

Original Article



# Assessment of Exocrine Pancreatic Insufficiency in Type 2 Diabetic Mellitus Patients Presenting with Dyspepsia: A Cross-sectional Observational Study

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**Abstract**

**Background:** Diabetes mellitus (DM) virtually affects the gastrointestinal (GI) tract in protean ways, including but not limited to small intestinal bacterial overgrowth, GI reflux disease, gastroparesis, neuropathy, pancreatopathy, and non-alcoholic fatty liver disease. The primary aim of the present study was to assess exocrine pancreatic insufficiency (EPI) in dyspeptic type 2 diabetes mellitus (T2DM) patients.

**Objectives:** The secondary objectives were to assess the correlation between the severity of EPI and the severity of dyspepsia and to evaluate the correlation between glycaemic control and the extent of EPI.

**Methods:** T2DM patients presenting with dyspepsia to the General Medicine and Gastroenterology Department of AIIMS Rishikesh, India, were screened for the inclusion and exclusion criteria, and the enrolled participants were subjected to glycated hemoglobin (HbA1c), the Short Form Leeds Dyspepsia Questionnaire, and pancreatic faecal elastase (PFE) by enzyme-linked immunosorbent assay.

**Results:** In 41 subjects, 36.6% (15) had EPI. Among the participants, 22.0% and 14.6% had mild-to-moderate and severe EPI, respectively. There was a significant correlation between glycaemic control (HbA1c%) and faecal elastase concentration ( $r=-0.51$ ,  $P<0.001$ ). No statistically significant correlation was found between the severity of dyspepsia (SF-LDQ) and pancreatic faecal elastase ( $\mu\text{g}$ ;  $r=-0.01$ ,  $P=0.957$ ).

**Conclusion:** Overall, a large number of T2DM patients with dyspepsia had EPI, and a significant correlation was observed between glycaemic control and EPI. Further studies are needed to determine if pancreatic enzyme supplementation can alleviate dyspeptic symptoms.

**Keywords:** Type 2 diabetes mellitus, Dyspepsia, Pancreatic exocrine insufficiency, Pancreatic faecal elastase, Gastrointestinal, HbA1c



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## Background

The prevalence of diabetes mellitus (DM) is rising exponentially as per the World Health Organization, the prevalence has increased to 830 million in 2022 (1). DM impacts nearly every organ in the body. Gastrointestinal (GI) affection is manifested as dyspepsia. The American College of Gastroenterology defines dyspepsia as predominant epigastric discomfort lasting at least one month, accompanied by other upper GI symptoms such as heartburn, epigastric fullness, nausea, or vomiting (2). GI complications of DM include pancreatopathy, small intestinal bacterial overgrowth, gastroesophageal reflux, gastroparesis, neuropathy, and non-alcoholic fatty liver disease. According to a population-based survey by Bytzer et al, the prevalence of upper and lower GI symptoms

was higher in DM patients, and the effect was linked to poor glycaemic control but not duration of diabetes (3). Constipation, indigestion, abdominal discomfort, gastroesophageal reflux, nausea, heartburn, and vomiting are among the chronic GI symptoms that affect almost 75% of patients in diabetes outpatient clinics (4).

Pancreatic dysfunction has been observed in 50% of individuals with diabetes. Pancreatic exocrine cells in type I diabetes suffer damage due to (a) the absence of insulin's trophic effect on acinar cells, (b) autoimmune destruction of islet cells, (c) autonomic diabetic neuropathy causing impairment of enteropancreatic reflexes, and (d) microvascular damage, leading to hypoxic injury to exocrine tissue. In type 2 DM (T2DM), autonomic neuropathy and microvascular damage are



major contributors to exocrine insufficiency (5). Exocrine pancreatic insufficiency (EPI) can be evaluated through various methods, including direct tests such as the secretin test, Lundh meal test, and indirect tests, such as faecal fat, faecal chymotrypsin, serum chymotrypsinogen, and pancreatic faecal elastase (PFE) test (6). Enzyme-linked immunosorbent assay (ELISA) was used to measure PEI, which is a low-cost, non-invasive method that has high sensitivity and specificity (7). The present study primarily aims to assess EPI in dyspeptic T2DM patients. The secondary objectives are to evaluate the correlation between the severity of EPI and severity of dyspepsia and to assess the correlation between glycaemic control and the extent of EPI.

### Materials and Methods

The sample size of this cross-sectional observational study included 41 patients. The study followed the Helsinki Declaration of 1975, as amended in 2013, and was approved by the Institutional Ethics Committee on December 23, 2022, via letter No. AIIMS/IEC/22/597, dated December 23, 2022. The study adheres to the Indian Council of Medical Research guidelines on biomedical research in human beings and Good Clinical Practices as advised by the institutional ethics committee. The recruitment duration was from December 2022 to September 2023. Informed written consent was obtained from participants for participation and use of data for research and educational purposes. Patients with T2DM presenting with dyspepsia at more than 18 years of age and less than 60 years of age were included in this study. However, patients with acute and known chronic pancreatitis, patients with T1DM, and pregnant females were excluded from the investigation. The sample size was based on the study by Osipenko et al, who reported the prevalence of 71% of examined patients with T2DM, with 42.3% due to organic GI causes and 57.7% due to non-organic pathology (8). The sample size was 41, with a 95% confidence level, a prevalence of 71%, and a relative precision of 20%.

All the participants were explained in detail about the purpose of the study. Informed consent was obtained, and participants were subjected to several tests, including glycated hemoglobin (HbA1c), PFE test by ELISA, and stool routine microscopy. The severity of dyspepsia was assessed by the Short Form Leeds Dyspepsia Questionnaire (SF-LDQ), which consists of four components, including indigestion, heartburn, regurgitation, and nausea. A score of zero on the SF-LDQ denotes no dyspepsia, and a score between 1 and 8 represents mild dyspepsia. In addition, a score between 9 and 15 demonstrates moderate dyspepsia, and a score greater than 15 indicates severe dyspepsia. Pancreatic fecal elastase was measured by ELISA, which is a low-cost, non-invasive method that has high sensitivity and specificity. This method has a sensitivity of 63% and 100% for mild and moderate-to-severe cases, respectively, and 93% overall for patients with EPI, with a specificity

of 93%. A fecal elastase 1 activity level above 200 µg/g is deemed normal, while levels in the range of 100–200 µg/g indicate mild PEI, and below 100 µg/g suggest severe insufficiency (7). The data were coded and recorded in the MS Excel spreadsheet program. SPSS (version 23, IBM Corp.) was used for data analysis. Means, medians, and modes were calculated, and data were presented based on means ± standard deviations (SD). The normality of data was determined using the Shapiro-Wilk test. Non-parametric tests, such as Spearman correlation, were employed for the non-normal data. A *P* value of <0.05 was considered statistically significant.

### Results

Overall, 41 participants were included in the study. The mean age of participants was 53.39 ± 7.94 years. Among the total sample, 42.5% (17) were male, and the remaining cases were female. Associated comorbidities were evaluated, and the results revealed that 57.5% (23) of participants had no comorbidities. Based on the obtained data, 37.5% (15) of participants had associated hypertension, while 2.5% (1) of them had decompensated chronic liver disease. The most predominant symptom was indigestion, observed in 63.4% (26) of participants, while heartburn was present in 24.3% (10). Further, nausea and regurgitation were present in 7.3% and 4.8% of participants, respectively. The mean SF-LDQ score and the mean HbA1c (%) were 7.68 ± 2.30 and 8.52 ± 1.52, respectively. HbA1c was ≤7% in 22% (9) of participants and >7% in the remaining. Non-parametric tests (Spearman correlation) were used to explore the correlation between HbA1c and SF-LDQ (degree of dyspepsia) as at least one of the variables was not normally distributed. There was no statistically significant correlation between HbA1c (%) and SF-LDQ ( $\rho = 0.18, P = 0.247$ ). Baseline characteristics of the study population are provided in Table 1. The stool routine exam was normal in 100% of participants. PFE was performed to rule out PEI. EPI was present in 36.6% (15), the rest had normal PFE (Table 2). About 22.0% (9) of participants had mild-to-moderate PEI, while 14.6% (6) of them had severe PEI (Table 3). Non-parametric tests (Spearman correlation) were employed to explore the correlation between HbA1c (%) and PFE, and this correlation was statistically significant ( $\rho = -0.51, P = <0.001$ , Table 4). Non-parametric tests (Spearman correlation) were utilized to examine the correlation between the severity of dyspepsia (SF-LDQ) and PFE (µg), and there was no statistically significant correlation between these two parameters ( $\rho = -0.01, P = 0.957$ ).

### Discussion

This study investigated how diabetes affects the GI tract, with a particular emphasis on dyspepsia and PEI. The results highlight that PEI may be present in many dyspeptic diabetics. To treat both organic and inorganic causes of dyspepsia in diabetics and achieve better glycaemic control, medication adherence, and symptom relief, a

**Table 1.** Baseline Characteristics of Population

Characteristics	Mean $\pm$ SD, Median (IQR), Min-Max OR N(%)
Age (years)	53.39 $\pm$ 7.94
<b>Age</b>	
21-30 years	1 (2.4%)
31-40 years	2 (4.9%)
41-50 years	9 (22.0%)
51-60 years	29 (70.7%)
<b>Gender</b>	
Male	17 (41.5%)
Female	24 (58.5%)
<b>Comorbidities</b>	
Nil	25 (61%)
HTN	5 (36.6%)
DCLD	1 (2.4%)
<b>Predominant symptom</b>	
Indigestion	26 (63.4%)
Heartburn	10 (24.4%)
Nausea	3 (7.3%)
Regurgitation	2 (4.9%)
SF-LDQ	7.68 $\pm$ 2.30
HbA1c (%)	8.52 $\pm$ 1.52
HbA1c $\leq$ 7 %	9 (22.0%)
HbA1c $>$ 7 %	32 (78.0%)

Note. DCLD: Decompensated chronic liver disease; HbA1c: Glycated haemoglobin; HTN: Hypertension; SF-LDQ: Short Form Leeds Dyspepsia Questionnaire.

methodical approach is essential. EPI is largely caused by autonomic neuropathy and microvascular damage in diabetes. Malabsorption resulting from inadequate digestion of nutrients, particularly lipids, is known as EPI (9,10). It shows up clinically as excess flatulence, weight loss, steatorrhea, pain in the abdomen, and vitamin deficiencies (10-12). Insulin inhibits its receptor in acinar cells and increases the production of digesting enzymes, causing trophic effects on acinar cells. In addition to insulin, endocrine pancreatic islets also generate ghrelin, glucagon, somatostatin, and pancreatic polypeptide. It is believed that diabetes-related hormone dysregulation plays a role in exocrine pancreatic dysfunction (13). Patients with T1DM were shown to have a considerably smaller pancreas on average (14). According to Phillippe et al, PEI is linked to smaller pancreatic sizes in patients with T1DM or T2DM (15). In addition to a change in size, research using animal models indicates that there is an increase in angiogenesis and a loss of extracellular matrix remodelling at the islet acinar interface (16). According to a meta-analysis by Mohapatra et al, histological evidence of exocrine pancreatic fibrosis was found in 59.4% of individuals with either T1DM or T2DM (17). EPI is also associated with pancreatic inflammation. In people with T1DM, the exocrine pancreas contained CD8+T, CD4+T, and CD11c+ cells. In T2DM, there was also a greater infiltration of immune cells (18,19). ELISA was

**Table 2.** Distribution of Participants in Terms of the Presence of 'Pancreatic Exocrine Insufficiency'

Pancreatic Exocrine Insufficiency	Frequency (%)	95% CI
Present	15 (36.6)	22.6-53.1%
Absent	26 (63.4)	46.9-77.4%

Note. CI: Confidence interval.

**Table 3.** Distribution of Participants in Terms of 'Extent of Pancreatic Exocrine Insufficiency'

Extent of Pancreatic Exocrine Insufficiency	Frequency (%)	95% CI
Absent	26 (63.4)	46.9-77.4%
Mild-moderate	9 (22)	11.1-38.0%
Severe	6 (14.6)	6.1-29.9%

Note. CI: Confidence interval.

**Table 4.** Correlation Between Pancreatic Faecal Elastase and HbA1c (%)

Correlation	Spearman Correlation Coefficient	P Value
Pancreatic faecal elastase ( $\mu$ g) vs. HbA1c (%)	-0.5	<0.001

Note. HbA1C: Glycated haemoglobin.

employed to assess PFE out of the numerous tests that were available. EPI, defined as PFE  $<$  200  $\mu$ g/g of stool, was present in 37.5% of T2DM patients with dyspepsia in our study. A cross-sectional study by Shashank et al revealed that patients with T1DM and T2DM had a 22.9% and 23.9% PEI prevalence, respectively (20). Faecal elastase concentrations were normal ( $>$  200  $\mu$ g/g) in 59.3% of type 1 and type 2 diabetic patients and severely reduced ( $<$  100  $\mu$ g/g) in 22.9%, according to a multi-center cross-sectional study conducted by Hardt et al (21). Shivaprasad et al recruited 90 healthy controls, 95 type 2 diabetes patients, and 89 type 1 diabetic patients in a cross-sectional study. ELISA was used to measure the levels of faecal elastase (FEC). Patients were diagnosed with EPI if their FEC was less than 200  $\mu$ g/g. T1DM, T2DM, and controls had a prevalence of PEI of 31.4%, 29.4%, and 4.4%, respectively ( $P <$  0.01). A significant negative correlation was observed between FEC levels and both FBS and HbA1c in diabetic patients (22). A study conducted by Larger et al analyzed 667 diabetic patients, with 195 having T1DM and 472 having T2DM. In 23% of patients, the concentration of elastase-1 was below 200  $\mu$ g/g (23). These findings, along with those of other studies, demonstrate the prevalence of EPI in many diabetic patients. The present study also confirms the existence of this condition in diabetic patients with dyspepsia. Rathmann et al performed a study on 544 type 2 diabetic patients and 544 controls, and PFE was found significantly lower in cases than controls (median: 308 mg/g and 418 mg/g for cases and controls, respectively,  $P <$  0.01). In diabetics, poor glycaemic control (HbA1c  $>$  7%) was associated with a higher risk of low elastase 1 level (odds ratio: 5.6) (24). The results of the present study also showed a significant correlation between HbA1C (%) and PFE ( $\rho = -0.51$ ,  $P = <$  0.001).

In contrast to the present study, in a study conducted by Yilmaztepe et al, there was no significant correlation between pancreatic elastase levels and glycaemic control, though exocrine function was decreased in 28% of type 2 diabetic patients, with no decrease in control subjects (25). Although many studies have demonstrated the high occurrence of EPI in individuals with T2DM, only a small number have investigated the impact of pancreatic enzyme supplementation in these groups. Heymann et al performed a similar study. In their retrospective study, individuals with both EPI and diabetes were compared after receiving pancreatic enzyme replacement therapy (PERT). PERT was performed on diabetes patients who were tested for faecal elastase 1 concentration but did not end up receiving the treatment. The focus was on determining how PERT affected the frequency and severity of hypoglycaemia, while secondary goals included examining its impact on GI issues, HbA1c levels, and body mass index. Approximately 80% of individuals who received PERT experienced a reduction in GI symptoms, including diarrhea, steatorrhea, nausea, and abdominal pain, compared to only 20% in the control group ( $P=0.02$ ) (26). Therefore, there is a need for more extensive multicentric studies to determine the precise prevalence of EPI in T2DM patients with indigestion and studies that investigate the impact of PERT on exocrine pancreatic dysfunction caused by diabetes.

### Conclusion

The findings revealed that a large proportion of T2DM patients with dyspepsia had EPI, and a significant correlation was observed between glycaemic control and EPI. Further studies are needed to determine if pancreatic enzyme supplementation can alleviate dyspeptic symptoms. In general, EPI can be an important cause of dyspepsia in T2DM patients, and further studies are needed to confirm its causative role.

### Authors' Contribution

**Conceptualization:** Nidhi Bhutra, Ravi Kant.

**Data curation:** Nidhi Bhutra, Ravi Kant.

**Formal analysis:** Nidhi Bhutra, Ravi Kant.

**Investigation:** Nidhi Bhutra.

**Methodology:** Nidhi Bhutra, Ravi Kant.

**Project administration:** Nidhi Bhutra, Ravi Kant.

**Resources:** Nidhi Bhutra, Ravi Kant.

**Software:** Nidhi Bhutra.

**Supervision:** Ravi Kant.

**Validation:** Nidhi Bhutra, Ravi Kant.

**Visualization:** Nidhi Bhutra, Ravi Kant.

**Writing—original draft:** Nidhi Bhutra.

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### Competing Interests

The authors declare that they have no competing interests.

### Ethical Approval

The AIIMS Rishikesh Institutional Ethics Committee approved the study on 23/12/22 (Letter No. – AIIMS/1EC/22/597).

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### References

1. World Health Organization (WHO). Diabetes [Internet]. Available from: <https://www.who.int/news-room/fact-sheets/detail/diabetes>. Accessed December 9, 2024.
2. Meldgaard T, Keller J, Olesen AE, Olesen SS, Krogh K, Borre M, et al. Pathophysiology and management of diabetic gastroenteropathy. *Therap Adv Gastroenterol*. 2019;12:1756284819852047. doi: 10.1177/1756284819852047.
3. Bytzer P, Talley NJ, Leemon M, Young LJ, Jones MP, Horowitz M. Prevalence of gastrointestinal symptoms associated with diabetes mellitus: a population-based survey of 15,000 adults. *Arch Intern Med*. 2001;161(16):1989-96. doi: 10.1001/archinte.161.16.1989.
4. Kadaj-Lipka R, Rydzewska G. Exocrine pancreatic insufficiency and causes of abdominal symptoms in diabetes patients. *Prz Gastroenterol*. 2020;15(4):289-93. doi: 10.5114/pg.2020.101556.
5. Piciucchi M, Capurso G, Archibugi L, Delle Fave MM, Capasso M, Delle Fave G. Exocrine pancreatic insufficiency in diabetic patients: prevalence, mechanisms, and treatment. *Int J Endocrinol*. 2015;2015:595649. doi: 10.1155/2015/595649.
6. Forsmark C, Adams PC. Pancreatic function testing—valuable but underused. *Can J Gastroenterol*. 2009;23(8):529-30. doi: 10.1155/2009/464326.
7. Radlinger B, Ramoser G, Kaser S. Exocrine pancreatic insufficiency in type 1 and type 2 diabetes. *Curr Diab Rep*. 2020;20(6):18. doi: 10.1007/s11892-020-01304-0.
8. Osipenko MF, Zhuk EA, Medvedeva OV. [Clinical characteristics of dyspepsia in patients with diabetes mellitus type 2]. *Ter Arkh*. 2013;85(2):43-7. [Russian].
9. Lindkvist B. Diagnosis and treatment of pancreatic exocrine insufficiency. *World J Gastroenterol*. 2013;19(42):7258-66. doi: 10.3748/wjg.v19.i42.7258.
10. Pezzilli R, Andriulli A, Bassi C, Balzano G, Cantore M, Delle Fave G, et al. Exocrine pancreatic insufficiency in adults: a shared position statement of the Italian Association for the Study of the Pancreas. *World J Gastroenterol*. 2013;19(44):7930-46. doi: 10.3748/wjg.v19.i44.7930.
11. Altay M. Which factors determine exocrine pancreatic dysfunction in diabetes mellitus? *World J Gastroenterol*. 2019;25(22):2699-705. doi: 10.3748/wjg.v25.i22.2699.
12. DiMagna EP, Go VL, Summerskill WH. Relations between pancreatic enzyme outputs and malabsorption in severe pancreatic insufficiency. *N Engl J Med*. 1973;288(16):813-5. doi: 10.1056/nejm197304192881603.
13. Barreto SG, Carati CJ, Toouli J, Saccone GT. The islet-acinar axis of the pancreas: more than just insulin. *Am J Physiol Gastrointest Liver Physiol*. 2010;299(1):G10-22. doi: 10.1152/ajpgi.00077.2010.
14. Alexandre-Heymann L, Mallone R, Boitard C, Scharfmann R, Larger E. Structure and function of the exocrine pancreas in patients with type 1 diabetes. *Rev Endocr Metab Disord*. 2019;20(2):129-49. doi: 10.1007/s11154-019-09501-3.
15. Philippe MF, Benabadji S, Barbot-Trystram L, Vadrot D, Boitard C, Larger E. Pancreatic volume and endocrine and exocrine functions in patients with diabetes. *Pancreas*. 2011;40(3):359-63. doi: 10.1097/MPA.0b013e3182072032.
16. Hayden MR, Karuparthi PR, Habibi J, Wasekar C, Lastra G, Manrique C, et al. Ultrastructural islet study of early fibrosis in the Ren2 rat model of hypertension. Emerging role of the islet pancreatic pericyte-stellate cell. *JOP*. 2007;8(6):725-38.
17. Hayden MR, Patel K, Habibi J, Gupta D, Tekwani SS, Whaley-Connell A, et al. Attenuation of endocrine-exocrine pancreatic communication in type 2 diabetes: pancreatic extracellular matrix ultrastructural abnormalities. *J Cardiometab Syndr*.

- 2008;3(4):234-43. doi: [10.1111/j.1559-4572.2008.00024.x](https://doi.org/10.1111/j.1559-4572.2008.00024.x).
18. Mohapatra S, Majumder S, Smyrk TC, Zhang L, Matveyenko A, Kudva YC, et al. Diabetes mellitus is associated with an exocrine pancreatopathy: conclusions from a review of literature. *Pancreas*. 2016;45(8):1104-10. doi: [10.1097/mpa.0000000000000609](https://doi.org/10.1097/mpa.0000000000000609).
  19. Rodríguez-Calvo T, Ekwall O, Amirian N, Zapardiel-Gonzalo J, von Herrath MG. Increased immune cell infiltration of the exocrine pancreas: a possible contribution to the pathogenesis of type 1 diabetes. *Diabetes*. 2014;63(11):3880-90. doi: [10.2337/db14-0549](https://doi.org/10.2337/db14-0549).
  20. Joshi SR, Chowdhury S, Dharmalingam M, Bhandari S, Deshmukh V, Cruz MD, et al. Prevalence of pancreatic exocrine insufficiency among patients with diabetes mellitus in India. *J Assoc Physicians India*. 2023;71(7):45-51. doi: [10.59556/japi.71.0316](https://doi.org/10.59556/japi.71.0316).
  21. Hardt PD, Hauenschild A, Nalop J, Marzeion AM, Jaeger C, Teichmann J, et al. High prevalence of exocrine pancreatic insufficiency in diabetes mellitus. A multicenter study screening fecal elastase 1 concentrations in 1,021 diabetic patients. *Pancreatology*. 2003;3(5):395-402. doi: [10.1159/000073655](https://doi.org/10.1159/000073655).
  22. Shivaprasad C, Pulikkal AA, Kumar KM. Pancreatic exocrine insufficiency in type 1 and type 2 diabetics of Indian origin. *Pancreatology*. 2015;15(6):616-9. doi: [10.1016/j.pan.2015.09.018](https://doi.org/10.1016/j.pan.2015.09.018).
  23. Larger E, Philippe MF, Barbot-Trystram L, Radu A, Rotariu M, Nobécourt E, et al. Pancreatic exocrine function in patients with diabetes. *Diabet Med*. 2012;29(8):1047-54. doi: [10.1111/j.1464-5491.2012.03597.x](https://doi.org/10.1111/j.1464-5491.2012.03597.x).
  24. Rathmann W, Haastert B, Icks A, Giani G, Hennings S, Mitchell J, et al. Low faecal elastase 1 concentrations in type 2 diabetes mellitus. *Scand J Gastroenterol*. 2001;36(10):1056-61. doi: [10.1080/003655201750422657](https://doi.org/10.1080/003655201750422657).
  25. Yilmaztepe A, Ulukaya E, Ersoy C, Yilmaz M, Tokullugil HA. Investigation of fecal pancreatic elastase-1 levels in type 2 diabetic patients. *Turk J Gastroenterol*. 2005;16(2):75-80.
  26. Alexandre-Heymann L, Yaker F, Lassen PB, Dubois-Laforgue D, Larger E. Pancreatic enzyme replacement therapy in subjects with exocrine pancreatic insufficiency and diabetes mellitus: a real-life, case-control study. *Diabetol Metab Syndr*. 2024;16(1):39. doi: [10.1186/s13098-024-01265-4](https://doi.org/10.1186/s13098-024-01265-4).