Original Article

Serum pancreatic enzymes and imaging in paediatric acute pancreatitis: Does lipase diagnostic superiority justify eliminating amylase testing?

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Abstract

Background: In acute pancreatitis (AP), serum amylase, lipase and imaging help establish a diagnosis with recognised lipase superiority. Recent literature has debated serum amylase testing and proposed its elimination, but little is known about the diagnostic role of simultaneously measured serum amylase levels in patients with non-diagnostic lipase. This study examined the contribution of pancreatic enzymes and imaging and the role of simultaneously measured serum amylase in children with non-diagnostic serum lipase.

Methods: Retrospective medical records review of children aged <18 years with a verified discharge diagnosis of first-attack AP between January 01, 1994, and December 31, 2016.

Results: First-attack AP was confirmed in 127 children (median age, 12.5 years). The sensitivity was 90.4%, 54.3%, 42.2% and 36.4% for lipase, amylase, contrast-enhanced computed tomography and ultrasonography (US), respectively. Combination US and lipase identified 96.6% of AP cases. Simultaneous amylase and lipase measurements in 125 children showed that either was ≥3× the upper limit of normal (ULN) in 95.2%, while both were <3× the ULN in 4.8% of cases. Nondiagnostic lipase was seen in 12 (9.6%) children, and diagnosis was based on amylase level ≥3× the ULN in six children and imaging in the other six.

Conclusions: Serum amylase, serum lipase and imaging should continue for the conclusive diagnosis of AP in children. Simultaneous serum amylase measurement helped diagnose AP with non-diagnostic lipase.

Keywords: Acute pancreatitis, amylase, lipase, non-diagnostic, simultaneous, supplemental

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Submitted: 16-Apr-2021 **Revised:** 24-Jul-2021 **Accepted:** 27-Jul-2021 **Published:** 30-Aug-2021

INTRODUCTION

Serum amylase, lipase and imaging are performed to fulfil the acute pancreatitis (AP) diagnostic criteria.[1-9] With the superior sensitivity and specificity of serum lipase, the need to measure both enzymes is debated, and the elimination of amylase testing has been proposed.[7,10-18] Nonetheless, AP presenting with non-diagnostic serum lipase has been reported while little is known about the diagnostic role of the simultaneous measurement of serum amylase in such a scenario.[19-25] This study aimed to examine the contribution

Access this article online	
Quick Response Code:	Website: www.saudijgastro.com
	DOI: 10.4103/sjg.sjg_204_21

How to cite this article: AlEdreesi MH, AlAwamy MB. Serum pancreatic enzymes and imaging in paediatric acute pancreatitis: Does lipase diagnostic superiority justify eliminating amylase testing? Saudi J Gastroenterol 2022;28:143-8.

of pancreatic enzymes and imaging in the diagnosis of first-attack AP in children and explore the diagnostic value of simultaneously measured serum amylase in children presenting with non-diagnostic serum lipase.

METHODS

The Johns Hopkins Aramco Healthcare Health Information Unit database was searched for all discharges between January 01, 1994, and December 31, 2016, with a diagnosis of pancreatitis (acute, recurrent or chronic) using International Classification of Diseases 9th and 10th edition coding. We included children younger than 18 years. The medical records were reviewed to verify the diagnosis of AP, recurrent pancreatitis and chronic pancreatitis, in compliance with the accepted diagnostic criteria.[1] AP was diagnosed if a patient had two of the following three criteria: abdominal pain, serum amylase, lipase ≥3× the upper limit of normal (ULN) or imaging findings suggestive of pancreatitis (enlarged pancreas, oedema, heterogeneous parenchyma, peripancreatic fluid collection). Patients who did not meet the diagnostic criteria were excluded. The date of the first-attack AP was verified, and if necessary, adjusted to accurately reflect the true date for patients who had their first attack prior to the index hospitalisation. Serum amylase and lipase measurements were simultaneously obtained within 24 h of hospitalization.

Data collected at the first-attack AP (excluding repeat attacks and chronic pancreatitis) included age, sex, total serum amylase and lipase levels, and imaging modality performed. Patients were divided into three groups (≤1 × ULN, >1 but <3× ULN and ≥3× ULN) based on the degree of pancreatic enzyme elevation and two groups (positive vs. negative for pancreatitis) based on imaging findings. Cross-tabulation of the aggregated groups was performed to study the agreement between the two serum enzymes and between the serum enzymes and the imaging modality. To study the impact of evolving laboratory and imaging technology on diagnostic outcomes, the study period was arbitrarily divided into two equal periods: period 1 (January 01, 1994 – June 30, 2005) and period 2 (July 01, 2005 – December 31, 2016).

Statistical analysis

Data were analysed using the Statistical Package for Social Studies (SPSS 21; IBM Corp., New York, NY, USA). The Chi-square test was used for categorical variables expressed as percentages (amylase, lipase and imaging subgroups). Age at the first-attack AP is expressed as mean, median and interquartile ratio. *P* value <0.05 and 95% confidence intervals were considered statistically significant.

Ethical considerations

This retrospective descriptive study was approved by the Institutional Review Board (IRB #18-20).

RESULTS

The health information unit electronic search identified 147 cases; of them, 20 were excluded because they did not meet the AP diagnostic criteria. The first-attack AP diagnosis was verified in 127 children aged 0–18 years, which constituted the study cohort.

Table 1 summarises the patient demographics, symptoms, number of children for whom serum amylase and lipase were tested, imaging modality performed and aetiology of pancreatitis. The median age at presentation was 12.5 years; and 56.7% were male. Abdominal pain was present in 113 of 118 (95.8%) children and vomiting in 87 of 119 (73.1%) children presenting with first-attack AP.

Table 2 shows the sensitivity of total serum amylase and lipase, and imaging, single and in combination, in the 127 children with first-attack AP. The sensitivity was 90.4%, 54.3%, 42.2% and 36.4% for lipase, amylase, contrast-enhanced computed tomography (CECT) and

Table 1: Characteristics, symptoms, diagnostic tests and aetiology of pancreatitis in 127 children with first-attack AP

Characteristic	Value
Age*, years	
Mean (SD)	11.9 (4.2)
Median (IQR)	12.5 (9.0-15.1)
Gender, *n* (%)	
Male	72 (56.7)
Female	55 (43.3)
Symptoms at first attack, *n* (%)	
Abdominal pain	113/118 (95.8)
Vomiting	87/119 (73.1)
Serum pancreatic enzymes measured, *n* (%)	
Amylase	127 (100)
Lipase	125 (98.4)
Imaging performed in 123 children, *n* (%)	
US	78 (63.4)
CECT	6 (4.9)
US and CECT	39 (31.7)
Aetiology of pancreatitis†	
Biliary, *n* (%)	42 (33.1)
Unknown, idiopathic, *n* (%)	29 (22.8)
Systemic disease, *n* (%)	13 (10.2)
Drug, *n* (%)	10 (7.9)
Metabolic, *n* (%)	9 (7.1)
Infection, *n* (%)	7 (5.5)
Genetic, *n* (%)	6 (4.7)
Diabetes mellitus, *n* (%)	6 (4.7)
Anatomical, *n* (%)	3 (2.4)
Autoimmune, *n* (%)	2 (1.6)

*Age at first-attack acute pancreatitis, SD=standard deviation, IQR=interquartile range, US=ultrasound, CECT=contrast-enhanced CT. †Aetiology of pancreatitis for children with single and recurrent attacks

Table 2: The sensitivity of total serum amylase and lipase, and imaging, single and in combination, in 127 children with first-attack AP

Test/s	Diagnosed* *n* (%) [95% CI]	Missed† *n* (%) [95% CI]	Total *n* (%)
Lipase	113 (90.4) [83.8-94.9]	12 (9.6) [5.1-16.2]	125 (100)
Amylase	69 (54.3) [45.3-63.2]	58 (45.7) [36.8-54.7]	127 (100)
Simultaneous amylase and lipase	119 (95.2) [89.8-98.2]	6 (4.8) [1.8-10.2]	125 (100)
US	43/118 (36.4) [27.8-45.8]	75 (63.6) [54.2-72.2]	118 (100
CECT	19/45 (42.2) [27.7-57.8]	26 (57.8) [42.2-72.3]	45 (100)
US and amylase	85 (72.0) [63.0-79.9]	33 (28.0) [20.1-37.0]	118 (100)
US and lipase	113 (96.6) [91.5-99.9]	4 (3.4) [0.1-8.5]	117 (100)
US, amylase and lipase	117 (100.0) [96.9-100.0]	0 (0.0) [0.0-3.1]	117 (100)
CECT and amylase	33 (73.3) [58.1-85.4]	12 (26.7) [14.6-41.9]	45 (100)
CECT and lipase	41 (91.1) [78.8-97.5]	4 (8.9) [2.5-21.2]	45 (100)
CECT, amylase and lipase	44 (97.8) [88.2-99.9]	1 (2.2) [0.1-11.8]	45 (100)

*Test sensitivity, †Test false-negative value. US=Ultrasound, CECT=contrast-enhanced CT

ultrasonography (US), respectively. A combination of US and serum lipase in 117 children identified 113 (96.6%), cases while adding US to simultaneously measure amylase and lipase identified all 117 cases. Specificity and other measures of test performance (positive and negative predictive value, likelihood ratios and receiver operating characteristic curve) could not be generated as all included children were confirmed cases of AP.

Table 3 demonstrates the results of the simultaneous measurement of amylase and lipase levels in 125 children. Either of the two enzymes was ≥3× the ULN in 119 (95.2%) cases, both enzymes were ≥3× the ULN in 62 (49.6%) cases, and the two enzymes were <3× the ULN in six (4.8%) cases. Nondiagnostic serum lipase was observed in 12 of 125 (9.6%) children; in six (50%) of them, the diagnosis was based on a serum amylase level ≥3× the ULN, and the other six (50%) were identified on imaging.

Table 4 shows the agreement of imaging (suggestive of pancreatitis) to serum pancreatic enzyme levels in 123 children with first-attack AP. Among the 64 children with an amylase level ≥3× the ULN, imaging suggestive of pancreatitis was seen in 22 of 64 (34.4%) and 12 of 26 (46.2%) cases for US and CECT, respectively. Similarly, in 106 children with a lipase level ≥3× the ULN, imaging suggestive of pancreatitis was seen in 35 of 106 (33.0%) and 15 of 37 (40.5%) cases for US and CECT, respectively. Of the children with levels of both enzymes ≥3× the ULN, findings suggestive of pancreatitis were seen in 34.5% on US and in 50% on CECT.

Table 3: Agreement of simultaneously measured amylase and lipase in 125 children with first-attack AP

	Amylase ≤1× ULN	Amylase >1 <3× ULN	Amylase ≥3× ULN	Total
Lipase ≤1× ULN	0 (0)	0 (0)	1 (0.8)	1 (0.8)
Lipase >1 <3× ULN	3 (2.4)	3 (2.4)	5 (4.0)	11 (8.8)
Lipase ≥3× ULN	8 (6.4)	43 (34.4)	62 (49.6)	113 (90.4)

ULN=Upper limit of normal

Table 5 displays the frequency of positive imaging and diagnostic serum enzymes across the two periods in the 127 children with first-attack AP. The frequency of a negative imaging study for pancreatitis was 51.2% and 53.7% for periods 1 and 2, respectively. The frequencies of lipase test levels <3× ULN were 18.6% and 4.9% ($P = 0.013$), while those for amylase <3× ULN were 33.3% and 53.4% ($P = 0.039$) for periods 1 and 2, respectively.

Table 6 summarises the clinical, laboratory and imaging findings at first-attack AP, and the number of recurrent attacks during follow-up in six children presenting with an amylase level ≥3× the ULN and a lipase level <3× the ULN.

DISCUSSION

In this retrospective study, we reported the contribution of pancreatic enzymes and imaging, single or in combination, to the diagnosis of first-attack AP in 127 children. Furthermore, we explored the diagnostic value of simultaneously measured serum amylase as a supplemental test in children with

Table 4: The agreement of imaging (suggestive of pancreatitis) to serum pancreatic enzyme levels in 123 children with first-attack AP

Pancreatic enzyme level	Pancreatitis on US	Pancreatitis on CECT
Amylase		
≤1× ULN	5/10 (50.0)	2/6 (33.3)
>1<3× ULN	16/44 (36.4)	5/13 (38.5)
≥3× ULN	22/64 (34.4)	12/26 (46.2)
Total*	43/118 (36.4)	19/45 (42.2)
P	0.594	0.805
Lipase		
≤1× ULN	0/1 (0)	1/1 (100)
>1<3× ULN	7/10 (70.0)	3/7 (42.9)
≥3× ULN	35/106 (33)	15/37 (40.5)
Total*	42/117 (35.9)	19/45 (42.2)
P	<0.001	0.493
Amylase and lipase		
≥3× ULN	20/58 (34.5)	11/22 (50.0)

*Add numbers vertically for each imaging modality and pancreatic enzyme group separately. A patient may have had more than one imaging modality. US=Ultrasound, CECT=contrast-enhanced CT, ULN=upper limit of normal

Table 5: The frequency of positive imaging and diagnostic serum enzymes across two periods in 127 children with first-attack AP

	Period 1 (January 1994 - June 2005)	Period 2 (July 2005 - December 2016)	*P*
Imaging* performed in 123 children			
Positive for pancreatitis	20 (48.8)	38 (46.3)	0.798
Negative for pancreatitis	21 (51.2)	44 (53.7)	
Serum lipase measured in 125 children			
Lipase <3× ULN	8 (18.6)	4 (4.9)	0.013
Lipase ≥3× ULN	35 (81.4)	78 (95.1)	
Serum Amylase measured in 127 children			
Amylase <3× ULN	15 (33.3)	43 (52.4)	0.039
Amylase ≥3× ULN	30 (66.7)	39 (47.6)	

*Ultrasound and/or contrast-enhanced CT, ULN=upper limit of normal

first-attack AP presenting with a serum lipase level <3× the ULN. We then highlighted several observations.

The sensitivity of serum amylase and lipase measurements was 69 of 127 (54.3%) and 113 of 125 (90.4%) cases, respectively. Our findings are in line with previously published figures in the paediatric literature showing the superiority of lipase over amylase. The reported diagnostic accuracy of serum amylase and lipase ranged from 25% to 86% and 73% to 100%, respectively.[26-32] This wide variation could be due to many factors, such as the gold standard against which the enzymes were compared, the enzyme cut-off level used, the interval between symptom onset and blood collection, the presence of alcoholic pancreatitis or hypertriglyceridemia, renal failure and macro-amylasemia.[5,33-35] However, some of these factors are less likely to occur in children. In our cohort, the US sensitivity of 36.4% was slightly higher than the 27% reported by Coffey *et al*.[31] but lower than the 52% reported by Orkin *et al*.[32] Other studies reported a wide range of positive imaging findings for AP that ranged between 24% and 86% and between 34% and 100% for US and CECT, respectively.[27,29,36-39] This difference could be attributed to several reasons, such as patients' heterogeneity of AP clinical severity, timing of imaging performed (early versus late) from symptom onset, inter-observer variability and AP imaging diagnostic criteria used.

Simultaneous serum lipase and amylase testing had better diagnostic accuracy and identified 119 of 125 (95.2%) of our cases compared to 113 of 125 (90.4%) cases for lipase-only testing. Orkin *et al*.[32] reported normal lipase in 9.6% of children with first-attack AP, with none having elevated amylase levels. However, amylase measurements were taken for only 76% of the cohort. Coffey *et al*.[31] studied children with acute and acute recurrent pancreatitis episodes, for whom amylase was measured in 78%. Those authors reported that lipase levels were <3× the ULN in 7%, while isolated amylase elevation was diagnosed in 2% of the pancreatitis episodes. However, the authors concluded that the combination of lipase and amylase provided a similar yield to that of lipase alone. The literature continues to debate performing lipase-only testing or simultaneous lipase and amylase testing in patients with suspected AP. Most of these studies examined amylase as an alternative to rather than a supplemental test for lipase. Few studies have shown no added diagnostic value of serum amylase over lipase-only testing and questioned the need for co-ordering amylase.[14,16-18] On the other hand, there are several reports of either normal or <3× ULN lipase levels in patients with radiologically confirmed AP, with little known about the value of simultaneously measured amylase.[19-23,40] In our cohort, 6 of 125 (4.8%) patients were diagnosed with elevated amylase levels. Despite the known low sensitivity, serum amylase was helpful as a supplemental test and identified a subset of AP patients presenting with non-diagnostic serum lipase levels.

There was no consistent agreement between serum enzyme levels and AP imaging findings. Among the 123 patients for whom both enzymes were measured and an imaging modality was performed, US and CECT findings suggestive of pancreatitis were seen in one-third

Table 6: Clinical, laboratory and imaging findings at first-attack AP, and the number of recurrent attacks during follow-up in six children presenting with an amylase level ≥3× ULN and a lipase level <3×ULN

Sex	Age (years)	Abdominal pain (days)	Vomiting	Abdominal tenderness	Imaging* pancreas	Follow-up (years)	Recurrent attacks
F	8.6	4	Yes	Yes	US and CT: normal	4.9	3
M	9.2	1/2	Yes	Yes	US and CT: Normal	5.8	0
F	9.6	7	Yes	No	CT: bulky	15.6	2
M	11.3	1	Yes	Yes	US: heterogeneous	4.6	2
F	14.6	1	No	Yes	US and CT: normal	18.2	2
M	17.4	1/2	Yes	Yes	US: bulky	1.7	0

ULN=Upper limit of normal. *Ultrasound and/or contrast-enhanced CT

to one-half with serum amylase and/or lipase levels <3× the ULN; conversely, normal imaging findings were reported in two-thirds of children with amylase and/or lipase levels ≥3× the ULN. However, the diagnosis of AP was based solely on US in 4.8% of our cases in which levels of both serum enzymes were below the diagnostic threshold. The lack of correlation between serum enzyme levels and AP imaging findings is consistent with findings of previous reports.[31,37,38]

Our study has several limitations. The study population was biased towards patients with serum lipase elevation ≥3× the ULN to satisfy the AP diagnostic criteria. Therefore, patients with abdominal pain and a serum lipase level <3× the ULN, who are potential AP cases, were under-represented in our cohort. We did not account for the timing between symptom onset and performance of pancreas imaging, which may have contributed to false-negative imaging findings if performed early or late in relation to symptom onset. Additionally, changes in imaging quality and techniques over the 23-year study period could have partially contributed to the relatively low rate of positive imaging findings in our cohort. However, there was no significant difference in the rate of positive imaging across periods 1 and 2, making this limitation likely insignificant in our cohort.

CONCLUSIONS

Neither serum pancreatic enzymes measurement nor pancreatic imaging is 100% sensitive for diagnosing children with AP. However, when performed simultaneously, they complement each other and may identify a proportion of patients who would otherwise have been missed. Children with abdominal pain and a non-diagnostic serum lipase elevation <3× the ULN for whom serum amylase measurements or imaging was not performed are potentially missed cases of AP. Further studies focusing on this subset of patients are needed to explore the diagnostic value of simultaneous serum amylase as a supplemental rather than alternative test to lipase.

We conclude that simultaneous measurement of serum amylase and lipase enzymes along with an imaging modality should be considered the standard for the conclusive diagnosis of AP in children. Eliminating serum amylase measurements, as suggested in recent adult literature, may not be applicable to children undergoing testing for AP. Collecting both serum amylase and lipase at presentation and performing reflex amylase testing, if the lipase level is <3× the ULN, can be an attractive option for improving diagnostic accuracy at minimal cost.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Morinville VD, Husain SZ, Bai H, Barth B, Alhosh R, Durie PR, *et al.* Definitions of pediatric pancreatitis and survey of present clinical practices. J Pediatr Gastroenterol Nutr 2012;55:261-5.
2. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, *et al.* Classification of acute pancreatitis - 2012: Revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102-11.
3. Elman R. The blood amylase in pancreatic disease. Proc Soc Exp Biol Med 1927;25:173-4.
4. Comfort MW, Osterberg AE. Serum amylase and serum lipase in the diagnosis of disease of the pancreas. Med Clin North Am 1940;24:1137-49.
5. Abruzzo JL, Homa M, Houck JC, Cofffy RJ. Significance of the serum amylase determination. Ann Surg 1958;147:921-30.
6. Johnson TA, Bockus HL. Diagnostic significance of determinations of serum lipase. Arch Intern Med 1940;66:62-77.
7. Lin X-Z, Wang S-S, Tsai Y-T, Lee S-D, Shiesh S-C, Pan H-B, *et al.* Serum amylase, isoamylase, and lipase in the acute abdomen. J Clin Gastroenterol 1989;11:47-52.
8. Elman R, Arneson N, GRAHAM EA. Value of blood amylase estimations in the diagnosis of pancreatic disease: A clinical study. Arch Surg 1929;19:943-67.
9. Wapshaw H. The blood diastase and lipase changes in acute pancreatitis. Br Med J 1948;2:68-70.
10. Ahmed S. Aljomah MMH. Superfluous amylase/lipase testing at a tertiary care hospital: A retrospective study. Ann Saudi Med 2019;39:354-8.
11. Kazmierczak SC, Catrou PG, Van Lente F. Diagnostic accuracy of pancreatic enzymes evaluated by use of multivariate data analysis. Clin Chem 1993;39:1960-5.
12. Vissers RJ, Abu-Laban RB, McHugh DF. Amylase and lipase in the emergency department evaluation of acute pancreatitis. J Emerg Med 1999;17:1027-37.
13. Sutton PA, Humes DJ, Purcell G, Smith JK, Whiting F, Wright T, *et al.* The role of routine assays of serum amylase and lipase for the diagnosis of acute abdominal pain. Ann R Coll Surg Engl 2009;91:381-4.
14. Chase CW, Barker DE, Russell WL, Burns RP. Serum amylase and lipase in the evaluation of acute abdominal pain. Am Surg 1996;62:1028-33.
15. Yadav D, Agarwal N, Pitchumoni CS. A critical evaluation of laboratory tests in acute pancreatitis. Am J Gastroenterol 2002;97:1309-18.
16. Smith RC, Southwell-Keely J, Chesher D. Should serum pancreatic lipase replace serum amylase as a biomarker of acute pancreatitis? ANZ J Surg 2005;75:399-404.
17. Hofmeyr S, Meyer C, Warren BL. Serum lipase should be the laboratory test of choice for suspected acute pancreatitis. South African J Surg 2014;52:72.
18. Ismail OZ, Bhayana V. Lipase or amylase for the diagnosis of acute pancreatitis? Clin Biochem 2017;50:1275-80.
19. Lankisch PG, Burchard-Reckert S, Lehnick D. Underestimation of acute pancreatitis: Patients with only a small increase in amylase/lipase levels can also have or develop severe acute pancreatitis. Gut 1999;44:542-4.
20. Shah AM, Eddi R, Kothari ST, Maksoud C, DiGiacomo WS, Baddoura W. Acute pancreatitis with normal serum lipase: A case series. J Pancreas 2010;11:369-72.
21. Shafqet MA, Brown TV, Sharma R. Normal lipase drug-induced

pancreatitis: A novel finding. Am J Emerg Med 2015;33:476.e5-6.
22. Singh A, Shrestha M, Anand C. Acute pancreatitis with normal amylase and lipase—an ED dilemma. Am J Emerg Med 2016;34:940.e5-7.
23. Avanesov M, Löser A, Keller S, Weinrich JM, Laqmani A, Adam G, *et al*. Diagnosing acute pancreatitis—Clinical and radiological characterisation of patients without threefold increase of serum lipase. Eur J Radiol 2017;95:278-85.
24. Song H, Tietz NW, Tan C. Usefulness of serum lipase, esterase, and amylase estimation in the diagnosis of pancreatitis--a comparison. Clin Chem 1970;16:264-8.
25. Corsetti JP, Cox C, Schulz TJ, Arvan DA. Combined serum amylase and lipase determinations for diagnosis of suspected acute pancreatitis. Clin Chem 1993;39:2495-9.
26. Tiao MM, Chuang JH, Ko SF, Kuo HW, Liang C Di, Chen CL. Pancreatitis in children: Clinical analysis of 61 cases in southern Taiwan. Chang Gung Med J 2002;25:162-8.
27. Werlin SL, Kugathasan S, Frautschy BC. Pancreatitis in children. J Pediatr Gastroenterol Nutr 2003;37:591-5.
28. Sánchez-Ramírez CA, Larrosa-Haro A, Flores-Martínez S, Sánchez-Corona J, Villa-Gómez A, Macías-Rosales R. Acute and recurrent pancreatitis in children: Etiological factors. Acta Paediatr Int J Paediatr 2007;96:534-7.
29. Park A, Latif SU, Shah AU, Tian J, Werlin S, Hsiao A, *et al*. Changing referral trends of acute pancreatitis in children: A 12-year single-center analysis. J Pediatr Gastroenterol Nutr 2009;49:316-22.
30. Bai HX, Lowe ME, Husain SZ. What have we learned about acute pancreatitis in children? J Pediatr Gastroenterol Nutr 2011;52:262-70.
31. Coffey MJ, Nightingale S, Ooi CY. Diagnosing acute pancreatitis in children: What is the diagnostic yield and concordance for serum pancreatic enzymes and imaging within 96 h of presentation? Pancreatology 2014;14:251-6.
32. Orkin SH, Trout AT, Fei L, Lin TK, Nathan JD, Thompson T, *et al*. Sensitivity of biochemical and imaging findings for the diagnosis of acute pancreatitis in children. J Pediatr 2019;213:143-8.e2.
33. Raffensperger EC. Elevated serum pancreatic enzyme values without primary intrinsic pancreatic disease. Ann Intern Med 1951;35:342.
34. Leclerc P, Forest JC. Variations in amylase isoenzymes and lipase during acute pancreatitis, and in other disorders causing hyperamylasemia. Clin Chem 1983;29:1020-3.
35. Hameed AM, Lam VWT, Pleass HC. Significant elevations of serum lipase not caused by pancreatitis: A systematic review. HPB 2015;17:99-112.
36. Yeung CY, Lee HC, Huang FY, Ho MY, Kao HA, Liang DC, *et al*. Pancreatitis in children - Experience with 43 cases. Eur J Pediatr 1996;155:458-63.
37. Chen C-F, Kong M-S, Lai M-W, Wang C-J. Acute pancreatitis in children: 10-year experience in a medical center. Acta Paediatr Taiwan 2006;47:192-6.
38. Kandula L, Lowe ME. Etiology and outcome of acute pancreatitis in infants and toddlers. J Pediatr 2008;152:106-10.
39. Lalith S, Ilangovan G. Comparative study of ultrasonography and computed tomography in diagnosis of acute pancreatitis. Int J Contemp Med Surg Radiol 2019;4. doi: 10.21276/ijcmsr.2019.4.3.6.
40. Neki NS, Shergill GS, Singh A, Rampal VK, Nizami S, Singh T. Acute pancreatitis with normal amylase and lipase levels. J Postgrad Med Inst 2017;31:199-202.