

World Journal of *Clinical Oncology*

World J Clin Oncol 2024 December 24; 15(12): 1459-1527



EDITORIAL

- 1459 Chronic pancreatitis as a driving factor for pancreatic cancer: An epidemiological understanding
Das A, Bararia A, Mukherjee S, Sikdar N
- 1463 Advancements and challenges in the treatment of esophageal cancer: A comprehensive review
Christodoulidis G, Agko SE, Koumarelas KE, Kouliou MN, Zacharoulis D

ORIGINAL ARTICLE**Retrospective Study**

- 1468 Paclitaxel for second-line treatment of squamous cell carcinoma of the head and neck: A multicenter retrospective Italian study
Fasano M, Pirozzi M, Vitale P, Damiano V, Ronzino G, Farese S, Carfora V, Ciccarella G, Di Giovanni I, Facchini S, Cennamo G, Caraglia M, Ciardiello F, Addeo R
- 1481 Germline pathogenic variants among high hereditary risk patients with breast and ovarian cancer and unaffected subjects in Lebanese Arab women
Moukadem HA, Fakhreddine MA, Assaf N, Safi N, Al Masry A, Al Darazi M, Mahfouz R, El Saghir NS

Clinical Trials Study

- 1491 New cheaper human papilloma virus mass screening strategy reduces cervical cancer incidence in Changsha city: A clinical trial
Zu YE, Wang SF, Peng XX, Wen YC, Shen XX, Wang XL, Liao WB, Jia D, Liu JY, Peng XW

CASE REPORT

- 1501 DEK::AFF2 fusion-associated middle ear non-keratinizing squamous cell carcinoma: A case report
Sun YW, Zhou Y, Liu XY, Shen DH
- 1507 Orbital and sinus rhabdomyosarcoma with concurrent central retinal artery occlusion: A case report
Ma Y, Jia B, He XJ, Cai YX, Chen JY, Zhong JX
- 1514 Diabetic ulcer with cutaneous squamous cell carcinoma: A case report
Luo Y, Li CY, Wang YQ, Xiang SM, Zhao C

LETTER TO THE EDITOR

- 1520 Exploring a new chapter in traditional Chinese medicine: The potential of *Calculus bovis* in liver cancer treatment
Du H, Chen HB, Zhao Y

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Oncology*, Tomoyuki Takura, PhD, Professor, Department of Healthcare Economics and Health policy, Graduate School of Medicine, The University of Tokyo, Tokyo 113-8655, Japan. ttakura@m.u-tokyo.ac.jp

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Oncology* (*WJCO*, *World J Clin Oncol*) is to provide scholars and readers from various fields of oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJCO mainly publishes articles reporting research results and findings obtained in the field of oncology and covering a wide range of topics including art of oncology, biology of neoplasia, breast cancer, cancer prevention and control, cancer-related complications, diagnosis in oncology, gastrointestinal cancer, genetic testing for cancer, gynecologic cancer, head and neck cancer, hematologic malignancy, lung cancer, melanoma, molecular oncology, neurooncology, palliative and supportive care, pediatric oncology, surgical oncology, translational oncology, and urologic oncology.

INDEXING/ABSTRACTING

The *WJCO* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJCO* as 2.6; JIF without journal self cites: 2.6; 5-year JIF: 2.7; JIF Rank: 175/322 in oncology; JIF Quartile: Q3; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yu-Qing Zhao*; Production Department Director: *Xu Guo*; Cover Editor: *Xu Guo*.

NAME OF JOURNAL

World Journal of Clinical Oncology

ISSN

ISSN 2218-4333 (online)

LAUNCH DATE

November 10, 2010

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Hiten RH Patel, Stephen Safe, Jian-Hua Mao, Ken H Young

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2218-4333/editorialboard.htm>

PUBLICATION DATE

December 24, 2024

COPYRIGHT

© 2024 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Chronic pancreatitis as a driving factor for pancreatic cancer: An epidemiological understanding

Amlan Das, Akash Bararia, Sanghamitra Mukherjee, Nilabja Sikdar

Specialty type: Oncology

Provenance and peer review:
Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade C

Novelty: Grade B, Grade C

Creativity or Innovation: Grade B, Grade C

Scientific Significance: Grade B, Grade C

P-Reviewer: Pan YZ; Vanella G

Received: May 21, 2024

Revised: September 21, 2024

Accepted: October 8, 2024

Published online: December 24, 2024

Processing time: 153 Days and 22.3 Hours



Amlan Das, Department of Biochemistry, Royal Global University, Guwahati 781035, India

Akash Bararia, Nilabja Sikdar, Human Genetics Unit, Indian Statistical Institute, Kolkata 700108, India

Sanghamitra Mukherjee, Department of Pathology, R. G. Kar Medical College and Hospital, Kolkata 700004, India

Nilabja Sikdar, Scientist G, Estaurine and Costal Studies Foundation, Howrah 711101, India

Corresponding author: Nilabja Sikdar, PhD, Research Scientist, Human Genetics Unit, Indian Statistical Institute, No. 203 Plot, Barrackpore Trunk Road, Dunlop, Bonhooghly Government Colony, Kolkata 700108, India. snilabja@gmail.com

Abstract

The retrospective study by Lew *et al* (2022) examined the rising hospitalization rates for chronic pancreatitis (CP) and its association with pancreatic ductal adenocarcinoma (PDAC), revealing significant ethno-racial disparities and risk factors. Overweight black men aged 40-59 years and white men over 40 years with higher incomes showed an elevated risk of PDAC among CP patients. The study, which included 14.2 million admissions from 2016-2017, found that 2.6% of adult patients were diagnosed with CP, with white males being the majority. Multi-variate regression analysis identified men, black individuals, those aged 40-59 years, and individuals with a body mass index (BMI) between 25 and 29.9 as having an increased risk for CP. Moreover, 0.78% of CP patients also had PDAC, with older age and BMI being significant risk factors for developing PDAC in CP patients. The study also highlighted disparities in healthcare access and utilization among different socioeconomic and ethno-racial groups, which may impact the risk and outcomes of CP and PDAC.

Key Words: Pancreatic ductal adenocarcinoma; Chronic pancreatitis; Acute pancreatitis; Epidemiological study, Pancreatic cancer

©The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: The United States has a high incidence of pancreatic cancer (PanCa) cases that result from chronic pancreatitis (CP). This link between diseases is well-established in many scientific studies and clinical practices. In CP, the chronic inflammation of the pancreas causes DNA mutations and cellular changes that may make one prone to cancerous tumors. The CP is responsible for the persistent damage and fibrosis as a consequence of continuous inflammation of the organ over time. Such chronic inflammation promotes DNA mutations and oxidative stress, and damages cells thus leading to an increased risk of carcinogenesis. On a long-term basis, these alterations can cause the development of pancreatic intraepithelial neoplasia, a precancerous stage prior to pancreatic ductal adenocarcinoma (PDAC), which is another name for PDAC; it's also regarded as the most prevalent type of this ailment. An example is that hereditary pancreatitis patients have up to 40% lifetime risk by age 70 years. Non-genetic CP also increases risks, although not very greatly. Development of PanCa is partly associated with CP risk factors like genetic mutations such as protease serine 1, serine protease inhibitor kazal type 1, cystic fibrosis transmembrane conductance regulator, heavy alcohol use, and smoking.

Citation: Das A, Bararia A, Mukherjee S, Sikdar N. Chronic pancreatitis as a driving factor for pancreatic cancer: An epidemiological understanding. *World J Clin Oncol* 2024; 15(12): 1459-1462

URL: <https://www.wjgnet.com/2218-4333/full/v15/i12/1459.htm>

DOI: <https://dx.doi.org/10.5306/wjco.v15.i12.1459>

INTRODUCTION

Our editorial addresses the retrospective study published by Lew *et al*[1] in 2022 which demonstrated an extensive nationwide study indicating a significant rising pattern in hospitalization rates for chronic pancreatitis (CP), particularly affecting overweight black men aged 40-59 years. Additionally, white men over 40 years who were overweight and had higher incomes showed an elevated risk of pancreatic ductal adenocarcinoma (PDAC) among CP patients. The primary objectives of the study included examining the ethno-racial disparities in hospital admissions for CP compared to the general population and between CP and PDAC. Additionally, the secondary outcome focused on assessing associations between ethnicity/race and hospitalization outcomes (mortality, length of stay, and expenses) among CP and PDAC patients. In their study sample covering the years 2016-2017, comprising 14.2 million admissions, 371275 adult patients (2.6%) were diagnosed with CP with the majority being white (64.8%) and male (55.7%). Interestingly, in multivariate regression analysis, certain demographic factors and health indicators exhibit associations with the likelihood of developing CP. Men [adjusted odds ratio (aOR) = 1.35], black individuals (aOR = 1.13), those aged 40-59 years (aOR = 2.60), and individuals with a body mass index (BMI) between 25 and 29.9 (aOR = 1.34), demonstrated an increased risk for CP. Furthermore, it was also observed that 0.78% of the adult patients admitted with CP, also had PDAC and the subsequent multivariate regression analysis revealed significant risk factors for developing PDAC in patients with CP, such as older age (> 40 years, aOR = 1.05) and BMI (between 25 and 29.9, aOR = 2.40). Contrary to the risk factors, certain demographics were found to be associated with a decreased likelihood of PDAC in CP patients: (1) Women (aOR = 0.77); (2) Blacks (aOR = 0.77); and (3) Hispanics (aOR = 0.66) respectively, highlighting the associations between sex as well as ethnicity/race and disease outcomes. Additionally, the study revealed that patients with CP and PDAC were significantly more likely to have higher median incomes, lower rates of being uninsured, and high rates of being admitted to large urban teaching hospitals when compared to CP patients alone. These findings suggest disparities in healthcare access and utilization among different socioeconomic and ethno-racial groups, which may impact the risk and outcomes of CP and PDAC[1]. One of the main risk categories for pancreatic cancer (PanCa) is people with CP, and research suggests that these patients may have a relative risk of PanCa of up to 7.6-68.1 times. Research on the incidence of PanCa in CP patients has mostly focused on Western nations, where estimates of the disease's frequency range from 1.0% to 2.6%. The incidence of PanCa was reported to be 0.9%-2.9% in a few research conducted in Asia.

CP SERVES AS A WELL-ESTABLISHED RISK FACTOR FOR PDAC

In contrast to the 9-fold to 16-fold increased risk reported in a recent cohort study, their finding of a average increase of PanCa among patients with pancreatitis-especially the chronic or recurrent forms-supports some previous clinical and case-control studies. There is no evidence of a heightened risk for pancreatitis 10 years or longer after the initial discharge, which contradicts a clear-cut causal relationship. Given the short time between pancreatitis and PanCa diagnosis, there's a chance that some types of pancreatitis precede PanCa or that common risk factors (like smoking cigarettes) could also be at play[2]. Several studies have proposed that risk factors associated with CP comprise newly diagnosed hyperglycemia, obesity, old age, smoking habits, alcohol consumption, physical inactiveness and diet to name a few[3]. Hence further validation of these risk factors is necessary, and identification of patient subgroups with CP for surveillance should be based on the risk factors for PDAC. Traditionally, CP and PDAC were considered distinct diseases originating from separate pancreatic cell types, acinar and ductal cells, respectively. However recent studies involving rodent models suggest a shared origin in acinar cells[4]. It has been observed that prolonged inflammation in CP leads to increased cell turnover and stellate cell proliferation, fostering a microenvironment conducive to carcinogenesis and inflammatory

mediators like Cyclooxygenase-2 (Cox-2), NF- κ B, and signal transducer and activator of transcription 3 (STAT3) play crucial roles, as sustained inflammation can trigger oxidative damage, exacerbating inflammatory infiltration and acinar cell injury[5,6]. While most PDAC patients exhibit constitutive activation of STAT3, which suggests that STAT3 may be a viable therapeutic target in this malignancy, STAT3 is not necessary for normal development. In PDAC, COX-2 is overexpressed. It's unclear, yet, how COX-2 encourages the development of PDAC. While prior research has assessed the effectiveness of COX-2 inhibition in PDAC models through the use of nonsteroidal anti-inflammatory drugs or the COX-2 inhibitor celecoxib, no study has examined the roles that COX-2 plays in modulating PDAC initiation and progression on a cell intrinsic versus microenvironment level[7].

In a recent study involving 1538 PanCa patients and 15380 controls, Ma *et al*[8] demonstrated that pancreatitis significantly raises the risk of PDAC, which escalates with the age of pancreatitis as well as the age of the individuals, with the highest risk observed in the age group between 61-70 years. Interestingly, the PanCa risk is significantly elevated within the first 3 years, but surprisingly the risk correlation diminishes after 10 years. Similarly, Kim *et al*[3], reported that, compared to individuals without PanCa, patients with CP showed an enhanced risk of PanCa development at older ages (60 years or older). Studies from Han *et al*[9] (2022) and Park *et al*[10] (2023) added some insights on the association of CP with the risk of PanCa in the Korean population. Han *et al*[9], observed that patients with CP posed a greater risk for both incidence and mortality of all cancers, particularly the pancreatic and esophageal cancers, compared with the sex- and age-matched control groups. Park *et al*[10], utilized Korean population-based data to identify 225811 patients with acute pancreatitis (AP) and 225685 with CP, each comprising 50.0% of the sample. Matching them with 4514960 age-matched and sex-matched controls, they analyzed PanCa incidence and adjusted hazard ratios in patients followed for over 2 years or 5 years. Additionally, they assessed risk changes over time in subgroups of AP, recurrent AP (RAP), CP with AP, and CP without AP groups, for both sexes. They observed that although the likelihood of PanCa diminished with time, it remained heightened in individuals with RAP and CP with AP for over 8 years. Female patients with RAP, severe AP (SAP), and CP with AP faced greater PanCa risks compared to men. Patients with RAP and CP with AP experienced prolonged and increased PanCa risks in contrast to those with SAP or CP without AP[10]. These studies added important insights into the age, sex, and ethnicity-related demographic factors, associated with the risk of PanCa for the Asian population, as a very limited number of studies were performed in this area.

CONCLUSION

Hence the findings revealed specific demographic and ethno-racial factors associated with an increased risk for admission with CP and PDAC, shedding light on potential disparities and risk factors for these conditions. The study also highlighted limitations, such as being limited to inpatient encounters and the inability to identify individual patients or the etiology of CP. Despite these limitations, the study provides valuable insights into the epidemiologic risk factors associated with CP and its association with PDAC, emphasizing the importance of understanding the prevalence and outcomes of these conditions.

ACKNOWLEDGEMENTS

We would like to thank the clinicians for sharing their valuable inputs, Ghosh S (Medical College and Hospital Kolkata), Chattopadhyay BK (IPGMER and SSKM Hospital), Baneerjee S (Tata Medical Center), Roy P (Tata Medical Center), Gulati S and Ghatak S (Apollo Multispeciality Hospitals) shared their valuable inputs during the discussion regarding the clinical part. We would also like to thank Bandyopadhyay A (Department of Surgery and Oncology, Command Hospital, Lucknow). Special thanks and acknowledgement are extended to Sikdar MS, who has been a constant source of encouragement.

FOOTNOTES

Author contributions: Das A and Bararia A wrote the manuscript; Mukherjee S did the clinical evaluation of the study; Sikdar N conceptualized, edited, proofread, and corresponded the manuscript; all of the authors read and approved the final version of the manuscript to be published.

Supported by The Department of Biotechnology, Government of India Grant Sanction, No. RLS/BT/Re-entry/05/2012.

Conflict-of-interest statement: The authors don't have any competing interests to disclose.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country of origin: India

ORCID number: Amlan Das [0000-0002-9295-3743](https://orcid.org/0000-0002-9295-3743); Akash Bararia [0000-0002-9069-3116](https://orcid.org/0000-0002-9069-3116); Nilabja Sikdar [0000-0003-4465-472X](https://orcid.org/0000-0003-4465-472X).

S-Editor: Luo ML

L-Editor: A

P-Editor: Zhao YQ

REFERENCES

- 1 **Lew D**, Kamal F, Phan K, Randhawa K, Cornwell S, Bangolo AI, Weissman S, Pandol SJ. Epidemiologic risk factors for patients admitted with chronic pancreatitis and pancreatic ductal adenocarcinoma in the United States. *World J Clin Oncol* 2022; **13**: 907-917 [PMID: [36483975](https://pubmed.ncbi.nlm.nih.gov/36483975/) DOI: [10.5306/wjco.v13.i11.907](https://doi.org/10.5306/wjco.v13.i11.907)]
- 2 **Ekbom A**, McLaughlin JK, Karlsson BM, Nyrén O, Gridley G, Adami HO, Fraumeni JF Jr. Pancreatitis and pancreatic cancer: a population-based study. *J Natl Cancer Inst* 1994; **86**: 625-627 [PMID: [8145277](https://pubmed.ncbi.nlm.nih.gov/8145277/) DOI: [10.1093/jnci/86.8.625](https://doi.org/10.1093/jnci/86.8.625)]
- 3 **Kim HS**, Gweon TG, Park SH, Kim TH, Kim CW, Chang JH. Incidence and risk of pancreatic cancer in patients with chronic pancreatitis: defining the optimal subgroup for surveillance. *Sci Rep* 2023; **13**: 106 [PMID: [36596818](https://pubmed.ncbi.nlm.nih.gov/36596818/) DOI: [10.1038/s41598-022-26411-8](https://doi.org/10.1038/s41598-022-26411-8)]
- 4 **Saiki Y**, Jiang C, Ohmuraya M, Furukawa T. Genetic Mutations of Pancreatic Cancer and Genetically Engineered Mouse Models. *Cancers (Basel)* 2021; **14**: 71 [PMID: [35008235](https://pubmed.ncbi.nlm.nih.gov/35008235/) DOI: [10.3390/cancers14010071](https://doi.org/10.3390/cancers14010071)]
- 5 **Bailey P**, Chang DK, Nones K, Johns AL, Patch AM, Gingras MC, Miller DK, Christ AN, Bruxner TJ, Quinn MC, Nourse C, Murtaugh LC, Harliwong I, Idrisoglu S, Manning S, Nourbakhsh E, Wani S, Fink L, Holmes O, Chin V, Anderson MJ, Kazakoff S, Leonard C, Newell F, Waddell N, Wood S, Xu Q, Wilson PJ, Cloonan N, Kassahn KS, Taylor D, Quek K, Robertson A, Pantano L, Mincarelli L, Sanchez LN, Evers L, Wu J, Pinese M, Cowley MJ, Jones MD, Colvin EK, Nagrial AM, Humphrey ES, Chantrill LA, Mawson A, Humphris J, Chou A, Pajic M, Scarlett CJ, Pinho AV, Giry-Laterriere M, Rooman I, Samra JS, Kench JG, Lovell JA, Merrett ND, Toon CW, Epari K, Nguyen NQ, Barbour A, Zeps N, Moran-Jones K, Jamieson NB, Graham JS, Duthie F, Oien K, Hair J, Grützmann R, Maitra A, Iacobuzio-Donahue CA, Wolfgang CL, Morgan RA, Lawlor RT, Corbo V, Bassi C, Rusev B, Capelli P, Salvia R, Tortora G, Mukhopadhyay D, Petersen GM; Australian Pancreatic Cancer Genome Initiative, Munzy DM, Fisher WE, Karim SA, Eshleman JR, Hruban RH, Pilarsky C, Morton JP, Sansom OJ, Scarpa A, Musgrove EA, Bailey UM, Hofmann O, Sutherland RL, Wheeler DA, Gill AJ, Gibbs RA, Pearson JV, Waddell N, Biankin AV, Grimmond SM. Genomic analyses identify molecular subtypes of pancreatic cancer. *Nature* 2016; **531**: 47-52 [PMID: [26909576](https://pubmed.ncbi.nlm.nih.gov/26909576/) DOI: [10.1038/nature16965](https://doi.org/10.1038/nature16965)]
- 6 **Pérez-Mancera PA**, Guerra C, Barbacid M, Tuveson DA. What we have learned about pancreatic cancer from mouse models. *Gastroenterology* 2012; **142**: 1079-1092 [PMID: [22406637](https://pubmed.ncbi.nlm.nih.gov/22406637/) DOI: [10.1053/j.gastro.2012.03.002](https://doi.org/10.1053/j.gastro.2012.03.002)]
- 7 **Hill R**, Li Y, Tran LM, Dry S, Calvopina JH, Garcia A, Kim C, Wang Y, Donahue TR, Herschman HR, Wu H. Cell intrinsic role of COX-2 in pancreatic cancer development. *Mol Cancer Ther* 2012; **11**: 2127-2137 [PMID: [22784710](https://pubmed.ncbi.nlm.nih.gov/22784710/) DOI: [10.1158/1535-7163.MCT-12-0342](https://doi.org/10.1158/1535-7163.MCT-12-0342)]
- 8 **Ma DM**, Dong XW, Han X, Ling Z, Lu GT, Sun YY, Yin XD. Pancreatitis and Pancreatic Cancer Risk. *Technol Cancer Res Treat* 2023; **22**: 15330338231164875 [PMID: [36972517](https://pubmed.ncbi.nlm.nih.gov/36972517/) DOI: [10.1177/15330338231164875](https://doi.org/10.1177/15330338231164875)]
- 9 **Han M**, Tran TPT, Oh JK. Chronic pancreatitis and cancer risk in a matched cohort study using national claims data in South Korea. *Sci Rep* 2022; **12**: 5545 [PMID: [35365692](https://pubmed.ncbi.nlm.nih.gov/35365692/) DOI: [10.1038/s41598-022-09426-z](https://doi.org/10.1038/s41598-022-09426-z)]
- 10 **Park SM**, Kim KB, Han JH, Kim N, Kang TU, Swan H, Kim HJ. Incidence and risk of pancreatic cancer in patients with acute or chronic pancreatitis: a population-based cohort study. *Sci Rep* 2023; **13**: 18930 [PMID: [37919344](https://pubmed.ncbi.nlm.nih.gov/37919344/) DOI: [10.1038/s41598-023-45382-y](https://doi.org/10.1038/s41598-023-45382-y)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

