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OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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Pediatrics 2009;124;509; originally published online July 20, 2009;

DOI: 10.1542/peds.2008-2348

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located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/124/2/509.full.html>

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American Academy of Pediatrics

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Utility of Hepatic Transaminases to Recognize Abuse in Children

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KEY WORDS

abdominal injuries, child abuse, liver function tests, sensitivity, specificity

ABBREVIATIONS

CT—computed tomography
GCS—Glasgow coma scale
ROC—receiver operating characteristics
AST—aspartate aminotransferase
ALT—alanine aminotransferase
CI—confidence interval
AUC—area under the curve

www.pediatrics.org/cgi/doi/10.1542/peds.2008-2348

doi:10.1542/peds.2008-2348

Accepted for publication Feb 2, 2009

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*



WHAT'S KNOWN ON THIS SUBJECT: Abdominal injury is an important cause of mortality in abused children, but it can be difficult to recognize clinically. Elevated hepatic transaminase levels can be a sign of occult injury. Experts recommend transaminase screening with any concern for physical abuse.



WHAT THIS STUDY ADDS: In this population of potentially abused children, abdominal injuries were identified in 3.2% of the patients. Using a threshold of 80 IU, transaminase levels had a sensitivity/specificity of 77%/82%. These results support recommendations for routine screening.

abstract

OBJECTIVE: Although experts recommend routine screening of hepatic transaminases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) in cases of potential child physical abuse, this practice is highly variable. Our objective was to determine the sensitivity and specificity of routine transaminase testing in young children who underwent consultation for physical abuse.

PATIENTS AND METHODS: This was a prospective, multicenter, observational study of all children younger than 60 months referred for subspecialty evaluation of possible physical abuse. The child abuse team at each center recommended screening transaminases routinely as standard of care for all cases with a reasonable concern for physical abuse. Sensitivity and specificity for transaminases and clinical examination findings to detect identified abdominal injuries were determined, and receiver operating characteristic analysis was undertaken.

RESULTS: Of 1676 consultations, 1272 (76%) patients underwent transaminase testing, and 54 (3.2% [95% confidence interval: 2.4–4.2]) had identified abdominal injuries. Area under the curve for the highest level of either transaminase was 0.85. Using a threshold level of 80 IU/L for either AST or ALT yielded a sensitivity of 77% and a specificity of 82% (positive likelihood ratio: 4.3; negative likelihood ratio: 0.3). Of injuries with elevated transaminase levels, 14 (26%) were clinically occult, lacking abdominal bruising, tenderness, and distention. Several clinical findings used to predict abdominal injury had high specificity but low sensitivity.

CONCLUSIONS: In the population of children with concern for physical abuse, abdominal injury is an important cause of morbidity and mortality, but it is not so common as to warrant universal imaging. Abdominal imaging should be considered for potentially abused children when either the AST or ALT level is >80 IU/L or with abdominal bruising, distention, or tenderness. *Pediatrics* 2009;124:509–516

Inflicted injury is an important cause of morbidity and mortality in young children.^{1–3} Nevertheless, diagnosis of inflicted injury is poor, and estimates of miss rates for abuse are 30% and higher.^{4,5} Abdominal injury is second only to head injury as a cause of mortality in children with inflicted injury.^{6,7} In young children, inflicted injury causes nearly as many abdominal injuries as motor vehicle crashes and is an independent predictor of poor outcome.^{8–10} Forensically, the discovery of abdominal injury can help determine if the history offered for a child's other injuries is plausible, because intraabdominal injuries are extremely rare with short falls or stairway falls.^{11–14}

The recognition of intraabdominal injury can be difficult. In studies of non-inflicted trauma, clinical examination has had limited sensitivity and specificity.^{7,8,15,16} Controversy exists regarding routine laboratory screening for intraabdominal injury with non-inflicted trauma when there is no forensic significance to finding an injury.^{17–20} In cases of potential abuse, expert statements^{21–23} have recommended routine screening on the basis of 1 small study ($N = 49$) that found occult hepatic injuries in 6% of the patients.²⁴ Yet, routine laboratory screening for intraabdominal injury remains controversial. Groups that recommend screening in accidental injury differ widely as to what threshold should be used to indicate the need for radiographic studies.^{15,18,20,25} Even less is known about useful thresholds in abused children in whom the time of injury is usually unknown. Our objective was to determine the sensitivity and specificity of routine transaminase screening relative to clinical examination for the identification of intraabdominal injury in a large population of potentially abused children in centers where such screening is the standard of care.

PATIENTS AND METHODS

This was a prospective, observational, multicenter trial. No interventions were undertaken for study purposes. The standard of care for all participating child abuse teams is to recommend transaminase screening routinely for consultations in children younger than 60 months with any reasonable concern for physical abuse. Nineteen child abuse teams collected data from all children younger than 60 months who were referred for consultation with concerns of physical abuse. Each participating center received approval from its local institutional review board with waiver of informed consent. Definitive testing for abdominal injuries (abdominal computed tomography [CT], MRI, autopsy, or surgical evaluation) was undertaken at the discretion of the clinical team.

Enrollment occurred between April 1, 2007, and March 31, 2008. Each center collected data from all consultations regardless of whether transaminase testing was undertaken. For the purpose of this study, consultation was considered to have occurred if a child abuse consultant had done any of the following: (1) written a note in the medical record; (2) performed a physical examination; or (3) recommended diagnostic or therapeutic management. In the absence of a reliable and validated scale of abuse likelihood,²⁶ we did not measure the ultimate level of concern for abuse. In some consultations, initial evaluation by the child abuse consultant led to the opinion that there was no reasonable concern for abuse (as when a mimic of abuse was identified) and that transaminase screening, therefore, was not recommended. These cases were not excluded from analysis. This category did not include patients in whom other evaluations for abuse (ophthalmologic examination, head CT, skeletal survey) were undertaken.

Enrollment was undertaken by a responsible child abuse consultant at the time of child abuse team disposition (discharge, sign-off, or death). To ensure complete enrollment, each center established an independent method of determining the census of eligible patients. Missed patients were identified by monthly checks, and missed data were entered retrospectively. It was established prospectively that centers that failed to enroll >90% of the eligible patients would be excluded from analysis.

Data Collected

Data were entered via a secure, Web-based data-entry form (Quickbase [Intuit, Waltham, MA]). Data included demographic information, details of the history offered by the patient or caretaker, symptoms (vomiting, fussiness, fever, abnormal oral intake, bleeding), physical examination findings (abdominal bruising, abdominal tenderness, bowel sounds, abdominal distention, shock, Glasgow coma scale [GCS] score), and results of any diagnostic testing. All data represented the final opinions of the responsible child abuse consultants, who were not blinded to transaminase results. Data included the opinions of the responsible child abuse consultants as to whether transaminase testing changed clinical, social, or legal management.

We used the following definition as our gold standard for identified intraabdominal injury: radiographic or pathologic evidence of solid organ (hepatic, splenic, pancreatic, adrenal, renal) laceration or contusion, hollow viscus hematoma or perforation, vascular injury, or mesenteric hematoma or tear. Nonspecific findings such as a small amount of free peritoneal fluid without further definition or bowel wall edema of unclear etiology do not meet this definition.²⁷ Intraabdominal injuries were considered to be occult if abdom-

inal bruising, tenderness, and distention were not noted, according to the definition used by Coant et al.²⁴

Statistical Analysis

Sensitivity, specificity, and likelihood ratios for identified abdominal injuries were determined for dichotomous variables. Analyses were performed by using Excel (Microsoft, Redmond, WA). Receiver operating characteristics (ROC) analysis was undertaken for aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels by using the highest value (AST or ALT) of the first transaminase levels obtained. The ROC curve was constructed by using SPSS 17 (SPSS Inc, Chicago, IL).

RESULTS

The centers completed 1676 consultations for physical abuse in children younger than 60 months. One consultation was excluded because the child was transferred between 2 participating institutions during 1 evaluation of abuse. One center enrolled 1 patient before subsequently withdrawing from the study. This patient was excluded from analysis. Demographic characteristics of enrolled patients are shown in Table 1. Patients had a broad range of injury severity from very mild to lethal. The most common injuries identified are listed in Table 2.

TABLE 1 Age and Gender of Enrolled Subjects

Age, mo	Injury Not Identified (<i>N</i> = 1622), <i>n</i> (%)	Abdominal Injury Identified (<i>N</i> = 54), <i>n</i> (%)	<i>P</i>
0–6	591 (36.4)	14 (25.9)	
6–12	369 (22.7)	7 (13.0)	
12–24	306 (18.8)	13 (24.1)	
24–36	163 (10.0)	10 (18.5)	
36–48	116 (7.1)	6 (11.1)	
48–60	77 (4.7)	4 (7.4)	
Mean age (SD), mo	14.4 (14.5)	19.8 (15.5)	.007
Male gender	929 (57.2)	34 (63.0)	.48

Children with injuries were slightly older than children without injuries.

TABLE 2 Identified Injuries

Identified Injury	<i>n</i> (%)
Cutaneous injury	889 (53.0)
Bruising	605 (36)
Bite marks	40 (2.4)
Burns	147 (8.8)
Other	170 (10.1)
Patterned injury	87 (5)
Fracture(s)	755 (45.0)
Traumatic brain injury	393 (23.4)
Retinal hemorrhage	
Any	151 (9.0)
Characteristic	97 (5.8)
Intra-abdominal injury	54 (3.2)
Total with any of these injuries	1452 (86.6)

Many subjects had >1 injury identified. Other cutaneous injuries included lacerations, crush injuries, rashes, petechiae, blisters, hematomas, etc.

Transaminase screening was not performed for 404 (24%) patients (Fig 1). Of these, 144 (36%) children did not undergo testing because, on initial evaluation, the child abuse consultant did not feel that there was a reasonable concern for physical abuse (“clearly not abuse”). In 141 (35%) cases, the child abuse consultant did not recommend

TABLE 3 Identified Abdominal Injuries

Organ	All Patients	AST and ALT <80 IU/L, <i>n</i>
Liver	26	2
Bowel/mesentery	10	4
Spleen	10	3
Pancreas	6	2
Adrenal	6	1
Kidney	3	1
Other	9	3

Seventy injured abdominal organs were identified among 54 patients. Each patient was counted no more than once for any given category. For example, a patient with 2 liver lacerations and 2 areas of perforated bowel would be counted once in “liver” and once in “bowel/mesentery.”

screening transaminases despite a reasonable concern for physical abuse (“oversight”). The treating team declined to obtain transaminase testing despite consultant recommendation in 110 (27%) of the cases.

At least 1 abdominal injury was identified in 54 patients (3.2% [95% confidence interval (CI): 2.4–4.2]; Table 3). Seventeen identified injuries were clinically occult (ie, no abdominal tender-

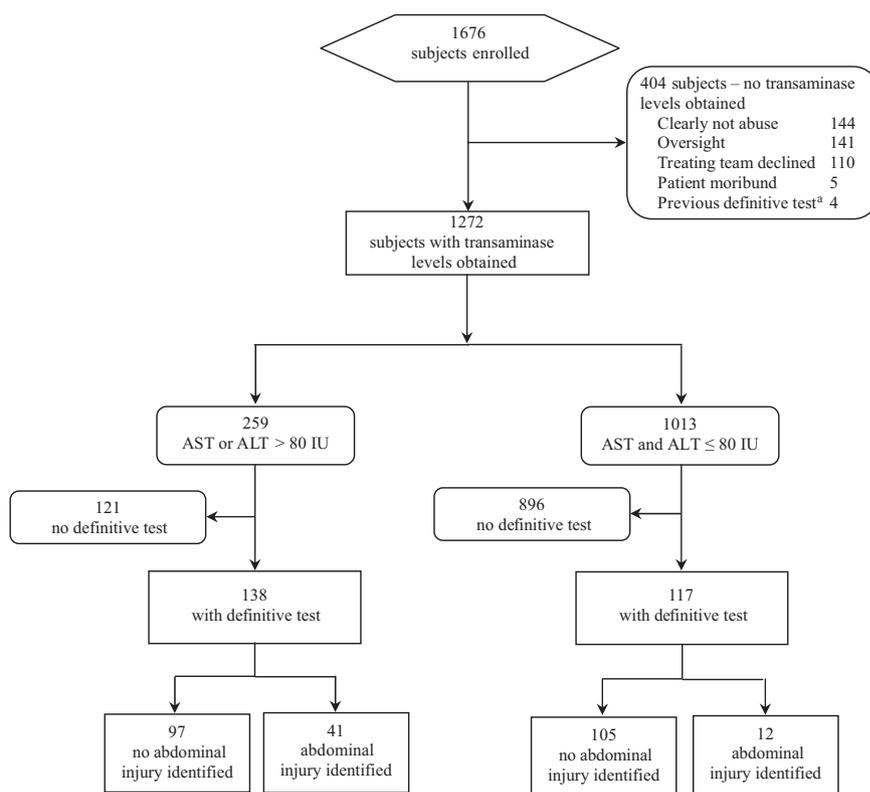


FIGURE 1

Patient flow. ^aOne subject with prior definitive testing had an injury identified.

ness, bruising, or distention). One abdominal injury was identified in a child without transaminase testing because imaging was obtained before the child abuse consultation was undertaken. Abdominal injuries were seen in a higher proportion of older patients (Table 1), and the mean age of children with abdominal injuries (19.8 months) was older than that of the general cohort (14.5 months) ($P = .007$).

ROC analysis was undertaken for the first set of transaminases by using the higher of the 2 tested levels (AST or ALT). Area under the curve (AUC) for transaminases as a test for identified abdominal injury was 0.85 (95% CI: 0.78–0.91; Fig 2). A cutoff of 80 IU/L identified 41 of 53 abdominal injuries, with 218 false-positives among 1219 children without identified abdominal injury (sensitivity: 77%; specificity: 82%). Previous studies of noninjured children have suggested using higher thresholds ranging from 100 to 400 IU/L.^{15,18,25} Test characteristics for these thresholds had lower sensitivity with moderately increased specificity (sensitivity/specificity: 68%/87% for 100 IU/L and 40%/98% for 400 IU/L). Abdominal and pelvic CT was performed in 256 patients, of whom 133 had either AST or

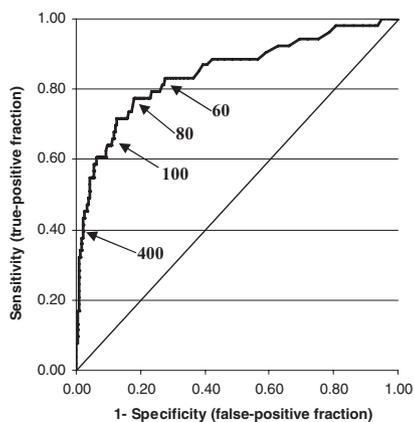


FIGURE 2 ROC curve for the higher of the initially obtained transaminase levels (AST or ALT). Arrows indicate test characteristics for various proposed transaminase cutoff levels. AUC is 0.85 (95% CI: 0.78–0.91). AUC for a perfect test will be 1.0, whereas AUC for a useless test is 0.5.

TABLE 4 Test Characteristics of Transaminase Levels and Several Clinical Examination Findings

Finding	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, %	NPV, %	LR ⁺	LR ⁻	<i>n</i>
AST or ALT > 80 IU/L	77 (65–87)	82 (80–84)	16	99	4.3	0.3	1272
Abdominal bruising	37 (25–50)	95 (94–96)	21	98	7.9	0.7	1657
Abdominal tenderness	52 (39–65)	99 (98–99)	55	98	36.9	0.5	1614
Abdominal distention	46 (33–60)	97 (96–98)	5	98	16.8	0.6	1658
Abnormal bowel sounds	47 (34–60)	93 (92–95)	19	98	7.2	0.6	1513
GCS score < 15	49 (36–63)	85 (85–87)	9	98	3.8	0.6	1592
Lipase > 100 K/μL	44 (28–60)	75 (72–79)	10	95	1.8	0.8	521
Vomiting	37 (25–51)	88 (87–90)	9	98	3.2	0.7	1633
WBCs > 11 K/μL	55 (41–68)	40 (38–43)	4	95	0.9	1.11	1182
Hematuria (any)	28 (16–45)	93 (90–95)	24	94	4.1	0.8	439
Abdominal bruising or tenderness or GCS score < 15	83 (71–91)	80 (78–82)	13	99	4.1	0.2	1562

PPV indicates positive predictive value; NPV, negative predictive value; LR⁺, positive likelihood ratio; LR⁻, negative likelihood ratio; *n*, number of patients for whom test results were documented; WBC, white blood cells.

ALT levels of >80 IU/L. Of 259 patients with elevated transaminase levels (>80 IU/L), 121 did not undergo CT or other definitive testing for abdominal injury.

Transaminase levels were elevated in 14 of 17 patients who had identified occult intraabdominal injuries. Transaminase levels were more sensitive than any single clinical characteristic examined, although several clinical findings had better specificity (Table 4). Combining abdominal bruising, abdominal tenderness, or an abnormal GCS score had similar test characteristics as transaminase levels. Twelve patients had abdominal injuries identified despite both transaminase levels being <80 IU/L. Injuries in these patients are listed in Table 3 and included 4 hollow viscus or mesenteric injuries with 1 small bowel perforation.

Investigators reported that the results of transaminase testing changed clinical management in 24 (44%) of the 54 patients with identified injuries. In most cases, transaminase levels were listed as the reason that imaging was obtained, even in several cases where other indicia (abdominal tenderness or bruising) of abdominal injury were present. Transaminase levels were reported to have changed the social or legal management of the patient in 8 (15%) cases with injuries.

DISCUSSION

In these 1676 patients, the pretest probability of finding abdominal injury was 3.2%, which seems to fall below the testing threshold to obtain abdominal CT for most clinicians. Using a threshold of 80 IU, hepatic transaminase levels identified 14 cases of occult abdominal injury in this group of children who underwent consultation for concerns of physical abuse. Using this threshold, the positive predictive value for identified abdominal injury was nearly 16%, potentially an underestimate because abdominal CT was omitted in nearly half of the children with such elevations and these patients were counted as having no injury. This yield is substantially higher than the yield in a recently published series of children who underwent CT in the setting of accidental trauma.²⁸ Given the clinical and forensic significance of these injuries, we recommend screening transaminase levels for all young children who undergo consultation for physical abuse who would not otherwise undergo definitive testing (abdominal CT, MRI, autopsy, or surgical evaluation).

Our estimate of the rate of abdominal injuries should be considered as a minimum. Nearly half of the children

with elevated transaminase levels did not undergo definitive diagnostic testing, and normal or minimally elevated transaminase levels were frequently cited as a reason to forego abdominal imaging. These results would be more robust if we had followed children for later evidence of abdominal injury or other abuse or if definitive testing had been performed in all children when either transaminase level was >80 IU/L. Because our inclusion criteria included concern for physical abuse, we required a waiver of informed consent and, therefore, were unable to require testing or follow-up by the clinical team.

Although the test characteristics of transaminase levels were generally superior to individual clinical examination findings, neither alone offered both universal sensitivity and acceptable specificity. Although less sensitive, the clinical findings of abdominal bruising, tenderness, and distention had very high specificity and positive predictive values. Twelve patients had abdominal injuries identified despite having normal transaminase levels.

It has been suggested that small bowel perforation may be specific for inflicted injury and that these injuries may be less likely to be associated with transaminase elevation.^{29,30} Only 1 of these 4 bowel/mesenteric injuries in the 12 patients with low transaminase levels was a small bowel (jejunal) perforation, whereas 5 such injuries were identified among patients with elevated transaminase levels. It is possible that bowel perforation is associated with local trauma or inflammation that may lead to transaminase elevation. Unlike solid organ injury, hollow viscus perforations are very likely to progress clinically and eventually to become clinically apparent.³¹

Authors who have advocated using screening transaminases have suggested a variety of levels as threshold values to suggest the need for further

imaging.^{15,18,25} Karam et al²⁰ identified several children with traumatic injuries whose transaminase levels were minimally elevated or normal. Our results suggest that a threshold of 80 IU/L provides a useful balance of sensitivity and specificity.

Although we reported all abdominal injuries, our rate of injury was lower than that of a group that excluded those with abdominal bruising, tenderness, or abnormal bowel sounds.²⁴ Although our rate is lower, it is within the CI reported in that small study. Our relatively higher rate of abdominal injuries in older children stands in distinction to the pattern seen in a review of a national trauma database by Trokel et al,³⁰ which suggests that transaminase testing remains useful among relatively older children.

First among the limitations of this study was our inability to clearly determine which abdominal injuries were truly "occult." Ideally, the management plan for a patient would be assessed both before and after transaminase results were available. Alternatively, a trial that randomly assigned centers to routine or judicious testing could theoretically better test transaminase utility. We felt that such a randomized trial would be unethical and impractical, because existing evidence and expert recommendations had led participating centers to consider routine testing to be standard of care.^{21–23}

Because we were unable to pursue either of these approaches, we chose 2 surrogate measures to determine the impact of transaminase testing. First, we used the Coant et al²⁴ definition to define occult injury (no abdominal bruising, tenderness, or distention). However, some injured patients without these signs underwent imaging before transaminase results were available, suggesting that their injuries were not truly occult. Conversely, other patients with clinical findings such as ab-

dominal bruising were nevertheless scheduled for discharge until the discovery of elevated transaminase levels drawn at the recommendation of the child abuse team, suggesting that these injuries were, in fact, occult.

Several clinical indicators besides those used by Coant et al may suggest injury (abdominal pain, fever, vomiting, fussiness, etc). Although the vast majority of injured children had at least 1 clinical finding that might be related to abdominal injury, this was also true of the majority of patients without injury.

We also used the opinion of the child abuse consultant to determine if transaminase testing changed management. Investigators reported that screening changed management in nearly half of the cases in which abdominal injury was identified, but this finding is limited by the potential for bias.

It is unclear if results would be similar in a population with noninflicted injuries. If abused children are more likely to have a delay in seeking care, the optimal threshold might be lower in abused children given the tendency of hepatic transaminase elevations to normalize rapidly.¹⁴ However, the dogma that abused children present later for care has been called into question in the case of abdominal injuries.³²

We are also limited by the variable nature of our key inclusion criterion: the decision to obtain child abuse consultation.^{26,33–35} Participating centers that serve similar populations had widely divergent rates of consultation, suggesting that the threshold to consult varies from center to center. This threshold also undoubtedly varies between clinicians at the same center and even within a single clinician from patient to patient.^{26,36} The proportion of identified abdominal injuries for each center did not correlate with the number of child abuse consults obtained, which likely represents "real-world" variability in clinical practice and,

thus, might be seen to further reinforce our suggested threshold for hepatic transaminase levels.

It should be emphasized that although our population included children who underwent consultation for abuse, some must have had noninflicted injury. We chose to include all children who underwent consultation for physical abuse rather than including only those with confirmed abuse for several reasons. First, we are aware of no objective and reliable standard for determining which children have been abused and no scale of abuse likelihood that has been rigorously validated.²⁶ Second, the decision to recommend transaminase testing must be made at the initiation of the child abuse workup rather than when it has been completed; to retrospectively exclude children ultimately determined not to have been abused might artificially inflate the utility of transaminase testing. Finally, results of transaminase testing can affect the perceived likelihood of abuse, which could lead to circular reasoning. Although we must have included some children with accidental injuries, we feel that this is as much a strength of our protocol as a weakness. By including all children with abuse consultations, we more closely approximated the real-world decision that faces child abuse consultants.

We did not measure interrater reliability of clinical examination findings, although some key findings (abdominal tenderness and GCS score) may be difficult to determine clearly in young children.³⁷ We did not enter data before the results of definitive testing were available. It is possible that the perception or recording of such clinical findings as abdominal tenderness,

bruising, and abnormal bowel sounds could have been biased by test results. If definitive testing biased recognition of these clinical signs, the result would have been to overestimate the accuracy of clinical examination findings.

Our results are also subject to confirmation bias, because patients with normal transaminase levels and no clinical findings were much less likely to undergo definitive testing with imaging or surgery. If, as we expect, the rate of unrecognized abdominal injury is higher in the group with elevated transaminase levels who did not undergo CT, relative to the group with normal transaminase levels, we would underestimate the utility of transaminase levels. If, however, the rate of unrecognized injury were higher in the group with normal transaminase levels, we would overestimate their utility.

It is possible that children with abdominal injuries had transaminase elevation at the initial time of their injury but that transaminase levels normalized before the evaluation for abuse. Although we collected data on the time of injury when it was available, these data were unavailable in >60% of the cases and could not be corroborated in the majority of others.

CONCLUSIONS

In young children undergoing subspecialty consultation with concerns for physical abuse, abdominal injuries are uncommon but not rare. We recommend using a threshold of 80 IU/L for either transaminase (AST or ALT) as an indication for pursuing definitive testing in a population with concern for abuse regardless of examination findings. However, neither transaminase levels nor

clinical examination are sufficient to identify all traumatic abdominal injuries and retain acceptable specificity. Mildly elevated or normal transaminase levels do not exclude abdominal injury, especially in children with clinical indicia of injury such as abdominal bruising, distention, or tenderness.

ACKNOWLEDGMENTS

This study was supported in part by a faculty collaborative grant from the Brigham and Women's Hospital Department of Emergency Medicine.

The ULTRA investigators included Megan McGraw, MD (Cincinnati Children's Hospital Medical Center, Cincinnati, OH), Judy Guinn, MD (Children's Hospital of Wisconsin, Milwaukee, WI), Marcella Donoruma-Kwoh, MD (Texas Children's Hospital, Houston, TX), Lori Frasier, MD (Primary Children's Medical Center, Salt Lake City, UT), Jonathan Thackeray, MD (Nationwide Children's Hospital, Columbus, OH), Christine Barron, MD (Hasbro Children's Hospital, Providence, RI), Rebecca Moles, MD, and Carolyn Keiper, MD (University of Massachusetts Memorial Medical Center, Worcester, MA), Alice Newton, MD (Children's Hospital Boston, Boston, MA), Lori Vavul-Roediger (Children's Medical Center of Dayton, Dayton, OH), Anne Lewis-O'Connor, NP, PhD, Boston Medical Center, Boston, MA), Kathryn McCans, MD (Cooper University Hospital, Camden, NJ), Paula Mazur, MD (Women and Children's Hospital of Buffalo, Buffalo, NY), Neha Mehta, MD (Sunrise Children's Hospital, Las Vegas, NV), Lisa Fink, RN, CNP (Mayo Clinic, Rochester, MN), and Marcus DeGraw, MD (St John Hospital, Detroit, MI). We thank Arun Rao for assistance with database creation and management.

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Utility of Hepatic Transaminases to Recognize Abuse in Children

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Pediatrics 2009;124;509; originally published online July 20, 2009;

DOI: 10.1542/peds.2008-2348

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