Pancreatology xxx (2014) 1–6

Contents lists available at ScienceDirect

Pancreatology

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

Original article

Diagnosing acute pancreatitis in children: What is the diagnostic yield and concordance for serum pancreatic enzymes and imaging within 96 h of presentation?

Michael J. Coffey [a], Scott Nightingale [b, c], Chee Y. Ooi [a, d, *]

[a] School of Women's and Children's Health, Faculty of Medicine, University of New South Wales, Sydney, NSW, Australia
[b] Department of Gastroenterology, John Hunter Children's Hospital, Newcastle, NSW, Australia
[c] Discipline of Paediatrics and Child Health, School of Medicine and Public Health, University of Newcastle, Newcastle, NSW, Australia
[d] Department of Gastroenterology, Sydney Children's Hospital Randwick, Sydney, NSW, Australia

Keywords:
Concordance
Enzymes
Imaging
Paediatrics
Pancreatitis
Lipase

A B S T R A C T

Background/objectives: There are limitations and challenges with the diagnosis of acute pancreatitis (AP) in children. We evaluated the diagnostic yield and concordance for serum pancreatic enzymes and imaging in children with AP.

Methods: A retrospective review of laboratory and radiographic results within 96 h of AP presentation (January 2000–July 2011) was performed at two paediatric hospitals. Observed agreement and kappa statistics (κ) were determined between outcomes of bloods (lipase and/or amylase) and imaging (ultrasound (US) and/or computed tomography (CT)).

Results: A total of 103/131 (79%) AP cases had both bloods and imaging performed (within 96 h). Overall, lipase, amylase, US and CT were consistent with an AP diagnosis in 93% (93/100), 54% (43/80), 27% (21/77) and 67% (28/42) of cases respectively. The diagnostic yield for combinations of blood(s) and imaging(s) tests was higher than any single test and blood tests alone. The observed agreement between bloods 'lipase or amylase' and imaging 'US or CT,' was 40%. The κ was −0.083 suggesting no agreement. In 55% of cases, enzymes were positive whilst imaging was negative and the converse was evident in 5% of cases. There was no agreement between the various diagnostic tests, except between amylase and US, which had fair agreement.

Conclusion: Elevations in serum lipase contributed to the diagnosis more often than other tests. Combinations of blood(s) and imaging(s) tests have an increased diagnostic yield. Serum enzyme elevation and imaging changes poorly correlated. At least 5% of cases of AP may be missed if imaging is not performed.

1. Introduction

The diagnosis of acute pancreatitis (AP) in children requires a high index of clinical suspicion. A recent consensus statement by The International Study Group of Paediatric Pancreatitis: In Search for a Cure (INSPPIRE) consortium recommended the use of the adult diagnostic criteria i.e. the diagnosis of AP requires 2 of the 3 criteria: (1) abdominal pain not due to other causes, (2) elevated serum lipase or amylase ≥3 times the upper limit of the normal reference range (×ULN), and/or (3) imaging evidence of pancreatitis [1,2]. Nonetheless, there are limitations associated with each criterion in children and, to our knowledge, a systematic evaluation of the laboratory and imaging criteria have not been performed.

Although abdominal pain is the most common presentation, up to one third of patients may not report abdominal pain and radiation of pain to the back occurs in ≤5% [3–6]. Pre-verbal children in particular may present with non-specific symptoms [7]. The clinical suspicion of AP is usually supported by the finding of increases in serum amylase and/or lipase levels. Serum lipase is considered superior to serum amylase and in a recent paediatric study [7], elevated serum lipase, amylase and 'lipase and/or amylase'

* Corresponding author. School of Women's and Children's Health, Sydney Children's Hospital, High Street, Randwick, NSW 2031, Australia. Tel.: +61 2 93821752; fax: +61 2 93821787.
E-mail address: keith.ooi@unsw.edu.au (C.Y. Ooi).

http://dx.doi.org/10.1016/j.pan.2014.05.383

performed with sensitivities of 77%, 52% and 81% respectively. Regarding imaging, the two most commonly used modalities for the diagnosis of AP are abdominal ultrasonography (US) and computed tomography (CT). Due to its wide availability and reluctance in subjecting children to ionizing radiation, US has been the imaging modality of choice, with 56–84% of children undergoing US upon presentation [7,8]. However, US has been reported to only identify morphologic changes of AP in about one third to one half of cases [3,6,7,9]. Approximately one third of children with AP undergo CT [8], which show pancreatic changes in only 60–75% of cases [6,7,10,11].

We retrospectively examined the contribution of both serum pancreatic enzymes and imaging to the diagnosis of AP in a cohort of children who already fulfilled the diagnostic criteria for AP. More specifically, we evaluated within 96 h of presentation: (1) the overall diagnostic yield of serum lipase, serum amylase, US and CT for AP; (2) the diagnostic yield when single *vs*. various combinations of tests were performed; and (3) the agreement between serum pancreatic enzyme(s) and imaging.

2. Methods

2.1. Study population

A retrospective review (January 2000 to July 2011) was performed in all patients admitted to the Sydney Children's Hospital Randwick (SCH) and John Hunter Children's Hospital (JHCH). Both hospitals are tertiary referral hospitals for their respective regions in the state of New South Wales, Australia. This study was approved by the human research ethics boards of both participating institutions: South Eastern Sydney Human Research Ethics Committee (10/188) and Hunter New England Human Research Ethics Committee (11/02/16/5.07).

Patients <18 years old at the time of presentation were eligible for inclusion if they had a diagnosis of AP or acute recurrent pancreatitis (ARP). Acute pancreatitis was defined as abdominal pain not due to other causes, *plus* either elevated serum lipase or amylase $\geq 3 \times$ ULN and/*or* imaging evidence of pancreatitis (e.g. pancreatic interstitial oedema, pancreatic or peripancreatic necrosis, peripancreatic inflammation, acute peripancreatic fluid collections, pancreatic haemorrhage, pancreatic abscess and pancreatic pseudocyst) [1,2]. Complete resolution of pain *and* at least one month pain free interval between episodes was required to be considered ARP. Each documented episode of ARP was analysed as a separate AP episode. Patients presenting with pain and elevation of serum pancreatic enzyme levels secondary to pseudocyst(s) rather than acute pancreatitis were excluded.

Demographic, clinical, laboratory and radiographic data were collected from medical records of patients with a confirmed diagnosis of AP. Laboratory and radiographic data within 96 h of initial hospital presentation were analysed. For the overall diagnostic test yield and concordance analysis, the following considerations were made: (i) If multiple lipase or amylase results were recorded, then the peak value (within 96 h of initial presentation) for each parameter was analysed; (ii) If one patient had two US or CT investigations recorded and these tests had different results, then a positive result took preference over a negative result. Unavailable data for a given parameter was recorded as missing.

To further evaluate the diagnostic yield according to whether they were performed as a single test or combination of tests, as well as to describe the trends and frequency of tests performed, information on tests performed were determined according to the following time frames from presentation: 0–24 h (24 h), 24–48 h (48 h), 48–72 h (72 h), and 72–96 h (96 h). Within each time period every patient was categorized into one of 16 testing categories, namely L, A, U, C, LA, LU, LC, AU, AC, UC, LAU, LAC, LUC, AUC, LAUC or no testing, with L as lipase, A as amylase, U as ultrasound and C as computed tomography. If a patient presented via a referring hospital, data was included and analysed from the time of initial presentation. Patients in this study have been previously reported in a different context [12,13].

2.2. Statistical analysis

The agreement between serum pancreatic enzymes and imaging modalities was evaluated by calculating observed agreement and Cohen's kappa coefficient (κ) [14]. Observed agreement was calculated as the number of patients with the same diagnostic finding divided by the total number of patients. Kappa values ranged from −1 (complete disagreement) to 1 (perfect agreement), and interpreted by the degree of agreement: $\kappa \leq 0$ is none, $\kappa = 0.01$–0.20 is poor, $\kappa = 0.21$–0.40 is fair, $\kappa = 0.41$–0.60 is moderate, $\kappa = 0.61$–0.80 is good and $\kappa = 0.81$–1.00 is excellent [15–17].

Descriptive analysis was utilized to describe the frequencies of test combinations within each 24 h period from presentation. Each patient was recorded as having none, one, two, three or all four tests (lipase, amylase, US and CT) performed within each time period (24 h, 48 h, 72 h, 96 h), with each category/combination of testing being mutually exclusive. Diagnostic criteria were satisfied if at least one test within the specified combination was positive (given all patients had abdominal pain). The diagnostic yield for each combination of testing (over 96 h from presentation) was calculated.

3. Results

3.1. Study population

A total of 131 AP episodes from 125 patients were identified from the two institutions. Of these, 28 cases (21%) did not have an US or CT performed within 96 h of presentation and were excluded from further analysis, leaving 103 episodes. Fifty-nine of these cases (57%) were from SCH and 44 (43%) were from JHCH.

The demographic data for the cases included in the analysis are summarized in Table 1. The median age (IQR) of all included AP episodes was 12.1 (9.5–15.1) years with a range of 0.9–17.9 years. Males represented 52% (54/103) of the cohort. The mean weight-for-age z-score (SD) for children during AP episodes was 0.10 (1.5) with a range of −6.07 to 3.14.

3.2. Yield of serum pancreatic enzymes and imaging in the diagnosis of AP

Lipase, amylase, US and CT within 96 h of initial presentation were performed in 97% (100/103), 78% (80/103), 75% (77/103) and 41% (42/103) of the 103 cases, respectively. Lipase, amylase, US and

Table 1
Episode and patient characteristics.

Characteristic	Values
Included episodes, *n*	103
Serum pancreatic enzymes measured, *n* (%)	
Lipase	100 (97)
Amylase	80 (78)
Imaging studies performed, *n* (%)	
Ultrasonography	77 (75)
Computed tomography	42 (41)
Patient age, years, median (IQR)	12.1 (9.5–15.1)
Male gender, *n* (%)	54 (52)
Weight *z*-score, mean (SD)	0.10 (1.53)

Please cite this article in press as: Coffey MJ, et al., 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), http://dx.doi.org/10.1016/j.pan.2014.05.383