Exploring the variations of the pancreatic ductal system: a systematic review and meta-analysis of observational studies

Adil Asghar[1], Ravi Kant Narayan[2], Nagavalli Basavanna Pushpa[3], Apurba Patra[4], Kumar Satish Ravi[5], R. Shane Tubbs[6]

[1]Department of Anatomy, All India Institute of Medical Sciences, Patna, [2]Department of Anatomy, ESIC Medical College & Hospital, Patna, [3]JSS Medical College, JSS Academy of Higher Education and Research, Mysore, [4]All India Institute of Medical Sciences, Bathinda, [5]All India Institute of Medical Sciences, Gorakhpur, India, [6]Tulane University School of Medicine, New Orleans, LA, USA

Abstract: The exocrine part of the pancreas has a duct system called the pancreatic ductal system (PDS). Its mechanism of development is complex, and any reorganization during early embryogenesis can give rise to anatomical variants. The aim of this study is to collect, classify, and analyze published evidence on the importance of anatomical variants of the PDS, addressing gaps in our understanding of such variations. The MEDLINE, Web of Science, Embase, and Google Scholar databases were searched to identify publications relevant to this review. R studio with meta-package was used for data extraction, risk of bias estimation, and statistical analysis. A total of 64 studies out of 1,778 proved suitable for this review and metanalysis. The meta-analysis computed the prevalence of normal variants of the PDS (92% of 10,514 subjects). Type 3 variants and "descending" subtypes of the main pancreatic duct (MPD) predominated in the pooled samples. The mean lengths of the MPD and accessory pancreatic duct (APD) were 16.53 cm and 3.36 cm, respectively. The mean diameters of the MPD at the head and the APD were 3.43 mm and 1.69 mm, respectively. The APD was present in only 41% of samples, and the long type predominated. The pancreatic ductal anatomy is highly variable, and the incorrect identification of variants may be challenging for surgeons during ductal anastomosis with gut, failure to which may often cause ductal obstruction or pseudocysts formation.

Key words: Cholangiopancreatography, Accessory pancreatic duct, Endoscopic retrograde cholangiopancreatography, Magnetic resonance cholangiopancreatography, Pancreatitis

Introduction

The pancreas is a retroperitoneal organ with endocrine and exocrine functions. The exocrine part of the gland drains into multiple lobular ducts which makes "herring-bone pattern" by uniting with the pancreatic duct or accessory duct. The single pancreatic duct starts in the tail of the pancreas and usually ends at the major duodenal papilla, which is also known as the pancreatic duct of Wirsung or the main pancreatic duct (MPD). The accessory duct starts in the head of the pancreas and usually has a small caliber and communicates with MPD or its inferior branch at the neck of the gland and terminates at the minor duodenal papilla about 2 cm proximal to the major duodenal papilla. The accessory duct is also known as the pancreatic duct of Santorini or the accessory pancreatic duct (APD). These duct

Corresponding author:
Ravi Kant Narayan (ORCID)
Department of Anatomy, ESIC Medical College & Hospital, Patna 801505, India
E-mail: narayanintouch@gmail.com

systems are called the pancreatic ductal system (PDS), which reflects variable embryological development of pancreatic buds along with their ducts. The pancreas develops by fusion of the ventral and dorsal endodermal pancreatic buds in the seventh week, and any divergence in this process can result in too many individual anatomical variants (Fig. 1) [1-5]. Anatomical variations of the PDS are commonly reported as incidental findings during imaging procedures during adulthood, but their prevalence is neither well documented nor well recognized [4]. The development of the PDS and its variations occur during embryogenesis when the pancreas begins to differentiate. Some examples of these variants include pancreas divisum, where there is no communication between the MPD and APD, and ansa pancreatica, which is a loop or S-shaped either in APD or in MPD. Except for pancreas divisum and ansa pancreatica, the effects of these variants on exocrine pancreatic function have not been extensively studied [6].

The methodology for studying the PDS has evolved over the years. Early methods used the injection of cadaveric specimens with delicate anatomical dissections and pancreatography. Duct visualization has evolved further during the last few decades, leading to endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) [7]. ERCP is still considered the gold standard for visualizing the ducts, but it has been replaced by non-invasive MRCP, which is safer and can also visualize the parenchyma. In addition, s-MRCP (secretin-stimulated MRCP), a newer technique that uses secretin to dilate the ducts temporarily, improves visualization and therefore the evaluation of duct morphology and the assessment of exocrine function [8]. Unfortunately, most studies on exocrine pancreatic function have provided little or no information about PDS variation, ductal morphology, and its

effects [9].

The present study focuses on the frequency and clinical significance of PDS variants other than pancreas divisum and determines the pooled prevalence of different types of ductal variations in different populations and ethnic groups. The aim of this review is to collect, organize, and interpret published data on the relevance of anatomical variants of the PDS in order to preclude diagnostic errors, fill gaps in our knowledge about pancreatic duct variations, and identify areas where further research is needed.

Materials and Methods

We adopted the SPIDER model for this systematic review and metanalysis of the PDS [10].

· Sample: cadaveric or dissection, pancreatography, ERCP, and MRCP.

· Phenomenon of interest: pancreatic ductal variation related to configuration, course, termination, and dimensions.

· Design: cross-sectional, prospective or retrospective study.

· Evaluation: proportion of variants and mean dimension of ducts.

· Research: quantitative estimation.

PRISMA guidelines provided the basis for the search strategy, data extraction, and statistical analysis. In order to be included in the review, a study had to meet the following criteria:

Inclusion criteria

(1) Studies reporting data on anatomical variants of the PDS along with morphometric measurements of the ducts.

(2) Studies including classification of PDS variants into three categories: "normal variant PDS", ansa pancreatica, and pancreas divisum or embryonic. Studies that provided
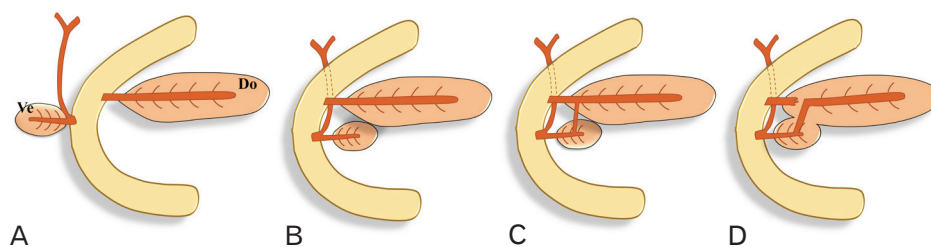
Fig. 1. Development of pancreas. (A) the ventral (Ve) and dorsal (Do) buds of the pancreas develop opposite to each other at the junction of foregut and midgut. (B) The ventral bud undergoes clockwise rotation around the caudal part of the foregut. (C) The dorsal and ventral pancreatic ducts fuse in the region of the neck of pancreas. (D) The fused ventral pancreatic duct and the proximal part of dorsal pancreatic duct forms the main pancreatic duct, while the remaining distal portion of the dorsal pancreatic duct may persist as accessory pancreatic duct.

further distinctions within the "normal PDS" category were also eligible.

Exclusion criteria

(1) Studies that only reported results for pancreas divisum and ansa pancreatica without data on other PDS variants.

(2) Systematic reviews, editorials, case reports, and case series.

(3) Studies reporting data associated with pancreatic disorders such as pseudocysts and tumors, which distorted the duct anatomy.

Search strategy

The MEDLINE, Web of Science, Embase, and Google Scholar databases were searched to identify publications relevant to this review. The search was limited to human subjects, but no time and language filters were applied. The included terms were "pancreas", "pánkreas", "duct", "ductus" "pancreatic", "pancreaticum" "ductal system", "variations", "variantes", "variants", "anatomic", "anatomico", and "anatomical". The references listed in the included studies were also hand-searched.

Data extraction

Two reviewers were assigned to search independently for the data, any discrepancies regarding study inclusion being resolved by senior investigators. The data extracted from the studies included information such as the authors and publication year, the country where the study was conducted, the setting of the study, the number and type of subjects involved, and the number and type of PDS variants described. The numerous inconsistent classification systems for such

variants are difficult to compare. Therefore, we adopted a literature-based classification system for anatomical variants of the PDS as follows:

1. Configuration variants, based on the drainage pattern of the PDS. The classification of the PDS was adopted from Bülow et al. [11] with slight modifications, including: normal variant (type 1–3), pancreas divisum or embryonic (type 4), and ansa pancreatica (type 5) (Fig. 2).

· Type 1: Bifid, dual duct configuration with MPD draining into the major papilla and APD opening into the minor papilla (Fig. 2).

· Type 2: Bifid configuration with MPD opening into the minor papilla and APD reaching the major papilla with or without patency (reverse of type 1) (Fig. 2).

· Type 3: MPD draining into the major papilla with or without communication with APD (Fig. 2).

· Type 4: Embryonic or pancreas divisum (subtype, "complete"; subtype, "absent APD"; subtype, "incomplete"; subtype "reverse divisum") (Fig. 2).

· Type 5: Ansa pancreatica: loop or S- or L-shaped communication between MPD and APD with or without patency (Fig. 2).

2. Variants of MPD: MPD are classified into five subtypes on the basis of course or shape: descending, vertical or ascending, sigmoid, loop, and horizontal or transverse (Fig. 3) [12].

3. Classification of the APD: In 2004, Kamisawa et al. [13] proposed a classification system for APDs based on their length relative to the MPD. This system is used to help identify and diagnose variations in PDS anatomy.

· The Long-type APD: a continuation of the main duct of
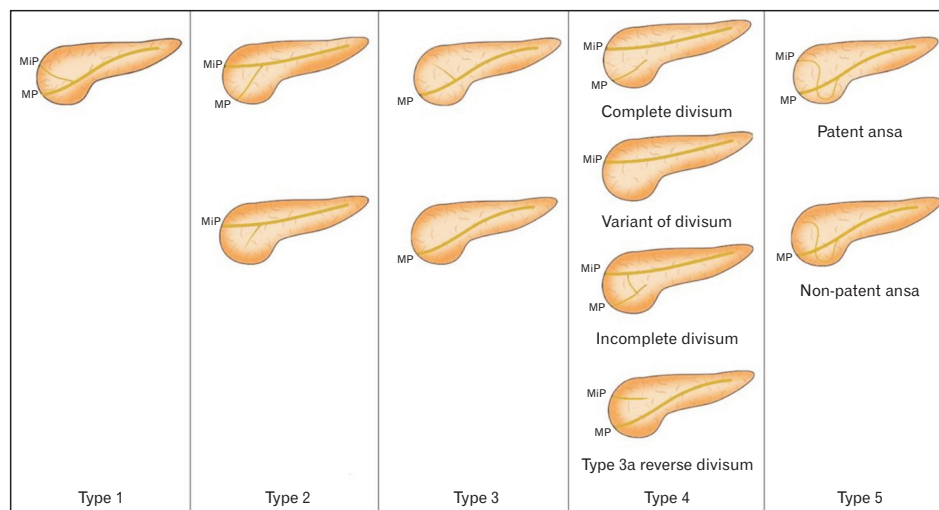

Fig. 2. Shows the configurational variants of the pancreatic ductal system (PDS). Types 1–3 shows normal pancreatic variants, and types 4, 5 shows variants of pancreas divisum. MP, major duodenal papilla; MiP, minor duodenal papilla.
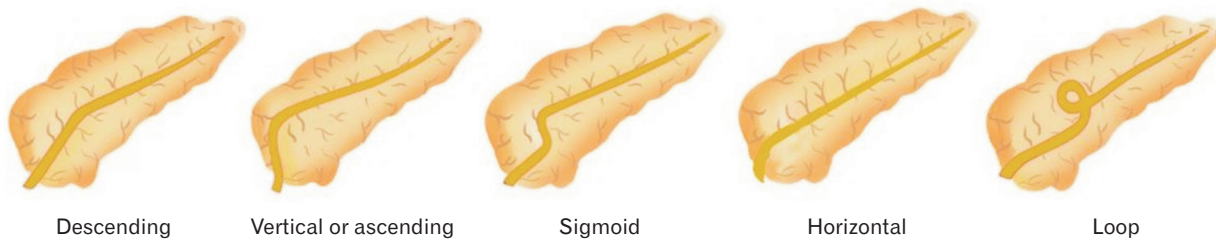
Fig. 3. Variants of the main pancreatic duct. Adapted from Türkvatan et al. Korean J Radiol 2013;14:905-13 [12].
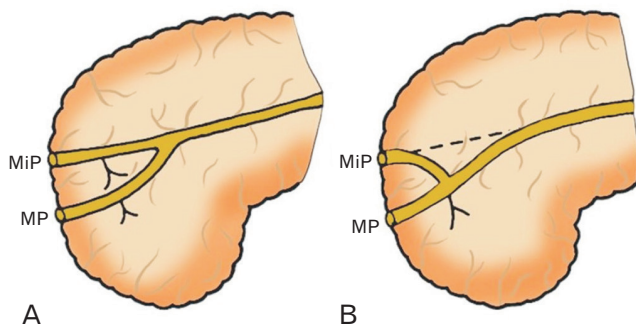

Fig. 4. Variants of the accessory pancreatic duct (A) long type, (B) short type. MP, major duodenal papilla; MiP, minor duodenal papilla. Adapted from Kamisawa et al. World J Gastroenterol 2010;16:4499-503 [17].

the dorsal primordium (Fig. 4).

· The Short-type APD: is formed by the continuation of the long inferior branch, with an obliterated connection with the main duct of the dorsal primordium (Fig. 4).

Variants of pancreaticobiliary junction (PBJ) arrangement: This classification is based on variations in the arrangement of the junction between the pancreas and the biliary system.

Risk of bias and statistical analysis

The risk of bias was estimated using the Newcastle–Ottawa score for observational studies [14]. R studio with meta package was used for statistical analyses. The effect size, *i.e.*, pooled weighted proportion and pooled weight mean, were computed using the generalized linear mixed (GLM) method and inverse variance (IV) method, respectively. Heterogeneity was examined using Higgins i^2 statistics, tau-square and Cochrane Q. If the heterogeneity was more than 50%, effect size computed with a random effect model was adopted in place of the fixed-effect model.

Results

The search strategy yielded 1,778 citations, of which 403 were duplicates. After these duplicates were removed, abstracts were screened, and 1,294 citations were excluded because they did not report outcomes of interest. The full texts of eighty-one citations were evaluated by further screening, and 17 were excluded during the data extraction phase because outcome data were missing. Therefore, only 64 citations were suitable for qualitative and quantitative analysis (Fig. 5 and Table 1) [1-4, 9, 11, 15-69]. Thirteen reported configuration variations of the PDS (types 1–5), and 12 concerned variations in its course (descending, sigmoid, vertical, horizontal, and loop). The citations were subgrouped into MPD and APD.

A. Configuration variants of PDS: the prevalence of the normal form of the PDS was 92% (0.87–0.95). The prevalence of types 1–3 PDS variants were 27% (0.18–0.37), 1% (0.00–0.04), and 50% (0.39–0.62), respectively. Type 3 was the most common variant. The prevalences of pancreatic divisum and ansa were 6% (0.05–0.08) and 2% (0.00–0.07) (Table 2). The most common subtypes of pancreas divisum were "complete," followed by "incomplete" and "absent APD." The distribution of "reverse divisum" was not reported in the original reports.

B. MPD (Table 3):

I. Course variants of MPD: the most common course of the MPD was the "descending" type (40%, 0.19–0.65), followed by the "sigmoid" type (22%, 0.17–0.27) and the "vertical" type (10%, 0.05–0.21) (Table 3).

II. Termination of MPD: the MPD terminated at the major duodenal papilla in 81% (0.48–0.95) and at the minor duodenal papilla in 19% (0.05–0.52).

III. Dimensions of MPD: the mean length of the MPD was 16.53 cm (15.67–17.39 cm). The pooled estimates of MPD diameter were 3.43 mm (3.21–3.65 mm) at the head, 2.43 mm
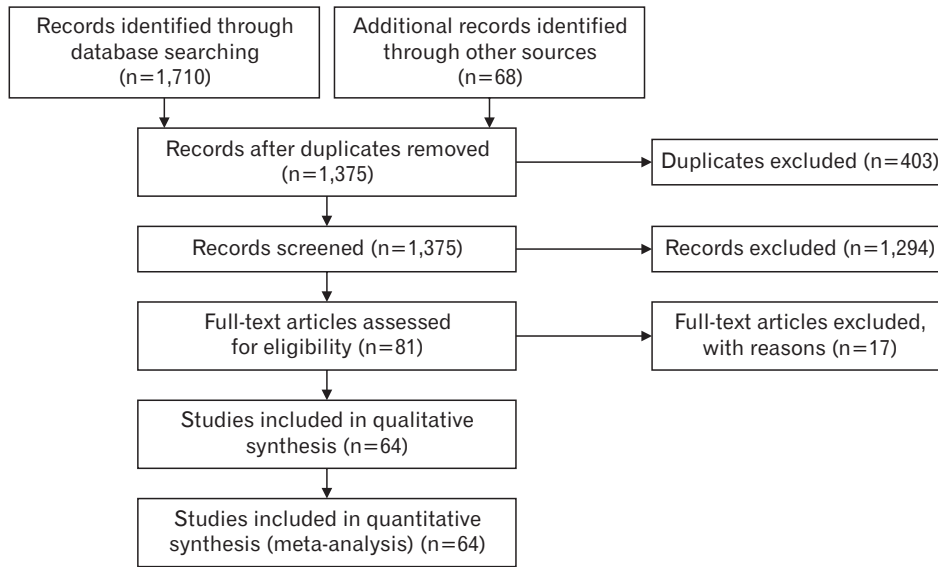
Fig. 5. PRISMA flow-diagram for systematic review.

Table 1. Characteristics of included studies

Author (yr)	Country	Ethnicity	Type of subject	Type of investigation	Type of article	Outcome	Selection	Comparability	Outcome	Total
De Filippo et al. (2008) [15]	Italy	European	Living patient	MRCP	Prospective study	Ductal variation	***	****	***	10
Adibelli et al. (2017) [9]	Turkey	Asian	Living patient	MRCP	Retrospective cohort study	Ductal variation	**	***	***	8
Bülow et al. (2014) [11]	Germany	European	Healthy volunteers	MRCP	Prospective study	Ductal variation	**	***	**	7
Bang et al. (2006) [16]	Korea	Asian	Living patient	ERCP	Retrospective cohort study	Ductal variation	***	**	***	8
Kamisawa et al. (2010) [17]	Japan	Asian	Living patient	ERCP	Retrospective cohort study	Ductal variation	***	***	***	9
Shahriah et al. (2014) [18]	Bangladesh	Asian	Cadaver	Dissection	Cross-sectional study	Ductal variation	**	**	**	6
Kim et al. (2002) [19]	Korea	Asian	Living patient	ERCP	Retrospective cohort study	Ductal variation	***	***	****	10
Oracz et al. (2006) [20]	Poland	European	Living patient	MRCP	Retrospective cohort study	Ductal variation	**	***	****	9
Uomo et al. (1995) [21]	Italy	European	Living patient	ERCP	Retrospective cohort study	Ductal variation	**	***	**	7
Prasanna et al. (2015) [22]	India	Asian	Cadaver	Duct injection	Cross-sectional study	Ductal variation	***	**	***	8
Prasad et al. (2019) [23]	India	Asian	Cadaver	Dissection	Cross-sectional study	Ductal variation	***	***	***	9

Table 1. Continued 1

Author (yr)	Country	Ethnicity	Type of subject	Type of investigation	Type of article	Outcome	Selection	Comparability	Outcome	Total
Prasad et al. (2019) [23]	India	Asian	Living patient	MRCP	Prospective study	Ductal variation	**	**	**	6
Abdelkareem et al. (2019) [3]	Palestine	Asian	Living patient	MRCP	Retrospective study	Ductal variation	***	***	****	10
Koshariya et al. (2019) [24]	India	Asian	Cadaver	Dissection	Cross-sectional study	Ductal variation	**	***	****	9
Gonoi et al. (2013) [25]	Japan	Asian	Living patient	MRCP	Prospective study	Ductal variation	***	***	***	9
Darnis et al. (1984) [26]	France	European	Living patient	ERCP	Prospective study	Ductal variation	**	**	**	6
Schmitt et al. (2010) [27]	France	European	Autopsy	Duct injection	Cross-sectional study	Ductal variation	***	***	****	10
Smanio (1969) [28]	Brazil	South American	Autopsy	Duct injection	Cross-sectional study	Ductal variation	**	***	****	9
Dawson and Langman (1961) [29]	Canada	North American	Autopsy	Duct injection	Cross-sectional study	Ductal variation	**	***	**	7
Berman et al. (1960) [30]	USA	North American	Autopsy	Duct injection	Cross-sectional study	Ductal variation	***	**	****	9
Ishaque et al. (2020) [31]	Pakistan	Asian	Living patient	MRCP	Prospective study	Ductal variation	***	***	***	9
Johansson et al. (2022) [32]	Finland	European	Living patient	MRCP	Prospective study	Ductal variation	**	**	**	6
Covantsev et al. (2022) [4]	Russia	European	Cadaver	Dissection	Cross-sectional study	Ductal variation & dimension	***	***	****	10
Malathi and Kishan Reddy (2019) [33]	India	Asian	Cadaver	Dissection	Cross-sectional study	Ductal variation	**	***	****	9
Shu et al. (2006) [34]	Chinese	Asian	Living patient	MRCP	Prospective study	Ductal variation & dimension	***	**	**	7
Kasugai et al. (1972) [35]	Japan	Asian	Living patient	ERCP	Prospective study	Ductal variation & dimension	***	***	****	9
Kreel and Sandin (1973) [36]	UK	European	Cadaver	Pancreatogram	Prospective study	Ductal variation & dimension	**	***	***	9
Kang et al. (1989) [37]	Korea	Asian	Living patient	ERCP	Prospective study	Ductal variation & dimension	***	**	**	6
Vinay Kumar and Lokanadham (2019) [38]	India	Asian	Cadaver	Dissection	Prospective study	Ductal variation & dimension	**	***	****	10

Table 1. Continued 2

Author (yr)	Country	Ethnicity	Type of subject	Type of investigation	Type of article	Outcome	Selection	Comparability	Outcome	Total
Hayashi et al. (2016) [39]	Japan	Asian	Living patient	MRCP	Prospective study	Ductal dimension	***	***	****	9
Govindraj and Shabna (2017) [40]	India	Asian	Cadaver	Dissection	Prospective study	Ductal dimension	**	**	**	6
Liessi et al. (2010) [41]	Italy	European	Living patient	MRCP	Prospective study	Ductal dimension	***	***	****	10
Varley et al. (1976) [42]	USA	North American	Living patient	ERCP	Prospective study	Ductal dimension	***	***	***	9
Classen et al. (1973) [43]	Germany	European	Living patient	ERCP	Prospective study	Ductal dimension	**	**	**	6
Kasugai et al. (1972) [35]	Japan	Asian	Living patient	ERCP	Prospective study	Ductal variation & dimension	***	***	****	10
Cotton (1974) [44]	UK	European	Living patient	ERCP	Prospective study	Ductal dimension	**	***	****	9
Seifert et al. (1973) [45]	Germany	European	Living patient	ERCP	Prospective study	Ductal dimension	**	***	**	7
Okuda et al. (1973) [46]	Japan	Asian	Living patient	ERCP	Prospective study	Ductal dimension	***	**	***	8
Sivak and Sullivan (1976) [47]	USA	North American	Living patient	ERCP	Prospective study	Ductal dimension	***	***	***	9
Ara et al. (2011) [48]	Bangladesh	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	**	**	**	6
Kochhar et al. (1996) [49]	India	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	***	***	****	10
Sahni et al. (2001) [50]	India	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	**	***	****	9
Fatima (2010) [51]	Bangladesh	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	***	***	***	9
Wilasrusmee and Pong-chairerks (1999) [52]	Thailand	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	**	**	**	6
Pina (2016) [53]	Argentina	South American	Cadaver	Dissection	Cross-sectional study	Ductal dimension	***	***	****	10
Anand et al. (1989) [1]	India	Asian	Living patient	ERCP	Prospective study	Ductal dimension	**	***	****	9
Hastier et al. (1998) [54]	France	European	Living patient	Pancreatogram	Prospective study	Ductal dimension	**	***	**	7
Akochi et al. (2018) [55]	Rwanda	African	Living patient	USG	Prospective study	Ductal dimension	***	***	****	10

Table 1. Continued 3

Author (yr)	Country	Ethnicity	Type of subject	Type of investigation	Type of article	Outcome	Selection	Comparability	Outcome	Total
Karak et al. (1991) [56]	India	Asian	Living patient	ERCP	Prospective study	Ductal dimension	**	***	**	7
Hadidi (1983) [57]	Iran	Asian	Living patient	USG	Prospective study	Ductal dimension	***	**	***	8
Cremer et al. (1976) [69]	Belgium	European	Living patient	ERCP	Prospective study	Ductal dimension	NA	NA	NA	NA
Millbourn (1960) [58]	Sweden	European	Living patient	Pancreatogram	Prospective study	Ductal dimension	***	***	***	9
Trapnell and Howard (1966) [59]	UK	European	Living patient	Pancreatogram	Prospective study	Ductal dimension	**	**	**	6
Hand (1963) [60]	USA	North American	Cadaver	Dissection	Cross-sectional	Ductal dimension	***	***	****	10
Ogoshi et al. (1973) [61]	Japan	Asian	Living patient	ERCP	Prospective study	Ductal variation & dimension	***	***	***	9
Birnstingl (1959) [62]	UK	European	Living patient	Pancreatogram	Prospective study	Ductal dimension	**	**	**	6
MacCarty et al. (1975) [63]	India	Asian	Living patient	Pancreatogram	Prospective study	Ductal dimension	***	***	****	10
Toda et al. (1998) [64]	Japan	Asian	Living patient	ERCP	Prospective study	Ductal dimension	**	***	****	9
Aubé et al. (2003) [65]	France	European	Living patient	MRCP	Prospective study	Ductal variation & dimension	**	***	**	7
Arora et al. (2011) [2]	India	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	***	***	****	10
Mchonde and Gesase (2014) [66]	Tanzania	African	Cadaver	Dissection	Cross-sectional study	Ductal dimension	**	***	****	9
Jirasiritham et al. (2016) [67]	Thailand	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	**	***	**	7
Malathi and Kishan Reddy (2019) [33]	India	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	***	***	****	10
Gosavi and Gaikwad (1980) [68]	India	Asian	Cadaver	Dissection	Cross-sectional study	Ductal dimension	**	***	**	7

MRCP, magnetic resonance cholangiopancreatography; ERCP, endoscopic retrograde cholangiopancreatography; USG, ultrasonography; NA, not available.
a)Secondary reference, manuscript NA. *Denotes quality rating of observational studies.

(2.27–2.59 mm) at the body, and 1.62 mm (1.41–1.81 mm) at the tail of the pancreas (Table 3 and Fig. 6A).

C. APD (Table 2):

I. Course variants: the prevalence of the APD was 41% (0.31–0.52) in 1,286 samples. The subtypes of the APD were studied in 467 samples. The long subtypes were the most common (52%, 0.37–0.67), followed by the short subtype (21%, 0.10–0.39). Both the embryonic and Ansa subtypes of the APD were 8% (Tables 2-4).

II. Termination of APD: the APD terminated at the major duodenal papilla in 18% (0.07–0.39) and at the minor duodenal papilla in 80% (0.58–0.95).

Table 2. Pooled estimates of morphometric parameters and morphological subtypes of accessory pancreatic duct

APD variations	Studies included	Subjects	Overall	Cadaveric sample	Pancreatography/ ductal injection	ERCP	MRCP	Hetero- geneity (i^2, %)
Prevalence of APD	15	1,286	0.41 (0.31–0.52)	0.47 (0.37–0.57)	0.29 (0.23–0.36)	0.19 (0.04–0.54)	0.68 (0.53–0.80)	95.7
Subtype "long"	5	467	0.52 (0.37–0.67)	0.50 (0.32–0.68)	NR	0.59 (0.53–0.64)	NR	80.8
Subtype "short"	5	467	0.21 (0.10–0.39)	0.18 (0.06–0.41)	NR	0.29 (0.24–0.35)	NR	70.2
Subtype "embryonic"	5	467	0.08 (0.04–0.15)	0.06 (0.02–0.16)	NR	0.12 (0.09–0.17)	NR	0.0
Subtype "ansa"	5	467	0.08 (0.06–0.11)	0.20 (0.15–0.27)	NR	NR	NR	0.1
Length (cm)	4	185	3.36 (2.62–4.09)	3.36 (2.62–4.09)	NR	NR	NR	96.7
Diameter (mm)	4	185	1.69 (1.60–1.77)	1.69 (1.60–1.77)	NR	NR	NR	42.8

Values are presented as number or mean (95% confidence interval). APD, accessory pancreatic duct; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; NR, not reported.

Table 3. Pooled estimates of morphometric parameters and morphological subtypes of main pancreatic duct

MPD variations	Studies included	Subjects	Overall	Cadaveric sample	Pancreatography/ ductal injection	ERCP	USG	Hetero- geneity (i^2, %)
Length (cm)	19	1,330	16.53 (15.67–17.39)	16.01 (14.72–17.30)	NR	16.84 (15.71–17.97)	NR	97.8
Diameter at head (mm)	23	1,859	3.43 (3.21–3.65)	2.97 (2.69–3.26)	3.97 (3.52–4.41)	3.52 (3.30–3.75)	2.72 (2.17–3.27)	97.7
Diameter at body (mm)	23	1,759	2.43 (2.27–2.59)	2.32 (2.23–2.41)	2.12 (1.97–2.27)	2.64 (2.42–2.87)	2.10 (2.08–2.12)	96.2
Diameter at tail (mm)	18	1,523	1.62 (1.42–1.81)	1.71 (1.08–2.33)	1.57 (0.94–2.19)	1.58 (1.30–1.86)	1.73 (1.48–1.98)	98.7
Descending	11	2,613	0.40 (0.19–0.65)	0.47 (0.22–0.75)	0.35 (0.25–0.46)	0.02 (0.00–0.14)	0.66 (0.57–0.75)	95.1
Sigmoid	11	2,613	0.22 (0.17–0.27)	0.24 (0.11–0.45)	0.17 (0.19–0.28)	0.23 (0.19–0.28)	0.21 (0.15–0.29)	85.3
Vertical/ascending	11	2,613	0.10 (0.05–0.21)	0.02 (0.01–0.06)	0.33 (0.22–0.44)	0.51 (0.46–0.56)	0.07 (0.05–0.10)	96.6
Horizontal	11	2,613	0.004 (0.00–0.11)	0.06 (0.00–0.59)	0.04 (0.01–0.11)	0.23 (0.19–0.28)	NR	31.1
Loop	11	2,613	0.01 (0.00–0.03)	0.01 (0.00–0.04)	0.07 (0.03–0.16)	NR	0.01 (0.00–0.06)	75.8

Values are presented as number or mean (95% confidence interval). MPD, main pancreatic duct; ERCP, endoscopic retrograde cholangiopancreatography; USG, ultrasonography; NR, not reported.

III. Dimensions of APD: the length of the APD was 3.36 cm (2.62–4.09), and its diameter was 1.69 mm (1.60–1.77) (Table 2 and Fig. 6B).

D. There was significant heterogeneity in almost every parameter owing to sample variations; subgroup analysis based on ethnicities and modalities of the investigation could not reduce this heterogeneity. There was publication bias in some parameters, corrected by trim-fill analysis.

Based on population normal variant of PDS was observed to be most prevalent in the Asians (0.96) while the embryonic variant was mostly seen in South Americans (0.11), and the ansa pancreatica was reported to be prevalent in North Americans (0.17). The Europeans were observed to possess the longest (18.05 cm) as well as the widest MPD (at head [3.88 mm] and body [2.49 mm]), whereas the diameter of the same at tail was widest for the South Americans (2.34 mm). Among the observed populations, only the South Americans (0.62) and Europeans (0.5) had APD prevalent in over half of their sample size (Table 4).

Discussion

The foetal development of the human pancreas is intricate leading to a wide range of congenital pancreatic and ductal abnormalities. The literature presents with distinct reports on prevalence of the normal form and the variants of the PDS across the globe. The study of pancreatic variation is important in medicine, medical imaging, surgery, and evolutionary biology, to elucidate the anatomy, function, and evolution of the pancreas.

Summary of findings

The present meta-analysis computed the prevalence of the normal form of the PDS, found in 92% of 10,514 subjects. Type 3 variants of the PDS and "descending" subtypes of the MPD predominated in the pooled samples. The MPD terminated at the major duodenal papilla in 80%, and a similar proportion of APDs terminated at minor duodenal papilla (81%). The mean lengths of the MPD and APD were 16.53

A **Forest plot estimating pooled estimate of length of main pancreatic duct (cm)**

Study or subgroup	Mean	SD	Total	Weight	Mean IV, random, 95% CI	Mean IV, random, 95% CI
Mode of investigation=ERCP						
[37] Kang et al. 1989	17.50	2.8000	126	5.1%	17.50 [17.01; 17.99]	
[42] Varley et al. 1976	16.90	2.7000	80	5.0%	16.90 [16.31; 17.49]	
[43] Classen et al. 1973	20.10	1.9500	48	5.1%	20.10 [19.55; 20.65]	
[35] Kasugai et al. 1972	16.20	2.5000	68	5.0%	16.20 [15.61; 16.79]	
[44] Cotton 1974	14.50	2.1250	57	5.1%	14.50 [13.95; 15.05]	
[45] Seifert et al. 1973	18.60	1.0000	28	5.1%	18.60 [18.23; 18.97]	
[46] Okuda et al. 1973	15.70	2.8000	20	4.7%	15.70 [14.47; 16.93]	
[47] Sivak and Sullivan 1976	15.40	1.7000	35	5.1%	15.40 [14.84; 15.96]	
[1] Anand et al. 1989	16.55	2.7600	55	5.0%	16.55 [15.82; 17.28]	
Total (95% CI)			**517**	**45.1%**	**16.84 [15.71; 17.97]**	

Heterogeneity: Tau^2=2.8747; Chi^2=314.37, df=8 (P<0.01); I^2=97%

Mode of investigation=dissection						
[22] Prasanna et al. 2015	17.30	2.5500	38	4.9%	17.30 [16.49; 18.11]	
[23] Prasad et al. 2019	16.17	1.5700	20	5.0%	16.17 [15.48; 16.86]	
[48] Ara et al. 2011	16.13	3.2600	50	4.9%	16.13 [15.23; 17.03]	
[40] Govindraj and Shabna 2017	11.10	2.0000	50	5.1%	11.10 [10.55; 11.65]	
[49] Kochhar et al. 1996	18.20	3.0000	93	5.0%	18.20 [17.59; 18.81]	
[50] Sahni et al. 2001	16.69	1.5500	275	5.2%	16.69 [16.51; 16.87]	
[51] Fatima 2010	14.76	2.3000	50	5.0%	14.76 [14.12; 15.40]	
[52] Wilasrusmee et al. 1999	15.60	1.8000	103	5.1%	15.60 [15.25; 15.95]	
[53] Pina 2016	15.76	3.5750	50	4.8%	15.76 [14.77; 16.75]	
[33] Malathi and Kishan Reddy 2019	18.40	2.4300	50	5.0%	18.40 [17.73; 19.07]	
Total (95% CI)			**779**	**50.1%**	**16.01 [14.72; 17.30]**	

Heterogeneity: Tau^2=4.2217; Chi^2=473.78, df=9 (P<0.01); I^2=98%

Mode of investigation=pancreaticogram						
[36] Kreel and Sandin 1973	19.04	2.8900	34	4.8%	19.04 [18.07; 20.01]	
Total (95% CI)			**1,330**	**100.0%**	**16.53 [15.67; 17.39]**	
Prediction interval					**[12.38; 20.68]**	

Heterogeneity: Tau^2=3.7082; Chi^2=886.70, df=19 (P<0.01); I^2=98%
Test for subgroup differences: Chi^2=16.00, df=2 (P<0.01)

B **Forest plot estimating pooled estimate of length of accessory pancreatic duct (cm)**

Study or subgroup	Mean	SD	Total	Weight	Mean IV, random, 95% CI	Mean IV, random, 95% CI
[1] Anand et al. 1989	2.52	0.9100	55	25.3%	2.52 [2.28; 2.76]	
[2] Arora et al. 2011	3.90	0.8467	30	24.9%	3.90 [3.60; 4.21]	
[70] Malathi and Chitra 2022	4.07	1.0700	50	25.0%	4.07 [3.77; 4.37]	
[53] Pina 2016	2.94	1.1400	50	24.8%	2.94 [2.62; 3.26]	
Total (95% CI)			**185**	**100.0%**	**3.36 [2.62; 4.09]**	

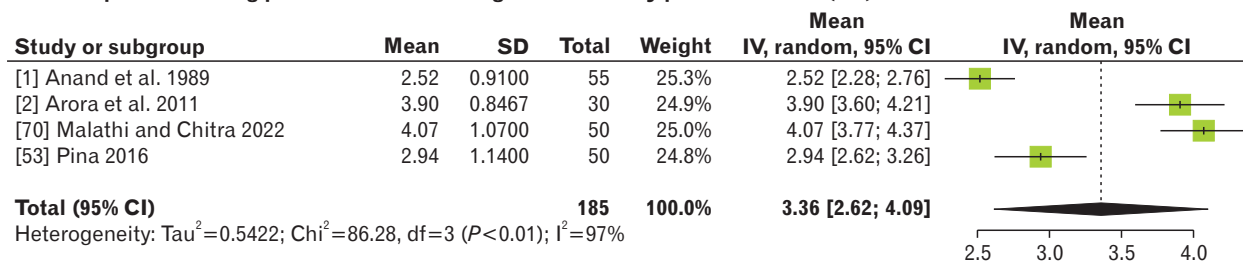Heterogeneity: Tau^2=0.5422; Chi^2=86.28, df=3 (P<0.01); I^2=97%

Fig. 6. Forest plot showing pooled estimate of the length of (A) the main pancreatic duct, and (B) the accessory pancreatic duct. SD, standard deviation; IV, inverse variance; CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography.

cm and 3.36 cm, respectively. The mean diameter of MPD at the head and that of the APD were 3.43 mm and 1.69 mm, respectively. The APD was present in only 41% of samples, and the long type predominated.

Comparison with earlier literature

A systematic review by Dimitriou et al. [7] revealed normal pancreatic ducts in 94.3% of 7,792 subjects. A review of nine studies by Dugic et al. [8] showed 89.9% of normal MPDs in 3,234 subjects. In both reviews, the MPD most commonly drained into the major papilla with or without communication with the APD [8]. The present study findings are similar to those of the two systematic reviews with respect to prevalence of MPDs. Furthermore, the present study adds the data related to the comparison between the dimensions of the MPD and APD, which has no prior mention in the literature.

Table 4. The distribution of variants of the pancreatic ductal system and pooled estimates of the length of the main pancreatic duct and accessory pancreatic in different populations

Pooled outcome of pancreatic duct variations	Asian	European	North American	South American	African
Proportion of normal variant (PDS)	0.96 (0.92–0.98)	0.86 (0.79–0.91)	0.76 (0.47–0.92)	0.67 (0.60–0.73)	NR
Proportion of PD or embryonic (PDS)	0.04 (0.02–0.07)	0.07 (0.05–0.09)	0.06 (0.03–0.09)	0.11 (0.07–0.16)	NR
Proportion of ansa pancreatica (PDS)	0.04 (0.01–0.11)	0.01 (0.00–0.03)	0.17 (0.10–0.25)	NR	NR
MPD length (cm)	16.18 (15.16–17.19)	18.05 (15.64–20.74)	16.15 (14.68–17.62)	15.76 (14.77–16.75)	NR
MPD diameter at head (mm)	3.28 (3.07–3.50)	3.88 (3.52–4.24)	3.23 (3.07–3.50)	2.90 (2.70–3.10)	2.44 (2.38–2.50)
MPD diameter at body (mm)	2.47 (2.25–2.69)	2.49 (2.16–2.81)	2.39 (1.88–2.90)	2.10 (2.07–2.13)	2.12 (2.07–2.17)
MPD diameter at tail (mm)	1.53 (1.38–1.68)	1.74 (1.22–2.26)	0.90 (0.81–0.99)	2.34 (2.18–2.50)	1.86 (1.81–1.91)
Proportion of APD	0.39 (0.26–0.54)	0.50 (0.26–0.74	0.40 (0.32–0.48)	0.62 (0.47–0.75)	0.29 (0.20–0.40)

Values are presented as mean (95% confidence interval). No data from Australian population. PDS, pancreatic ductal system; PD, pancreatic duct; MPD, main pancreatic duct; APD, accessory pancreatic duct; NR, not reported.

Clinical implications

Pancreatic duct variations can have several clinical implications. The ductal anastomosis with gut usually performed for chronic pancreatitis, trauma, tumor and other causes of ductal obstruction. Adequate identification pancreatic duct and its long inferior branch often confused with accessory duct. For example, a long APD can make a pancreaticoduodenectomy (a surgical procedure to remove the head of the pancreas) without injuring the duct more challenging [13]. Variations in pancreatic ductal anatomy can lead to the formation of pancreatic pseudocysts, fluid-filled sacs formed within the pancreas [11, 13, 17, 70, 71]. Pancreas divisum and ansa pancreatica can cause ductal obstruction, leading to chronic pancreatitis and recurrent acute episodes. However, not all patients with those variations develop pancreatitis; other factors such as genetics, lifestyle, and environment can also be involved [9, 12, 72, 73].

In ERCP, variations in pancreatic ductal anatomy, particularly if there is a long APD, can make it difficult to identify the MPD and to locate any blockages or strictures. This can lead to diagnostic errors, such as mistaking a blockage in the APD for one in the MPD or failing to identify a blockage in the MPD. Variations in pancreatic ductal anatomy can also increase the risk of complications during endoscopic procedures such as ERCP. For example, a long APD entails the risk of the contrast medium accidentally entering the duct, causing inflammation and infection during ERCP [73]. PDS variations can make therapeutic interventions such as stent placement more difficult to perform during ERCP, leading to diagnostic errors. They can also make it more difficult to diagnose conditions such as chronic pancreatitis, as the changes in ductal anatomy can mimic those seen in

this condition [74, 75]. Pancreatic duct length and width can influence the diagnosis and management of pancreatic pathologies, both clinically and surgically, and can be used as indicators of pancreatic inflammation or injury. For example, in acute pancreatitis, the pancreas is often enlarged and wider; in chronic pancreatitis, it can be shrunken and narrower. Pancreatic length and width can also affect the surgical management of pancreatic pathologies. For example, in pancreatic cancer, a longer pancreas can make it more difficult to perform a pancreaticoduodenectomy (removal of the head of the pancreas) because it increases the risk of injuring adjacent structures. Similarly, a wider pancreas can make a distal pancreatectomy (removal of the tail of the pancreas) more difficult [71, 76]. Overall, knowledge of pancreatic ductal anatomy variations is vital for diagnosing, treating, and managing pancreatic conditions.

There are some flaws in our study. First, data from several studies that used different categories to define the PDS in their subjects were evaluated together. Second, the studies were either prospective or retrospective, and their subjects came from various demographic groups. Our study is also limited by the variety of subjects we used: healthy volunteers, active patients, and cadavers. The key problem was the dearth of population studies with enough information to calculate the prevalence of each particular type of MPD and APD. Morphometric data appropriate for the subtypes of PDS were not available for further meta-analysis of estimates.

In conclusion, the meta-analysis showed a 92% prevalence of the normal PDS. The most common variant subtype was type 3, followed by type 1. The MPD was mostly of the "descending type" followed by the "sigmoid" and "vertical"

types, while a long APD was most common. The pancreatic divisum and ansa pancreatica were noticeably prevalent. Most of the MPDs (81%) terminated at the major duodenal papilla and the APDs at the minor duodenal papilla. Variations in pancreatic ductal anatomy can lead to the formation of pancreatic pseudocysts and can affect the surgical management of conditions such as pancreatic cancer and chronic pancreatitis. Variants such as pancreas divisum and ansa pancreatica can cause ductal obstruction, which can lead to further complications depending upon other factors such as genetics, lifestyle, and environment. Many of these variants can hinder ERCP, potentially cause diagnostic errors, and make therapeutic interventions difficult to perform. Variations in ductal length and width can affect the diagnosis of pancreatic inflammation or injury, and the surgical management of pancreatic pathologies.

Understanding the anatomical variations of the pancreatic ducts is critical for helping general surgeons to perform pancreatic anastomoses safely and effectively. Such knowledge is essential for invasive gastroenterology and ERCP as diagnostic and therapeutic methods. Rare structural alterations of the pancreatic ducts, such as pancreas divisum, afflict less than 6%.

ORCID

Adil Asghar: https://orcid.org/0000-0002-1404-1298
Ravi Kant Narayan:
https://orcid.org/0000-0003-2510-6744
Nagavalli Basavanna Pushpa:
https://orcid.org/0000-0001-6417-5350
Apurba Patra: https://orcid.org/0000-0002-1107-4481
Kumar Satish Ravi:
https://orcid.org/0000-0003-0527-2825
R. Shane Tubbs: https://orcid.org/0000-0003-1317-1047

Author Contributions

Conceptualization: AA. Data acquisition: AA. Data analysis or interpretation: AA, RKN. Drafting of the manuscript: AA, RKN, NBP, KSR. Critical revision of the manuscript: RKN, NBP, KSR, RST. Approval of the final version of the manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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