

Pancreatic cancer in Pakistan: A lens into the research landscape

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Abstract

Objective: To identify and categorise the types of research conducted on pancreatic cancer in Pakistan, to analyse gaps in the knowledge and focus areas within the existing research, and to prioritise research areas requiring immediate attention to improve patient care.

Method: The scoping review comprised literature search on PubMed, ScienceDirect, GoogleScholar and PakMedinet databases for research on pancreatic cancer done in the Pakistani population and published between January 1, 1998, and December 1, 2021. Key words included 'pancreatic neoplasms', 'pancreatic cancer', 'Pakistan' and their medical subject heading derivatives. Data about type of study, research methodology, geospatial location of the study site, date of publication and level of evidence was extracted by two independent evaluators. Cancer-specific variables included tumour location and histology. Interventions studied were grouped into surgical resections, systemic therapeutics and diagnostic modalities.

Results: Of 3,120 studies identified, 84(0.02%) were analysed. The most common study types were descriptive studies 25(30%), case reports 19(23%) and retrospective cohorts 11(13%). The trend of research showed an overall increase from 2-4 articles per annum in 2011-13 to 14 in 2021. The most studied neoplasm was located in the pancreatic head 32(38%), followed by neoplasms of the periampullary region 24(29%). Most studies were on surgical intervention 42(50%), followed by adjuvant and neoadjuvant chemotherapy 8(10%).

Conclusion: There was found to be little data about pancreatic cancer in Pakistan along all aspects of the disease process, including mechanistic, epidemiological, treatment, or outcome elements. Most research was found to be focussed on surgical care and short-term outcomes.

Keywords: Pancreatic neoplasms, Pancreatic cancer, Pakistan, Epidemiology, Health research priorities, Disease burden, Surgical outcomes, Chemotherapy, Low-and-middle income countries, LMICs. (JPMA 76: 1918; 2026)

DOI: <https://doi.org/10.47391/JPMA.10554>

Introduction

Pancreatic neoplasms consist of both benign and malignant pathologies. Pancreatic cancer (PC) is a deadly disease characterised by its aggressive nature and high mortality rate worldwide. Global incidence and mortality rates in 2020 reached up to 500,000 and 466,000, respectively.¹ While mortality rates have improved for many cancers, PC outcomes remain poor with 5-year survival rates remaining at <10%.

Pakistan is a middle-income country in South Asia with a population of over 212 million. Like many low- and middle-income countries (LMICs), Pakistan suffers from a burden of disease marked by a combination of communicable diseases and non-communicable diseases, and emerging globalisation-related health conditions, like pandemics.² Since public priority has been given to infectious and

cardiovascular diseases, cancers have often been neglected. The cancers with the highest incidence in Pakistan in 2020 were the breast (25,928), lip/oral cavity (16,959) and lung (10,538). Also, mortality with breast cancer (13,725), lip/oral cavity (10,617) and oesophageal cancer (9,443) contributing to overall cancer-related deaths in Pakistan.¹ These cancers have relatively prominent symptomatology, are more readily detected, and have more effective treatment strategies. PC, however, requires intensive resources from both the patient and the healthcare system, treatments are complex, and are often not effective.³ Therefore, PC has received little attention from policy-makers. While data is limited, the current burden of PC in Pakistan is estimated to be 1,162 new cases and 1,129 deaths each year.^{1,4} PC is responsible for 66,790 disability-adjusted life years (DALYs) per 100,000 population in Pakistan, which is an increase of 65.3% in age-standardised rates from 1990.⁵ However, these numbers likely underestimate the true burden as diagnostic services for PC is unavailable or inaccessible to most of the population. Development of infrastructure to address the burden of this deadly disease requires targetted intervention in line with the resource constraints of the country.

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Submission complete: 10-03-2024 **1st Revision received:** 26-11-2024

Acceptance: 25-07-2026

Last Revision received: 24-07-2026

Annexure 1: Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist.⁵

Section	Item	Prisma-ScR checklist item	Reported on page #
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	4
Objectives	3	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	N/A
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	5
Information sources	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	S1 File
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	5
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	N/A
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	N/A
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	6
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	6
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	6
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	N/A
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	7
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	7
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	8
Limitations	20	Discuss the limitations of the scoping review process.	9
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	9
FUNDING			
FUNDING	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	N/A

JBI: Joanna Briggs Institute; * Where sources of evidence (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and websites; † A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with information sources (see first footnote); ‡ The frameworks by Arksey and O'Malley(6) and Levac et al. (7) and the JBI guidelines (4,5) refer to the process of data extraction in a scoping review as data charting; § The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

For strategies how to better address PC in Pakistan, the first step is to generate local data. It is imperative to understand disease epidemiology, management options and outcomes. The current scoping review was planned to synthesise all available literature on pancreatic neoplasms in Pakistan to better provide insight into this deadly disease from the perspective of an LMIC, and to identify gaps in the literature to help prioritise research needs.

Annexure 2: Search strategies.

Search Engines: PubMed, GoogleScholar, ScienceDirect, PakMediNet

PubMed:

("pancreatic neoplasms"[MeSH Terms] OR ("pancreatic neoplasms"[MeSH Terms] OR ("pancreatic"[All Fields] AND "neoplasms"[All Fields]) OR "pancreatic neoplasms"[All Fields] OR ("pancreatic"[All Fields] AND "cancer"[All Fields]) OR "pancreatic cancer"[All Fields]) OR ("pancreas"[MeSH Terms] OR "pancreas"[All Fields] OR "pancreatic"[All Fields] OR "pancreatitides"[All Fields] OR "pancreatitis"[MeSH Terms] OR "pancreatitis"[All Fields]) AND ("neuroendocrine tumours"[All Fields] OR "neuroendocrine tumors"[MeSH Terms] OR "neuroendocrine"[All Fields] AND "tumors"[All Fields]) OR "neuroendocrine tumors"[All Fields])) OR (("pancrea"[All Fields] OR "pancreas"[MeSH Terms] OR "pancreas"[All Fields]) AND ("cancer s"[All Fields] OR "cancerated"[All Fields] OR "canceration"[All Fields] OR "cancerization"[All Fields] OR "cancerized"[All Fields] OR "cancerous"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields] OR "cancers"[All Fields])) AND ("pakistan"[MeSH Terms] OR "pakistan"[All Fields] OR "pakistan s"[All Fields])

For GoogleScholar:

All in title: "pancreatic oncology" OR "pancreatic neoplasms" OR "pancreatic cancer" OR ("pancreatic" AND "neoplasms") OR "neuroendocrine tumours" OR ("pancreas" OR "pancreas" OR "pancreas") AND "cancer") AND ("pakistan" OR "pakistanis")

For ScienceDirect:

(pancreatic cancer OR pancreatic adenocarcinoma OR ((pancreatic) AND (cancer OR tumor OR adenocarcinoma)) OR periampullary OR Pancreatoduodenectomy) AND Pakistan

For PakMediNet:

PakMediNet requires individual search phrases: "Pancreatic cancer", "Pancreatic neoplasm", "Pancreatic tumor", "Pancreatic metastasis", "Insulinoma"

Materials and Methods

The scoping review comprised literature search on PubMed, ScienceDirect, GoogleScholar and PakMedinet databases for research on pancreatic cancer done in the Pakistani population and published between January 1, 1998, and December 1, 2021. The review was performed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines.⁶ Databases were searched with the help of medical subjects heading (MeSH), Emtree terms and/or key words in Title, Abstract and Key word fields. The Search was limited to studies published in the English language. Articles on non-cancer pathologies were excluded. Eligible articles were those that reported data about PC detection, diagnosis and/or treatment services, including articles on cancer that referred to PC in Pakistan or available services for PC.

Publications identified through the database search were organised by title and abstract using Covidence. Two reviewers screened the articles for inclusion, and any conflict was resolved by two other reviewers. Full-text articles were then screened for eligibility based on the inclusion/exclusion criteria, and the shortlisted articles were chosen for the scoping review.

Data were extracted by two independent evaluators, and it was stored in Microsoft Excel. Data was extracted on the type of study (epidemiology, diagnosis, treatment, basic sciences and unique presentations), research methodology (cross-sectional, case reports, prospective and retrospective cohorts), geospatial location of where a study was performed, date of publication, and level of evidence. Cancer-specific variables included tumour location and histology. Interventions studied were grouped into surgical resections, systemic therapeutics, and diagnostic modalities.

Results

Of the 3,125 studies identified initially, 134(4.3%) were subjected to full-text review, and, of them, 84(63%) were included for detailed analysis (Figure).⁷⁻⁹⁰

There were 25(29%) descriptive studies, 11(13%) retrospective cohort studies, 6(7%) basic science studies, 2(2.4%) case-control studies, 19(23%) case reports, 8(10%) case series, and 7(8%) cross-sectional studies (Table). Most studies had II-B level of evidence 44(52%), consisting mainly of observational studies, followed by level IV 26(31%), and level III-B 7(8%) (Table). An overall increase in research over the past 24 years was observed, rising from

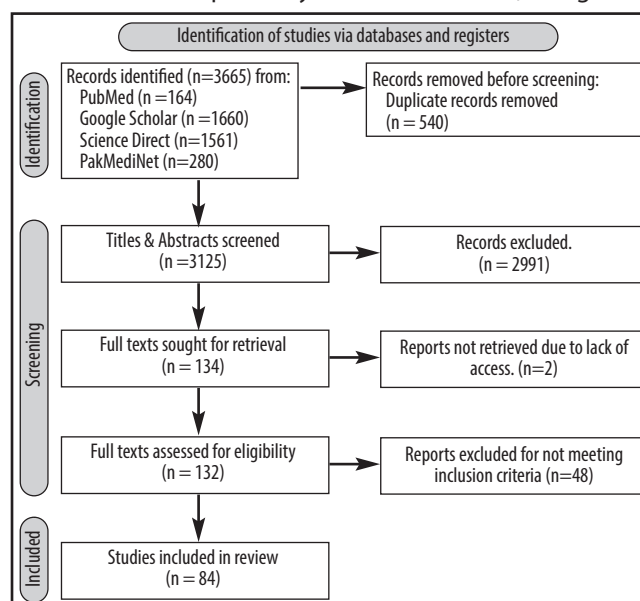


Figure: Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 flow diagram.

Table: Summary of the studies analysed.

Author	Title	Date of Publication	Location of study	Type of study
Ahmed et al. ⁷	Molecular Basis of Treatment with Heat Ablation, Cryoablation or Dual Thermal Ablation in Pancreatic Cancer Cells	1/10/19	Faisalabad	Basic Science
Ali et al. ⁸	Genetic landscape of pancreatic adenocarcinoma patients: a pilot study from Pakistan	11/23/21	Karachi	Basic Science
Fakhar et al. ⁹	Antagonistic role of Klotho-derived peptides dynamics in the pancreatic cancer treatment through obstructing WNT-1 and Frizzled binding	9/1/18	Islamabad	Basic Science
Naeem et al. ¹⁰	Clinicopathological Study of Solid Pseudopapillary Tumor of Pancreas	1/1/17	Lahore	Basic Science
Nisar et al. ¹¹	Integrated Analysis of Microarray and RNA-Seq Data for the Identification of Hub Genes and Networks Involved in Pancreatic Cancer	6/23/21	Islamabad	Basic Science
Raja et al. ¹²	Genomic relevance of FGF14 and associated genes on the prognosis of pancreatic cancer	6/1/21	Islamabad	Basic Science
Alam et al. ¹³	Evaluation of Carcino-Embryonic Antigen (CEA) and Diagnostic Significance in Adult Patients Suffering from Colorectal	1/12/10	Karachi	Case Control Study
Choudhary et al. ¹⁴	Comparison of CEA and CA 19-9 with CA 72-4 in patients with upper gastrointestinal carcinomas in local population	6/1/10	Lahore	Case Control Study
Afzal et al. ⁸⁷	Pancreatic lymphangioma	1/1/14	Karachi	Case Report
Ahmed et al. ¹⁵	Solid and cystic epithelial neoplasm of pancreas with metastasis: report of a highly unusual case	1/1/01	Islamabad	Case Report
Amini et al. ¹⁶	Periapillary Neuroendocrine (Carcinoid) Tumor in a Patient with Neurofibromatosis Type I	1/1/15	Karachi	Case Report
Aurangzeb et al. ¹⁷	Synchronous Adenocarcinoma of gall bladder and Ampulla of Vater	4/1/08	Sialkot	Case Report
Bhatti et al. ¹⁸	Multivisceral central pancreatectomy for pancreatic neuroendocrine tumor: A case report on a novel surgical technique	1/1/21	Islamabad	Case Report
Fatima et al. ²⁵	Fine Needle Aspiration Cytology of Pseudopapillary Tumour of Pancreas	09/1/08	Karachi	Case Report
Husen et al. ¹⁹	Acinar Cell Carcinoma of Pancreas in a Child: A Radiological Perspective	10/1/15	Karachi	Case Report
Khokhar et al. ²⁰	Missed Carcinoma of Pancreas at open Cholecystectomy	4/1/03	Islamabad	Case Report
Malik et al. ²¹	Moderately differentiated ductal carcinoma pancreas involving periampullary region	4/1/15	Lahore	Case Report
Mehmood et al. ²²	Removal of Malfunctioning Biliary Plastic Stent Via Percutaneous Transhepatic Cholangiography	1/1/17	Karachi	Case Report
Rashid et al. ²³	Localizing an occult insulinoma by selective calcium arterial stimulation test: first ever experience and a new dimension to diagnosis in Pakistan	9/1/20	Karachi	Case Report
Rathore et al. ²⁴	Serous cystadenocarcinoma of pancreas	1/1/13	Quetta	Case Report
Rehman et al. ²⁶	Insulinoma - a deceptive endocrine tumour	9/1/11	Islamabad	Case Report
Sahaab et al. ²⁷	Successful outcome after Pancreaticoduodenectomy in an elderly cirrhotic patient: A case report.	4/10/19	Islamabad	Case Report
Sajid et al. ²⁸	Paediatric pseudo papillary pancreatic tumour: A case based review	6/1/21	Karachi	Case Report
Salahuddin et al. ²⁹	Unusual presentation of metastatic pancreatic carcinoma	5/1/21	Karachi	Case Report
Shafique et al. ³⁰	Ampullary carcinoid tumour presenting with extrahepatic biliary obstruction	8/1/15	Rawalpindi	Case Report
Tariq et al. ³¹	Extra pancreatic solid pseudopapillary tumour in a young male	10/1/16	Islamabad	Case Report
Zahid et al. ³²	Neuroendocrine tumour of the ampulla of Vater: A rare neoplasm at an atypical site	5/1/21	Lahore	Case Report
Ahmed et al. ³³	Solid cystic Papillary Epithelial neoplasm of Pancreas: a series of three cases with review of literature	7/1/04	Karachi	Case Series
Amin et al. ³⁴	Role of MDCT in detecting patterns of recurrence after Whipple procedure in follow-up of pancreatic malignancy.	4/1/14	Islamabad	Case Series
Batool et al. ³⁵	Vascular Resection and Reconstruction in Pancreatic Tumours	1/1/18	Lahore	Case Series
Gondal et al. ⁸⁶	Treatment Options for Pancreatic Tumours	4/1/02	Lahore	Case Series
Malik et al. ³⁶	Validity of surgical bypass in unresectable pancreatic cancer	4/1/13	Jamshoro	Case Series
Shah et al. ³⁷	Surgical Outcome of Pancreaticoduodenectomy in Pancreatic and Periampullary Neoplasms	9/21/17	Lahore	Case Series
Tariq et al. ³⁹	Serous cystadenoma of pancreas: A clinicopathologic experience of 23 cases from a major tertiary care center.	1/1/18	Karachi	Case Series
Tufail et al. ⁹⁰	Pancreaticoduodenectomy for Periampullary Carcinoma - A Five Years Experience	1/1/00	Lahore	Case Series
Ahmad et al. ⁴⁰	Extrahepatic Biliary Obstruction: A study of etiological factors in a teaching Hospital	12/1/20	Lahore	Cross-sectional Study
Aziz et al. ⁴¹	Incidence of malignant Obstructive Jaundice - a study of hundred patients at Nishtar Hospital Multan	1/1/04	Multan	Cross-sectional Study
Lail et al. ⁴²	Reports of gastrointestinal cancers at Bahawal Victoria Hospital, Bahawalpur Pakistan	2/1/12	Bahawalpur	Cross-sectional Study
Mehdi et al. ⁴³	Frequency of Gastrointestinal Tumours at A Teaching Hospital in Karachi	1/1/98	Karachi	Cross-sectional Study
Qureshi et al. ⁴⁴	Diagnostic utility of endoscopic ultrasound guided aspiration cytology in evaluation of pancreatic masses	1/1/13	Lahore	Cross-sectional Study
Salim et al. ⁴⁵	Management and Outcome of Jaundice Secondary To Malignancies of the Gall Bladder, Biliary Tree and Pancreas: a Single Centre Experience	10/1/18	Lahore	Cross-sectional Study
Yousaf et al. ⁴⁶	Surgical Outcome Of Upper Gastrointestinal Malignancies	2/1/16	Peshawar	Cross-sectional Study
Abrar et al. ⁴⁷	Predictive value of CA 19-9 in patients with pancreatic tumours	1/1/20	Lahore	Descriptive Study
Aslam et al. ⁴⁸	Early complications following Pancreaticoduodenectomy	11/1/05	Karachi	Descriptive Study
Bari et al. ⁴⁹	Managing pancreatic cancer; experience from an HBP unit of oncology center of Pakistan	1/1/18	Lahore	Descriptive Study
Bhatti et al. ⁵⁰	Long term outcomes after pancreaticoduodenectomy: A single center experience from Pakistan	7/1/21	Islamabad	Descriptive Study
Bilal et al. ⁵¹	Whipple Resection: Concordance Between Frozen Section and Permanent Section Diagnosis of Surgical Margins	1/1/18	Islamabad	Descriptive Study
Chawla et al. ⁵²	Pancreaticogastrostomy – An alternate for dealing with pancreatic remnant after pancreaticoduodenectomy – Experience from a tertiary care center of Pakistan	10/1/18	Karachi	Descriptive Study
Dalwani et al. ⁸⁹	Evaluation of Various Causes and Treatment of Obstructive Jaundice at Liaquat University Hospital	6/1/13	Hyderabad/Jamshoro	Descriptive Study
Din et al. ⁵³	Solid pseudopapillary neoplasm of the pancreas. A clinicopathologic study of 25 cases from Pakistan and review of Literature.	1/1/14	Karachi	Descriptive Study
Hanif et al. ⁵⁴	Diagnostic accuracy of ultrasound in evaluation of obstructive jaundice with MRCP as gold standard Accuracy of ultrasound in obstructive jaundice	5/1/20	Karachi	Descriptive Study
Haq et al. ⁵⁵	Outcome of Surgical Management of Carcinoma of the pancreas	1/10/05	Lahore	Descriptive Study
Jahan et al. ⁵⁶	Fine-Needle Aspiration Cytology in the Diagnosis of Pancreatic Neuroendocrine Tumors: A Single-Center Experience of 25 Cases	4/1/15	Lahore	Descriptive Study
Khanum et al. ⁵⁷	Accuracy of Diagnostic Ultrasound Detection of Pancreatic Head Carcinoma	10/1/17	Lahore	Descriptive Study
Majid et al. ⁵⁸	Ultrasound Guided Biopsy- a Useful Method of Extraction of Sample Tissues to Examine the Diagnostic Accuracy of Malignant and Benign Lesions	10/1/18	Peshawar	Descriptive Study

Continued on next page.....

Table: *Continued from previous page.*

Author	Title	Date of Publication	Location of study	Type of study
Mamoon et al. ⁵⁹	Endoscopic ultrasound guided aspiration cytology - a useful diagnostic tool	4/1/11	Rawalpindi	Descriptive Study
Mamoon et al. ⁶⁰	Gastroenteropancreatic neuroendocrine tumours: Clinicopathological evaluation at Shifa International Hospital, Islamabad	2/1/21	Islamabad	Descriptive Study
Manzoor et al. ⁶¹	Are Gastrointestinal Tract Malignancies, Diseases of Old Age? In South Western Region of Pakistan Too	1/1/15	Quetta	Descriptive Study
Masud et al. ⁶²	Role of radiology in pancreatic disorders	1/1/09	Muzaffarabad/ Sialkot	Descriptive Study
Mumtaz et al. ⁶³	Comparison of magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography in hepatobiliary disorders	1/1/11	Rawalpindi	Descriptive Study
Nasim et al. ⁶⁴	Pancreaticoduodenectomy – A tertiary care hospital experience	1/1/12	Karachi	Descriptive Study
Pal et al. ⁶⁵	Pancreaticoduodenectomy: a developing country perspective	3/1/11	Karachi	Descriptive Study
Raouf et al. ⁶⁶	Diagnostic accuracy of perfusion-CT using Peak Enhancement Intensity (PEI) in detecting high grade pancreatic ductal adenocarcinoma keeping histopathology as gold standard	11/1/19	Faisalabad	Descriptive Study
Rauf et al. ⁶⁷	Periampullary Carcinoma: Clinical Presentation and Diagnosis - a hospital based study	7/1/03	Multan	Descriptive Study
Rehman et al. ⁶⁸	The CT Criteria of Non Resectability for Pancreatic Carcinoma	1/6/17	Karachi	Descriptive Study
Siddique et al. ⁶⁸	Evaluation of the aetiological spectrum of obstructive jaundice	10/1/08	Rawalpindi	Descriptive Study
Yawar et al. ⁶⁹	Multidetector CT Patterns of Peritoneal Involvement in Patients with Abdominopelvic Malignancies	3/1/15	Islamabad	Descriptive Study
Garland et al. ⁷⁰	Cloud cover-adjusted ultraviolet B irradiance and pancreatic cancer incidence in 172 countries	4/1/15	California	Epidemiological
Yasmeen et al. ⁸⁵	Efficacy of neoadjuvant chemotherapy for locally advanced pancreatic cancer: a single institution retrospective review	1/1/17	Lahore	Interventional Study
Ahmed et al. ⁷²	Pancreaticojejunostomy or pancreaticogastrostomy to prevent pancreatic fistula formation after pancreaticoduodenectomy	1/1/16	Rawalpindi	Prospective Cohort Study
Bhatti et al. ⁷³	Survival advantage with para aortic lymphadenectomy in peri-ampullary cancer: A retrospective cohort study.	7/1/16	Islamabad	Retrospective Cohort Study
Bhatti et al. ⁷⁴	Preoperative Endoscopic Biliary Stenting Before Pancreaticoduodenectomy: Does Timing Matter?	10/1/21	Islamabad	Retrospective Cohort Study
Dar et al. ⁷⁵	Is pancreaticoduodenectomy with vascular resection a safe procedure in developing country? Early outcomes and review of national literature	9/1/15	Islamabad	Retrospective Cohort Study
Hussain et al. ⁷⁶	Surgical palliation for unresectable Pancreatic carcinoma	12/1/04	Karachi	Retrospective Cohort Study
Jamal et al. ⁷⁷	Pancreaticoduodenectomy: Outcomes of a complex surgical procedure from a developing country.	1/1/20	Lahore	Retrospective Cohort Study
Khan et al. ⁷⁸	Impact of Different Treatment Modalities on the Outcome of Pancreatic Cancer	8/1/17	Lahore	Retrospective Cohort Study
Malik et al. ⁷⁹	Coeliac Plexus Neurolysis for Pancreatic Cancer patients; Retrospective Analysis of Shaikat Khanum Memorial Cancer Hospital & Research Centre Experience	10/1/18	Lahore	Retrospective Cohort Study
Noor et al. ⁸⁰	Pancreaticogastrostomy: a Safe Option in Pancreaticoduodenectomy for Pancreatic Head and Periampullary Neoplasms.	1/1/20	Lahore	Retrospective Cohort Study
Qureshi et al. ⁸¹	Anatomic Level of Biliary Obstruction and Outcome of Pre-Operative Biliary Stenting in Malignant Obstructive Jaundice - A Shaikh Zayed Hospital Experience	1/1/08	Lahore	Retrospective Cohort Study
Yasmeen et al. ⁷¹	Efficacy of chemotherapy for locally advanced and metastatic pancreatic cancer: A single institution experience from a third world country	10/1/17	Lahore	Retrospective Cohort Study
Zahir et al. ⁸²	Metastatic pancreatic carcinoma and experience with FOLFIRINOX: A cross-sectional analysis from a developing country	1/1/15	Karachi	Retrospective Cohort Study
Zafar et al. ⁸⁸	A comprehensive review on anticancer mechanism of bazedoxifene	3/24/21	Lahore	Review
Zahra et al. ⁸³	Synthesis and Therapeutic Potential of Nanoceria against Cancer: An Update	1/1/21	Faisalabad	Review
Pourhoseingholi et al. ⁸⁴	Systematic review of pancreatic cancer epidemiology in Asia-Pacific Region: major patterns in GLOBACON 2012	9/30/17	Tehran	Systematic Review

11 articles in 8 years between 1998 and 2005, to 55 articles published between 2015 and 2021 (Table). Most articles were published from major cities of Lahore 24(29%), Karachi 21(25%), and Islamabad 17(20%) (Table).

Among the articles that specified histopathological diagnosis of the lesions, the most studied neoplasms were adenocarcinomas 20(24%), carcinoma unspecified 18(21%), neuroendocrine tumours 8(10%) and pseudopapillary tumours 6(5%). Other pathologies reported included cystadenocarcinoma 1(1%), and multiple/others 13(15%). The studies that specified location of the lesions predominantly reported tumours in the head 32(38%) and ampullary/periampullary 24(29%) region.

Other locations included the body 10(12%), tail 6(7%), intraductal 3(4%) and others 1(1%).

Most studies focussed on surgical intervention 42(50%), followed by adjuvant chemotherapy 7(8%), neoadjuvant chemotherapy 2(2%) and neoadjuvant radiation 2(2%). Neoadjuvant studies focussed on 5-FU-based, gemcitabine-based and capecitabine-based therapy and their efficacy in locally-advanced PC. Further, 1(1%) study compared the efficacy of folfrinix vs gemcitabine-based therapy on stage IV PC patients, finding that folfrinix therapy had significantly better median overall survival for the cohort ($p=0.002$). The surgical technique most often studied was the Whipple procedure 19(23%). Only a few

studies used other techniques, such as distal pancreatectomy 4(5%), central pancreatectomy 2(2%), total pancreatectomy 2(2%) and enucleation 2(2%). Outcomes of interest pertained to mortality in 29(35%) studies, morbidity 19(23%), postoperative complications 23(27%), intraoperative complications 7(8%), surgical technique 22(26%), length of hospital stay 4(5%), and long-term outcomes 12(14%). No study was found that explored quality of life, end-of-life care and palliation for PC patients in Pakistan.

Discussion

The current review demonstrates a dearth of PC research in Pakistan. Although the increasing trend of publications has offered some reassurance, studies have largely relied on retrospective data, with a severe lack of prospective studies and randomised data, as well as negligible basic science research. Most clinical studies have focussed on post-surgical outcome data, with very few population-level studies or those on specific chemotherapeutic efficacy or radiation therapy. Research gaps were noted in all aspects of the cancer care continuum, from epidemiology to survivorship, with the largest gap in survivorship.

Most PC research was from a handful of tertiary centres. Therefore, patients without ready access to these locations may be unaccounted for, and not represented in local research. Additionally, due to the absence of a national registry, estimates of the true PC burden is severely limited.^{91,92} Lack of epidemiological studies also prevents meaningful insight into population-specific risk factors for the disease, as certain areas in Pakistan see higher than average proportions of patients being exposed to specific risk factors, such as betel nut use, unique dietary intakes, and environmental exposures.⁹²⁻⁹⁴ It may be useful to know these risk factors to understand differences in tumour biology and patterns of disease in the people of Pakistan. Local data has shown that religious beliefs and attitudes towards healthcare also act as problematic barriers to healthcare, coupled with system failures due to political instability and institutional corruption. Although certain cancers (e.g. breast) have seen a significant amount of efforts made to increase literary works and evidence-based practises, significant limitations in infrastructure, allocation of resources, qualified researchers, and formal research-centric training and development have resulted in severely neglected areas.⁹⁵

Furthermore, the focussed nature of publications out of these specific hubs provides evidence to the barriers that plague healthcare delivery as a whole in Pakistan. Patients with significant issues accessing these specific high-volume centres (e.g. distant areas, poor infrastructure for

transportation, and lack of literacy) may not receive quality care, and, hence, may have suboptimal disease management and greater mortality. As such, efforts need to be made to understand and optimise methods of work-up and care delivery for PC in resource-limited settings. Patients often travel large distances to tertiary care centres for each clinical visit, and possibly require management that is applicable in the local context as opposed to importing management guidelines from high-income countries.⁹⁶

To improve the current research landscape in Pakistan, priority should be given to the creation of an effective national cancer registry to adequately assess the burden of cancer in the country. Once at-risk populations are identified, public health experts, policymakers and trained research staff should be recruited to devise focussed strategies to incentivise ethical research. Collaborations should be promoted between high-volume centres across the country, and outreach programmes should be devised. Development of multidisciplinary task forces consisting of surgeons, oncologists, gastroenterologists and others should define research goals, and outline strategies to realistically see them to fruition. These can help focus efforts to areas currently known to be severely lacking, such as population-specific chemotherapeutic use, randomised trials and survivorship. Local trials need to be conducted to formulate diagnostic, surveillance and therapeutic guidelines that may ensure adequate care delivery.

A key limitation to the current review is the inability to obtain full texts for two manuscripts that met the inclusion criteria. This was mostly due to an inadequate online archive and poor website design, with no links to full-text articles and lack of author contact information. However, these manuscripts were from lower quality journals, and would not have significantly impacted the findings.

Conclusion

PC research is limited in Pakistan, and efforts need to be made to systematically broaden research in all phases of the cancer continuum, including cancer aetiology, prevention, early detection, diagnosis, treatment, survivorship, and end-of-life care.

Acknowledgements: The authors would like to thank Aashir Aslam for his contribution in writing and editing of the manuscript.

Disclaimer: The text was presented at the Academic Surgical Congress 2022 in Orlando, Florida, United States.

Conflict of Interest: None.

Source of Funding: None.

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MeSH: Medical subject heading.

Annexure 3: Citations for the studies analysed

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Author Contribution:

SAP & KSA: Concept, literature search, methodology, data analysis, writing and review.

MK & NA: Data extraction, analysis, writing and review.

SNZ: Concept, methodology, writing, review and supervision.