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Similarities and Differences of New-Onset Hyperglycemia Secondary to Different Types of Acute Pancreatitis

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ABSTRACT

With the increasing incidence of acute pancreatitis (AP), new-onset hyperglycemia (prediabetes and diabetes) secondary to AP attracts more attention as one of chronic complications. There are numerous causes of AP, including cholelithiasis, hypertriglyceridemia, alcoholism and so forth, which are both diabetic high-risk factors. Unfortunately, it is still unknown whether the hazards of secondary glucose metabolism impairment resulting from different types of AP are equal. In addition, person suffered from pancreatitis or diabetes is with high-risk for future pancreatic cancer. Thus, identification and analyzation on factors for different types of pancreatogenic diabetes is crucial. The literature review summarizes the incidence of new hyperglycemia after different causes of APs and explores the risk factors of different pancreatic backgrounds and potential mechanisms behind them.

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Introduction

Acute pancreatitis (AP) is one of the most common digestive emergencies worldwide, with global incidence rate increasing [1]. There are numerous etiologies of AP, and in China, gallstone (cholelithiasis) remains the main cause, followed by hypertriglyceridemia (HTG) and excessive alcohol consumption [2].

Diabetes of the exocrine pancreas (DEP) derives from the dysfunction of exocrine pancreas, with terms such as pancreatic, pancreatogenic and type 3c diabetes, also used for this condition, as the second most common subtype of diabetes after type 2 diabetes mellitus (T2DM) [3]. Wherein, approximately four fifths of DEP cases are caused by pancreatitis, namely, post-pancreatitis diabetes mellitus (PPDM) [4]. Furthermore, the pancreatitis giving rise to diabetes can be acute or chronic, thus, it is reasonable to divide PPDM into post-acute pancreatitis diabetes mellitus (PPDM-A) and post-chronic pancreatitis diabetes mellitus (PPDM-C). Recently, the statistical results of the New Zealand national population database have indicated that PPDM-A accounts for 61% of all DEP [5]. Moreover, 27% of patients with AP have been reported to develop PPDM-A after discharge [6]. Importantly, new-onset prediabetes (PD) after AP is also frequent, with the combined incidence rate of PD and DM to be 35% in first year following the AP attack, and increasing to 59% after 5 years [7]. Besides, PPDM-A is characterized by poor glycemic control, frequent hypoglycemia attacks and high risk of pancreatic cancer [3,8,9]. Therefore, it is crucial to understand the risk factors of new-onset hyperglycemia (PD and DM) after AP and identify high-risk populations.

In the last decade, researches on the risk factors of new-onset hyperglycemia after AP have boomed. The potential factors affect the development of PPDM-A, including the severity of AP, pancreatic necrosis, stress hyperglycemia as well as the circulating levels of IL-6. However, the risk factors are not clearly confirmed now [10-13].

This article reviews the incidence rates of new-onset hyperglycemia after AP with different etiologies, leading to an assumption that the risk factors of etiologies of AP influence the development of hyperglycemia after AP attack.

Incidence of New-Onset Hypeglycemia after AP with Different Etiologies

A Medline search was done with search terms AP ("acute pancreatitis" or "pancreatitis, acute") combined with "endocrine function" OR "endocrine insufficiency" OR "impaired glucose tolerance" OR "glucose homeostasis" OR "diabetes mellitus" OR "prediabetic state" OR "type 2 diabetes mellitus" OR "type 1 diabetes mellitus" OR "adult-onset diabetes mellitus" OR "maturity onset diabetes" OR "non-insulin dependent diabetes" OR "insulin dependent diabetes", based on the criteria as follows

Eligibility criteria:

1. Adult (age equal to or greater than 18 years) AP patients without a history of pre-existing pre-diabetes or diabetes at discharge;
2. Measurements of glucose metabolism at least one month after hospital discharge;
3. The studies used standard diagnosis methods for AP;

And 4. The reports provided incidence rates or raw data to calculate the rates of new-onset hyperglycemia secondary to AP with different etiologies.

Exclusion criteria:

1. Studies that specifically focused on AP patients with pancreatic surgery (invasive percutaneous and/or endoscopic procedures), hereditary pancreatitis or autoimmune pancreatitis;

2. Studies that provided incomplete or no definition of glycemic outcomes;
3. Reports in which the number of new-onset hyperglycemia patients was unavailable (not reported);
4. Studies where less than 50% of the patients provided information during the follow-up or there was no report on the percentage of patients providing data during follow-up.

The search yielded 6023 records, with 32 articles eligible for inclusion, however 27 studies used to analyze due to duplicated data reported (Figure 1) [10,11,13-42]. Critical study characteristics are summarized in Table 1. After data collection (Table 2), the incidence rates of new-onset hyperglycemia after AP with different etiologies were calculated, stated as median (quartile 1, quartile 3) with 34.5% (12.2%,40.9%) of AAP, 18.3% (7.4%,35.1%) of ABP and 46.9% (25.0%,100%) of HTGAP (Figure 2A).

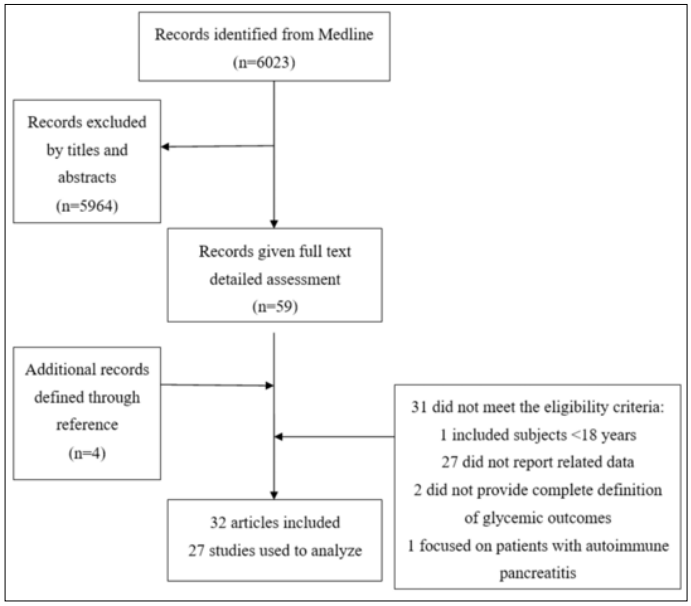


Figure 1: Flowchart for identification of studies included

Table 1: Basic characteristics of included studies [10,11,13-42]

Authors	Date	Country or Area	Population	Total No. of participants (male %)	Age(year)	Glucose measurement	Outcome	Duration of follow-up(month)*
Johansen and Ornsholt	1972	Denmark	AP	22 (45.5%)	37	OGTT	DM	24
Ibars et al.	2002	Spain	ABP	55 (27%)	62	OGTT, Arginine test	PD, DM	1,6,12
Malecka-Panas et al.	2002	Poland	AP	82 (67.1%)	47	OGTT, Insulin test	PD, DM	56
Boreham and Ammori	2003	UK	AP	23 (56.5%)	55, median	FBG	DM	3
Hochman et al.	2006	Canada	SAP	25 (57.1%)	62	Questionnaire	DM	24,36
Yasuda et al.	2008	Japan	SAP	41 (81.3%)	52	FBG	DM	56
Pelli et al.	2009	Finland	AAP	46 (87%)	49, median	OGTT, HbA1c	PD, DM	23, median
Andersson et al.	2010	Sweden	AP	39 (40%)	59	OGTT, Insulin, FBG	DM	45
Wu et al.	2011	China	AP	59 (56%)	59	FBG	PD, DM	42
Ho et al.	2015	Taiwan	AP	12284 (70.6%)	50.2	Medical records	DM	>24
Gillies et al.	2016	New Zealand	AP	83 (61%)	Group1:48, median	HbA1c	PD, DM	Group1:17.5, median
					Group2:63, median			Group2:37, median
Pendharkar et al.	2016	New Zealand	AP	83 (60%)	Group1:47	FBG, HbA1c	PD, DM	Group1:33
					Group2:57			Group2:23

Nikkola et al.	2017	Finland	AAP	47 (90%)	48	Medical records	PD, DM	126
Pendharkar et al.**	2017	New Zealand	AP	83 (60%)	Group1:47	FBG, HbA1c	PD, DM	Group1:33
					Group2:57			Group2:23
Pendharkar et al.**	2017	New Zealand	AP	83 (60%)	Group1:47	FBG, HbA1c	PD, DM	Group1:33
					Group2:57			Group2:23
Pendharkar et al.**	2018	New Zealand	AP	83 (60%)	Group1:47	FBG, HbA1c	PD, DM	Group1:33
					Group2:57			Group2:23
Ma et al.	2019	China	AP	616 (62.7%)	47, median	OGTT, HbA1c	DM	>3
Bharmal et al.**	2019	New Zealand	AP	83 (61%)	Group1:48, median	HbA1c	PD, DM	Group1:17.5, median
					Group1:63, median			Group2:37, median
Bharmal et al.	2020	New Zealand	AP	79 (62%)	50, median	FBG, HbA1c	PD	26, median
Cho et al.	2020	New Zealand	AP with gout	9471 (48%)	56	Medical records	DM	46
Gold-Smith et al.	2020	New Zealand	AP	93 (61%)	53, median	FBG, HbA1c	DM	22, median
Yu et al.	2020	China	AP	361 (56%)	48.6	FBG, OGTT	PD, DM	24
Li et al.	2021	New Zealand	AP	72 (67%)	Group1:60, median	FBG, HbA1c	PD, DM	27
					Group2:51, median			
Norbitt et al.	2021	New Zealand	AP	69 (59.4%)	Group1:58.9	FBG, HbA1c	PD, DM	26
					Group2:51.6			
Bharmal et al.	2022	New Zealand	AP	120 (58%)	Group1:48	HbA1c	DM	6,12,18,24
					Group2:54			
					Group3:53			
Bharmal et al.	2022	New Zealand	AP	68 (47%)	Group1:60	FBG, HbA1c	PD	6,12,18,24
					Group2:55			
					Group3:48			
Lv et al.	2022	China	AP	1804 (63.1%)	48, median	Telephone survey	DM	36.5, median
Man et al.	2022	Romania	AP	308 (54%)	Group1:60, median	FBG, OGTT	DM	1,3,12
					Group2:45.5, median			
Norbitt et al.**	2022	New Zealand	AP	69 (59.4%)	Group1:58.9	FBG, HbA1c	PD, DM	26
					Group2:51.6			
Tu et al.	2023	China	HTGAP	88 (NA)	Group1:45, median	FBG, OGTT,	DM	>6
					Group2:42, median	HbA1c		
Bejjani et al.	2023	USA	AP	68 (NA)	Group1:54, median	HbA1c	DM	3,12
					Group2:59, median			
Zhong et al.	2023	China	AP	244 (65.6%)	46	FBG, OGTT	DM	18

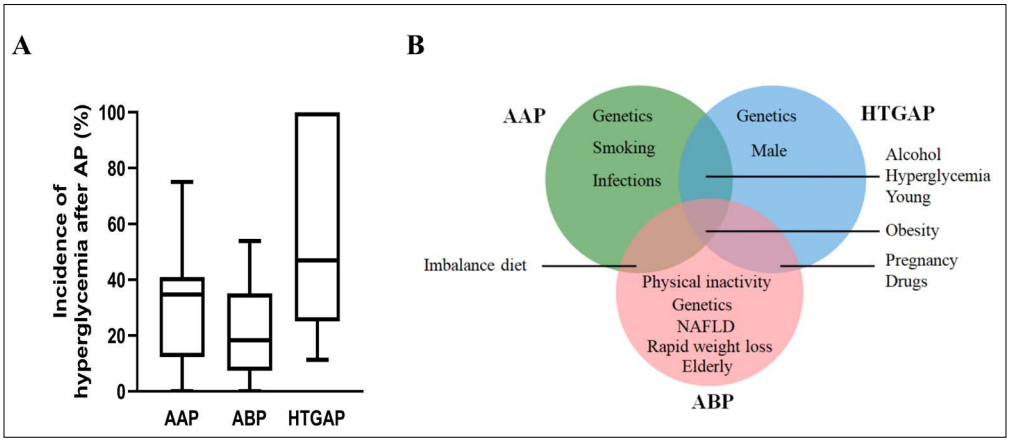
"AP, Acute pancreatitis; AAP, Acute alcoholic pancreatitis; ABP, Acute biliary pancreatitis; HTGAP, Hypertriglyceridemia-related AP; SAP, Severe acute pancreatitis; OGTT, Oral glucose tolerance test; FBG, Fasting blood glucose; HbA1c, Glycohaemoglobin A1c; NA, not available; DM, Diabetes mellitus; PD, Prediabetes.
*The age and duration of following up were presented as mean if not stated as median or a range.
**Studies were not included in the analysis with duplicated data".

Table 2: Hyperglycemia occurrence of AP participants with different etiologies [10,11,13-25,29,31-38,40-42]

Study	AAP		ABP		HTGAP	
	Hyperglycemia (n=541)	Total No. (n=6316)	Hyperglycemia (n=697)	Total No. (n=11458)	Hyperglycemia (n=130)	Total No. (n=494)
Johansen	2	4	1	11	NA	NA
Ibars	NA	NA	13	55	NA	NA
Malecka-Panas	13	36	4	29	NA	NA
Boreham	0	5	2	13	1	1
Hochman	2	4	0	11	2	2
Yasuda	8	21	4	9	NA	NA
Pelli	17	46	NA	NA	NA	NA
Andersson	4	10	3	19	NA	NA
Wu	2	7	10	42	6	7
Ho	383	5728	235	6556	NA	NA
Gillies	3	18	9	37	NA	NA
Pendharkar	6	18	13	37	NA	NA
Nikkola	20	47	NA	NA	NA	NA
Ma	18	86	48	263	11	26
Bharmal	5	17	13	37	NA	NA
Cho	NA	NA	171	2775	NA	NA
Gold-Smith	4	72	NA	NA	NA	NA
Yu	21	52	63	166	61	130
Li	10	17	14	26	NA	NA
Norbitt	12	16	14	26	NA	NA
Bharmal	3	26	5	64	NA	NA
Bharmal	4	10	8	29	NA	NA
Lv	3	68	44	971	27	240
Man	NA	NA	3	204	NA	NA
Tu	NA	NA	NA	NA	22	88
Bejjani	1	8	2	27	NA	NA
Zhong	NA	NA	18	51	NA	NA

NA, not available.

Figure 2: Incidence rates and risk factors of new-onset hyperglycemia secondary to different types of AP



AAP, Acute alcoholic pancreatitis; ABP, Acute biliary pancreatitis; HTGAP, Hypertriglycemia-related AP; NAFLD, Nonalcoholic fatty liver disease.

The susceptibility genes of different types of AP are distinct. ABCG8, ABCG5 and UGT1A1 are potentially associated with ABP; LPLD increases the risk for HTGAP; PRSS1, SPINK and CTRC are related to AAP.

Risk Factors of AP with Different Etiologies

Acute biliary pancreatitis

Biliary pancreatitis results from impaction or temporary obstruction of the major duodenal papilla due to the migration of a gallstone to the common bile duct. Generally, ABP attacks are not severe, and self-limiting. Gallstones (cholelithiasis) are masses in the gall bladder or biliary tract that are caused by abnormally high levels of either cholesterol or bilirubin (a breakdown product of haem) in bile. Based on composition, gallstones are classified into cholesterol gallstones (composed mainly of cholesterol) and other stone types, represented by black and brown pigment stones; wherein, more than 90% of gallstones are cholesterol gallstones. Studies have indicated exogenous and genetic risk factors for cholesterol gallstones formation

Exogenous factors

Numerous exogenous risk factors for cholesterol gallstones have been reported. Specifically, the formation of cholesterol stones is profoundly affected by abnormal metabolism, including obesity (particularly central adiposity), physical inactivity and nonalcoholic fatty liver disease. Moreover, dietary factors such as high calorie or carbohydrate, low fibre and high haem iron intake also increase the risk for the formation of cholesterol stones. Previous study has shown that rapid weight loss (that means, >1.5kg per week reduced by a very-low-calorie diet or after bariatric surgery) leads to the formation of gallstones in up to 30% individuals. Importantly, pregnancy also is a well-known risk factor for gallstones formation. Additionally, some drugs (such as octreotide, fibrates and estrogens) predispose to gallstone formation [43].

Genetic susceptibility

In addition to the aforementioned risk factors, a genetic predisposition to gallstones is well recognized. The heritability of gallstones has been reported to exceed 50% in Hispanics with high Native American ancestry [44]. Associations between multiple lithogenic gene variants and gallstone formation indicate that the contributing genes are highly heterogeneous [45]. In humans, mutations in some of the lithogenic genes may represent the cause of gallstone formation, for example, the common gallstone associated variants in hepatobiliary cholesterol transporter (ABCG8) and ABCG5 as well as UDP glucuronosyltransferase family member A1 (UGT1A1) [46].

Hypertriglyceridemia-related acute pancreatitis

The chief characteristic of patients with HTGAP is the presence of abnormal lipid metabolism, particularly triglycerides.

Primary HTG exposures to increase the risk of AP

Based on Fredrickson classification, primary HTG can be caused by five types of hyperlipidemias. Patients with type I, IV, and V hyperlipidemia were found that have an increased risk of HTG pancreatitis (HTGP). In type1 hyperlipidemia, primarily the chylomicron metabolism is influenced, resulting in high levels of circulating triglyceride-rich chylomicrons (chylomicronemia). Specifically, familial lipoprotein lipase deficiency (LPLD) is a genetic disorder characterized by severe HTG and chylomicronemia, and patients with LPLD are at higher risk of pancreatitis than those with HTG from other causes. Type IV (familial combined hyperlipidemia) is characterized by elevated very-low-density lipoproteins (VLDLs) levels, and results from mutations in several genes with an environmental effect [47]. Patients with type V hyperlipidemia present with both chylomicrons and VLDL elevated, which caused by alterations of genes that induce a reduction in catabolism. Furthermore, in patients with type IV or V hyperlipidemia, environmental factors, including obesity, excessive alcohol consumption and diet affect the elevated triglycerides [47].

Secondary HTG exposures to increase the risk of AP

Previous study found that excess alcohol consumption may cause elevated serum triglyceride levels in patients with underlying HTG that increases the risk of AP. In addition, obesity, pregnancy, and medications (such as estrogens, tamoxifen, thiazides, β-blockers) may also trigger elevations in serum cholesterol and triglycerides, leading to the increase of the risk for HTGP [48].

Demographic characteristics

In addition to abnormal lipid metabolism, it has been reported that in younger patients (aged<50 years), HTGP appears to be more prevalent in males than females, while ABP seems to affect a greater percentage of older patients (aged>70 years) [49].

Acute alcoholic pancreatitis

Alcohol is considered to be one of the major causes of AP; however, alcohol alone at social drinking level (10-20 mM) or even at moderate (50 mM) or severe intoxication (>100 mM) were noted to have little effects on causing pancreatitis. Therefore, this led to the hypothesis that other compounding factors are required for the development of alcoholic pancreatitis, including smoking, dietary habits and genetic background [50].

Most alcoholic pancreatitis cases present as AP, but AAP frequently progresses to alcoholic chronic pancreatitis particularly in habitual alcohol drinkers, many with intervening RAP. There are several reported potential factors increasing the risk for alcoholic pancreatitis as follows:

Susceptibility genes

Cationic trypsinogen gene (PRSS1) mutations were found to increase the risk for alcoholic pancreatitis in Europeans [51]. Moreover, higher prevalence of serine protease inhibitor Kazal-type 1 (SPINK) mutations (N34S) was noted in alcoholic pancreatitis. In addition, variants of chymotrypsin C (CTRC), which regulates cationic trypsin activity, and FAFE synthase enzyme carboxyl ester lipase (CEL), were reported to be higher in patients with alcoholic pancreatitis [52]. In terms of Asians, alcoholic pancreatitis patients are far more likely to have the ADH1B*2 allele than alcoholics not prone to pancreatitis [53].

Exogenous risk factors

Previously published study of meta-analyses have shown a significant association between smoking and alcoholic pancreatitis [54]. Importantly, a linear relationship between alcohol consumption and plasma triglycerides has been clearly evident, being 0.37-0.46 mmol/L higher in those consuming >5 alcoholic drinks/day compared to non-drinkers [55]. This leads to an assumption that the increment of alcohol consumption increases the risk for pancreatitis, along with the elevated plasma triglycerides. Additionally, high alcohol consumption (≥ 30 g/d) frequently contributes to weight gain and obesity, raising the postulate of an association of obesity and high fat diet with alcoholic pancreatitis [56]. Intriguingly, it is noted that infections are associated with alcoholic pancreatitis. Especially, lipopolysaccharide (LPS), found on Gram-negative bacteria, when administered intravenously into alcohol-fed rats showed a dose-dependent increase in pancreatic damage [57].This ultimately has become a model of alcoholic pancreatitis.

Demographic characteristics

Besides, alcoholic pancreatitis also has its demographic characteristics different from ABP. Alcoholic pancreatitis typically affects individuals between 35 to 55 years of age, with peak exposure in the preceding 15 to 20 years. Moreover, after this age, the risk of new-onset alcohol-related pancreatitis decreases [58]. On the contrary, the risk for ABP increases along with age, and is the highest among the elderly.

The risk factors of AP with different etiologies are generalized in Figure 2B, with some factors overlapped, and the majority of non-genetic factors also increasing the risk for type 2 diabetes mellitus (T2DM), such as obesity, male and inactivity [59].

Discussion

This review shows that the incidence rates of new-onset hyperglycemia after AAP, ABP and HTGAP attack are different, with 46.9% of HTGAP highest, followed by 34.5% of AAP and 18.3% of ABP. In addition, the risk factors of AAP, ABP and HTGAP are partly overlapped, with most exogenous factors increasing the risk for T2DM. However, it should be noted that AP patients with different etiologies have diverse genetic backgrounds. Specifically, the development of ABP may result from the mutations in some of the lithogenic genes (such as ABCG8, ABCG5 and UGT1A1). But, patients with type I, IV or V hyperlipidemia could be prone to HTGAP, particularly in those with LPLD. In addition, the mutations of PRSS1, SPINK or CTRC predispose to alcoholic pancreatitis. Therefore, it is necessary to focus on the distinct genetic susceptibility of AP patients to identify high-risk populations of new-onset hyperglycemia after AP attack. With respect to the underlying genetic risk factors, further research is warranted to understand the relationship between susceptibility genes and the development of hyperglycemia after AP.

In summary, the incidence rates of new-onset hyperglycemia after distinct AP with distinct etiologies are different. Hence, focusing on the risk factors of different etiologies, especially genetic factors, may help identify high-risk populations and guide their personalized prevention and treatment.

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References

1. Bingjun Yu 1, Nianshuang Li 1, Jiarong Li 1, Jianhua Wan 1, Wenhua He, et al. (2020) The Clinical Characteristics of Acute Pancreatitis in Gerontal Patients: A Retrospective Study. Clin Interv Aging 15: 1541-1553.
2. Pancreatic Surgery Group of the Surgery Branch of the Chinese Medical Association. Chinese Guidelines for the Diagnosis and Treatment of Acute Pancreatitis (2021). Zhejiang Practical Medicine 26: 511-519+535.
3. Woodmansey C, McGovern AP, McCullough KA, et al. (2017) Incidence, Demographics, and Clinical Characteristics of Diabetes of the Exocrine Pancreas (Type 3c): A Retrospective Cohort Study. Diabetes Care 40: 1486-1493.
4. Petrov MS, Yadav D (2019) Global epidemiology and holistic prevention of pancreatitis. Nat Rev Gastroenterol Hepatol 16: 175-184.
5. Pendharkar SA, Mathew J, Petrov MS (2017) Age- and sex-specific prevalence of diabetes associated with diseases of the exocrine pancreas: A population-based study. Dig Liver Dis 49: 540-544.
6. Zhi M, Zhu X, Lugea A, Waldron RT, Pandol SJ, et al. (2019) Incidence of New Onset Diabetes Mellitus Secondary to Acute Pancreatitis: A Systematic Review and Meta-Analysis. Front Physiol 10: 637.
7. Das SL, Singh PP, Phillips AR, Murphy R, Windsor JA, et al. (2014) Newly diagnosed diabetes mellitus after acute pancreatitis: a systematic review and meta-analysis. Gut 63: 818-831.
8. Cho J, Scragg R, Petrov MS (2020) Postpancreatitis Diabetes Confers Higher Risk for Pancreatic Cancer Than Type 2 Diabetes: Results From a Nationwide Cancer Registry. Diabetes Care 43: 2106-2112.
9. Cho J, Pandol SJ, Petrov MS (2021) Risk of cause-specific death, its sex and age differences, and life expectancy in post-pancreatitis diabetes mellitus. Acta Diabetol 58: 797-807.
10. Yu BJ, Li NS, He WH, Cong He, Jian-Hua Wan, et al. (2020) Pancreatic necrosis and severity are independent risk factors for pancreatic endocrine insufficiency after acute pancreatitis: A long-term follow-up study. World J Gastroenterol 26: 3260-3270.
11. Bharmal SH, Cho J, Ko J, Petrov MS (2022) Glucose variability during the early course of acute pancreatitis predicts two-year probability of new-onset diabetes: A prospective longitudinal cohort study. United European Gastroenterol J 10: 179-189.
12. Bharmal SH, Cho J, Alarcon Ramos GC, Juyeon Ko, Charlotte Elizabeth Stuart et al. (2020) Trajectories of glycaemia following acute pancreatitis: a prospective longitudinal cohort study with 24 months follow-up. J Gastroenterol 55: 775-788.
13. Gillies N, Pendharkar SA, Asrani VM, Mathew J, Windsor JA, et al. (2016) Interleukin-6 is associated with chronic hyperglycemia and insulin resistance in patients after acute pancreatitis. Pancreatology 16: 748-755.
14. Johansen K, Ornsholt J (1972) Frequency of diabetes after acute pancreatitis. Metabolism 21: 291-296.
15. Ibars EP, Sánchez de Rojas EA, Quereda LA, Ramis RF, Sanjuan VM, et al. (2002) Pancreatic function after acute biliary pancreatitis: does it change? World J Surg 26: 479-486.
16. Malecka-Panas E, Gasiorowska A, Kropiwnicka A, Zlobinska A, Drzewoski J. (2002) Endocrine pancreatic function in patients after acute pancreatitis. Hepatogastroenterology 49: 1707-1712.
17. Boreham B, Ammori BJ (2003) A prospective evaluation of pancreatic exocrine function in patients with acute pancreatitis: correlation with extent of necrosis and pancreatic endocrine insufficiency. Pancreatology 3: 303-308.
18. Hochman D, Louie B, Bailey R (2006) Determination of patient quality of life following severe acute pancreatitis. Can J Surg 49: 101-106.
19. Yasuda T, Ueda T, Takeyama Y, Makoto Shinzeki, Hidehiro Sawa, et al. (2008) Long-term outcome of severe acute pancreatitis. J Hepatobiliary Pancreat Surg 15: 397-402.
20. Pelli H, Lappalainen-Lehto R, Piironen A, Järvinen S, Sand J, et al. (2009) Nordback I. Pancreatic damage after the first episode of acute alcoholic pancreatitis and its association with the later recurrence rate. Pancreatology 9: 245-251.
21. Andersson B, Pendse ML, Andersson R (2010) Pancreatic function, quality of life and costs at long-term follow-up after acute pancreatitis. World J Gastroenterol 16: 4944-4951.
22. Wu D, Xu Y, Zeng Y, Wang X (2011) Endocrine pancreatic function changes after acute pancreatitis. Pancreas 40: 1006-1011.
23. Ho TW, Wu JM, Kuo TC, Ching-Yao Yang, Hong-Shiee Lai, et al. (2015) Change of Both Endocrine and Exocrine

Insufficiencies After Acute Pancreatitis in Non-Diabetic Patients: A Nationwide Population-Based Study. Medicine (Baltimore) 94: e1123.

24. Pendharkar SA, Asrani VM, Xiao AY, Harry D Yoon, Rinki Murphy, et al. (2016) Relationship between pancreatic hormones and glucose metabolism: A cross-sectional study in patients after acute pancreatitis. Am J Physiol Gastrointest Liver Physiol 311: G50-58.
25. Nikkola J, Laukkarinen J, Lahtela J, Hanna Seppänen, Satu Järvinen, et al. (2017) The Long-term Prospective Follow-up of Pancreatic Function After the First Episode of Acute Alcoholic Pancreatitis: Recurrence Predisposes One to Pancreatic Dysfunction and Pancreatogenic Diabetes. J Clin Gastroenterol 51: 183-190.
26. Pendharkar SA, Asrani VM, Murphy R, Cutfield R, Windsor JA, et al. (2017) The Role of Gut-brain Axis in Regulating Glucose Metabolism After Acute Pancreatitis. Clin Transl Gastroenterol 8: e210.
27. Pendharkar SA, Drury M, Walia M, Korc M, Petrov MS (2017) Gastrin-Releasing Peptide and Glucose Metabolism Following Pancreatitis. Gastroenterology Res 10: 224-234.
28. Pendharkar SA, Singh RG, Petrov MS (2018) Pro-inflammatory cytokine-induced lipolysis after an episode of acute pancreatitis. Arch Physiol Biochem 124: 401-409.
29. Ma JH, Yuan YJ, Lin SH, Pan JY (2019) Nomogram for predicting diabetes mellitus after the first attack of acute pancreatitis. Eur J Gastroenterol Hepatol 31: 323-328.
30. Bharmal SH, Pendharkar S, Singh RG, Cho J, Petrov MS (2019) Glucose Counter-regulation After Acute Pancreatitis. Pancreas 2019;48(5): 670-681.
31. Bharmal SH, Pendharkar SA, Singh RG, Cameron-Smith D, Petrov MS (2020) Associations between ketone bodies and fasting plasma glucose in individuals with post-pancreatitis prediabetes. Arch Physiol Biochem 126: 308-319.
32. Cho J, Dalbeth N, Petrov MS (2020) Relationship between Gout and Diabetes Mellitus after Acute Pancreatitis: A Nationwide Cohort Study. J Rheumatol 47: 917-923.
33. Gold-Smith FD, Singh RG, Petrov MS (2020) Elevated Circulating Levels of Motilin are Associated with Diabetes in Individuals after Acute Pancreatitis. Exp Clin Endocrinol Diabetes 128: 43-51.
34. Li X, Kimita W, Cho J, Ko J, Bharmal SH, et al. (2021) Dietary Fibre Intake in Type 2 and New-Onset Prediabetes/Diabetes after Acute Pancreatitis: A Nested Cross-Sectional Study. Nutrients 13: 1112.
35. Norbitt CF, Kimita W, Ko J, Bharmal SH, Petrov MS (2021) Associations of Habitual Mineral Intake with New-Onset Prediabetes/Diabetes after Acute Pancreatitis. Nutrients 13: 3978.
36. Bharmal SH, Kimita W, Ko J, Petrov MS (2022) Cytokine signature for predicting new-onset prediabetes after acute pancreatitis: A prospective longitudinal cohort study. Cytokine 150: 155768.
37. Lv Y, Zhang J, Yang T, Jinfang Sun, Jiaying Hou, et al. (2022) Non-Alcoholic Fatty Liver Disease (NAFLD) Is an Independent Risk Factor for Developing New-Onset Diabetes After Acute Pancreatitis: A Multicenter Retrospective Cohort Study in Chinese Population. Front Endocrinol (Lausanne) 13: 903731.
38. Man T, Seicean R, Lucaciu L, Istrate A, Seicean A (2022) Risk factors for new-onset diabetes mellitus following acute pancreatitis: a prospective study. Eur Rev Med Pharmacol Sci 26: 5745-5754.
39. Norbitt CF, Kimita W, Bharmal SH, Ko J, Petrov MS (2022) Relationship between Habitual Intake of Vitamins and New-Onset Prediabetes/Diabetes after Acute Pancreatitis. Nutrients 14: 1480.
40. Tu X, Liu Q, Chen L, Jie Li, Xiaoping Yu, et al. (2023) Number of recurrences is significantly associated with the post-acute pancreatitis diabetes mellitus in a population with hypertriglyceridemic acute pancreatitis. Lipids Health Dis 22: 82.
41. Bejjani J, Papachristou GI, Dungan K, Anna Evans Phillips, Vikesh Singh, et al. (2023) Incident diabetes following acute pancreatitis in a multicenter prospective observational cohort. Pancreatology 23: 900-903.
42. Zhong S, Du Q, Liu N, Yuwei Chen, Tianyue Yang, et al. (2023) Developing a CT-based radiomics nomogram for predicting post-acute pancreatitis diabetes mellitus incidence. Br J Radiol 96: 20230382.
43. Tsirline VB, Keilani ZM, El Djouzi S, Ryan C Phillips, Timothy S Kuwada, et al. (2014) How frequently and when do patients undergo cholecystectomy after bariatric surgery? Surg Obes Relat Dis 10: 313-321.
44. Méndez-Sánchez N, King-Martínez AC, Ramos MH, Pichardo-Bahena R, Uribe M (2004) The Amerindian's genes in the Mexican population are associated with development of gallstone disease. Am J Gastroenterol 99: 2166-2170.
45. Wang DQ, Cohen DE, Carey MC (2009) Biliary lipids and cholesterol gallstone disease. J Lipid Res 50 :S406-S411.
46. Buch S, Schafmayer C, Völzke H, Marcus Seeger, Juan F Miquel, et al. (2010) Loci from a genome-wide analysis of bilirubin levels are associated with gallstone risk and composition. Gastroenterology 139: 1942-1951.
47. Brahm A, Hegele RA (2013) Hypertriglyceridemia. Nutrients 5: 981-1001.
48. Yadav D, Pitchumoni CS (2003) Issues in hyperlipidemic pancreatitis. J Clin Gastroenterol 36: 54-62.
49. Yamin Zheng 1, Zhen Zhou, Haichao Li, Jia Li, Ang Li, Binrong Ma, et al. (2015) A multicenter study on etiology of acute pancreatitis in Beijing during 5 years. Pancreas 44: 409-414.
50. Stephen J Pandol, Aurelia Lugea, Olga A Mareninova, Duane Smoot, Fred S Gorelick, et al. (2011) Investigating the pathobiology of alcoholic pancreatitis. Alcohol Clin Exp Res 35: 830-837.
51. Monique H Derikx, Peter Kovacs, Markus Scholz, Emmanuelle Masson, Jian-Min Chen, et al. (2015) Polymorphisms at PRSS1-PRSS2 and CLDN2-MORC4 loci associate with alcoholic and non-alcoholic chronic pancreatitis in a European replication study. Gut 64: 1426-1433.
52. Jonas Rosendahl, Heiko Witt, Richárd Szmola, Eesh Bhatia, Béla Ozsvári, et al. (2008) Chymotrypsin C (CTRC) variants that diminish activity or secretion are associated with chronic pancreatitis. Nat Genet 40: 78-82.
53. Zhong Y, Cao J, Zou R, Peng M (2015) Genetic polymorphisms in alcohol dehydrogenase, aldehyde dehydrogenase and alcoholic chronic pancreatitis susceptibility: a meta-analysis. Gastroenterol Hepatol 38: 417-425.
54. Majumder S, Gierisch JM, Bastian LA (2015) The association of smoking and acute pancreatitis: a systematic review and meta-analysis. Pancreas 44: 540-546.
55. Jean-Bernard Ruidavets, Pierre Ducimetière, Alun Evans, Michèle Montaye, Bernadette Haas, et al. (2010) Patterns of alcohol consumption and ischaemic heart disease in culturally divergent countries: the Prospective Epidemiological Study of Myocardial Infarction (PRIME). Bmj 341: c6077.
56. Wannamethee SG, Shaper AG (2003) Alcohol, body weight,

and weight gain in middle-aged men. Am J Clin Nutr 77: 1312-1317.

57. Franco Fortunato, Xiaoying Deng, Lawrence K Gates, Craig J McClain, Daniel Bimmler, et al. (2006) Pancreatic response to endotoxin after chronic alcohol exposure: switch from apoptosis to necrosis? Am J Physiol Gastrointest Liver Physiol 290: G232-241.
58. Lankisch PG, Assmus C, Maisonneuve P, Lowenfels AB (2002) Epidemiology of pancreatic diseases in Lüneburg County. A study in a defined german population. Pancreatology 2: 469-477.
59. Nuha A ElSayed, Grazia Aleppo, Raveendhara R Bannuru, Dennis Bruemmer, Billy S Collins (2024) 2 Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes Care 47 : S20-s42.