FOLIA MEDICA CRACOVIENSIA
Vol. LXIV, 3, 2024: 91–101
PL ISSN 0015-5616 eISSN 2957-0557
DOI: 10.24425/fmc.2024.152169

# Vitamin D levels in early phase of acute pancreatitis — preliminary study

Mateusz Sporek[1,2]#, Paulina Dumnicka[3]#, Barbara Maziarz[4], Anna Laskowska[5], Beata Kuśnierz-Cabala[3]

[1] Department of Anatomy, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland
[2] Surgery Department of the District Hospital in Sucha Beskidzka, Poland
[3] Chair of Medical Biochemistry, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland
[4] University Hospital in Krakow, Poland
[5] Student's Scientific Group of Medical Biochemistry, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland
#These authors contributed equally to this paper

**Corresponding author:** Prof. Beata Kuśnierz-Cabala, Ph.D.
Chair of Medical Biochemistry, Faculty of Medicine, Jagiellonian University Medical College
ul. Kopernika 7, 31-034 Kraków, Poland
Phone: +48 12 422 74 00; E-mail: beata.kusnierz-cabala@uj.edu.pl

**Abstract:** Introduction: Recent decades brought important insights into the role of vitamin D, showing, among others, its anti-inflammatory properties. Studies linked vitamin D deficiency with higher incidence and worse outcomes of acute inflammatory conditions. Several studies reported low vitamin D status in acute pancreatitis (AP), however, its association with AP severity is not clear, and there are no such studies in Polish population. The aim of the study was to evaluate the concentrations of 25-OH-D at the early phase (the first three days) of AP, to assess the changes in vitamin D concentrations in that period, and to study the relationship with AP severity.
Materials and Methods: The prospective observational study included adult patients with AP admitted within the first 24 h from the onset of symptoms. Total 25-hydroxyvitamin D was measured at 24, 48 and 72 h from the AP onset, using electrochemiluminescent assay.
Results: Initial 25-OH-D was not associated with AP severity. In patients who developed moderately severe to severe AP and pancreatic necrosis, the decrease in 25-OH-D over two consecutive days was higher comparing to mild AP. The change in 25-OH-D concentrations during the first three days of AP was significantly correlated with inflammatory markers (C-reactive protein, leukocyte count), D-dimer, total calcium, hematocrit, and platelet count.
Conclusions: Our study confirmed the decrease in 25-OH-D in AP; however, it cannot be reliably used as an early prognostic factor of severity in AP as it appears too late from the onset of symptoms and its diagnostic accuracy is low.

**Keywords:** vitamin D, severe acute pancreatitis, early phase of acute pancreatitis.

**Submitted:** 03-Sep-2024; **Accepted in the final form:** 03-Nov-2024; **Published:** 26-Dec-2024.

## Introduction

Recent decades brought significant insights into the metabolism and function of vitamin D. Initially known solely as an anti-rickets substance, now it is not only considered a "pro-hormone" engaged in calcium-phosphate homeostasis but also a compound associated with pleiotropic effects important for overall body homeostasis [1]. The active form, 1,25-$(OH)_2$-vitamin D (calcitriol) working through a vitamin D receptor (VDR) has been shown to affect immune functions, cell proliferation, differentiation and apoptosis, endothelial and epithelial cells homeostasis. Moreover, vitamin D deficiency has been associated with poor outcomes in various settings, including patients of intensive care units [2–5]. The change in thinking about the role of vitamin D resulted from the identification of VDR in more than 30 different tissues and the discovery of extrarenal activity of 1-alpha hydroxylase (CYP27B1) that converts 25-hydroxyvitamin D (25-OH-D) into a biologically active form [1]. The participation of vitamin D metabolites in the processes of cell proliferation, differentiation and apoptosis indicates a significant relationship between vitamin D and various inflammatory, neoplastic (including pancreatic cancer), and metabolic diseases (including type 1 and 2 diabetes) [2, 5–9].

According to the current consensus, serum concentration of 25-OH-D is used as a marker of vitamin D status [1]. Based on epidemiological studies, the European Calcified Tissue Society (ECTS) Working Group recognized serum total 25-OH-D below 20 ng/mL (50 nmol/L) as indicating vitamin D deficiency, a recommendation also valid for the Polish population [10]. According to the Endocrine Society [11], concentrations above 30 ng/mL up to 100 ng/mL (75–250 nmol/L) are considered sufficient.

The proper absorption of dietary vitamin D, its metabolism and function requires adequate function of digestive tract (the small intestine, liver and pancreas). Low vitamin D status is observed in cholestasis, cystic fibrosis, or alcoholism, and can be present in chronic pancreatitis [12]. The study of El-Mahdy *et al.* [13] linked VDR gene polymorphism (the predominance of TaqI rs731236 T allele and TT genotype) with increased odds of developing acute pancreatitis (AP). More VDR polymorphisms were also studied in this context by Cieślińska *et al.* [14] and reviewed by Li *et al.* in 2021 [15]. Huh *et al.* [2] have shown that the concentration of $25(OH)D_3$ is significantly reduced in the days following the diagnosis of AP and is inversely correlated with the concentration of C-reactive protein. However, the relationship between low vitamin D levels and acute pancreatitis has not yet been conclusively explained. Serum 25-OH-D levels in AP may be influenced by the decrease in liver synthesis observed in the course of the inflammatory process, and by the increased degradation of 25-OH-D mediated by CYP24A1 in the early phase of the disease. It has also been noted that an increase in vitamin D levels improves the function of the pancreas and its ability to produce insulin, although vitamin D supplementation in the acute phase is still strongly debated and requires further research [5, 16].

The aim of the study was to evaluate the concentrations of 25-OH-D at the early phase (the first three days) of AP, to assess the changes in vitamin D concentrations in that period, and to study the relationship with AP severity.

## Materials and Methods

### *Study design and patients*

The prospective observational study was consistent with the Declaration of Helsinki. The study protocol was approved by the Bioethics Committee of the Jagiellonian University in Cracow (Poland) (approval no. KBET/247/B/2013 issued on 13th November 2013).

The study included adult (≥18 years of age) patients admitted with the diagnosis of AP, treated in the Surgery Department of the District Hospital in Sucha Beskidzka in 2014 (January to December). The study included patients who were admitted no later than 24 hours from the onset of symptoms of AP and only those who signed the informed consent for the study. The diagnosis of AP was consistent with the revised Atlanta classification [17]. Patients with the following comorbidities: chronic pancreatitis, liver diseases, and kidney diseases were excluded.

The study protocol of this observational study required blood sampling for non-standard laboratory tests performed trice: at 24, 48 and 72 hours from the onset of AP symptoms. Otherwise, the patients underwent a standard care, according to the published guidelines [17]; the results of non-standard laboratory tests were not known for the team providing the care.

The severity of AP was based on the revised Atlanta classification [17] which assigned patients to one of three subgroups: (1) mild acute pancreatitis (MAP) — patients without organ dysfunction or local complications during the hospital stay; (2) moderately severe acute pancreatitis (MSAP) — patients with transient (<48 hours) organ failure, local complications (acute peripancreatic fluid, pancreatic pseudocyst, acute necrotic collection, walled-off necrosis), or exacerbation of comorbidities; and (3) severe acute pancreatitis (SAP) — patients with persistent (>48 hours) organ failure and ≥1 local complications [17, 18].

### *Laboratory tests*

The routine laboratory tests, including the complete blood count (WBC), serum amylase, alanine and aspartate aminotransferases (ALT and AST), glucose, bilirubin, urea, creatinine, calcium, C-reactive protein (CRP), albumin, plasma fibrinogen, D-dimer and clotting times were performed on the day of blood sampling in the Medical Diagnostic Laboratory in Sucha Beskidzka, Poland. Serum 25-OH-D was measured with the electrochemiluminescence binding assay designed to determine the total concentrations of 25-hydroxyvitamin D using Cobas 6000 analyzer (Roche Diagnostics, Mannheim, Germany) in the Department of Diagnostics, University Hospital in Krakow, Poland.

### *Statistical analysis*

Quantitative data were summarized as mean ± standard deviation (SD) or median, lower quartile (Q1) and upper quartile (Q3), depending on distribution (normal or significantly different from normal in Shapiro–Wilk test, respectively). Number of patients (n) and percentage of the respective group was given for categories. The 25-OH-D concentrations and change in 25-OH-D were compared between subgroups of patients using Mann–Whitney test because of non-normal distributions of the variables. The 25-OH-D concentrations were compared between the time-points using Friedman test (a non-parametric comparison of dependent variables). Receiver operating

characteristic (ROC) curve analysis was used to determine the diagnostic accuracy and cut-off value of change in 25-OH-D in prediction of AP severity. The correlations between 25-OH-D concentrations and change were studied using Spearman rank correlation coefficient. The statistical tests were two-tailed. The results were considered significant at $p < 0.05$. Statistica 13 data analysis software (Tibco Software Inc., Tulsa, OK, USA) was used for computations.

## Results

The study included 53 patients whose serum was available for 25-OH-D measurements (Table 1). Most patients (60%) had mild course of AP, despite the high percentage (57%) of patients with chronic comorbidities. The maximum BISAP score at admission was 4 points. In the course of AP, the pancreatic necrosis was observed in eight patients, and four were diagnosed with SAP. The length of hospital stay in the whole studied group was in range of 1–35 days. The overall mortality was low (3.8%): the two patients diagnosed with SAP died on the 27$^{th}$ and 31$^{st}$ day of hospital stay. The results of routine laboratory tests in the studied group (Table 2) showed abnormalities typical for the early phase of AP.

**Table 1.** Clinical characteristics of the studied patients with acute pancreatitis (AP).

| Variable | Patients with AP (n = 53) |
|---|---|
| Mean age ± SD, years | 53.2 ± 18.1 |
| Sex: male / female, n (%) | 31 (58.5) / 22 (41.5) |
| AP etiology:<br>Gallstones, n (%)<br>Alcohol, n (%)<br>Hypertriglyceridemia, n (%)<br>Other / idiopathic, n (%) | <br>20 (37.7)<br>18 (34.0)<br>4 (7.5)<br>11 (20.8) |
| AP severity: MAP / MSAP / SAP, n (%) | 32 (60.4) / 17 (30.1) / 4 (7.5) |
| Median BISAP score on admission (Q1–Q3), points | 2 (1–4) |
| BISAP >3 points, n (%) | 8 (15.1) |
| SIRS, n (%) | 23 (43.4) |
| Comorbidities, n (%)<br>Ischemic heart disease, n (%)<br>Obesity, n (%)<br>Diabetes, n (%) | 30 (56.6)<br>14 (26.4)<br>7 (13.2)<br>5 (9.4) |
| Organ failure: transient / persistent, n (%) | 7 (13.2) / 4 (7.5) |
| Pancreatic necrosis, n (%) | 8 (15.1) |
| Median length of hospital stay (Q1–Q3), days | 10 (7–15) |
| Mortality, n (%) | 2 (3.8) |

Abbreviations: BISAP — bedside index of severity in acute pancreatitis; MAP — mild acute pancreatitis; MSAP — moderately severe acute pancreatitis; SAP — severe acute pancreatitis; SIRS — systemic inflammatory response syndrome; SD — standard deviation; Q1 — lower quartile; Q3 — upper quartile; n — number of patients

**Table 2.** The results of laboratory tests in the studied group of 53 patients with acute pancreatitis (AP) at 24, 48, and 72 h from the onset of AP symptoms.

| Laboratory test | 24 hours | 48 hours | 72 hours | Reference interval |
|---|---|---|---|---|
| 25-OH-D, ng/mL | 26.3 (18.4–31.40) | 20.3 (14.8–26.9) | 20.6 (14.1–26.3) | 30.0–80.0 |
| Amylase, U/L | 1046 (411–1909) | 162 (94–375) | 84 (57–136) | 62–220 |
| ALT, U/L | 169.5 (53.6–526.4) | 86.0 (32.8–230.6) | 72.0 (27.0–127.5) | 10.0–37.0 |
| AST, U/L | 128.5 (65.0–313.5) | 59.0 (34.0–90.2) | 37.0 (25.9–57.0) | 10.0–37.0 |
| Bilirubin, μmol/L | 33.6 (19.5–56.3) | 24.8 (16.4–35.2) | 18.7 (7.35–120.5) | 0–21.0 |
| Glucose, mmol/L | 7.77 (4.61–15.71) | 5.27 (2.94–12.61) | 5.07 (13.20–32.20) | 3.30–5.60 |
| Total calcium, mmol/L | 2.21 (1.99–2.36) | 2.09 (2.00–2.33) | 2.13 (2.01–2.31) | 2.02–2.61 |
| Urea, mmol/L | 5.04 (3.33–6.88) | 4.07 (2.86–6.00) | 4.30 (3.37–5.22) | 2.76–8.07 |
| Creatinine, μmol/L | 71.4 (64.4–94.0) | 67.4 (57.2–77.1) | 65.9 (55.3–74.3) | 45.0–97.0 |
| PT, s | 13.8 (12.9–15.3) | 14.6 (13.7–16.2) | 14.5 (13.9–15.2) | 10.4–13.0 |
| APTT, s | 26.1 (23.1–28.8) | 32.8 (28.5–39.5) | 33.4 (30.0–36.5) | 26.0–36.0 |
| D-dimer, mg FEU/L | 1.67 (0.95–3.68) | 3.96 (1.31–6.41) | 3.78 (1.06–7.27) | <0.55 |
| Fibrinogen, g/L | 2.73 (2.22–5.10) | 4.30 (3.34–6.00) | 5.21 (3.77–7.41) | 2.0–4.0 |
| CRP, mg/L | 13.8 (5.0–75.5) | 169.4 (52.4–292.5) | 173.4 (48.0–282.5) | <5.0 |
| Albumin, g/L | 41.4 (35.4–45.5) | 37.8 (31.7–40.7) | 34.7 (27.9–41.9) | 35.0–50.0 |
| WBC, $\times 10^3/\mu L$ | 12.98 (9.55–15.67) | 9.62 (6.82–12.53) | 7.79 (6.44–11.15) | 4.0–10.0 |
| Neutrophils, $\times 10^3/\mu L$ | 3.24 (7.66–14.06) | 6.58 (5.03–10.61) | 6.34 (4.60–8.87) | 1.8–8.0 |
| Lymphocytes, $\times 10^3/\mu L$ | 1.17 (0.73–1.69) | 1.17 (0.75–1.65) | 1.30 (0.82–1.80) | 1.0–5.0 |
| Monocytes, $\times 10^3/\mu L$ | 0.58 (0.44–0.76) | 0.65 (0.47–0.96) | 0.66 (0.51–0.82) | 0.03–0.80 |
| Hematocrit, % | 44.1 (41.3–46.6) | 40.4 (36.8–42.8) | 38.4 (35.9–40.6) | W: 37–47; M: 40–54 |
| Platelets, $\times 10^3/\mu L$ | 200 (171–242) | 170 (138–201) | 184 (137–221) | 150–350 |

Abbreviations: 25-OH-D — total 25-hydroxyvitamin D; ALT — alanine aminotransferase; APTT — activated partial thromboplastin time; AST — aspartate aminotransferase; CRP — C-reactive protein; FEU — fibrinogen equivalent units; PT — prothrombin time; WBC — white blood cell count

At the beginning of the study (24 h from the onset of AP symptoms), serum 25-OH-D was low (i.e. below the concentration of 30 ng/mL, indicating sufficient vitamin D status) in 36 (67.9%) patients. We did not observe significant differences in the initial concentrations of 25-OH-D according to the severity of AP. Also, there were no significant association between the initial status of vitamin D and patients' age, comorbidities, or AP etiology.

In the whole studied group, the concentrations decreased further at 48 h from the onset of AP ($p < 0.001$) and stabilized thereafter (Table 2). However, the decrease was more evident in patients with more severe disease (MSAP or SAP; pancreatic necrosis), and in those patients, serum 25-OH-D concentrations at 72 h from the onset of AP were lower that at 24 or 48 h (Fig. 1). At 72 h, serum 25-OH-D was significantly lower among patients who developed pancreatic necrosis

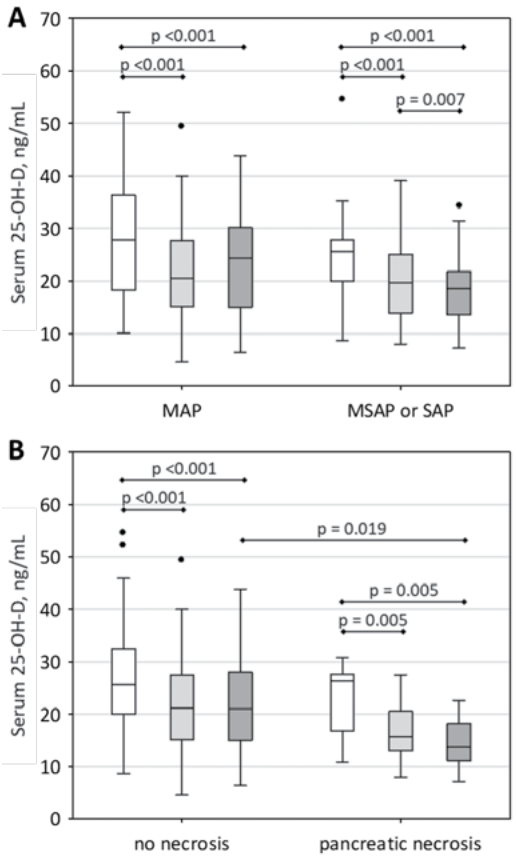


**Fig. 1.** Serum concentrations of total 25-hydroxyvitamin D (25-OH-D) in patients with early phase of acute pancreatitis (AP) over the course of the study (first 72 hours from the onset of AP symptoms). Time from the onset of AP symptoms is denoted with different colors of the boxes: white — 24 h, light grey — 48 h and dark grey — 72 h. Data are shown as median (central bar), interquartile range (box), non-outlier range (whiskers) and outliers (points). Significant differences between the groups and time-points are shown on the graphs. Panel A compares patients with mild (MAP) versus moderately severe to severe AP (MSAP or SAP). Panel B compares patients without and with pancreatic necrosis.

during the hospital stay as compared to those without necrosis (p = 0.019; Fig. 1B). Moreover, the change in 25-OH-D concentrations between 24 and 72 h from the onset of symptoms was significantly higher among patients with MSAP to SAP comparing to those with MAP (median change of 5.65 versus 3.45 ng/mL, respectively; p = 0.032; Fig. 2). The change of more than 3.58 ng/mL predicted moderately severe to severe AP with a high sensitivity of 90%, although relatively low specificity of 54% (Fig. 2).

Serum 25-OH-D concentrations correlated positively with monocyte count at 24 h (R = 0.36; p = 0.020), with total calcium at 72 h (R = 0.33; p = 0.042), and negatively with serum amylase at 72 h (R = –0.30; p = 0.046). Otherwise, we did not observe significant correlations of serum 25-OH-D with the results of routine laboratory tests. To the contrary, the change in 25-OH-D concentrations (calculated as the concentration at 24 h minus the concentration at 72 h) correlated positively with inflammatory markers (CRP, WBC, neutrophil and monocyte counts), hematocrit (at 24 h) and plasma D-dimer (Table 3). Also, larger decrease in 25-OH-D was associated with lower total calcium at 48 h as well as with lower platelet count at 24 and 72 h (Table 3). Moreover, the change in 25-OH-D concentrations correlated significantly with the length of hospital stay (R = 0.34; p = 0.021). Larger decrease in 25-OH-D between 24 and 72 h was associated with increasing severity in Atlanta classification (MAP, MSAP, SAP): R = 0.31; p = 0.032.

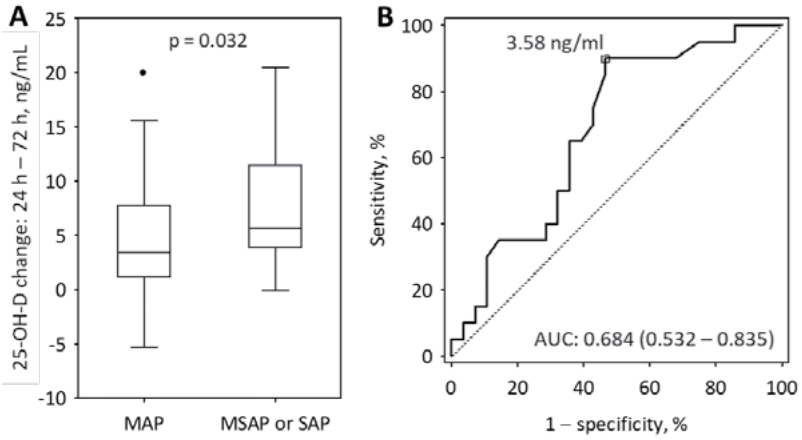


**Fig. 2.** Panel A: The change in total 25-hydroxyvitamin D (25-OH-D) concentrations (calculated as: serum 25-OH-D at 24 h from the onset of AP symptoms minus serum 25-OH-D at 72 h) among patients with mild acute pancreatitis (MAP) as compared to moderately severe or severe disease (MSAP or SAP). Panel B: Receiver operating characteristic (ROC) curve for the change in serum 25-OH-D (24–72 h) in prediction of MSAP or SAP. The selected cut-off is shown on the graph. The area under the ROC curve (AUC) is shown together with 95% confidence interval (in brackets).

**Table 3.** Statistically significant correlations between the change in total 25-hydroxyvitamin D (25-OH-D) concentrations during the study (calculated as: serum 25-OH-D at 24 h from the onset of AP symptoms minus serum 25-OH-D at 72 h) and the results of routine laboratory tests performed at each time point (24, 48 and 72 h from the onset of symptoms) in the whole studied group of 53 patients with acute pancreatitis.

| Laboratory test | 24 hours | | 48 hours | | 72 hours | |
|---|---|---|---|---|---|---|
| | R | p | R | p | R | p |
| Total calcium | NS | | –0.35 | 0.021 | NS | |
| D-dimer | NS | | 0.48 | <0.001 | 0.48 | <0.001 |
| CRP | NS | | 0.47 | <0.001 | 0.42 | 0.004 |
| WBC | NS | | 0.35 | 0.016 | 0.38 | 0.008 |
| Neutrophils | NS | | 0.39 | 0.009 | 0.37 | 0.012 |
| Monocytes | NS | | NS | | 0.33 | 0.029 |
| Hematocrit | 0.40 | 0.005 | NS | | NS | |
| Platelets | –0.31 | 0.033 | NS | | –0.35 | 0.016 |

Abbreviations: CRP — C-reactive protein; NS — non-significant result; WBC — white blood cell count

## Discussion

Our study assessed vitamin D status in patients with early phase of AP. Although we failed to show significant association between the initial vitamin D status (at 24 h from the onset of symptoms) with patients' characteristics or with subsequent AP severity, we observed higher decrease in 25-OH-D concentrations in subsequent two days among patients who were eventually diagnosed

with more severe AP (MSAP or SAP). This led to lower 25-OH-D concentrations observed at 72 h from the onset of AP in patients who subsequently developed pancreatic necrosis. The decrease in 25-OH-D concentrations during the first three days of AP was significantly correlated with inflammatory markers.

In previous studies, serum 25-OH-D level was inversely associated with the severity of AP and inflammatory markers such C-reactive protein (CRP) [2, 4, 15]. It has been noted that in the course of acute inflammation, including AP, there may be accelerated degradation of 25-OH-D mediated by CVP24A1 (24-hydroxylase) and a significant decrease in the synthesis of 25-OH-D in the liver; these observations led some authors to compare vitamin D to negative acute phase reactants [5]. However, decreased total 25-OH-D concentrations in acute inflammation may to some extend reflect the decrease in binding proteins including albumin [1]. In our study, over two thirds of patients had initial 25-OH-D concentrations below 30 ng/mL (75 nmol/L). This is similar to the study of Tilg *et al.* [19], who showed that on the first day of AP, 23% of patients presented a severe vitamin D deficit (25-OH-D <13 nmol/L), in about 20% the concentration were in range of 13–25 nmol/L, and in 40% in the range of 26–50 nmol/L [19]. The most common causes of AP are the diseases of the bile ducts and excessive alcohol consumption [17]. We expected vitamin D deficiency in patients with alcohol etiology of AP, associated with a broader spectrum of nutritional deficiencies in such patients. Also, cholestasis may lead to worsened absorption of this fat-soluble vitamin in the intestine. It should also be noted that epidemiological studies have shown a widespread vitamin D deficiency in Eastern-European (including Polish) population, which is considered to be caused by insufficient dietary supply, avoidance of sunlight, and impaired skin synthesis or insufficient metabolism to active forms in chronic diseases [10].

Although we have not observed the correlation between initial vitamin D status with AP severity, our results indicate the associations between the decrease in 25-OH-D over the early phase of AP and several known markers of unfavorable prognosis in AP. In our patients, higher decrease in 25-OH-D was associated with lower total calcium. At 72 h, the 25-OH-D concentrations were positively correlated with total calcium. The relationship between vitamin D concentration and calcium metabolism is well understood. However, severe AP is associated with a decrease in total calcium, resulting from several processes: decreased binding by serum albumin (a negative acute phase protein), catecholamine-mediated translocation to cells (including pancreatic cells), or binding with fatty acids and precipitation of soaps [20, 21]. Low calcium level is a known predictor of SAP [4]. In 2017, Peng *et al.* [21] showed that total calcium concentration below 1.97 mmol/L predicts persistent organ failure in AP with almost 90% sensitivity. On the other hand, hypercalcemia (also resulting from vitamin D intoxication) may be a trigger for AP and increased intracellular calcium levels are involved in the pathomechanism of pancreatic injury [20, 22].

In our study, higher decrease in 25-OH-D was associated with higher hematocrit at 24 h from the onset of AP. High hematocrit (>44%) at admission indicates early hemodynamic abnormalities in AP and is a known predictor of severe course of AP [23]. Also, in our study, higher decrease in 25-OH-D was associated with higher D-dimer level and lower platelets. Both high D-dimers and low platelets are associated with prothrombotic endothelial dysfunction which plays a role in the development of systemic complications and organ failure in AP [24].

Recent decades brought the evidence that vitamin D is involved not only in the metabolic processes of bone remodeling, but also in immunological processes and anti-inflammatory and anti-cancer effects [2, 6]. Epigenetic, transcriptomic and proteomic studies revealed biological mechanisms mediated by vitamin D, associated with cell differentiation, proliferation, neoplastic

transformation and death of cancer cells [6]. Vitamin D has anti-inflammatory effects and the its deficits are associated with acute and chronic inflammatory conditions [3, 7]. Yet, most large studies failed to show a clear advantage of vitamin D supplementation in chronic and acute inflammatory conditions [1, 3].

Our study has several limitations. Most importantly, the studied group was relatively small, therefore, our study might have missed weak associations. This may be the main reason why we failed to observe the association between the initial vitamin D status and the clinical characteristics of our patients (e.g. chronic comorbidities or age). On the other hand, our study only recruited patients in the first 24 hours from the onset of AP symptoms, which may be the reason why we did not observe the association between initial 25-OH-D concentrations and AP severity. Some discrepancies between our results and the previous studies may also be explained by the differences in laboratory test used to assess vitamin D status. Despite significant methodological improvement, some important analytical issues implicating differences in results obtained with various methodologies have not been solved [1].

In conclusion, our study confirms the association of decreased 25-OH-D concentrations with the severity of AP as an acute inflammatory disease. At the same time, our results suggest that 25-OH-D concentration (or the change in its concentrations) cannot serve as an early predictor of severe course of AP, since a significant decrease in 25-OH-D occurs relatively late (72 h from the onset of AP symptoms). Considering the literature data, there is need for further studies to fully explain the changes in vitamin D metabolism in acute inflammation, and the possibilities of clinical interventions utilizing the anti-inflammatory potential of vitamin D metabolites in such diseases.

## Author contributions

Conceptualization, B.K.-C., M.S. and P.D.; methodology, B.K.-C.; validation, B.K.-C., P.D., and M.S.; formal analysis, P.D.; data curation, M.S.; investigation, B.M., and B.K.-C.; searching for the publications used in the part in this work, A.L.; project administration B.K.-C. and M.S.; writing-review, B.K.-C. and P.D.; final proofreading, B.K.-C. and P.D.; cooperation in the preparation of figures, A.L. and P.D.; supervision, B.K.-C. and P.D. All authors have read and approved the contest of the manuscript.

## Acknowledgements

The study was financed by Jagiellonian University Medical College grants No K/ZDS/002844 and K/DSC/003118.

## Conflict of interest

None declared.

## References

1. *Cavalier E., Makris K., Heijboer E.C., Herrmann M., Souberbielle J.V.*: Vitamin D: Analytical Advances, Clinical Impact, and Ongoing Debates on Health Perspectives. Clin Chem. 2024; 70: 1104–1121. doi: 10.1093/clinchem/hvae056.

2. *Huh J.H., Kim J.W., Lee K.J.*: Vitamin D deficiency predicts severe acute pancreatitis. United Eur Gastroenterol J. 2019; 7: 90–95. doi: 10.1177/2050640618811489.
3. *The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network*: Early high-dose Vitamin D3 for critically ill, vitamin D–deficient patients. N Engl J Med. 2019; 381: 2529–2540. doi: 10.10.56/NEJMoa1911124.
4. *Kolosovych I., Hanol I., Bystrytska M., Uzun H.:* Changes in vitamin D and calcium-phosphorus metabolism in patients with severe acute pancreatitis. Turk J Surg. 2022; 38: 327–333. doi: 10.47717/turjsurg.2022.5669.
5. *Han Z., Margulies S.L., Kurlan D., Elliott M.S.*: Vitamin D deficiency in patients with pancreatitis: is vitamin D replacement required? Pancreat Disord Ther. 2016; 6. doi. 10.4172/2165-7092.1000172.
6. *Seraphin G., Rieger S., Hewison M., Capobianco E., Lisse T.S.*: The impact of vitamin D on cancer. A mini review. J Steroid Biochem Mol Biol. 2023; 231. doi: org/10.1016/j.jsbmb.2023.106308.
7. *Dancer R.C.A., Pareh D., Lax S., D'Souza V., Zheng S., Bassford C.R., et al.*: Vitamin D deficiency contributes directly to the acute respiratory distress syndrome (ARDS). Thorax. 2015; 70: 617–624. doi. 10.1136/thoraxjnl-2014-206680.
8. *Cho M., Peddi P.F., Ding K., Chen L., Thomas D., Wang J., et al.*: Vitamin D deficiency and prognosis among patients with pancreatic adenocarcinoma. J Transl Med. 2013; 11: 206. doi: 10.1186/1479-5876-11-206.
9. *Altieri B., Grant W.B., Casa S.D., Orio F., Pontecorvi A., Colao A., et al.*: Vitamin D and pancreas: The role of sunshine vitamin in the pathogenesis of diabetes mellitus and pancreatic cancer. Crit Rev Food Sci Nutr. 2017; 57: 3472–3488. doi: 10.1080/10408398.2015.1136922.
10. *Lips P., Cashman K.D., Lamberg-Allardt Ch., Bischoff-Ferarri H.A., Obermayer-Pietsch B., et al.*: Current vitamin D status in European and Middle East countries and strategies to prevent vitamin D deficiency: a position statement of the European Calcified Tissue Society. Eur J Endocrinol. 2019; 180: 23–54. doi: 10.1530/EJE-18-0736.
11. *Holick M.F., Binkley N.C., Bischoff-Ferrari H.A., Gordon C.M., Hanley D.A., Heaney R.P., et al.*: Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011; 96: 1911–1930. doi: 10.1210/jc.2011-0385.
12. *Saleh M.A., Alkhayyat M., Mansoor E., Khoudari G., Simons-Linares C.R., Vargo J., et al.*: The risk of Vitamin D deficiency, osteoporosis, and fractures in acute pancreatitis. Pancreas. 2020; 49: 629–633. doi: 10.1097/MPA.0000000000001538.
13. *El-Mahdy R.I., Ramadan H.K.-A., Sharaf H., Mohammed H.S.E.D., Ahmed E.H., et al.*: Impact of the etiology and vitamin D receptor TaqI rs731236 gene polymorphism on the severity of acute pancreatitis. J Hepatobiliary Pancreat Sci. 2020; 27: 896–906. doi: 10.1002/jhbp.817.
14. *Cieślińska A., Kostyra E., Fiedorowicz E., Snarska J., Kordulewska N., Koper K., 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: 1919. doi: 10.3390/ijms19071919.
15. *Li X., Gan X., Gong J., Mou T., Zhou H., Li M.*: Association between vitamin D receptor polymorphism and acute pancreatitis. A protocol for systemic review and meta-analysis. Medicine (Baltimore). 2021; 100: e25508. doi: org/10.1097/MD.0000000000025508.
16. *Cai F., Hu C., Chen C.-J., Han Y.-P., Lin Z.-Q., Deng L.-H., Xia Q.*: Vitamin D and pancreatitis: a narrative review of current evidence. Nutrients. 2022; 14: 2113. doi: 10.3390/nu14102113.
17. *Banks P.A., Bollen T.L., Dervenis Ch., Gooszen H.G., Johnson C.J., Sarr M.G., et al.*: Classification of acute pancreatitis — 2012 revision of the Atlanta classification and definitions by international consensus. Gut. 2013; 62: 102–111. doi: 10.1136/gutjnl-2012-302779.
18. *Lee P.J., Papachristou G.I.*: Management of severe acute pancreatitis. Curr Treat Options Gastroenterol. 2020; 18: 670–681. doi: 10.1007/s11938-020-00322-x.

19. *Tilg H., Moschen A.R., Kaser A., Pines A., Doton I.*: Gut, inflammation and osteoporosis: basic and clinical concepts. Gut. 2008; 57: 684–694. doi: 10.1136/gut.2006.117382.
20. *Frick T.W.*: The role of calcium in acute pancreatitis. Surgery. 2012; 152: S157–163. doi: 10.1016/j.surg.2012.05.013.
21. *Peng T., Peng. T., Huang M., Zhang Y., Wu H., et al.*: Serum calcium as an indicator of persistent organ failure in acute pancreatitis. Am J Emerg Med. 2017; 35: 978–982. doi: 10.1016/j.ajem.2017.02.006.
22. *Singh R., Balwani M.R., Godhani U., Ghule P., Tolani P., Kute V.*: Iatrogenic vitamin D overdose resulting in acute pancreatitis with acute kidney disease. J Parathyroid Dis. 2018; 6: 29–31. doi: 10.15171/jpd.2018.10.
23. *Li L., Jin T., Wen S., Shi N., Zhang R., Zhu P., et al.*: Early Rapid Fluid Therapy Is Associated with Increased Rate of Noninvasive Positive-Pressure Ventilation in Hemoconcentrated Patients with Severe Acute Pancreatitis. Dig Dis Sci. 2020; 65: 2700–2711. doi: 10.1007/s10620-019-05985-w.
24. *Dumnicka P.*, *Maduzia D., Ceranowicz P., Olszanecki R., Drożdż R., Kuśnierz-Cabala B.*: The Interplay between Inflammation, Coagulation and Endothelial Injury in the Early Phase of Acute Pancreatitis: Clinical Implications. Int J Mol Sci. 2017; 18: 354. doi: 10.3390/ijms18020354.