Practical Laboratory Medicine 42 (2024) e00429

Contents lists available at ScienceDirect

Practical Laboratory Medicine

journal homepage: www.elsevier.com/locate/plabm

Registered Report Stage II

Biochemical indices of patients with enteric fever and pancreatitis: A comparative cross-sectional study

Nathaniel Ebo Aidoo [a,b], Emmanuel Kwaku Ofori [a,*], Vincent Boima [c], Eric Nana Yaw Nyarko [a], John Cletus Osei [a], Clement G. Darkwah [a,d], Morris O. Gayflor [a], Seth K. Amponsah [e], Henry Asare-Anane [a]

[a] Department of Chemical Pathology, University of Ghana Medical School, Accra, Ghana
[b] MDS-Lancet Laboratories Ghana Ltd, East Legon, Accra, Ghana
[c] Department of Medicine and Therapeutics, University of Ghana Medical School, Ghana
[d] University of Ghana Legon Hospital, Accra, Ghana
[e] Department of Medical Pharmacology, University of Ghana Medical School, Accra, Ghana

ARTICLE INFO

Keywords:
Enteric fever
Acute pancreatitis
Amylase
Lipase
Elastase-1

ABSTRACT

Objective: Enteric fever (EF), a potentially fatal febrile illness, is prevalent in developing countries. Elevated levels of lipase and amylase in serum, typically associated with acute pancreatitis (AP), have been observed in patients with EF. The elevated enzymes in both conditions may lead to diagnostic confusion and care delays. This study aimed to determine biochemical indices that are peculiar to EF and AP.

Methods: A cross-sectional comparative study was conducted at the Korle-Bu Teaching Hospital, Ghana. Volunteers were categorized into three groups: EF (n = 32), AP (n = 30) and healthy controls (n = 31). A standard questionnaire was used to collect socio-demographic and clinical information from the participants. Blood and stool samples were obtained, followed by biochemical analysis: total amylase, lipase, pancreatic amylase, serum elastase 1, hepatic enzymes, calcium, magnesium, phosphate, stool colour, stool pH, and stool fat presence.

Results: The AP group displayed higher total amylase, lipase, elastase-1, alkaline phosphatase, aspartate aminotransferase, and gamma-glutamyl transferase levels compared to the EF and control groups ($p < 0.05$ respectively). Elastase 1 levels were found to be high in all AP participants, whereas no elevations were observed in the EF group. Positive associations were observed in the AP and EF groups for lipase vs total amylase ($\rho = .543$, $p = 0.001$; $\rho = .543$, $p = 0.001$ for both).

Conclusions: Elevated levels of total/pancreatic amylase and lipase were found to be indicative of a patient with AP and EF. Further, elastase-1 was found to be a good biomarker to distinguish between AP and EF.

* Corresponding author.
E-mail addresses: neaidoo20@gmail.com (N.E. Aidoo), ekofori1@ug.edu.gh (E.K. Ofori), vboima@ug.edu.gh (V. Boima), eynyarko@ug.edu.gh (E.N.Y. Nyarko), jcosei001@st.ug.edu.gh (J.C. Osei), clezzil@yahoo.com (C.G. Darkwah), gomorris@st.ug.edu.gh (M.O. Gayflor), skamponsah@ug.edu.gh (S.K. Amponsah), henryasare-anane.gh@hotmail.com (H. Asare-Anane).

https://doi.org/10.1016/j.plabm.2024.e00429
Received 11 July 2024; Received in revised form 30 August 2024; Accepted 15 September 2024
Available online 18 September 2024

1. Introduction

Enteric fever (EF), or typhoid fever, is a potentially life-threatening febrile condition [1,2]. EF encompasses a range of complications, and the disease is usually endemic in developing countries [3]. Notably, around 10–15 % of hospitalized patients with EF can present with encephalopathy, gastrointestinal haemorrhage due to intestinal perforation, pancreatitis, and peritonitis, with a higher vulnerability observed in children [4,5].

Historically, acute pancreatitis (AP) has been associated with elevated serum lipase and amylase levels. Additionally, some studies have reported high serum amylase and lipase levels in EF patients [6–8]. Importantly, none of the participants in the aforementioned studies had a prior diagnosis of pancreatitis, whether clinically, biochemically, or radiologically. A conundrum may present itself when there is the need to diagnose EF or AP biochemically.

A notable case report from India presented an 18-year-old male with EF who manifested symptoms such as fever, chills, and rigours. Following the fever, he experienced a sudden onset of dull, aching, non-radiating pain in the epigastric region, accompanied by bilious vomiting and bleeding per rectum [6]. Laboratory results showed elevated serum lipase and amylase in this patient. This puzzled clinicians, leading to uncertainty about whether the elevation was linked to EF or potentially complicating pancreatitis. Sequential biochemical assessments indicated a decline in lipase and amylase levels as the patient's condition improved. Due to the similar biochemical patterns between EF and AP patients, further investigation of the intriguing biochemical association is needed.

Reports suggest that EF typically will not lead to hyperamylasemia and hyperlipasemia; biochemical manifestations associated with AP [9,10]. Therefore, routine biochemical assessment may not consider these markers in EF patients. Indeed, these two conditions can give rise to biochemical abnormalities, including hepatic enzyme derangements [11,12]. EF, with its non-specific symptoms, often mimics other febrile illnesses, leading to misdiagnosis and inappropriate treatment [3,13]. Furthermore, AP has a broad spectrum of causative factors, including hypertriglyceridemia, genetic predispositions, and medication-induced pancreatitis, making diagnosis and treatment more intricate. Understanding the biochemical underpinnings of both EF and AP can potentially facilitate the implementation of early intervention strategies. This study evaluated the biochemical indices of patients with EF and AP at a teaching hospital in Ghana.

2. Materials and Methods

2.1. Study design, site, participants and ethical considerations

This comparative cross-sectional study was conducted at the Korle-Bu Teaching Hospital, Accra, Ghana. A total of ninety-three (93) consented participants were enrolled. Of the participants, 32 were diagnosed with EF, 30 with AP, and 31 healthy volunteers served as control. Participants were within the age range of 18–60 years. Adult patients diagnosed with AP or EF confirmed by ultrasonography and a positive typhidot test (IgM or both IgM and IgG), respectively, were included in the study. Healthy adults with no history of pancreatitis and with a negative typhidot test were included in the study as controls. Patients who had both EF and AP were excluded from the study. The research received approval from the Ethical and Protocol Review Committee (EPRC) of the College of Health Sciences, University of Ghana (ID: CHS-Et/M.5 – P 4.11/2022–2023) and the Institutional Review Board (IRB) of the Korle-Bu Teaching Hospital (KBTH) (ID: KBTH-STC/IRB/000216/2022). The minimum sample size was calculated using an EF prevalence rate of .943 % [14].

2.2. Socio-demographics, clinical data and sample collection

A standard questionnaire and patient folders were used to collect socio-demographic and clinical information of the participants. Five (5) mls of venous blood were drawn from participants into gel-activated tubes and centrifuged within 15 min of the blood draw at 4000 rpm for 5 min. The resultant serum was aliquoted in .5 ml tubes and stored at −80°C until analyzed. Additionally, a stool sample was collected from each participant in a clean, dry, screw-top plastic container and analyzed on the same day.

2.3. Laboratory procedures

Total amylase, lipase, calcium, magnesium, phosphates, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine transaminase (ALT) and gamma-glutamyl transferase (GGT) in serum were assayed using Beckman Coulter DXC 700 AU480 (Japan) and Cobas Integra 400 plus (Switzerland) clinical chemistry analyzers. Serum elastase 1 and pancreatic amylase were measured using the sandwich enzyme-linked immunosorbent assay (ELISA) method (Sunlong Biotech Co. LTD, China). Stool samples were assessed for colour, pH and fat content using a stool colour chat, nitrazine paper and qualitative faecal fat test (Biopharma, Virginia, USA).

2.4. Statistical analysis

Data was initially entered into Microsoft Excel and analyzed using the Statistical Package for Social Sciences (SPSS) version 26. Descriptive data were summarised into frequencies and percentages. Continuous data were presented as means and standard error of mean where appropriate. The Shapiro-Wilk test assessed whether the dataset exhibited a normal distribution. Levene's test was employed to determine the equality of variances among groups. Given the presence of unequal sample sizes, unequal variances among groups, and non-normal distribution of the data, Welch's ANOVA and chi-square statistic were used to investigate differences among

the groups at a significance level of .05. Furthermore, a post hoc test was conducted to identify specific differences between individual pairs of means. Principal component analysis (PCA) with varimax rotation was conducted to reduce dimensionality and identify underlying patterns in the data. The scree plot was used to determine the optimal number of components to retain: three components for both the enteric fever and acute pancreatitis groups, and two components for the combined analysis of all three groups. Spearman rank correlation (ρ) was used to assess the strength and direction of associations between variables.

3. Results

3.1. Demographic and clinical characteristics

Table 1 summarizes demographic characteristics. The study had 93 participants, the average age of whom was 39.4. Male participants were 50.5 % (Table 1).

Table 2 provides the clinical information on the EF group. About a quarter, 28.1 %, sought medical care before joining the study. Common symptoms experienced in the EF group included abdominal pain (n = 23, 71.9 %), headache (n = 27, 84.4 %), fever (n = 29, 90.6 %), and chills (n = 24, 75 %). All EF participants (100 %) had no knowledge of ever receiving a typhoid vaccination (Table 2).

In the AP group, a minority (6.7 %, n = 2) sought medical care before joining the study. Common symptoms experienced in the AP group included abdominal pains (n = 30, 100 %), nausea and vomiting (n = 27, 90 %), fever (n = 25, 83.3 %) and loose stool or diarrhoea (n = 14, 46.7 %). A minority in the AP group (n = 1, 3.3 %) had a history of gallstones, with 10 % reporting a history of alcoholism (Table 3).

3.2. Serum biochemical markers in the study participants

Total amylase, pancreatic amylase, elastase 1, lipase, AST, ALT, ALP and GGT were higher in the AP group than in the EF and control groups (p-value < .05 for all). EF participants also displayed higher total amylase, pancreatic amylase and AST levels than controls (p-value <.05 for all). No significant differences were found between the EF and control groups regarding lipase, ALP, and GGT serum levels. On the other hand, calcium, phosphate, and magnesium levels were notably lower in the AP and EF groups compared to the control group (p value < .05). AP subjects showed lower stool pH than EF and control subjects (p value < .05), with no significant difference found between the EF and control groups (Table 4).

3.3. Distribution of serum biomarkers based on reference ranges in the enteric fever and acute pancreatitis groups

In the EF group, most participants had normal total amylase levels (65.62 %), whereas in AP, all patients had markedly elevated total amylase levels. For lipase and ALP in EF, the vast majority (96.87 % and 96.87 %, respectively) had normal levels, whereas in AP, most (96.67 %) exhibited elevated levels of lipase, with a quarter (20 %) having high ALP levels. In EF, a minority had elevated AST, ALT, and GGT levels (12.50 %, 6.25 %, and 6.25 %, respectively), whereas in AP, the majority had elevated AST (63.33 %), ALT (33.33 %), and GGT (33.33 %) levels. Calcium, magnesium and phosphate levels were mainly within the normal range in both groups (Fig. 1).

3.4. Stool analysis findings

The majority in the control group (96.8 %) had brown stool, with the rest (3.2 %) having black stool. The EF group also had brown stool (93.8 %), with less than a tenth (6.3 %) having green stool. In the AP group, a significant proportion (90.0 %) had brown stool, with a minority (10.0 %) having yellow stool (Fig. 2). A majority (96.8 % and 90.6 %, respectively) in the control and EF groups had no detectable stool fat. The AP group had the highest percentage of individuals with stool fat (26.7 %), with the rest having no detectable stool fat (Fig. 2). Chi-Square analysis revealed a significant association between AP and stool fat ($\chi^2 = 6.661$, $p = 0.006$) (Table 6). In contrast, no relationship existed between EP and stool variables (Table 5).

Table 1
Socio-demographic characteristics of study participants.

Variables	Controls (n = 31, %)	Enteric fever (n = 32, %)	Acute pancreatitis (n = 30, %)	χ^2 (p-value)
Age groups (years)				
20–29	5, (16.1)	11, (34.4)	4, (13.3)	45.68 (.026)
30–39	11, (35.5)	7, (21.9)	11, (36.7)	
40–49	12, (38.7)	6, (18.7)	4, (13.3)	
50–59	3, (9.7)	8, (25.0)	11, (36.7)	
Gender				
Males	18, (58.1)	12, (37.5)	17, (56.7)	3.33 (.187)
Females	13, (41.9)	20, (62.5)	13, (43.3)	

Values presented as frequencies (n) and percentages (%); Age (years, mean ± SD): 39.43 ± 11.2.
χ^2 is chi-square; p < 0.05 was significant.

Table 2
Clinical information on study participants with enteric fever.

Variables	Frequency (n = 32)	Percentage (%)
Medical Facility attendance		
Participants who sought care from another facility before visiting the hospital	9	28.1
Main clinical symptoms experienced		
Abdominal pains	23	71.9
Headaches	27	84.4
Fever	29	90.6
Loose stool/diarrhoea	13	40.6
Coughing	11	34.4
Rigors	24	75.0
Medical history		
Typhoid vaccination (unknown)	32	100.0
Travel to/Arrive from a poor sanitation area in the 28 days prior to illness	4	12.5

Values presented as frequencies (n) and percentages (%); Mean duration of illness (days): 9.38 ± 6.598.

Table 3
Clinical information on study participants with acute pancreatitis.

Variables	Frequency (n = 30)	Percentage (%)
Duration of illness		
Minimum duration (days)	2	
Maximum duration (days)	14	
Medical Facility attendance		
Participants who sought care from another facility prior to visiting the hospital	2	6.7
Main clinical symptoms experienced		
Abdominal pains	30	100
Nausea and Vomiting	27	90
Fever	25	83.3
Loose stool/diarrhoea	14	46.7
Medical history		
Gallstones	1	3.3
Alcoholism	3	10
Pancreatic cancer	0	0
Cystic fibrosis	0	0
Abdominal surgery	2	6.7
Injury to the abdomen	1	3.3
Obesity	0	0
Trauma	2	6.7
Hypertriglyceridemia	3	10
Hypercalcemia	0	0
Diagnosed of Diabetes	3	10

Values presented as frequencies (n) and percentages (%); Mean duration of illness (days): 5.97 ± 2.918.

3.5. Associations in biomarkers between enteric fever and acute pancreatitis groups

Correlation analysis revealed significant associations between serum biomarkers in the EF and AP groups (Tables 7 and 8). In the EF group, positive relationships were observed for ALT vs AST ($\rho = .711$, $p < 0.001$), lipase vs total amylase ($\rho = .543$, $p = 0.001$), AST vs ALP ($\rho = .573$ $p = 0.001$), ALT vs ALP ($\rho = .570$, $p = 0.001$), and pancreatic amylase vs lipase ($\rho = .513$, $p = 0.003$). At the same time, a negative association was observed between magnesium and lipase ($\rho = -.391$, $p = 0.027$) (Table 7).

In the AP group, positive correlations were found between ALT and AST ($\rho = .822$, $p < 0.001$), ALT vs ALP ($\rho = .525$, $p = 0.003$), GGT vs AST ($\rho = .660$, $p < 0.001$), lipase vs total amylase ($\rho = .451$, $p = 0.012$), and pancreatic amylase vs lipase ($\rho = .392$, $p = 0.032$). Notably, negative associations were observed between pancreatic amylase and magnesium ($\rho = -.529$, $p = 0.003$) and between magnesium and total amylase ($\rho = -.559$, $p = 0.001$) (Table 8).

3.6. Principal component analysis of biomarkers

We extracted three separate components that accounted for 61.5 % and 59.2 % of the variations in the AP and EF groups, respectively (Table 9). When analyzing all three groups combined, the first two components accounted for approximately 60.32 % of the total variance (Table 10).

Tables 11 and 12, respectively, give the factor loadings of the biomarkers in separate and combined models. For enteric fever, the rotated component matrix revealed high loadings for Total amylase, pancreatic amylase, stool pH, and lipase in the first component

Table 4
Biochemical indices in the enteric fever, acute pancreatitis and control groups.

VARIABLES	Subjects			
	Controls	Enteric Fever	Acute Pancreatitis	*p*-value
	(n = 31)	(n = 32)	(n = 30)	
Total Amylase (U/L)	68.39 ± 3.58^{A}	102.78 ± 7.59^{B}	347.23 ± 21.11^{C}	<.001
Lipase (U/L)	26.72 ± 2.26^{A}	33.79 ± 2.28^{A}	242.45 ± 27.87^{B}	<.001
ALP (U/L)	65.84 ± 2.36^{A}	73.50 ± 4.24^{A}	106.87 ± 11.30^{B}	.002
AST (U/L)	18.71 ± 0.97^{A}	24.44 ± 1.84^{B}	107.37 ± 32.23^{C}	.002
GGT (U/L)	31.25 ± 2.12^{A}	35.31 ± 6.22^{A}	117.27 ± 23.60^{B}	.003
ALT (U/L)	16.91 ± 1.32	15.68 ± 2.18	74.73 ± 24.38	.064
Calcium (mmol/L)	2.43 ± 0.02^{A}	2.33 ± 0.03^{B}	2.21 ± 0.04^{B}	<.001
Magnesium (mmol/L)	$.87 \pm 0.01^{A}$	$.81 \pm 0.02^{B}$	$.76 \pm 0.02^{B}$	.004
Phosphate (mmol/L)	1.26 ± 0.02^{A}	1.10 ± 0.04^{B}	1.02 ± 0.04^{B}	<.001
Pancreatic amylase (U/L)	42.13 ± 2.95^{A}	71.97 ± 6.98^{B}	291.67 ± 19.70^{C}	.001
Serum Elastase 1 (ng/dl)	247.00 ± 19.22^{A}	299.44 ± 19.34^{A}	571.17 ± 37.23^{B}	<.001
Stool pH	6.55 ± 0.04^{A}	6.45 ± 0.04^{A}	6.3 ± 0.04^{B}	.021

Values are given as mean ± SEM. A, B, and C denote significant differences ($p < 0.001$) (Welch's ANOVA with Games-Howell post-hoc analyses). The difference between the means is not statistically significant for variables with the same letter.

and AST, ALT, GGT, and ALP in the second component. The third component indicated high loadings for Magnesium, Calcium, and Phosphate (Table 11).

In the case of acute pancreatitis, the component matrix revealed high loadings for GGT, ALT, AST, and ALP for the first component and Magnesium, Calcium, Stool pH, Total amylase, and pancreatic amylase for the second component. The third component indicated high loadings for Total amylase, pancreatic amylase, lipase, and serum elastase (Table 11).

For all three groups, the rotated component matrix revealed high loadings for AST, ALT, GGT, ALP, and pancreatic amylase in the first component and high loadings for Serum Elastase, Lipase, Total Amylase, Pancreatic amylase, Calcium, and Magnesium in the second component (Table 12). A scatter diagram visually presented the separated groups based on principal components 1 and 2 (Fig. 3).

4. Discussion

The primary aim of this study was to evaluate biochemical indices in patients diagnosed with EF and AP. Total and pancreatic amylase were markedly higher in the AP cohort than in the control and EF cohorts. In the EF cohort, 34.38 % showed high amylase levels, corroborating the 23 % in another EF population reported by Baert et al. [7] but lower than the 62 % observed by Renner et al. [15]. These differences may reflect population features and disease severity. High levels of amylase were detected across all AP subjects, affirming amylase's key diagnostic role in AP [16,17]. This aligns with prior evidence demonstrating elevations in serum amylase, often three-to four-fold higher than normal limits in AP [16]. The high amylase levels could be due to pancreatic injury, triggering the release of digestive enzymes like amylase into circulation [18]. The moderately raised amylase in some EF patients accords with previous findings [6] and may originate from intestinal mucosal disruption, enabling enzyme leakage. However, the mechanisms likely differ, with gastrointestinal inflammation eliciting modest amylase elevations in EF while direct pancreatic damage leads to relatively higher levels in AP. While the current study did not specifically investigate S- and P-type amylase levels, it is well-documented that S- and P-type amylase forms can be elevated in various conditions, including pancreatitis and gastrointestinal disorders. The elevation of one or both isoforms may depend on factors such as the severity of the condition, the underlying cause, and individual patient variations.

Furthermore, variations were observed in lipase levels between the 3 groups, with higher mean levels in AP patients. Generally, the lipase profile differed from amylase in the EF subjects, most in the normal range, highlighting the complexity of enzyme dynamics across disease states. Notably, serum elastase-1 levels varied between the AP and EF patients (Table 4). This highlights elastase-1 as a vital differential biomarker to distinguish between AP and EF patients.

There were significant differences in liver enzymes between the AP and EF groups. These align with previous observations of elevated levels of ALP in specific AP subtypes, namely biliary pancreatitis [19]. Reports suggest that ALP levels exceeding 246 U/L may indicate ductal obstruction [19]. ALP and GGT elevations can reflect hepatobiliary dysfunction or damage [20]. Their relatively preserved levels in EF patients may signify that EF rarely impacts the hepatobiliary system. ALP and GGT differences between EF and AP groups suggest that conditions like AP potentially inflict more significant damage on the liver and biliary structures [21]. Few EF patients demonstrated ALP, AST or ALT aberrations. This differs from Abro et al.'s observations of more prevalent enzyme perturbations in EF [22]. Notably, a subset of AP patients exhibited elevated ALP, a potential marker of biliary pancreatitis and corroborated prior studies [23,24]. The strong correlations observed between ALT and AST in both conditions likely reflect coordinated enzymatic responses to liver injury from systemic effects of the disease, as described previously [21,25].

Calcium, phosphate and magnesium levels showed differences between AP patients and control/EF subjects, with AP patients exhibiting lower mean levels (Table 4). The underlying drivers for this observation may relate to proposed mechanisms, including pancreatic enzyme-mediated mesenteric fat digestion, releasing free fatty acids that bind serum calcium, and intestinal absorptive

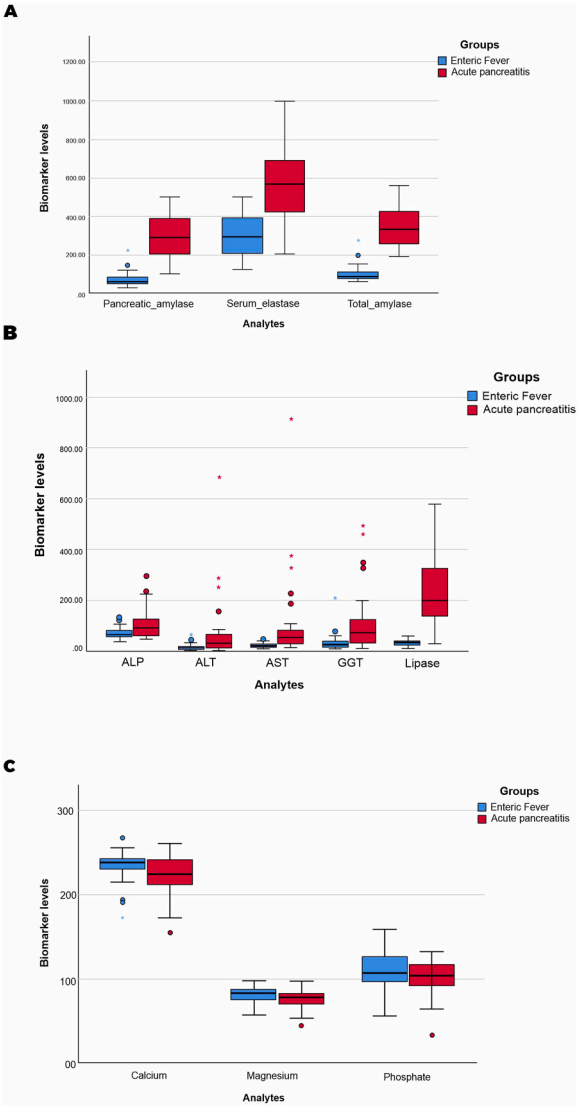

Fig. 1. Box plot comparison of serum biomarker levels in EF and AP

impairment, which can arise during infection and hypomagnesemia [26,27]. As magnesium is relevant for vital processes like immune function and electrolyte equilibrium [28,29], depletion may augment infection susceptibility and worsen diarrheal fluid/electrolyte losses. Intriguingly, around a tenth of EF patients had high calcium levels, which had potential clinical implications. Decreased magnesium levels were found to be linked to the occurrence of acute renal injury in patients diagnosed with AP [30].

Stool findings demonstrated some parallels between groups (Fig. 2). Most subjects across cohorts exhibited normal stool colouration. However, subsets showed green (in EF) and yellow (in AP) discolourations indicative of rapid intestinal transit and fat malabsorption, respectively [31]. Pancreatic damage in AP can reduce bicarbonate output, contributing to stool acidity, as seen in the present study and previous studies [32,33].

Furthermore, the possible impairment of pancreatic function may lead to decreased fat digestion, resulting in steatorrhea. The present study corroborates this by the significant association observed between AP and the presence of stool fat. The implications include optimizing treatment approaches to counteract stool pH derangements and considering the possibility of steatorrhea, which may result from pancreatic dysfunction in AP.

Principal Component Analysis (PCA) unveiled distinct biochemical patterns in enteric fever and acute pancreatitis, reflecting the complex nature of these conditions. In the enteric fever group, the first principal component was primarily linked to pancreatic function, the second to liver function, and the third to electrolyte balance. Conversely, in the acute pancreatitis group, the first component was associated with liver function, the second with a combination of pancreatic and electrolyte factors, and the third with pancreatic function based on the high loadings observed. (Table 11). Despite some overlapping patterns, the differences in the composition of these components between the two groups suggest underlying variations in the pathophysiological mechanisms driving

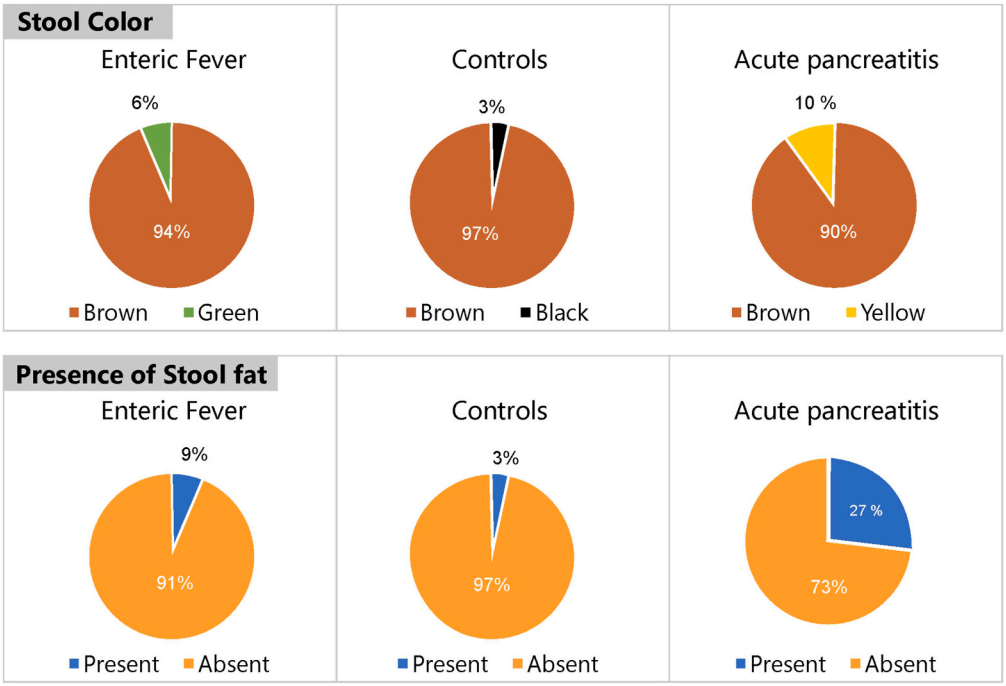

Fig. 2. Distribution of stool colour and presence of stool fat in the control, enteric fever and acute pancreatitis patients. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 5
Chi-square analysis: Enteric fever and stool variables.

Variable	Chi-square value	df	*p*-value	Phi(φ)/Cramer's V (V)
Stool color	2.985	2	.126	.218 (V)
Stool fat	1.001	1	.306	.126 (V)

χ^2 = Chi-square value. df = Degrees of freedom. Φ = Phi. V = Cramer's v.

Table 6
Chi-Square Analysis: Acute pancreatitis and Stool Variables.

Variable	Chi-square value	df	p value	Phi(φ)/Cramer's V (V)
Stool color	4.143	2	.126	.218 (V)
Stool fat	6.661	1	**.006**	.330 (V)

χ^2 = Chi-square value. df = Degrees of freedom. Φ = Phi. V = Cramer's v.

each condition. These findings offer deeper insights into the specific biochemical dynamics in enteric fever and acute pancreatitis, underscoring the importance of tailored diagnostic and therapeutic approaches.

This study had some limitations. The relatively small sample size reduces the study's ability to detect more subtle differences between patient groups. Additionally, it is imperative to emphasize the need for future longitudinal studies to understand biochemical dynamics in disease progression. Furthermore, the inability to assess insulin resistance and parathyroid hormone levels in the study subjects posed a notable limitation, as these factors could influence biochemical dynamics and levels of electrolytes.

5. Conclusion

Notable serum biomarker signatures like total amylase, lipase, ALP, AST, and GGT exhibited distinctions in patients with AP and EF, emphasising the nuanced biochemical divergence between the two groups. Generally, AP patients had higher lipase, amylase and elastase 1 levels. Arguably, serum elastase 1 levels may be an important marker in differentiating AP and EF cases. The findings represent a noteworthy stride in interpreting subtle biochemical variations and enhancing the diagnosis and treatment of both EF and AP.

Table 7
Correlation analysis of biomarkers in enteric fever patients.

		Total Amylase levels	Lipase levels	ALP levels	AST levels	ALT levels	GGT levels	Calcium levels	Magnesium levels	Phosphate levels	Serum Elastase 1	Pancreatic amylase	Stool pH
Lipase levels	ρ	**.543**	1.000										
	Sig. (2-tailed)	**.001**	.										
ALP levels	ρ	.044	.104	1.000									
	Sig. (2-tailed)	.813	.570	.									
AST levels	ρ	.286	.089	**.573**	1.000								
	Sig. (2-tailed)	.113	.628	**.001**	.								
ALT levels	ρ	.170	.016	**.570**	**.711**	1.000							
	Sig. (2-tailed)	.353	.930	**.001**	**.000**	.							
GGT levels	ρ	−.232	−.147	.222	**.365**	**.470**	1.000						
	Sig. (2-tailed)	.202	.421	.222	**.040**	**.007**	.						
Calcium levels	ρ	−.120	.035	.025	.317	.339	**.358**	1.000					
	Sig. (2-tailed)	.513	.847	.891	.077	.058	**.044**	.					
Magnesium levels	ρ	−.047	**−.391**	.150	−.189	−.135	.070	.119	1.000				
	Sig. (2-tailed)	.797	**.027**	.413	.301	.463	.702	.516	.				
Phosphate levels	ρ	.108	.332	−.202	−.087	−.108	−.080	.219	.274	1.000			
	Sig. (2-tailed)	.555	.063	.267	.637	.555	.665	.229	.129	.			
Serum Elastase 1	ρ	.037	−.102	−.074	.248	.097	.179	.111	−.310	−.278	1.000		
	Sig. (2-tailed)	.840	.579	.688	.171	.596	.326	.544	.084	.124	.		
Pancreatic amylase	ρ	**.865**	**.513**	.104	.321	.328	−.018	−.070	−.086	.153	.015	1.000	
	Sig. (2-tailed)	**.000**	**.003**	.573	.073	.067	.924	.703	.639	.404	.936	.	
Stool pH	ρ	−.163	−.270	−.250	−.109	.043	.258	.029	−.024	−.270	.046	−.175	1.000
	Sig. (2-tailed)	.374	.135	.168	.551	.816	.154	.875	.898	.135	.804	.339	.

ρ = spearman's correlation coefficient. Correlation is significant at .05 (2 tailed). Significant co-efficient (ρ) and p-values in bold.

Table 8
Correlation analysis of biomarkers in acute pancreatitis patients.

		Total Amylase levels	Lipase levels	ALP levels	AST levels	ALT levels	GGT levels	Calcium levels	Magnesium levels	Phosphate levels	Serum Elastase 1	Pancreatic amylase	Stool pH
Lipase levels	ρ	**.451**	1.000										
	Sig. (2-tailed)	**.012**	.										
ALP levels	ρ	.055	.081	1.000									
	Sig. (2-tailed)	.773	.671	.									
AST levels	ρ	.246	.226	**.468**	1.000								
	Sig. (2-tailed)	.190	.229	**.009**	.								
ALT levels	ρ	.280	.110	**.525**	**.822**	1.000							
	Sig. (2-tailed)	.134	.563	**.003**	**.000**	.							
GGT levels	ρ	.164	.282	**.477**	**.660**	**.578**	1.000						
	Sig. (2-tailed)	.387	.131	**.008**	**.000**	**.001**	.						
Calcium levels	ρ	.081	−.083	.113	.154	.164	−.037	1.000					
	Sig. (2-tailed)	.672	.662	.552	.415	.386	.844	.					
Magnesium levels	ρ	**−.559**	.035	.050	.235	−.392	.124	.221	1.000				
	Sig. (2-tailed)	**.001**	.855	.791	.212	.032	.513	.241	.				
Phosphate levels	ρ	−.120	−.148	−.256	−.026	−.091	−.262	.011	−.032	1.000			
	Sig. (2-tailed)	.526	.436	.173	.891	.632	.162	.953	.867	.			
Serum Elastase 1	ρ	.240	.230	−.176	−.165	−.238	−.160	−.140	−.142	−.085	1.000		
	Sig. (2-tailed)	.202	.221	.353	.385	.206	.398	.460	.454	.653	.		
Pancreatic amylase	ρ	**.963**	**.392**	.084	.192	.274	.184	.107	**.529**	−.182	.246	1.000	
	Sig. (2-tailed)	**.000**	**.032**	.661	.310	.143	.331	.573	**.003**	.335	.191	.	
Stool pH	ρ	.071	−.024	.020	.236	.185	−.020	.185	.102	−.153	.051	.098	1.000
	Sig. (2-tailed)	.710	.902	.918	.209	.328	.918	.328	.590	.418	.789	.605	.

ρ = spearman's correlation coefficient. Correlation is significant at .05 (2 tailed). Significant co-efficient (ρ) and p-values in bold.

Table 9
Total variance explained.

Acute Pancreatitis				Enteric Fever			
Component	Initial Eigenvalues	% of Variance	Cumulative %	Component	Initial Eigenvalues	% of Variance	Cumulative %
1	3.700	30.832	30.832	1	2.771	23.091	23.091
2	2.064	17.203	48.035	2	2.267	18.893	41.984
3	1.619	13.492	61.526	3	2.067	17.226	59.210

Only the first three components are shown, as they account for most of the variance.

Table 10
Total Variance Explained (All three groups combined).

Component	Initial Eigenvalues	% of Variance	Cumulative %
1	5.016	41.800	41.800
2	2.222	18.518	60.318

Only the first two components are shown, as they account for most of the variance.

Table 11
Rotated Component matrix.

Acute Pancreatitis				Enteric Fever			
	Component				Component		
Biomarkers	1	2	3	Biomarkers	1	2	3
Total Amylase	.099	**.549**	**.773**	Total Amylase	**.945**	.034	−.190
Pancreatic amylase	.158	**.556**	**.756**	Pancreatic amylase	**.939**	.073	−.179
Lipase	.162	−.224	**.692**	Lipase levels	**.667**	.084	.432
Stool pH	−.078	**.502**	−.059	Stool pH	**−.508**	−.027	−.245
AST	**.800**	.376	−.081	AST levels	.180	**.850**	.020
ALT	**.828**	.380	−.049	ALT levels	.101	**.706**	−.030
GGT	**.875**	−.014	.123	GGT levels	−.131	**.655**	−.059
ALP	**.712**	.025	.001	ALP levels	.076	**.525**	.113
Magnesium	.154	**.787**	.148	Magnesium	−.130	.132	**.842**
Calcium	.212	**.571**	−.226	Calcium levels	−.146	.387	**.648**
Phosphate	−.469	.207	−.192	Phosphate levels	.232	−.220	**.646**
Serum Elastase	−.146	−.282	**.597**	Serum Elastase	−.240	.0384	−.480

Rotation Method: Varimax with kaiser normalization.
Component loadings represent the correlation between each variable and the principal components.
Loadings greater than |.5| are considered significant.

Table 12
Rotated component matrix for all three groups combined.

Biomarkers	Component	
	1	2
ALT	**.939**	−.039
AST	**.925**	−.010
GGT	**.799**	.230
ALP	**.663**	.219
Serum Elastase	.203	**.774**
Lipase	.370	**.746**
Total Amylase	.496	**.743**
Pancreatic amylase	**.519**	**.729**
Calcium	.148	**−.680**
Magnesium	.188	**−.613**
Stool pH	−.070	−.460
Phosphate	−.255	−.459

Rotation Method: Varimax with kaiser normalization.
Component loadings represent the correlation between each variable and the principal components.
Loadings greater than |.5| are considered significant.

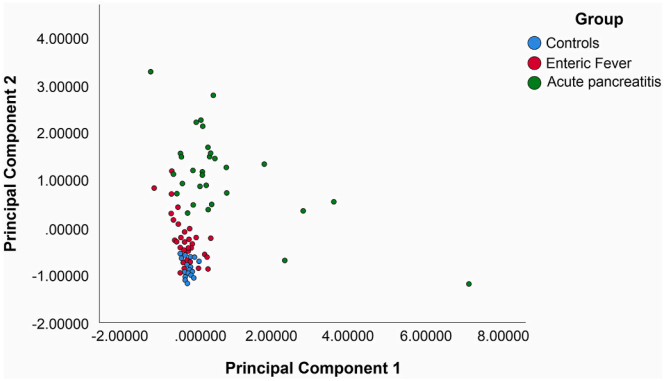

Fig. 3. The scatter plot shows the separation of Control, Enteric Fever, and Acute Pancreatitis groups based on Principal Components 1 and 2, highlighting distinct clustering patterns among the groups.

Ethical approval and consent to participate

Ethical approval for this work was obtained from the Ethical and Protocol Review Committee of the College of Health Sciences (CHS), University of Ghana (EPRC) (ID: CHS-Et/M.5 – P 4.11/2022–2023) and the Institutional Review Board (IRB) of the Korle-Bu Teaching Hospital (KBTH) (ID: KBTH-STC/IRB/000216/2022). All participants signed a consent form after obtaining the necessary information about the study. The consent process provided participants with the study purpose, duration, potential benefits, the materials utilized for sample collection, and any associated risks involved in the sampling procedure.

Funding

No funding was received for this project.

Availability of data and material

Emmanuel Kwaku Ofori and Nathaniel Ebo Aidoo will make the datasets used throughout this study available to the interested party upon reasonable request.

CRediT authorship contribution statement

Nathaniel Ebo Aidoo: Writing – original draft, Methodology, Investigation, Conceptualization. **Emmanuel Kwaku Ofori:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Vincent Boima:** Writing – review & editing, Supervision. **Eric Nana Yaw Nyarko:** Writing – review & editing, Resources. **John Cletus Osei:** Methodology, Investigation. **Clement G. Darkwah:** Methodology, Investigation. **Morris O. Gayflor:** Methodology, Investigation. **Seth K. Amponsah:** Writing – review & editing, Software. **Henry Asare-Anane:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgement

The authors would like to thank the management and personnel of MDS-Lancet Laboratories Ghana Ltd. The authors also acknowledge the Department of Chemical Pathology at the University of Ghana for their institutional assistance.

References

[1] D.P. Neupane, H.P. Dulal, J. Song, Enteric fever diagnosis: current challenges and future directions, Pathogens 10 (4) (2021) 410.
[2] K. Aiemjoy, et al., Seroepidemiology for enteric fever: emerging approaches and opportunities, in: Open Forum Infectious Diseases, Oxford University Press US, 2023.

[3] S. Baker, et al., The current status of enteric fever diagnostics and implications for disease control, Clin. Infect. Dis. 71 (Supplement_2) (2020) S64–S70.
[4] L.M. Cruz Espinoza, et al., Occurrence of typhoid fever complications and their relation to duration of illness preceding hospitalization: a systematic literature review and meta-analysis, Clin. Infect. Dis. 69 (Supplement_6) (2019) S435–S448.
[5] C.S. Marchello, M. Birkhold, J.A. Crump, Complications and mortality of typhoid fever: a global systematic review and meta-analysis, J. Infect. 81 (6) (2020) 902–910.
[6] M. Kapoor, A. Parchani, M. Dhar, Raised amylase/lipase levels in enteric fever: prognostic marker or a sign of pancreatitis?–case report, J. Fam. Med. Prim. Care 10 (10) (2021) 3913–3915.
[7] D. Baert, et al., Infectious gastroenteritis: are they all the same, Acta Clin. Belg. 50 (5) (1995) 269–273.
[8] A. Jansen, et al., Aetiology of community-acquired, acute gastroenteritis in hospitalised adults: a prospective cohort study, BMC Infect. Dis. 8 (2008) 1–7.
[9] S. Ben-Horin, Z. Farfel, M. Mouallem, Gastroenteritis-associated hyperamylasemia: prevalence and clinical significance, Arch. Intern. Med. 162 (6) (2002) 689–692.
[10] O.Z. Ismail, V. Bhayana, Lipase or amylase for the diagnosis of acute pancreatitis? Clin. Biochem. 50 (18) (2017) 1275–1280.
[11] R. Karoli, et al., Salmonella hepatitis: an uncommon complication of a common disease, J. Fam. Med. Prim. Care 1 (2) (2012) 160–162.
[12] S. Bhatia, M. Prabhu, Spectrum of hepatic dysfunction in enteric fever, Int. J. Infect. Dis. 14 (2010) e215–e216.
[13] K. Mitsakakis, et al., Diagnostic tools for tackling febrile illness and enhancing patient management, Microelectron. Eng. 201 (2018) 26–59.
[14] A. Fusheini, S.K. Gyawu, Prevalence of typhoid and paratyphoid fever in the hohoe municipality of the Volta region, Ghana: a five-year retrospective trend analysis, Annals of global health 86 (1) (2020).
[15] F. Renner, C. Nimeth, N. Demmelbauer, High frequency of concomitant pancreatitis in Salmonella enteritis, Lancet 337 (8757) (1991) 1611.
[16] H. Batra, et al., Comparative study of serum amylase and lipase in acute pancreatitis patients, Indian J. Clin. Biochem. 30 (2015) 230–233.
[17] R.C. Smith, J. Southwell-Keely, D. Chesher, Should serum pancreatic lipase replace serum amylase as a biomarker of acute pancreatitis? ANZ J. Surg. 75 (6) (2005) 399–404.
[18] P. Singh, P.K. Garg, Pathophysiological mechanisms in acute pancreatitis: current understanding, Indian J. Gastroenterol. 35 (2016) 153–166.
[19] B. Güngör, et al., The predictivity of serum biochemical markers in acute biliary pancreatitis, Int. Sch. Res. Notices 2011 (2011).
[20] S. Gowda, et al., A review on laboratory liver function tests, The Pan african medical journal 3 (2009).
[21] W. Liu, et al., Liver injury associated with acute pancreatitis: the current status of clinical evaluation and involved mechanisms, World Journal of Clinical Cases 9 (34) (2021) 10418.
[22] A.H. Abro, et al., Hematological and biochemical changes in typhoid fever, Pakistan J. Med. Sci. 25 (2) (2009) 166–171.
[23] E. Amerine, Get optimum outcomes for acute pancreatitis patients, Nurse Pract. Am. J. Prim Health Care 32 (6) (2007) 44–48.
[24] T.P. Bohara, A.P. Anuj Parajuli, M.R. Joshi, Role of Biochemical Investigation in Prediction of Biliary Etiology in Acute Pancreatitis, 2013.
[25] J. Ozer, et al., The current state of serum biomarkers of hepatotoxicity, Toxicology 245 (3) (2008) 194–205.
[26] P. Chhabra, et al., Hypocalcemic tetany: a simple bedside marker of poor outcome in acute pancreatitis, Ann. Gastroenterol.: Quarterly Publication of the Hellenic Society of Gastroenterology 29 (2) (2016) 214.
[27] A. Ahmed, et al., Hypocalcemia in acute pancreatitis revisited, Indian J. Crit. Care Med.: peer-reviewed, official publication of Indian Society of Critical Care Medicine 20 (3) (2016) 173.
[28] V. Trapani, et al., The relevance of magnesium homeostasis in COVID-19, Eur. J. Nutr. (2022) 1–12.
[29] L.J. Dominguez, et al., Magnesium in infectious diseases in older people, Nutrients 13 (1) (2021) 180.
[30] X.-Q. Yu, et al., Serum magnesium level as a predictor of acute kidney injury in patients with acute pancreatitis, World Journal of Clinical Cases 9 (35) (2021) 10899.
[31] S. Brewer, S. Seth, Stool characteristics explained, Nurs. Made Incred. Easy 16 (3) (2018) 14–19.
[32] H. Ishiguro, et al., Physiology and pathophysiology of bicarbonate secretion by pancreatic duct epithelium, Nagoya J. Med. Sci. 74 (1–2) (2012) 1.
[33] C.D. Ulrich II, Bicarbonate secretion and CFTR: continuing the paradigm shift, Gastroenterology 118 (6) (2000) 1258–1261.