)	2600	2.4	1:1083	0.092%
8.	38 Weeks (3)	1.900	2.1	1:904	0.11%
9.	Full term	2800	2.6	1:1166	0.09%

Table: 04: Ratio of Foetal weight and Pancreas weight at different gestational ages

Ratio of Foetal weight and Pancreas weight at different gestational ages shown in (Table: 04), There is gradual increase in the organ weight at different groups with the increase in foetal weight. When average weight of pancreas at different gestational ages was compared with the body weight of fetus there is gradual increase in the ratios between the two except in one female fetus of 32weeks where the proportion was 1: 3714.

HISTOLOGICAL OBSERVATIONS

8 – 10weeks: The specimen was 30 mm CR length female embryo. The pancreatic parenchyma consisted of multiple branched epithelial tubules that terminated distally either as solid cords or as small clumps of cells. These findings are in agreement with those reported in the literature by Cirea and Conklin (1962). The cytoplasm of the bud cells was basophilic in nature. Few para tubular buds were observed which were loosely differentiated. Most probably these may be islet cells. (Figure: 02) shows the section of 6-8 weeks embryo consists of developing pancreatic buds, pancreatic ducts, stomach and duodenum

16 – 18 weeks: Few groups of undifferentiated cells were seen. The parenchyma had begun to organize into lobes and lobules with abundant mesenchymal tissue surrounding it (Figure: 03). The islets were small and mainly spherical, well-defined constituents of pancreatic parenchyma (Figure: 04).The cells of islets were aggregated in the centre in clusters with a wide peripheral space. The mesenchymal connective tissue formed an ill-defined capsule around the islets. The H&E stain showed the presence of more number of alpha cells than beta cells. Capillaries were not seen with in the islets but were present in the surrounding mesenchyme.

28 - 30 weeks: The intra lobular connective tissue was well differentiated while the inter lobular one still had some mesenchymal cells. The ducts were better formed and the connective tissue condensation was visible around the ducts though not very compact. The islets were markedly increased in number and widely distributed (Figure: 05). Some were lying close to acini while an occasional one seen within the inter lobar connective tissue. Acini are fully formed and are arranged in groups separated by connective tissue. Ducts are numerous and still showing signs of budding. Large islets were seen scattered all over in relation to blood vessels and clusters of acini.

36 weeks: Well-defined pancreatic architecture was seen at this stage. Some amount of undifferentiated mesenchymal tissue was seen. Islets were large and prominent and more concentrated towards the tail region. These findings are more or

less in agreement with those reported in literature.

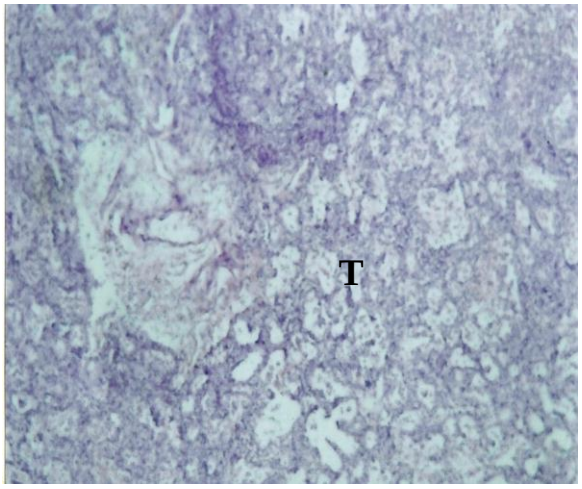

Figure: 03:16 weeks pancreatic H&E section showing tubular cells budding (T) magnification 10 ×10 X.

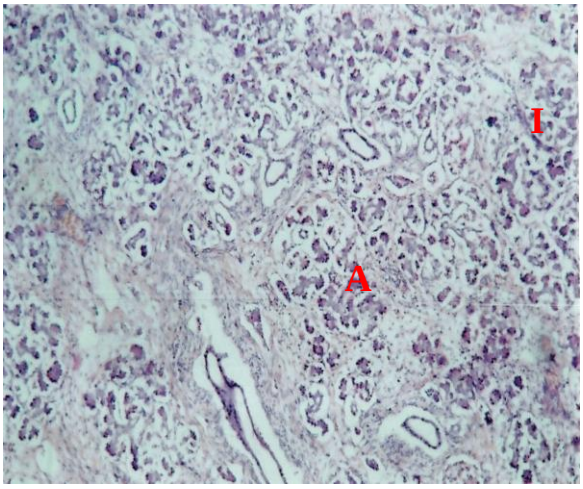

Figure: 04: 18 weeks of pancreatic section showing Acini (A), Islets (I), magnification 10 ×10 X.

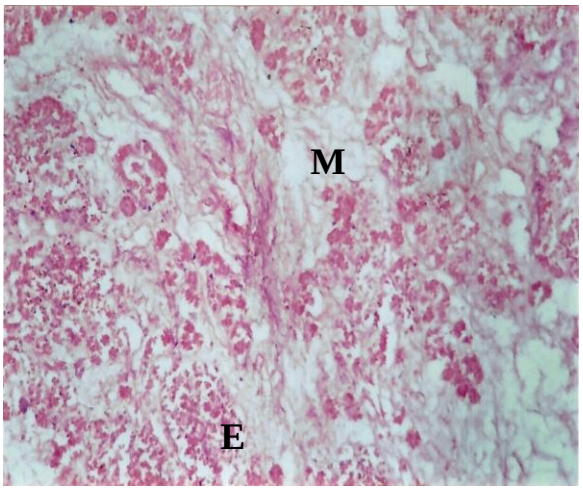

Figure: 05: 28 weeks of pancreatic section showing endocrine tissue (E) and Mesenchyme (M) magnification 10 ×10 X.

DISCUSSION

A study of Bensley [2] in guinea pigs described that both acini and islets of pancreas have separate origin from tubules and overlapping of islets and acinar cells sometimes gives an intermediate picture that might suggest a transformation between the two. Vincent [3] on human fetal pancreas although reported the development of islets and acini from tubules but inferred that transition from islets to acini or vice-versa can occur and developmentally they are not independent structures. Bencosme [4] however found that the mature islets develop from differentiated acini and not from the tubules. According to Elayat [5] Structural organization of cells of islet in different species has a functional significance. The study by Saito on human adult pancreas reported highest volume density of islets in tail region of pancreas.

According to Achaya and Anand [6] in 8-11 weeks: (30-65mm) throughout the phase of the fetal period there is an increase in the number of epithelial buds at many sites along the duct system. Early in the period, certain of the cell buds along the course of the tubule system and the cells of terminal buds gradually acquire a basophilic cytoplasm. Nucleoli are not visible in the duct epithelium at this stage and the nuclei are darkly stained. According to Gupta [7] in11-12.5 weeks (65-90mm CR) the interval between adjacent tubule is filled by a loose stoma of argyrophilic fibers. The cell buds increase in size by cellular proliferation and by the end of the period, Para tubular cell buds from adjacent tubules begins to merge

with each other. Many of these expanding cell buds grow towards capillaries within the stroma and as the buds undergo fusion as the capillaries become enveloped with in a mass of cells at 85 mm stage of fetus. This gives rise to the configuration of a cord like clusters of cell penetrated by a capillary bed and corresponds to the Inselfeld stage of Neubert (1927). Robb [8] stated the primitive islets budding out from tubules, evident in the youngest fetus (12 weeks)

According to Conklin [9] in 14.5-17 weeks (110-150mm CR) stage the acinar epithelium demonstrates the greatest change. The cytoplasm of these cells becomes basophilic. The alpha cells are observed to undergo similar morphological changes. Sandler [10] reported a positive correlation between the pancreatic insulin content and crown rump length. Dense aggregations of granules were seen in A and B cells of at the age of 22 – 24 week fetuses.

CONCLUSION

The present study concluded the morphometric results of foetal pancreas and also the pancreatic parenchyma consisted of multiple branched epithelial tubules observed in 8-10 weeks, the parenchyma had begun to organize into lobes and lobules with abundant mesenchymal tissue and the cells of islets were aggregated in the centre in clusters with a wide peripheral space in 16-18 weeks, the islets were markedly increased in number and widely distributed and acini are fully formed and are arranged in groups separated by connective tissue In 28-30 weeks.

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