

Percentile reference curves for normal pancreatic dimensions in Indian children

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Abstract

Objectives: This study aims at determining the normal pancreatic dimensions in pediatric age groups considering demographic parameters and thus developing percentile reference curves for normal pancreatic dimensions in Indian children. **Setting and Design:** It is a cross-sectional study. **Materials and Methods:** A hospital-based cross-sectional study was planned at a children hospital during July 2016–December 2017, in which the pancreatic dimensions of 1078 normal children in the age range of 1 month to 19 years were obtained through abdominal ultrasonography (USG). The demographic details like age and gender were obtained for each child. **Statistical Analysis Used:** Percentile reference curves were obtained with reference to age for each gender type independently. Generalized additive models for location, scale, and shape were used to obtain percentile plots for each pancreatic part. **Results:** The mean age of children was 6.65 ± 4.43 years and the male-to-female ratio was 1.63:1. The head, body, and tail dimensions increased with the age. For head, up to 25th percentile, the curves were similar for both genders, while subsequent curves were higher in males as compared to females. Similar was the observation for body of pancreas. For tail, up to 75th percentile, the curves were similar for both genders. **Conclusion:** The normal ranges can be supportive in diagnosis of illness related to pancreas. The dimensions within 5–95th percentile along with iso-echogenicity can be regarded as normal, while the dimensions beyond these limits along with change of echogenicity can be suspected for pancreatic disorders.

Key words: Generalized additive models; pancreas; percentile curves

Introduction

The dimensions of abdominal organs like kidney, spleen, and pancreas have potential significance. A multitude of medical conditions is associated with the changes in the volume and size of these organs. The pancreas continues to grow until approximately the age of 25 years. Normal pancreas across individuals seems to show a great variation in size.^[1] The assessment of normal pancreatic size is an integral part of the evaluation of pancreatic diseases for both diagnostic and prognostic purposes.

Currently, sonography is used as a radiologic noninvasive procedure of choice in the examination of children with symptoms referable to pancreas.^[2-11] The most widely used criteria for determining the presence or absence of pancreatic diseases are based on alterations of pancreatic size, contour, and echotexture. Hence, it becomes important to evaluate the normal size, morphology, and echogenicity of pancreas at various stages of development.^[3,4] Data on normal pancreatic dimensions are available on western population.^[3,4] The question is, whether these can be extrapolated to Indian children,

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as there is no reference for pancreatic size in the Indian population.

The main purpose of this study was to determine the variability of anteroposterior (AP) diameters of head, body, and tail of pancreas ultrasonically by considering demographic and anthropometric parameters and develop percentile reference values for normal pancreatic dimensions for children under Indian context.

Materials and Methods

This was a cross-sectional study in which 1078 children in the age range of 1 month to 19 years attending a pediatric center during the period July 2016 to December 2017 were considered. The inclusion criteria were (a) normal healthy siblings of patients attending outpatient department and those visiting for vaccination, and (b) those children without any clinical or laboratory evidence of pancreatic disorder, like acute pancreatitis, which is most common among pancreatic disorders. Children with protein energy malnutrition (according to Indian Academy of Pediatrics classification),^[12] type I diabetes mellitus,^[13] cystic fibrosis,^[14] premature infants^[3] and clinical or laboratory evidence of hepatic diseases,^[3,15] and obesity,^[16] where echogenicity gets altered, were excluded from the study. Proper consent was obtained from accompanying parents for ultrasonography (USG) evaluation, and the protocol was approved by the institutional ethics committee. A single radiological center from the city was identified for abdominal sonography. Parameters like age, gender, height, and weight of the subjects were recorded at the time of examination. The Goldtech instrument from Precision electronic instruments company, New Delhi was used for weighing infants, while older children were measured using instrument by Detecto Medic Scales Inc., USA. Weights were recorded to the nearest 100 g. The supine lengths were measured on an infantometer in children below 2 years and standing height was measured on stadiometer in children above 2 years to the nearest 1 mm.

Abdominal sonography

A single qualified radiologist with over 25 years of experience was involved in the USG evaluations. Observations were repeated thrice to account for the intra-observer reliability. The average of three observations was reported for analysis. While selecting the abdominal sonogram, emphasis was on pancreatic dimensions, shape, echogenicity, calcification, and the status of the main pancreatic duct. The echogenicity of pancreas was compared to the texture of the region in the left lobe of liver. The sonographic examination was mostly conducted in morning hours, in supine position to eliminate the difference of dimensions in different positions.^[4,15] Some children required nearly 200–400 ml of water to drink to delineate the image of pancreas, which could have been obscured by the gas in the stomach. No

other pretreatment was used.^[4,15] A well-calibrated Sonoacc X8 Medison-Korean (SAX8) with 3.5, 5.0, and 7.5 MHz sector electronic probes properly focused on the pancreas after adequate gain setting was used during the course of study. A sample abdominal USG showing pancreatic parts with L1 vertebra is shown in Figure 1.

Anatomical landmarks for head, body, and tail of pancreas

The diameters of head, body, and tail were measured perpendicular to the long axis of the organ. A reliable diagnosis depends on the analysis of adjacent structures of pancreas. For measuring head of pancreas, duodenum, which envelops the lateral and caudal contour of the head, was taken as a landmark for measurement.^[3,4] The superior mesenteric artery and splenic vein serve as important landmarks, for localization of the body of pancreas.^[3,4] The splenic vein has a major contribution for localizing the tail of pancreas.^[3]

The maximum AP diameters of head, body, and tail of pancreas were measured on transverse/oblique images. If pancreas was oriented transversely across the abdomen, the entire gland could be seen in one image. However, the pancreas often had varying degree of obliquity, with the tail lying more cranial than the head and body. In such cases, multiple images were necessary to demonstrate the entire gland.^[3] Pancreatic echogenicity was determined by comparison with the adjacent liver at a similar depth on both transverse and longitudinal views. Pancreatic echogenicity was categorized as less than, equal to, or greater than liver echogenicity.^[3,17] The data on dimensions were analyzed along with anthropometric data using robust statistical methods.

Statistical methods

The descriptive statistics like mean and standard deviation of the dimensions of head, body, and tail were obtained for different age, height, and weight categories. The percentile curves for the three pancreatic parts were obtained as a function of age using generalized additive models for

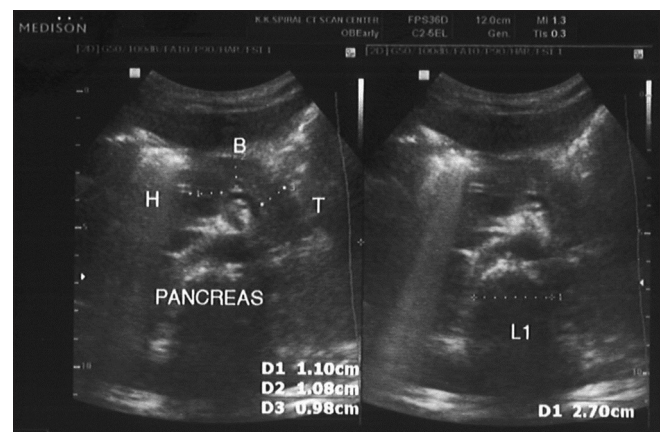


Figure 1: A sample abdominal USG showing pancreatic parts with L1 vertebra

location, scale, and shape (GAMLSS) stratified by gender. GAMLSS are semi-parametric regression models, which require a parametric distribution assumption for response variable, and it is “semi” because modeling parameters of the distribution may involve nonparametric smoothing functions.^[18] GAMLSS are more suited for modeling response variable wherein the shape and scale of the distribution of response variable change with explanatory variable. In the present study, each pancreatic dimension was referred as response variable, while *age* was treated as explanatory variable. GAMLSS models four parameters as a function of explanatory variable: the median, the coefficient of variation, the skewness, and the kurtosis of the best distribution. Different distributions like the Box–Cox power exponential, the Box–Cox *t*, the Box–Cox Cole, and Green distribution were fitted to the distribution of each pancreatic dimension. The goodness of fit was evaluated using GAIC (*k*) criterion. Finally, the selected models for each pancreatic dimension were used to calculate the curves for 5th, 10th, 25th, 50th, 75th, and 95th percentiles. The curves were obtained separately for males and females according to age. All the analyses were performed using GAMLSS package from R – 3.4.3 (R Core Team, Vienna, Austria).

The percentile reference curves were digitized wherein the inputs required are the *age* of child and the pancreatic dimensions. A point appears on the reference curves for head, body, and tail indicating the percentile limits for each pancreatic dimension. The application is available at

<https://mdsclin.in> and can be accessed by keying *pancreas* as username and password.

Results

The mean age of 1078 children at the time of USG was 6.65 ± 4.43 years and the male-to-female ratio was 1.63:1. The length/height of subjects ranged from 43 to 166 cm, while weight ranged from 2.6 to 65 kg and body surface area ranged from 0.18 to 1.54 m². The descriptive statistics like mean and standard deviation for each pancreatic section according to age, height, and weight are given in Table 1. It shows that the mean dimension for each part increased with the increasing age. Moreover, the standard deviation also showed increasing trend with age, indicating heteroscedasticity in the measurements with age. *Studentized Breusch-Pagan* method revealed significant heteroscedasticity in *head* measurements, with a *P* value of 0.0003, while for body and tail, heteroscedasticity was insignificant across age. Further, mean dimension of each part increased with the increasing height, while heteroscedasticity was statistically insignificant for all the three measurements. For weight, the mean dimension for all the three sections increased with the increasing weight, while heteroscedasticity was statistically insignificant.

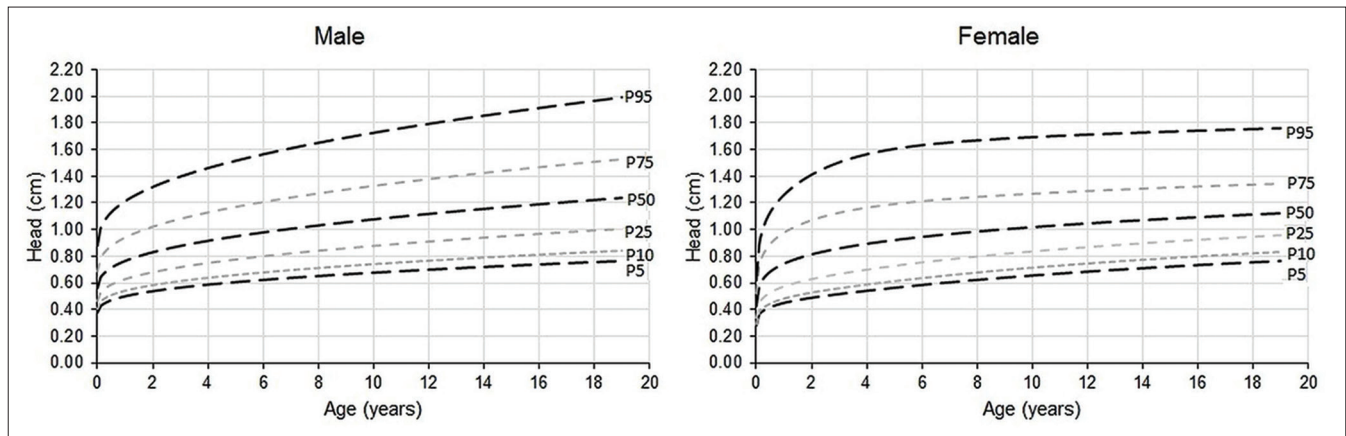
The percentile reference values for head measurement according to age and gender are shown in Table 2 and depicted in Figure 2. The head dimension increased with age

Table 1: Dimensions of pancreatic part according to age, height, and weight observed in three studies

Characteristic	Levels	n	Present study (n=1078)			n	Study by Siegel et al. (n=273)			n	Study by Ueda (n=93)	
			Head	Body	Tail		Head	Body	Tail		Head	Body
Age	<1 month	30	0.53±0.13	0.49±0.11	0.51±0.13	15	1.0±0.4	0.6±0.2	1.0±0.4			
	1 month-1 year	73	0.74±0.19	0.70±0.15	0.71±0.18	23	1.5±0.5	0.8±0.3	1.2±0.4	5	0.7±0.2	0.6±0.1
	1-5 years	351	0.93±0.30	0.86±0.23	0.91±0.26	49	1.7±0.3	1.0±0.2	1.8±0.4	35	1.5±0.2	0.8±0.2
	5-10 years	393	1.07±0.31	0.98±0.23	1.05±0.25	69	1.6±0.4	1.0±0.3	1.8±0.4	27	1.7±0.3	0.9±0.2
	10-19 years	231	1.18±0.34	1.04±0.23	1.11±0.25	117	2.0±0.5	1.1±0.3	2.0±0.4	26	1.8±0.2	0.9±0.1
Height (cm)	<90	298	0.81±0.25	0.76±0.21	0.79±0.25						1.1±0.4	0.7±0.1
	90-99	75	0.99±0.30	0.90±0.23	0.96±0.25						1.5±0.2	0.8±0.1
	100-109	147	1.01±0.32	0.97±0.26	0.99±0.25						1.6±0.2	0.9±0.1
	110-119	117	1.14±0.32	1.02±0.25	1.09±0.26						1.6±0.2	0.8±0.1
	120-129	129	1.10±0.32	0.98±0.20	1.09±0.26						1.7±0.3	0.8±0.2
	130-139	129	1.12±0.29	1.01±0.22	1.06±0.25						1.6±0.4	1.0±0.1
	140-149	93	1.11±0.39	1.01±0.23	1.07±0.26						1.7±0.2	0.9±0.2
	150-159	44	1.21±0.41	1.09±0.29	1.11±0.25						1.8±0.2	1.0±0.1
	160-169	46	1.11±0.25	1.02±0.23	1.13±0.25						2.0±0.2	1.0±0.1
Weight (kg)	1-10	205	0.79±0.26	0.73±0.22	0.76±0.24							
	10-20	402	0.99±0.30	0.91±0.23	0.98±0.25							
	20-30	264	1.11±0.31	1.00±0.23	1.08±0.25							
	30-40	106	1.11±0.30	1.01±0.20	1.07±0.26							
	40-50	56	1.27±0.42	1.11±0.30	1.17±0.25							
	50-60	37	1.31±0.33	1.09±0.26	1.17±0.27							
	60-70	8	1.18±0.37	0.89±0.13	0.98±0.31							

Table 2: Percentile reference values for head of pancreas using generalized additive models for location, scale, and shape in normal Indian children

Age (years)	Percentile for male						Age (years)	Percentile for female					
	5	10	25	50	75	95		5	10	25	50	75	95
0.01-1	0.50	0.54	0.63	0.77	0.94	1.21	0.01-1	0.45	0.48	0.57	0.75	0.98	1.26
1-3	0.56	0.61	0.72	0.88	1.08	1.40	1-3	0.51	0.56	0.67	0.86	1.13	1.51
3-6	0.62	0.68	0.80	0.98	1.21	1.57	3-6	0.58	0.63	0.75	0.95	1.21	1.64
6-9	0.66	0.73	0.86	1.06	1.30	1.69	6-9	0.64	0.69	0.81	1.01	1.26	1.68
9-12	0.70	0.77	0.91	1.12	1.38	1.79	9-12	0.68	0.74	0.87	1.05	1.29	1.71
12-15	0.73	0.80	0.95	1.18	1.45	1.88	12-15	0.72	0.78	0.91	1.09	1.31	1.74
15-19	0.76	0.84	1.01	1.24	1.53	1.99	15-19	0.76	0.83	0.95	1.13	1.34	1.76

**Figure 2: Percentile curves of head of pancreas according to gender in normal Indian children**

for both males and females. The plots revealed that the 5th, 10th, and 25th percentile curves for both males and females were almost the same. However, 50th, 75th, and 95th percentile curves for males were higher than that of females, and the difference was wider for age greater than 12 years. For instance, the 50th percentile value for age group 9–12 years in males was 1.12, which was higher than that of females with value 1.05. For age group 15–19 years, 50th percentile value was 1.24 in males, which was further higher than that of females with 1.13. The difference of centile values of head between males and females ranged between 0.01 and 0.23.

On similar lines, the percentile reference values were obtained for body of pancreas as shown in Table 3 and the curves are shown in Figure 3. The body dimension also increased with age for both males and females. The percentile values for males were marginally higher as compared to females in each group as evident from the table and also evident through figure. For instance, the 50th percentile value for age group 9–12 years in males was 1.01, which was higher than females with value of 0.98. The difference of centile values between males and females ranged between 0.01 and 0.08.

Table 4 provides the percentile reference values for tail of pancreas and Figure 4 shows the percentile curves as per gender. The percentile values increased with the increasing

age for both gender types. Up to 75th percentile, the increase in dimension with age was almost similar for both males and females. However, beyond 6 years, the 95th percentile values for females were higher than that of males. The difference of centile values between males and females ranged between 0.01 and 0.16.

Discussion

The dimensions of normal pancreas show great variation,^[1] as observed in the present study. The study revealed that mean dimension of head and tail for the study group was smaller than that reported by Seigel *et al.*,^[3] while the mean dimension for body was nearly similar. The dimensions of head and tail were nearly same in each age group, which corroborates with the findings by Seigel *et al.*^[3] Normal dimensions described by Ueda^[4] in short axis for head are more in all age groups as compared to those observed in this study; however, the observations for body were quite close with his study. Normal dimensions of each part were also studied as a function of height. The mean diameter of head was smaller compared to the diameter on short axis, as reported by Ueda, while the mean diameter of body observed in the study was quite close to that reported by Ueda.^[4] The reason for this discrepancy is not clear but may reflect the difference of physical constitution according to races in same age groups, and also perhaps the influence

Table 3: Percentile reference values for body of pancreas using generalized additive models for location, scale, and shape in normal Indian children

Age (years)	Percentile for male						Age (years)	Percentile for female					
	5	10	25	50	75	95		5	10	25	50	75	95
0.01-1	0.48	0.54	0.63	0.74	0.87	1.07	0.01-1	0.44	0.49	0.58	0.70	0.84	1.12
1-3	0.57	0.62	0.71	0.84	0.98	1.21	1-3	0.52	0.57	0.67	0.80	0.97	1.28
3-6	0.63	0.69	0.79	0.91	1.06	1.33	3-6	0.58	0.64	0.75	0.89	1.06	1.37
6-9	0.68	0.73	0.83	0.97	1.13	1.41	6-9	0.64	0.69	0.80	0.94	1.11	1.42
9-12	0.72	0.77	0.87	1.01	1.18	1.48	9-12	0.68	0.73	0.84	0.98	1.15	1.45
12-15	0.75	0.80	0.91	1.05	1.22	1.54	12-15	0.71	0.77	0.88	1.02	1.19	1.48
15-19	0.78	0.84	0.94	1.09	1.26	1.60	15-19	0.75	0.81	0.92	1.06	1.23	1.52

Table 4: Percentile reference values for tail of pancreas using generalized additive models for location, scale, and shape in normal Indian children

Age (years)	Percentile for male						Age (years)	Percentile for female					
	5	10	25	50	75	95		5	10	25	50	75	95
0.01-1	0.50	0.55	0.65	0.77	0.92	1.16	0.01-1	0.48	0.52	0.60	0.74	0.91	1.13
1-3	0.58	0.64	0.75	0.89	1.05	1.33	1-3	0.56	0.61	0.71	0.86	1.04	1.32
3-6	0.65	0.71	0.83	0.98	1.15	1.44	3-6	0.62	0.68	0.80	0.96	1.15	1.47
6-9	0.70	0.77	0.89	1.04	1.21	1.50	6-9	0.67	0.74	0.86	1.02	1.21	1.57
9-12	0.74	0.81	0.93	1.08	1.26	1.55	9-12	0.70	0.78	0.91	1.08	1.27	1.65
12-15	0.77	0.84	0.97	1.12	1.30	1.59	12-15	0.73	0.82	0.96	1.12	1.31	1.71
15-19	0.81	0.88	1.01	1.16	1.34	1.63	15-19	0.77	0.86	1.01	1.17	1.35	1.79

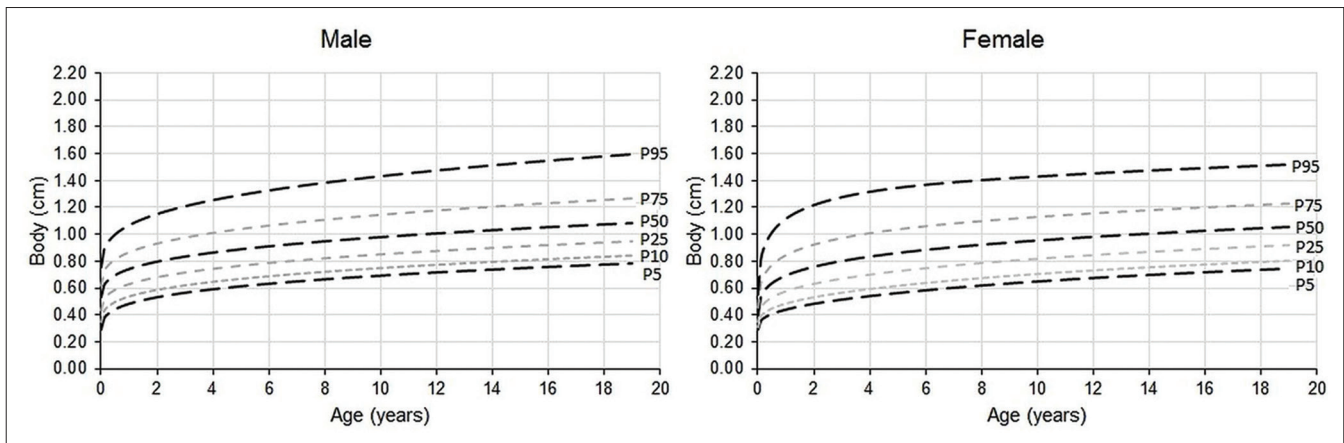


Figure 3: Percentile curves for body of pancreas according to gender in normal Indian children

of genetic and environmental factors across population.^[1] Pancreatic iso-echogenicity was observed in all the studied cases. Hypoechoenicity was reported in 10% cases by Seigal *et al.*^[3]

This study provides age- and gender-specific percentile reference values for the three pancreatic parts based on a sample of 1078 normal children. At present, such data are not available under Indian context. The age-specific percentile values of head and body for males were higher than that of females. However, for tail, the values were close for gender types till 75th percentile, but differed in 95th percentile, and were higher for females as compared to males.

Utility of Percentile Curves

The derived centile plots for three pancreatic parts can be referred by radiologists or clinicians to opine about the normal or abnormal dimensions of pancreas in children. For a new subject with specific age and gender, the pancreatic dimensions as obtained through USG can be mapped onto the respective percentile plots and may be interpreted.

Moreover, certain disease conditions are known to influence the dimensions of pancreas. Diseases like acute pancreatitis result in the enlargement of pancreatic size, while some may diminish in size, as observed in cystic fibrosis. USG findings under disease condition and the findings when the patient is

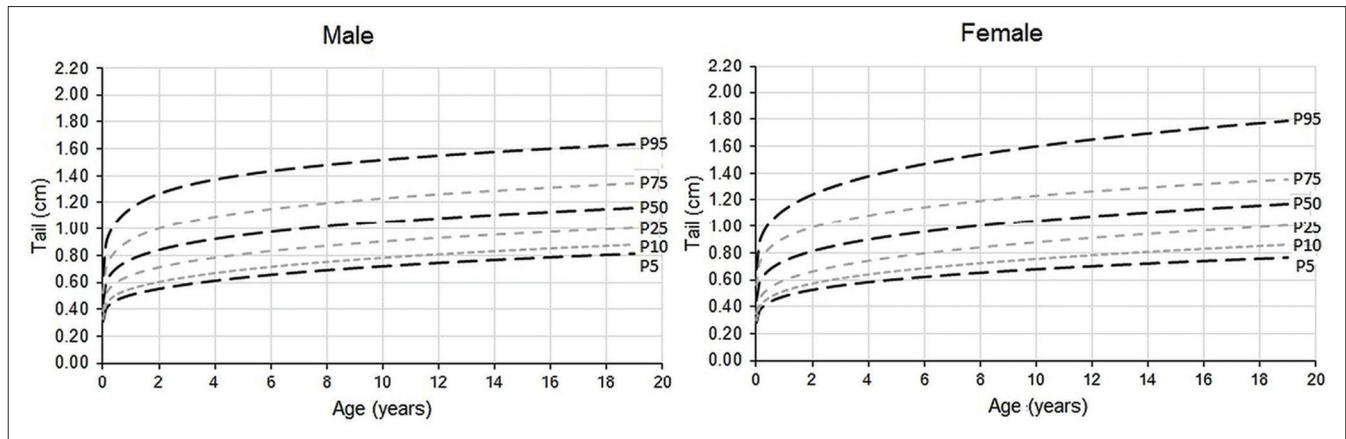


Figure 4: Percentile reference curves for tail of pancreas according to gender in normal Indian children

asymptomatic for the disease can be used to understand the percentile shift in the dimensions of each part and thereby increase the diagnostic strength of pancreatic-related illness.

In summary, this study has established the normal size limits for the pediatric pancreas as determined by the measurement of AP diameter with real-time sonography. Based on this study, the dimensions falling within 5th and 95th percentile along with iso-echogenicity can be regarded as normal. If the dimensions lie outside these limits, along with change of echogenicity, then such cases may be screened further for pancreatic disorders. We believe that a more comprehensive effort is needed to include representative samples from different parts of the country so as to address the biological diversity in pancreatic measurements.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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