



A STUDY ON HUMAN CADAVERIC PANCREAS: VARIATIONS IN NUMBERS OF ISLETS OF LANGERHANS IN DIFFERENT AGE GROUP

Baro Banerwar	Associate Professor, Department of Anatomy, Diphu Medical College, Diphu, Karbi Anglong, Assam, India,
Sarma Usha	Professor, Department of Pathology, Gauhati Medical College, Guwahati, Assam, India
Talukdar KL	Ex-HOD, Department of Anatomy, Gauhati Medical College, Guwahati, Assam & Principal, MGM Medical College and LSK Hospital, Kishanganj, India
Dutta BC	Professor and HOD, Department of Anatomy, Diphu Medical College, Diphu, Karbi Anglong, Assam, India
Rabha Gunamani*	Assistant Professor, Department of Anatomy, Diphu Medical College, Diphu, Karbi Anglong, Assam, India*Corresponding Author

ABSTRACT

INTRODUCTION: Pancreatic islets (of Langerhans) constitute the endocrine component of the pancreas. The human pancreas may contain more than a million islets distributed throughout the gland but most numerous in the tail. **MATERIALS AND METHODS:** This descriptive and cross-sectional study was done in the Department of Anatomy, Forensic Medicine & Pathology of Gauhati Medical College, Guwahati from May, 2016 to December 2019, based on collection of 103 human pancreas aging from 13 to 78 years of both sexes. The collected samples were divided into seven age groups: A (10-19 years), B (20-29 years), C (30-39 years), D (40-49 years), E (50-59 years), F (60-69 years) and G (≥ 70 years). **RESULTS :** The number of islets per unit area of the head of the pancreas were 1.4 ± 0.55 , 1.4 ± 0.55 , 1.2 ± 0.45 , 1.00 ± 0.00 , 1.80 ± 0.45 , 1.00 ± 0.00 and 1.40 ± 0.55 ; in the body 1.2 ± 0.45 , 2.6 ± 0.55 , 1.6 ± 0.55 , 2.60 ± 0.55 , 2.20 ± 0.45 and 1.40 ± 0.55 ; in the tail region 2.4 ± 0.55 , $2.2 \pm 0.1.3$, 2.6 ± 0.55 , 2.80 ± 1.10 , 2.00 ± 1.41 , 3.20 ± 0.84 and 3.60 ± 0.55 in group A, B, C, D, E, F and G respectively. **CONCLUSIONS:** The number of the islets was much higher in the tail part than the body and head region. Racial variation and geographical distribution may attribute dissimilarities among different age group.

KEYWORDS : Islets of Langerhans, Pancreas, different age group, variations in number

INTRODUCTION

Pancreatic islets (of Langerhans) constitute the endocrine component of the pancreas. The human pancreas may contain more than a million islets distributed throughout the gland but most numerous in the tail.¹ Pancreatic islets may contain a few cells or many hundreds of polygonal cells arranged in short irregular cords that are abundantly invested with a network of fenestrated capillaries.² Specifically, the total mass of pancreatic beta cells is a critical factor in the regulation of glucose homeostasis.³

In haematoxylin and eosin (H & E) stained sections, the islets of Langerhans appear as cluster of pale staining cells surrounded by more darkly staining pancreatic acini.^{4,5} The pancreatic islet function is closely associated with the morphologic changes in islet cells.⁶ The most common disease of the endocrine pancreas is diabetes mellitus associated with changes in the size and number of islets.^{7,8} Moreover, male population predominantly suffers from diabetes mellitus.⁹

Recently, islet cells were successfully generated in vitro from human pancreatic stem cells.⁹ However, sufficient investigation has not been made into how many islets are contained in a unit volume of pancreas, or how differently they behave in their size distribution and still there are scopes to gain insight into their functional relationships and changes in disease process.¹⁰ Scientists have made many advances in islet transplantation in recent years. However, most recipients returned to using insulin because the transplanted islets lost their ability to function over time. Besides, the researchers also noted that many transplant recipients were able to reduce their need for insulin, achieve better glucose stability, and reduce problems with hypoglycaemia.¹¹

It is important to study the beta cell mass of pancreas to know

the endocrine function of pancreas. Hence histology is the gold standard to determine the beta cell mass. Literature in this regard is very scanty from this part of the country (North East India). That is why the study was carried out to calculate the average numbers of islet of langerhans in different locations of pancreas on routine histology and to observe if any variability exists in the study population.

MATERIALS AND METHODS

This descriptive and cross-sectional study was conducted in the Department of Anatomy, Forensic Medicine & Pathology of Gauhati Medical College, Guwahati from May, 2016 to December 2019. A total of 103 specimens of human pancreas were collected from 13 to 78 years age of both sexes, excluding any visible signs of pathological changes of the viscera, any doubtful injury in pancreas, death due to known poisoning, pancreatic diseases and specimens of medicolegal cases. Simple random samplings were used for sampling method.

The collected samples were divided into seven age groups: A (10-19 years), B (20-29 years), C (30-39 years), D (40-49 years), E (50-59 years), F (60-69 years) and G (≥ 70 years), for convenient description of their various age related changes (according to Varley et al.).¹²

Preparation of the slides: Selection of the tissue was done according to Wolfe-Coote & duToit,¹³ and 3 mm \times 3 mm were cut with scissors for histological study (table 1). The histological slides were prepared by using standard procedure with Harris' Haematoxylin and Eosin (H & E) stain.

Counting and calculation of number of islets of Langerhans in head, body and tail regions: Slides were reported using a compound microscope (Olympus CH20, Singapore). Five best prepared and stained slides were taken from each of the regions (i.e. head, body and tail) of each group. Finally a total

of 105 slides were observed. The slides were focused under low magnification (×10 objectives, ×10 eyepiece) to count the number of islets. The average number of islets per unit area of microscopic field for each slide was calculated and their mean is recorded.

Statistical analysis of data: Data were collected and appropriate statistical analyses were done by using IBM SPSS version 26. Paired sample t-test was conducted to check for significant difference in the average number of islets in head, body and tail. A p-value of less than 0.05 indicates significant difference in the average number of islets between two groups.

Ethical clearance: The study was approved by the Institutional Ethics Committee of Gauhati Medical College, Guwahati. Written informed consent had been taken in English as well as in local languages from the attendants and permission from concerned authority of post mortem cases.

RESULTS

Number of Islets of Langerhans in the head of the pancreas: The mean number of islets in the head of the pancreas were 1.4 ± 0.55 , 1.4 ± 0.55 , 1.2 ± 0.45 , 1.00 ± 0.00 , 1.80 ± 0.45 , 1.00 ± 0.00 and 1.40 ± 0.55 in group A, B, C, D, E, F and G respectively. The differences were statistically significant in C vs E, D vs E and E vs F (table 9 and 10).

Number of Islets of Langerhans in the body of the pancreas: The mean number of islets in the body of the pancreas were found 1.2 ± 0.45 , 2.6 ± 0.55 , 1.6 ± 0.55 , 2.60 ± 0.55 , 2.60 ± 0.55 , 2.20 ± 0.45 and 1.40 ± 0.55 in group A, B, C, D, E, F and G respectively. The differences were statistically significant in A vs B, A vs D, A vs E, A vs F, B vs C, B vs G, C vs D, C vs E, C vs F, D vs G, E vs G and F vs G (table 9 and 10).

Number of Islets of Langerhans in the tail of the pancreas: The mean number of islets of in the tail of the pancreas in different group was 2.4 ± 0.55 , 2.2 ± 0.13 , 2.6 ± 0.55 , 2.80 ± 1.10 , 2.00 ± 1.41 , 3.20 ± 0.84 and 3.60 ± 0.55 . in group A, B, C, D, E, F and G respectively. The differences were statistically significant in A vs G, B vs G, C vs G and E vs G groups (table 9 and 10).

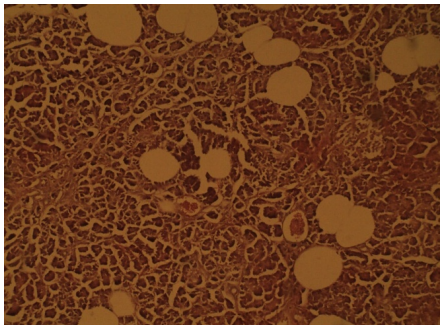


Figure 1: Islets of Langerhans in the head part of pancreas under low power microscope

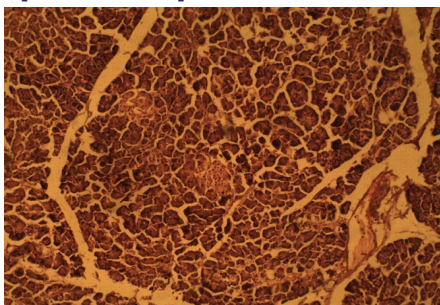


Figure 2: Islets of Langerhans in the body part of pancreas under low power microscope

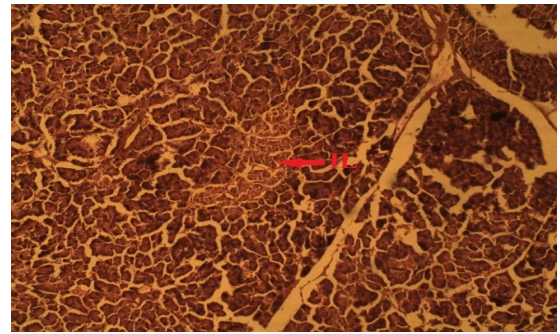


Figure 3: Islets of Langerhans in the tail part of pancreas (Low power, IL= Islets of Langerhans)

TABLE – 1 LOCATION OF THE TISSUES COLLECTED FROM EACH SAMPLE

Parts	Head	Body	Tail
Area	1 inch proximal to tail end from horizontal portion of pancreas lateral to superior mesenteric vessels.	Apparently central region.	Portion lying between inner curve of second part of duodenum and superior mesenteric vessels.

TABLE – 2 ANALYSIS REPORT OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP A (10 to 19 Years):

Slide No	Head	Body	Tail
1	2	1	2
2	1	1	3
3	1	1	3
4	1	2	2
5	2	1	2
Sum	7	6	12
Mean	1.4	1.2	2.4
SD	0.55	0.45	0.55

TABLE – 3 ANALYSIS REPORT OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP B (20 to 29 Years):

Slide No	Head	Body	Tail
1	1	3	1
2	2	3	1
3	1	2	3
4	2	2	2
5	1	3	4
Sum	7	13	11
Mean	1.4	2.6	2.2
SD	0.55	0.55	1.3

TABLE – 4 ANALYSIS REPORT OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP C (30 to 39 Years):

Slide No	Head	Body	Tail
1	2	2	3
2	1	2	2
3	1	1	3
4	1	2	2
5	1	1	3
Sum	6	8	13
Mean	1.20	1.60	2.60
SD	0.45	0.55	0.55

TABLE – 5 ANALYSIS REPORT OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP D (40 to 49 Years):

Slide No	Head	Body	Tail
1	1	2	2
2	1	3	2
3	1	3	4
4	1	2	4
5	1	3	2
Sum	5	13	14
Mean	1.00	2.60	2.80
SD	0.00	0.55	1.10

TABLE – 9 NUMBER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN DIFFERENT AGE GROUP

Group (n)	Number of islets of Langerhans per unit area of microscopic field		
	Head Mean±SD	Body Mean±SD	Tail Mean±SD
A (5)	1.4±0.55 (1-2)	1.2±0.45 (1-2)	2.4±0.55 (2-3)
B (5)	1.4±0.55 (1-2)	2.6±0.55 (2-3)	2.2±0.1.3 (1-4)
C (5)	1.2±0.45 (1-2)	1.6±0.55 (1-2)	2.6±0.55 (2-3)
D (5)	1.00±0.00 (1-1)	2.60±0.55 (2-3)	2.80±1.10 (2-4)
E (5)	1.80±0.45 (1-2)	2.60±0.55 (2-3)	2.00±1.41 (1-4)
F (5)	1.00±0.00 (1-1)	2.20±0.45 (2-3)	3.20±0.84 (2-4)
G (5)	1.40±0.55 (1-2)	1.40±0.55 (1-2)	3.60±0.55 (2-4)

TABLE – 10 NUMBER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN DIFFERENT AGE GROUP

Comparisons of groups	Number of p-Value in the different parts of pancreas		
	Head p-Value	Body p-Value	Tail p-Value
A vs B	1.00	<0.01	>0.50
A vs C	>0.50	>0.20	>0.50
A vs D	>0.10	<0.01	>0.40
A vs E	>0.20	<0.01	>0.50
A vs F	>0.10	<0.10	>0.10
A vs G	1.00	>0.50	<0.01
B vs C	>0.50	<0.05	>0.50
B vs D	>0.10	1.00	>0.40
B vs E	>0.20	1.00	>0.80
B vs F	>0.10	>0.20	>0.10
B vs G	1.00	<0.10	<0.05
C vs D	>0.30	<0.05	>0.70
C vs E	<0.10	<0.05	>0.40
C vs F	>0.30	<0.10	>0.20
C vs G	>0.50	>0.50	<0.05
D vs E	<0.01	1.00	>0.30
D vs F	1.00	>0.20	>0.50
D vs G	>0.10	<0.01	>0.10
E vs F	<0.01	>0.20	>0.10
E vs G	>0.20	<0.01	<0.05
F vs G	>0.10	<0.05	>0.30

DISCUSSION

Saito et al.14 found that the islet number per mm³ pancreatic volume varied with a wide range of 43.26 to 583.42. Hellman15 reported that the number of the pancreatic islets in unit area of tissue in non-diabetic humans varied with the range of 10.6

to 43.8, which was independent of age. Benner et al16 and Korsgren et al17 found in their studies the total number of islets varied between 3.6 and 14.8 million in 3D map study. Murtaugh & Melton18 mentioned that the islets contain an average of 3000 cells.

Constantin Ionescu-Tirgoviste et al19 found the maximum number of islets found on a slide has been encountered in the body slide of the pancreas (233 islets), whereas the minimum number of islets was found in the neck slice in their 3D map of the islet of pancreas study. Xiaojun Wang et al20 found that islet distribution/density is similar between the head and body regions, but is 2-fold higher in the tail region. Jerry Wittingen et al21 found that the islet concentration of the tail is significantly greater than the concentration in the head and body. The mean number in their study were in the head, neck and tail 25.544±9.888, 28.067±8.795 and 45.700±17.03 respectively. Shahriah et al22 and our study found that the values are roughly several times smaller than that of previous researchers. Dissimilarities mentioned above may attribute to racial variation and geographical distribution.

In our study, the lowest mean number of islets of Langerhans was 1.00±0.00 in D group (40-49 years) and F group (60-69 years) and highest was 3.60±0.55 in G group (≥70 years). Similar findings were found with the study by Shahriah et al22. Shahriah et al22 found the lowest mean number 1.00±0.00 in the age group of 40-49 years and 60-69 years and highest was 3.20±0.45 in the age group ≥70 years.

CONCLUSIONS

In the head and body regions of pancreas few variations in number of islets of Langerhans cells in relation to age were found. The number of the islets was much higher in the tail part than the body and head region. Racial variation and geographical distribution may attribute dissimilarities among different age group.

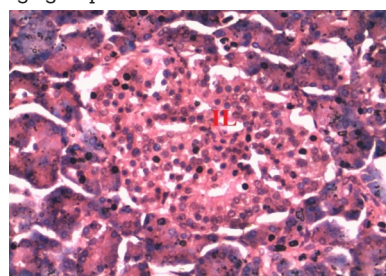


Figure 4: Islets of Langerhans in the tail part of pancreas (40×10 power, IL= Islets of Langerhans)

REFERENCES:

- Standing S, Stringer MD, Rela M, Reddy MS (2016), Gray's Anatomy: The Anatomical Basis Of Clinical Practice. 41st ed. Edinburgh: Elsevier Churchill Livingstone; PP-1187.
- Mescher AL (2010). Junqueira's basic histology: text and atlas. 12th ed. Baltimore: McGraw-Hill; 2010.
- Elayat AA, el Naggar MM, Tahir M. (1995). An immunocytochemical and morphometric study of the rat pancreatic islets. J Anat. 1995; 186: 629-37.
- Kumar V, Abbas AK, Fausto N, (2004). Robbins and Cotran pathologic basis of disease. 7th ed. New Delhi: Saunders.
- Ross MH, Pawlina W. (2006). Histology: a text and atlas with correlated cell and molecular biology. 5th ed. Baltimore: Lippincott Williams & Wilkins.
- Kreel L, Sandin B. (1973). Changes in pancreatic morphology associated with ageing. Gut; 14:962-70. <http://dx.doi.org/10.1136/gut.14.12.962>
- Burghen GA, Murrell LR. (1989). Factors influencing isolation of islets of Langerhans. Diabetes 1989;38:129-32. <http://dx.doi.org/10.2337/diab.38.1.S129>
- Robertson RP (2004). Islet transplantation as a treatment for diabetes - a work in progress. New Engl J Med; 350:694-705. <http://dx.doi.org/10.1056/NEJMra032425>
- Yeo ZX, Zhou DS (2004). In vitro cultivation of human fetal pancreatic ductal stem cells and their differentiation into insulin-producing cells. World J Gastroenterol; 10:1452-6.
- Kaihoh T, Masuda T, Sasano N, et al. (1986). The size and number of Langerhans islets correlated with their endocrine function: a morphometry on immunostained serial sections of adult human pancreases. Tohoku J Exp Med; 149:1-10. <http://dx.doi.org/10.1620/tjem.149.1>
- Gepts W. (1981). Islet changes in human diabetes. In: Cooperstein SJ, Watkins D, eds. The islets of Langerhans. New York: Academic Press.
- Varley PF, Rohrmann CA Jr., Silvis SE, et al. (1976). The normal endoscopic

- pancreatogram. *Radiology*;118:295-300.
- [13] Wolfe-Coote SA, duToit DF.(1987). Distribution of cell types of the islets of Langerhans throughout the pancreas of the Chacma baboon. *Anat Rec*;217:172-7. <http://dx.doi.org/10.1002/ar.1092170209>
- [14] Saito K, Iwama N, Takahashi T.(1978). Morphometrical analysis on topographical difference of size distribution, number and volume of islets in the human pancreas. *Tohoku J Exp Med*;124:17786. <http://dx.doi.org/10.1620/tjem.124.177>
- [15] Hellman B.(1959). The frequency distribution of the number and volume of the islets of Langerhans in man. I. Studies on non-diabetic adults. *Acta Soc Med Ups*; 64: 432-60.
- [16] Benner, C. et al. (2014). The transcriptional landscape of mouse beta cells compared to human beta cells reveals notable species differences in long non-coding RNA and protein-coding gene expression. *BMC Genomics* 15, 620.
- [17] Korsgren, O. et al.(2005). Current status of clinical islet transplantation. *Transplantation* 79, 1289–93.
- [18] Murtaugh LC, Melton DA. (2003). Genes, signals, and lineages in pancreas development. *Annu Rev Cell Dev Biol*;19:71-89. <http://dx.doi.org/10.1146/annurev.cellbio.19.111301.144752>
- [19] Constantin Ionescu-Tirgoviste1, Paul A. Gagniu, Elvira Gubceac, Liliana Mardare, Irinel Popescu, Simona Dima & Manuella Militaru.(2015).A 3D map of the islet routes throughout the healthy human pancreas. *Sci. Rep.* 5, 14634; doi: 10.1038/srep14634.
- [20] Xiaojun Wang, Ryosuke Misawa, Mark C. Zielinski, Peter Cowen, Junghyo Jo, Vipul Periwal, Camillo Ricordi, Aisha Khan, Joel Szust, Junhui Shen, J. Michael Millis, Piotr Witkowski, Manami Hara(2013). Regional Differences in Islet Distribution in the Human Pancreas - Preferential Beta-Cell Loss in the Head Region in Patients with Type 2 Diabetes, June 2013, Volume 8, Issue 6, e67454, PLOS ONE | www.plosone.org
- [21] Jerry Wittingen and Charles F. Frey(1974).Islet Concentration in the Head, Body, Tail and Uncinate Process of the Pancreas, *Ann. Surg.* Vol. 179 , No. 4,p412-414.
- [22] Shahriah S, Nurunnabi ASM, Begum GN, Kabir R.(2014). Histomorphometric Changes of Pancreatic Islets with Advancing Age – A Postmortem Study in A Bangladeshi Male Population. *Nepal Journal of Medical Sciences* 2014;3(1):63-7.