Diagnostic and Interventional Endoscopy

Research Article

Baseline Vitamin D Levels Do Not Have Any Impact on Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Retrospective Cohort Study

Adil Duman[1], Serdar Akca[1], Osman Cagin Buldukoglu[1], Besir Kaya[1], Galip Egemen Atar[1], Tolga Yalcinkaya[1], Ferda Akbay Harmandar[1], Serkan Ocal[1], Haldun Selcuk[2], Ayhan Hilmi Cekin[1]

[1]Department of Gastroenterology, Antalya Training and Research Hospital, Antalya, Türkiye
[2]Department of Gastroenterology, Başkent University Hospital, Ankara, Türkiye

Cite this article as: Duman A, Akca S, Buldukoglu OC, et al. Baseline vitamin D levels do not have any impact on post-endoscopic retrograde cholangiopancreatography pancreatitis: A retrospective cohort study. *Diagn Interv Endosc.* 2024;3(1):5-7.

Corresponding author: Osman Cagin Buldukoglu, e-mail: cbuldukoglu@hotmail.com

Received: February 20, 2024 **Revision Requested:** March 18, 2024 **Last Revision Received:** March 18, 2024 **Accepted:** March 22, 2024
Publication Date: May 16, 2024 **DOI:** 10.5152/DiagnIntervEndosc.2024.24106

Abstract

Objective: Post-ERCP pancreatitis (PEP) is a recognized complication following endoscopic retrograde cholangiopancreatography (ERCP), with the inflammatory cascade playing a crucial role in the pathogenesis of PEP. Vitamin D, reported as a significant component of the immune system, influences inflammation and may correlate with acute pancreatitis. In this study, we aimed to investigate the role of vitamin D in the development of PEP.

Methods: This study analyzed the results of 147 consecutive patients with common bile duct stones treated with ERCP at Antalya Training and Research Hospital, Department of Gastroenterology. We compared demographic data and baseline vitamin D levels of patients who developed PEP with those of uncomplicated patients.

Results: Our findings indicate that baseline vitamin D levels were not associated with an increased risk of PEP in this cohort. Vitamin D levels were sufficient in only 25.9% of the study population.

Conclusion: Vitamin D deficiency is a common problem in the general population. Although this retrospective study did not reveal a correlation between vitamin D levels and PEP development, further studies would reveal more on this important topic.

Keywords: Vitamin D, common bile duct stone, endoscopic retrograde cholangiopancreatography, pancreatitis, pep

INTRODUCTION

Post-ERCP pancreatitis (PEP) is a recognized complication following endoscopic retrograde cholangiopancreatography (ERCP). It is thought to arise from a combination of factors including the skill and experience of the endoscopist, procedural aspects, and patient-specific factors.[1-3] Among patient-specific factors, the impact of the inflammatory cascade plays a crucial role in the pathogenesis of PEP.[4,5] Consequently, agents aimed at controlling the inflammatory cascade have been employed in the prevention of PEP.[6-8]

Additionally, beyond its role in calcium and phosphate metabolism, vitamin D is acknowledged as a significant component of the immune system, influencing inflammation.[9-12] There is growing evidence to suggest a possible association between vitamin D deficiency and pancreatic diseases, including both acute and chronic pancreatitis. Vitamin D receptors have been identified in pancreatic tissues, indicating that vitamin D can regulate immune responses and inflammation, which are key factors in the development of pancreatitis.[13-20] A handful of studies have also indicated a potential link between vitamin D deficiency and the onset and severity of acute pancreatitis.[21-24]

Despite these findings, the impact of baseline vitamin D status on the risk of developing PEP has not been previously explored. We propose that a deficiency in baseline vitamin D levels may affect the risk of PEP. The aim of this study is to investigate the relationship between vitamin D levels and the occurrence of PEP.

METHODS

This retrospective study was carried out at Antalya Training and Research Hospital. We reviewed data from 551 consecutive therapeutic ERCP procedures—comprising sphincterotomy, balloon sweeping, and, when necessary, plastic stent insertion—performed between July 1, 2022, and June 30, 2023, at our tertiary care center. Of the 551 patients, only ERCP-naive patients with common bile duct stones and documented baseline vitamin D levels were included. Vitamin D deficiency was classified for levels below 10 ng/mL, insufficiency for levels between 10 and 19 ng/mL, and sufficiency for levels of 20 ng/mL or higher. Magnetic resonance cholangiopancreatography (MRCP) confirmed the presence of CBD stones in all patients. Exclusion criteria were applied to patients with elevated amylase or lipase levels, cholangitis, or kidney disease (creatinine above 1.3 gr/dL prior to the ERCP procedure), resulting in 147 patients deemed suitable for statistical analysis.

All ERCP procedures were performed by the same experienced endoscopist, who handled over 300 cases annually for a decade. Standard preparatory measures included 100 mg of rectal indomethacin administered immediately before ERCP and aggressive hydration at 3 mL/kg/h for 4 hours prior to the procedure using Ringer's lactate. Anesthesiology preparation preceded additional interventions, with all procedures conducted under sedation and anesthesiologist supervision. We abstain from using prophylactic pancreatic stenting for high-risk patients; thus, none had a pancreatic stent. Post-ERCP assessment involved checking amylase and lipase levels 4-6 hours after the procedure, with overnight discharge considered for those without enzyme elevation or pain. Post-ERCP pancreatitis was defined according to the 2020 European Society of Gastrointestinal Endoscopy (ESGE) guidelines, and treatment was administered as necessary. Patients were categorized based on the presence or absence of PEP, and baseline vitamin D levels were compared between these groups.

We performed all statistical analyses using Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM SPSS Corp.; Armonk, NY, USA). Categorical data were presented as counts and percentages, and patient ages as mean ± SD. The Fisher's exact test or the Student's *t*-test was applied as appropriate for continuous and categorical variables. Continuous data were reported as means ± SD or range, and categorical data as percentages. A two-tailed *P*-value of less than .05 was deemed statistically significant.

This study received approval from the Ethical Board of Clinical Research at Antalya Training and Research Hospital, University of Health Sciences, Antalya (Approval number 10/14 2023-190; Date: July 20, 2023). Since the study was a retrospective study, no informed consent was required.

MAIN POINTS

- Post-ERCP pancreatitis (PEP) is a serious complication following endoscopic retrograde cholangiopancreatography (ERCP).
- Serum vitamin D levels were not found to be correlated with PEP development.
- Vitamin D levels were sufficient in only 25.9% of the study population, revealing an important deficiency.

Table 1. Age, Sex, and Vitamin D level Comparisons of Study Population

	PEP+, n = 14	PEP–, n = 133	*P*
Age years old	62.2 ± 23.2	60.1 ± 19.5	.70 NS
Sex (female%)	n = 6 (42.9%)	n = 75 (56.4%)	.24 NS
Vitamin D levels ng/mL	22.2 ± 13.3	18.9 ± 14.5	.51 NS
Vitamin D sufficient %	n = 5 (35.7%)	n = 33 (24.8%)	.70 NS

RESULTS

The study included 147 patients, with an average age of 60.3 ± 19.8 years, ranging from 19 to 90 years; 55.1% were female. Vitamin D levels indicated deficiency in 34%, insufficiency in 40.1%, and sufficiency in 25.9% of patients, with males displaying higher levels than females ($P < .05$). Post-ERCP pancreatitis occurred in 9.5% of patients, with one case being severe and the rest mild to moderate. There was no difference in vitamin D levels of patients with and without PEP. The ages of patients with and without PEP were comparable between the groups (Table 1).

Males have slightly higher vitamin D levels than female, though the difference was not statistically significant (22.6 ± 13.5 versus 16.6 ± 11.5, $P = .06$). Males experienced a higher incidence of pancreatitis (12.1%) compared to females (7.4%), though the difference was not statistically significant ($P = .33$).

DISCUSSION

Our study found no significant correlation between baseline vitamin D levels and the occurrence of PEP. Despite prior studies suggesting a link between vitamin D deficiency and pancreatic diseases (20-24), our findings do not support an association between baseline vitamin D levels and PEP in patients undergoing ERCP for common bile duct stone(s). Although we did not establish a direct link between vitamin D levels and PEP, the retrospective nature of our study and the limited patient number are notable limitations. Also, baseline values were not evaluated in previous studies. Our cohort consisted exclusively of patients with common bile duct stones, which may not represent the broader ERCP patient population where different or additional risk factors could be more influential. Although beyond the scope of this study design, we believe that our results suggest that procedural complexity, pancreatic ductal anatomy, and other individual patient characteristics might have a more substantial impact on the development of PEP in this special cohort.

One interesting result is the frequent vitamin D deficiency/insufficiency in our study population. Similar results were reported from Türkiye previously,[25,26] highlighting the need for heightened awareness of this issue in our region, irrespective of the ERCP procedure.

Future prospective studies with larger sample sizes and a more detailed evaluation of vitamin D status and pancreatic health are needed for a clearer understanding of the possible connection between vitamin D and PEP.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Antalya Training and Research Hospital, University of Health Sciences, Antalya (Approval number 10/14 2023-190; Date: July 20, 2023).

Informed Consent: Since the study was a retrospective study, no informed consent was required.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.D., S.A., O.C.B., S.O.; Design – A.D., S.A., O.C.B., F.A.H., A.H.C.; Supervision – S.A., F.A.H., S.O., H.S., A.H.C.; Resource – A.D., S.A., O.C.B., B.K., G.E.A., T.Y., F.A.H., S.O.; Materials – A.D., S.A., O.C.B., B.K., G.E.A., T.Y., F.A.H., S.O.; Data Collection and/or Processing – S.A., O.C.B., F.A.H., S.O.; Analysis and/or Interpretation – S.A., O.C.B., F.A.H., S.O., A.H.C.; Literature Search – S.A., O.C.B., B.K., G.E.A., F.A.H., S.O., A.H.C.; Writing – A.D., S.A., O.C.B., F.A.H., S.O., H.S., A.H.C.; Critical Review – F.A.H., S.O., H.S., A.H.C.

Declaration of Interests: Serkan Ocal is serving as one of the associate editors of this journal. We declare that Serkan Ocal had no involvement in the peer review of this article and has no access to information regarding its peer review. The other authors have no conflicts of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. *Am J Gastroenterol*. 2007;102(8):1781-1788. [CrossRef]
2. Kochar B, Akshintala VS, Afghani E, et al. Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials. *Gastrointest Endosc*. 2015;81(1):143-149.e9. [CrossRef]
3. Torun S, Parlak E, Yıldız H, et al. Assessment of the endoscopic retrograde cholangiopancreatography grading system: a prospective study from a tertiary care center. *Turk J Gastroenterol*. 2016;27(2):187-191. [CrossRef]
4. Cai F, Hu C, Chen CJ, et al. Vitamin D and pancreatitis: a narrative review of current evidence. *Nutrients*. 2022;14(10):2113. [CrossRef]
5. Pekgöz M. Post-endoscopic retrograde cholangiopancreatography pancreatitis: a systematic review for prevention and treatment. *World J Gastroenterol*. 2019;25(29):4019-4042. [CrossRef]
6. Kang X, Zheng L, Zeng W, et al. Risk factors for post-ERCP pancreatitis in high-risk patients receiving post-procedure rectal indomethacin. *J Gastrointest Surg*. 2018;22(11):1903-1910. [CrossRef]
7. Elmunzer BJ, Scheiman JM, Lehman GA, et al. U.S. Cooperative for outcomes research in endoscopy (USCORE). A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *N Engl J Med*. 2012;366(15):1414-1422. [CrossRef]
8. Otsuka T, Kawazoe S, Nakashita S, et al. Low-dose rectal diclofenac for prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis: a randomized controlled trial. *J Gastroenterol*. 2012;47(8):912-917. [CrossRef]
9. Sîrbe C, Rednic S, Grama A, Pop TL. An update on the effects of vitamin D on the immune system and autoimmune diseases. *Int J Mol Sci*. 2022;23(17):9784. [CrossRef]
10. Christakos S, Hewison M, Gardner DG, et al. Vitamin D: beyond bone. *Ann N Y Acad Sci*. 2013;1287(1):45-58. [CrossRef]
11. Li J, Zhou R, Zhang J, Li ZF. Calcium signaling of pancreatic acinar cells in the pathogenesis of pancreatitis. *World J Gastroenterol*. 2014;20(43):16146-16152. [CrossRef]
12. Cieślińska A, Kostyra E, Fiedorowicz E, et al. Single nucleotide polymorphisms in the vitamin D receptor gene (VDR) may have an impact on acute pancreatitis (AP) development: a prospective study in populations of AP patients and alcohol-abuse controls. *Int J Mol Sci*. 2018;19(7):1919. [CrossRef]
13. Cates MC, Singh SM, Peick AL, Harvey MH, Reber HA. Acute hypercalcemia, pancreatic duct permeability, and pancreatitis in cats. *Surgery*. 1988;104(2):137-141.
14. Kim DI, Kim H, Son P, Kang JH, Kang BT, Yang MP. Serum 25-hydroxyvitamin D concentrations in dogs with suspected acute pancreatitis. *J Vet Med Sci*. 2017;79(8):1366-1373. [CrossRef]
15. Mann ST, Stracke H, Lange U, Klör HU, Teichmann J. Vitamin D3 in patients with various grades of chronic pancreatitis, according to morphological and functional criteria of the pancreas. *Dig Dis Sci*. 2003;48(3):533-538. [CrossRef]
16. Löhr JM, Dominguez-Munoz E, Rosendahl J, et al. United European gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *U Eur Gastroenterol J*. 2017;5(2):153-199. [CrossRef]
17. Frulloni L, Falconi M, Gabbrielli A, et al. Italian consensus guidelines for chronic pancreatitis. *Dig Liver Dis*. 2010;42: S381-S406. [CrossRef]
18. Martínez J, Abad-González A, Aparicio JR, et al. The Spanish Pancreatic Club recommendations for the diagnosis and treatment of chronic pancreatitis: Part 1 (diagnosis). *Pancreatology*. 2013;13(1):8-17. [CrossRef]
19. Dominguez-Munoz JE, Drewes AM, Lindkvist B, et al. Recommendations from the United European gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis. *Pancreatology*. 2018;18(8):847-854. [CrossRef]
20. Arvanitakis M, Ockenga J, Bezmarevic M, et al. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. *Clin Nutr*. 2020;39(3):612-631. [CrossRef]
21. Ocal S, Cerci K, Buldukoglu OC, Atar GE, Harmandar FA, Cekin AH. Effect of serum vitamin D levels on the severity of acute pancreatitis: a prospective study. *Pancreatology*. 2024;24(2):206-210. [CrossRef]
22. Bang UC, Novovic S, Andersen AM, Fenger M, Hansen MB, Jensen JE. Variations in serum 25-hydroxyvitamin D during acute pancreatitis: an exploratory longitudinal study. *Endocr Res*. 2011;36(4):135-141. [CrossRef]
23. Huh JH, Kim JW, Lee KJ. Vitamin D deficiency predicts severe acute pancreatitis. *U Eur Gastroenterol J*. 2019;7(1):90-95. [CrossRef]
24. Abou Saleh M, Alkhayyat M, Mansoor E, et al. The risk of vitamin D deficiency, osteoporosis, and fractures in acute pancreatitis. *Pancreas*. 2020;49(5):629-633. [CrossRef]
25. Yeşiltepe-Mutlu G, Aksu ED, Bereket A, Hatun Ş. Vitamin D status across age groups in Turkey: results of 108,742 samples from a single laboratory. *J Clin Res Pediatr Endocrinol*. 2020;12(3):248-255. [CrossRef]
26. Göktaş O, Ersoy C, Ercan I, Can FE. Vitamin D status in the adult population of Bursa-Turkey. *Eur J Gen Pract*. 2020;26(1):156-162. [CrossRef]