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MICROSCPOIC AND MORPHOMETRIC STUDY OF HUMAN FETAL PANCREAS

Anatomy

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ABSTRACT

Background and Aim: Pancreas is unique for its dual role of exocrine and endocrine function, well known for its association with Diabetes mellitus, a very common endocrine disorder. The research of fetal pancreas has great implication in clinical practice and treatment protocol as it is a suitable organ for transplantation in patients of insulin dependent diabetes mellitus as cell replacement therapy.
Aim of this study was to observe the gross anatomical and light microscopic changes undergone by human fetal pancreas in its different developmental stages.
Materials and Methods: The present study was conducted on 24 fresh aborted human foetuses belonging to both sexes obtained from the Department Of Obstetrics And Gynaecology, Institute of Maternal and Child Health (IMCH) Calicut. After noting the gross anatomical features of the tissue bits, light microscopic and morphometric study was conducted. Statistical analysis was done using SSPS16.
Results: Early fetal pancreas differed considerably from the near term foetuses in the acini appearance, islet size and distribution of connective tissue which was discussed in details.
Conclusion: The various changes observed in the exocrine and endocrine parts of pancreas of human foetuses belonging to different gestational age will help research scholars and is of utmost importance in its implication in replacement therapy.

KEYWORDS

Human Fetal Pancreas, Islets , Acini

INTRODUCTION

The pancreas (pan= all; kreas = flesh) is a soft lobulated retroperitoneal organ, occupying epigastrium and left hypochondrium measuring about 12-15 cms and weighs 80-90 gms. The main bulk of the gland is constituted by its exocrine part which is in the form of serous, compound tubulo-alveolar gland, embedded in this exocrine part are the pancreatic islets of endocrine cells of langerhans most numerous in the tail region of pancreas.

The organ is best known for its association with diabetes, which is probably the oldest known endocrine disorder. The various cell populations of the islets, especially the beta cells owing to its essential role in glucose regulation and general metabolism implications have attracted many research scholars. The therapy of diabetes has undergone many transitions from various types of diets, insulin, oral hypoglycemic drugs and more recently, to islet cell transplantation and stem cell treatment. The human infant and fetal pancreas are a potential source of islet tissue for transplantation. However it is crucial to identify an appropriate stage of fetal pancreas development that will be an optimal transplant material. This study aims at studying the gross anatomy and histogenesis of pancreas in human foetuses in view of existing literature.

MATERIALS AND METHODS

The present study was conducted on 24fresh aborted human foetuses belonging to both sexes obtained from the Labour room, IMCH, Calicut. The age of the foetuses were calculated from obstetrical history and crown-rump length (CRL). In all the foetuses, a cruciate abdominal incision was made and fixed in 10% formal-saline, for 1 – 2 hours. The pancreas was then dissected out, the length and weight noted. Tissue bits were taken from the 3 regions of each pancreas – head, body and tail. The bits were fixed in 10% formal saline for 48 – 72 hours and then processed for paraffin sections. The tissue sections were stained with haematoxylin and eosin and studied under binocular compound light microscope and microphotography was done. Statistical analysis of the different parameters was done using SPSS 16. The various tests used were Pearson Correlation test, ANOVA (Analysis of variants) and Independent t test.

RESULTS

The specimens were divided into 3 groups;
Group 1 (10^{th} to 20^{th} week) –The length of the pancreas ranged from 1.5cm to 2.5 cm. The weight of the pancreas ranged from 10 gms to 19 gms. The pancreatic parenchyma consisted of mesenchymal tissue in which were embedded, numerous branched tubules with wide lumen. The tubules were lined by simple cuboidal epithelium with large vesicular nuclei. At various places along the tubules, budding was seen, probably forming primitive acini and islets. The typical acinar pattern of the parenchyma couldn't be recognized. Abundant mesenchymal connective tissue masked the organization of parenchyma into lobes and lobules. The endocrine islets could be well appreciated as small, mainly spherical masses of cells which were well vascularised. The cells were round or oval in shape and had a dark nucleus. The islets appeared larger probably because of the poorly developed acinar tissue. The number of cells per islet was more in the tail region as compared to head and body of pancreas.

Group 2 (21^{st} to 30^{th} week) – The length of the pancreas ranged from 2.7cm to 3.5 cm and the weight ranged from 20 grams to 25 grams. The parenchyma showed organisation into lobes and lobules. The mesenchymal connective tissue was reduced. The sections of tubules were reduced as these were differentiated into ducts, both intralobular and inter lobular. Acinar formation could be appreciated though the typical adult pattern was not observed. The islets were larger and well encapsulated. The largest fetal islets could be seen during this period of fetal development. The islets were seen in close relation to the duct system. The islets were richly vascularised. Different types of cells constituting the islets were seen, but could not be differentiated with the H & E staining. The number of cells per islet was more in the tail region as compared to head and body of pancreas.

Group 3 (31^{st} to 40^{th} week) – The length of the pancreas ranged from 3.6 cm to 4 cm. The weight of the pancreas ranged from 29 grams to 35 grams. As the fetal age advanced the connective tissue decreased and the acini became more typical with pyramidal cells. A definite lobular pattern was present. Centroacinar cells could be seen. The ducts were better formed with some connective tissue condensation around them. The section appeared to be highly vascular. The islets were seen as well defined spherical pale staining areas among the exocrine "ocean" of the pancreas. The number of islets increased and many of them were seen in close relation to the duct system. The size of the islets decreased in all the 3 regions of pancreas studied .This decrease was found to be statistically significant using Pearson correlation test. The islets were more in the sections from the tail region of the pancreas. The number of cells per islet of all 3 regions decreased compared to the midgestational foetuses. The islets in tail region appeared to be larger and they contained more number of cells than islets in the head and body of the pancreas.

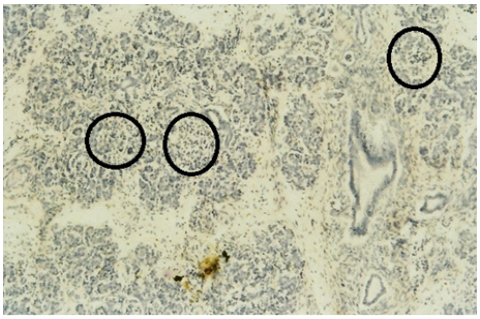

Fig:1 Section of the pancreatic body region of a 14 week fetus showing numerous cross section of primitive tubules.Well developed are the islets.Haemetoxylin and Eosin staining. Magnification x 100

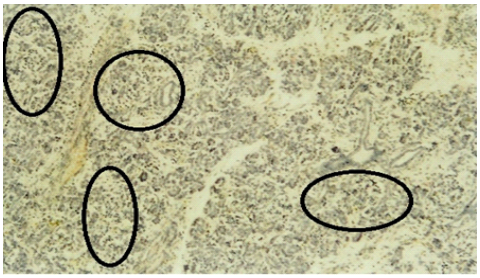

Fig:2 Section of the pancreatic tail region of a 14 week fetus showing islets and numerous cross section of primitive tubule. Haemetoxylin and Eosin staining. Magnificationx100.

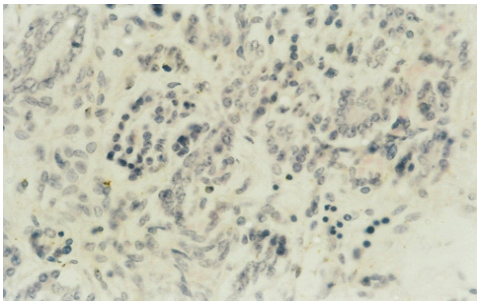

Fig:3 Different cells constituting an Islet of 14 week fetus. Haemetoxylin and Eosin staining. Magnification x400.

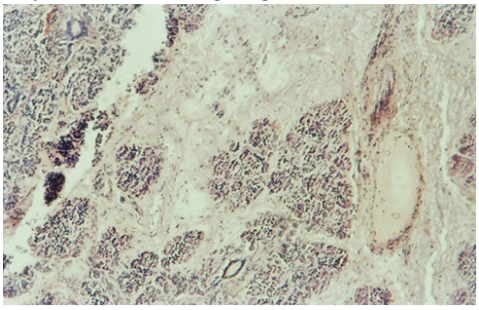

Fig:4 Section of the pancreatic body region of a 18 week old fetus.Note the abundant connective tissue. Haemetoxylin and Eosin staining. Magnification x100

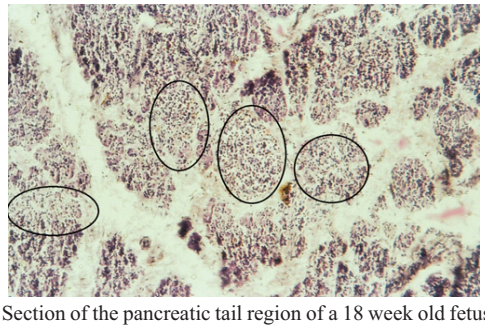

Fig:5 Section of the pancreatic tail region of a 18 week old fetus.Note the many islets.Typical acini not found. Haemetoxylin and Eosin staining. Magnification 10X.

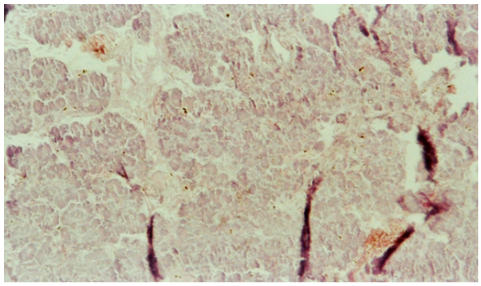

Fig:6 Developing acini in the pancreas of a 24 week fetus. Haemetoxylin and Eosin staining. Magnification X100.

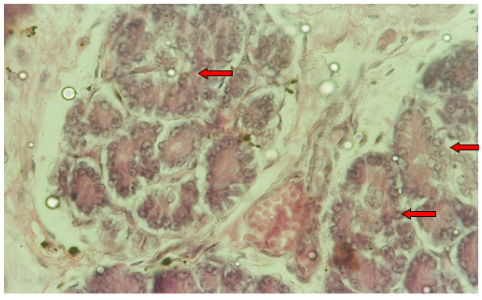

Fig:7 Developing acini of a 24 week fetus. Haemetoxylin and Eosin staining. MagnificationX 400.

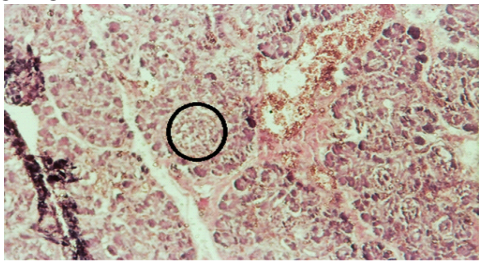

Fig : 8 Section of the pancreatic body region of a 38 week fetus.Islets with surrounding acini seen. Haemetoxylin and Eosin staining. Magnification x100.

Table : 1 , Table showing the distribution , size and umber of cells per islet in diffrent regions of pancreas.

Age (weeks)	Sex	No:of Islets /LPF			Greatest diameter of Islet			Averageno:of cells per islet		
		A	B	C	A	B	C	A	B	C
14	F	2 - 3	3 - 4	3 – 4	60	80	100	110	115	130
16	M	2-3	3 - 4	3-4	58	65	85	115	120	158
16	M	2 - 3	3 - 4	2 -3	55	50	95	118	110	170
17	M	2 - 3	2 - 3	4 – 5	60	95	115	110	160	220
18	F	1 - 2	2 - 3	3-4	75	95	105	130	150	200
18	M	2-3	2-3	3-4	80	90	95	125	160	195
19	M	2 - 3	2 - 3	4 – 5	70	90	95	130	155	195
20	F	1-2	2-3	4-5	75	80	90	130	125	160
20	M	1 - 2	2 - 3	3-4	75	70	80	125	110	110
23	F	1 - 2	2 - 3	4 – 5	50	45	65	110	118	108
23	M	1 - 2	3-4	3-4	45	25	45	88	90	90
24	F	2 - 3	2 - 3	3-4	25	55	65	60	110	100
26	F	2-3	2-3	3-4	30	50	70	70	100	100
27	M	2-3	2-3	3-4	30	40	60	65	110	110
28	M	2 - 3	1- 2	3 - 4	35	30	70	60	110	120
30	F	1-2	1-2	3-4	35	35	75	65	100	115
30	M	1-2	1-2	4-5	30	40	75	75	95	100
32	M	0 - 1	1- 2	3 - 4	30	40	80	90	90	120
33	M	1 - 2	1- 2	3- 4	40	45	55	94	94	135
35	F	0-1	2-3	3-4	40	40	55	90	95	120
36	M	1-2	1-2	3-4	35	35	50	95	100	110
38	F	1 - 2	2-3	4- 5	35	35	55	95	105	120
40	M	1 - 2	1- 2	4 - 5	50	40	60	100	100	110
40	F	1-2	1-2	4-5	55	45	60	105	100	105

A-Head region of pancreas ; B- Body of Pancreas ; C- Tail of pancreas

DISCUSSION

The pancreas measured 1.5cm in the youngest foetus studied (14 weeks). As the age of the foetus advanced the pancreas showed an increase in length reaching up to 4cm in the full term foetus. The weight of the pancreas also showed a positive linear relationship with gestational age of the fetus.

In group 1 and group 2 foetuses studied, typical acini consisting of pyramidal cells arranged around a small lumen could not be seen. Instead, there were numerous branched tubules lined by simple cuboidal cells with wide lumen. They were embedded in the mesenchymal tissue. Budding of the tubules were evident in group 2 foetuses and early group3 foetuses. James L. Conklin[1] in his study on human foetuses of various age groups has reported that, at the beginning of the fetal development, the pancreatic parenchyma consists of a system of multibranched epithelial tubules which terminate distally either as solid cords or as small clumps of cells which ultimately give rise to both acinar and islet epithelium. This picture persisted up till about 15 weeks of gestation. L. I. Falin[2] and Gupta, et.al.,[3] has also noted a similar picture of primitive pancreatic tubules, which ultimately give rise to the ducts, acini and the pancreatic islets.

The presence of acini and centroacinar cells in early foetuses less than 20 weeks of gestation has been observed by some investigators[1]. In the present study beginning of acini formation with centroacinar cells could be identified in group2 foetuses but typical acini with pyramidal cells and centroacinar cells were observed only in group3 foetuses. This is similar to the observations made by M. Laito et.al.,[4] and Liu and Potter[5] who supports the observation of acini in midtrimester foetuses and older.

Present study observed abundant connective tissue in younger foetuses and hence the lobar and lobular arrangement of the pancreas was not fairly well appreciated. There were many undifferentiated cells in the connective tissue. As the age of the foetus increased, the connective tissue component decreased and then the lobar and lobular arrangement became more evident in group 2 and 3 foetuses. It resembled more of an adult pattern by about 24 week's fetal age. Organisation of pancreatic parenchyma into well defined lobes and lobules occur by 12 weeks as per Clark and Grant[6] and by 14 – 15 weeks as per others[1,3]. The progressive decrease in the interstitial connective tissue with age of the fetus and rapid maturation of the exocrine acini which begins by midgestation has been attributed a reason for observing organized lobular pattern in midgestational and older foetuses[4].

The exact time at which the islets of Langerhans make their first appearance in the pancreas of the human foetus has been a topic of study by many workers[7,8,9]. This aspect in the study of human pancreas is significant because the selection of an appropriate developmental stage of fetal pancreas is of paramount importance for the successful transplant of pancreas in patients of insulin dependent diabetes mellitus. The time is 12th – 14th week of human fetallife[7] and a much earlier period, 10th – 11th weeks [8]. Since the islets of Langerhans were present even in the youngest foetus of 14 weeks studied, any comment on the time of appearance of islets in this study could not be made.

The primitive islets are said to be formed from primitive pancreatic tubules[1,3,8,9]. The islets during early stages of development were connected to the tubules by a cord of cells[1,3,9]. In the present study too the close proximity of islets to the tubules could be appreciated. The observation of islets before typical acinar formation is in accordance with Seyfarth[8] who suggested the inductive effect of islets on the acinar development.

Cells differing in the staining properties of their nucleus and cytoplasm could be seen within the islets of all the fetal groups but the cell types could not be differentiated into alpha, beta and delta cells with haematoxylin and eosin staining. The identification of alpha and beta cells of islets at 12 weeks of age has been reported[1,3,9].

The rich vascular supply of the islets is an important factor that helps in their function[1,9]. The islets irrespective of the groups were found to be richly provided with sinusoids and capillaries. The presence of rich capillary supply in the islets of young foetuses suggests that the secretion of insulin and glucagon begins during the earliest stages of human embryonic development, soon after formation of the islets and differentiation of their cells.

On comparing the head, body and tail region of the pancreas it could be seen that the islets were concentrated towards the tail of the pancreas in all the groups studied. This is in accordance with the previous studies[3,10]. The average number of islets per low power field in the head and body were more in group1 and early group 2 foetuses compared to group 3. This can be due to the formation of new islets from the walls of small ducts lying in the head and body of pancreas up till midgestation[2]. There after the distribution gradually resembled that of adults. The islets measured larger in group 1 and 2. The sizes of the islets were decreased with the development of the acinar tissue in older foetuses.

CONCLUSION

This study conducted on 24 human foetuses have observed various developmental changes occurring in the gross anatomy and histogenesis of human pancreas .The light microscopic study shows that it is endocrine cells of Islets of pancreas that first differentiate followed by the pancreatic acini which has got a functional correlation. The changes observed in the number, size and distribution of fetal islets will be helpful to anatomists and other research scholars. The near term fetal pancreas shows a picture similar to adult pancreas. So a light microscopic study of childhood and adult pancreas and observing the changes in the exocrine and endocrine parts with increasing age can further augment this study.

REFERENCES

1. Conklin,J. A."Cytogenesis of human fetalpancreas". Amer. Jl. Anat.(1962)111:181 – 193.
2. Falin,L. I. "The development and cytodifferentiation of the islets of Langerhans in human embryos and foetuses". Acta Anat.(1967) 68: 147 – 168,
3. Gupta,V., Garg,K., Raheja,S. And Tuli,A. "The histogenesis of islets in the human fetal pancreas". J. Anat. Soc. India (2002). 51 (1) : 23 – 26.
4. Laito. M, Robert Lev, Donald Orlic. The developing human pancreas : an ultra structural and histochemical study with special reference to exocrine cells. Jl. of Anat 117 : 619 – 634,1974.
5. Liu H. M., Potter E. L. (1962). Development of the human pancreas. Arch,Pathol;74:439-452. Cited in Williams Textbook of Endocrinology 9th Edition pp. 1286.
6. Clark,A. and Grant,A. M (1983). Diabetologia 25:31 – 35. Cited in J. Anat. Soc. India 51 (1): 23 – 26, (2002).
7. Gartier,E. E.. Pancreatic gland of human foetuses and newborn children. Acta. Anat(1900) 68: 147 – 168,1967.
8. Seyfarth,C., Gustav Fischer, Jena. Cytogenesis of human fetal pancreas. Amer. Jl. Anat(1920)111:181 – 193.
9. Robb,P. The development of the islets of Langerhans in man. Arch. Dis. Child. 36: 229, 1961.
10. Elayat,A., Naggar E., Mostafa M., An immunocytochemical and morphometric study on the pancreatic islets. Jl. of Anatomy,(1995), 186: 629 – 637.