Which clinical features distinguish inflicted from non-inflicted brain injury? A systematic review

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ABSTRACT

Aim: A systematic review of the scientific literature to define clinical indicators distinguishing inflicted (iBI) from non-inflicted brain injury (niBI).

Methods: An all language literature search of 20 electronic databases, websites, references and bibliographies from 1970–2008 was carried out. Relevant studies were independently reviewed by two trained reviewers, with a third review where required. Inclusion criteria included primary comparative studies of iBI and niBI in children aged <18 years, with high surety of diagnosis describing key clinical features. Multilevel logistic regression analysis was conducted, determining the positive predictive value (PPV) and odds ratios (OR) with p values for retinal haemorrhage, rib/long bone/skull fractures, apnoea, seizures and bruising to head/neck.

Results: 8151 studies were identified, 320 were reviewed and 14 included, representing 1655 children, 779 with iBI. Gender was not a discriminatory feature. In a child with intracranial injury, apnoea (PPV 93%, OR 17.06, p = 0.001) and retinal haemorrhage (PPV 71%, OR 3.504, p = 0.03) were the features most predictive of iBI. Rib fractures (PPV 73%, OR 3.03, p = 0.13) had a similar PPV to retinal haemorrhages, but there was less data for analysis. Seizures and long bone fractures were not discriminatory, and skull fracture and head/neck bruising were more associated with niBI, although not significantly so.

Conclusions: This systematic review shows that apnoea and retinal haemorrhage have a high odds ratio for association with iBI. This review identifies key features that should be recorded in the assessment of children where iBI is suspected and may help clinicians to define the likelihood of iBI.

In 1974, radiologist John Caffey published his paper “The whiplash shaken infant syndrome: manual shaking by the extremities with whiplash induced intracranial and intraocular bleedings, linked with residual permanent brain damage and mental retardation”. The title captured a proposed association with iBI. This review identifies key features that should be recorded in the assessment of children where iBI is suspected and may help clinicians to define the likelihood of iBI. Considerable scepticism is being expressed as to how to distinguish inflicted (iBI) from non-inflicted brain injury (niBI). Varying weight has been given to specific clinical features of iBI in previous publications. Apnoea, retinal haemorrhages and rib fractures are felt to be important but there is no comprehensive statistical estimate of predictive power regarding iBI.

What is already known on this topic

- Considerable scepticism is being expressed as to how to distinguish inflicted (iBI) from non-inflicted brain injury (niBI).
- Varying weight has been given to specific clinical features of iBI in previous publications.
- Apnoea, retinal haemorrhages and rib fractures are felt to be important but there is no comprehensive statistical estimate of predictive power regarding iBI.

What this study adds

- The finding of apnoea and/or retinal haemorrhage in a child with a brain injury is more strongly associated with iBI than niBI.
- Children where iBI may be a differential diagnosis should undergo fundoscopy by an ophthalmologist and if <2 years old should have a skeletal survey.
- Infants less than 6 months of age with a brain injury are more likely to have sustained an iBI than older infants.
incidence of inflicted head injury is 21–24 per 100,000 infants under the age of 1 year.\textsuperscript{10,11} Cases may present regularly to specialist neurology units but present infrequently to general paediatric units. Clinicians in all settings need to be aware of the clinical indicators for this condition to make evidence-based decisions as to when they should consider investigating an infant where iBI is a possible cause and to inform a final diagnosis. Many are asked to present their professional or expert opinion in the family or criminal courts as part of the child protection process and they must be able to cite relevant evidence to back up their statements. Although there is a considerable amount of published scientific literature in this field, there have been few attempts to systematically review and critically appraise the world literature. We have attempted to repair this deficit and have addressed the question: “What are the clinical features that distinguish inflicted from non-inflicted brain injury?”\textsuperscript{12} The neuro-radiological features of iBI/niBI are the subject of a separate review.

**METHODS**

We conducted an all-language literature search from 1970–2008, searching 20 databases, websites, references and bibliographies, using over 100 keyword combinations (box 1, table 1). This yielded 520 studies for review by reviewers, drawn from paediatricians, paediatric neurologists, neuro-radiologists and ophthalmologists, designated and named doctors/nurses in child protection. All reviewers underwent standardised critical appraisal training, based on the NHS Centre for Reviews and Dissemination critical appraisal standards,\textsuperscript{12} supported by a dedicated electronic critical appraisal module. All studies underwent two independent reviews and a third if there was disagreement (fig 1).

**Inclusion/exclusion criteria and quality standards**

We defined the term “brain injury” as extra-axial haemorrhage (subdural, extradural, subarachnoid) and/or injury to the brain (hypoxic ischaemic injury, parenchymal injury, contusion, diffuse axonal injury, cerebral oedema). Inclusion/exclusion criteria are listed in box 2. Inflicted brain injury (iBI), the item of interest, refers to children who had sustained brain injury from physical child abuse. Those with non-inflicted brain injury (niBI) had other causative mechanisms including accidental trauma, and medical causes of intracranial lesions.

Given the nature of this research field, our optimal study type was population-based studies that compared the clinical features of iBI and niBI with consecutive case ascertainment. As only studies with both niBI and iBI cases could be used for any analysis of predictive power of the features identified, many oft cited (non-comparative) studies were not eligible for inclusion. The included studies detailed the clinical features of interest but did not rely solely on these for the determination of diagnosis (iBI vs niBI). Only studies after 1970 were considered for inclusion, as radiological techniques prior to this would not be relevant to current practice. Included studies had a high surety of diagnosis of iBI\textsuperscript{13} and confirmation of cause in niBI. To determine a high surety of abuse, we implemented our previously published “ranking of abuse”, that is, children stated as “abused” in the study had had that outcome confirmed by multi-agency child protection teams, legal decision, witnessed abuse or perpetrator admission (rank 1–2)\textsuperscript{13} (table 2). Studies where the decision of abuse had relied solely on clinical features were excluded to minimise selection bias and circularity. Where studies included a category “aetiology indeterminate”, these cases were excluded from the final analysis.

**Statistical analysis**

The analysis was limited by the items that the authors chose to report and we were able to analyse the following features:

- apnoea
- retinal haemorrhages
- rib fractures
- long bone fractures
- bruising to the head and/or neck
- seizures
- skull fractures.

We were dependent on the primary authors’ definitions of the above terms. “Apnoea” reflects either recorded or reported apnoea in the two studies that recorded this item.\textsuperscript{14–16} “Seizures” were not always defined, but some authors did report that some children presented in status epilepticus.\textsuperscript{17} “Long bone fractures” included any fracture to the femur, tibia, fibula, radius, ulna or humerus. Likewise, “skull” or “rib fractures” included any type or location of fracture, respectively.

We included only data from studies where a key feature was explicitly mentioned by the authors. Further, even when a feature was included in the study, not all children in each group were examined for the feature in question. For example, not all children in the niBI group had a fundoscopy examination to look for retinal haemorrhages. We have elected to adopt an
<table>
<thead>
<tr>
<th>Set 1</th>
<th>Keywords</th>
<th>Search Terms</th>
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<tbody>
<tr>
<td>battered child</td>
<td>child protection</td>
<td>non-accidental injury</td>
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<tr>
<td>shaken baby</td>
<td>children</td>
<td>non-accidental trauma</td>
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<tr>
<td>battered baby</td>
<td>inflicted brain injury</td>
<td>physical abuse</td>
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<tr>
<td>battered infant or shaken infant</td>
<td>inflicted cerebral injury</td>
<td>shaking baby syndrome</td>
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<td>child</td>
<td>inflicted traumatic head injury</td>
<td>shaking impact syndrome</td>
</tr>
<tr>
<td>child abuse</td>
<td>inflicted traumatic brain</td>
<td>soft tissue injury</td>
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<tr>
<td>child maltreatment</td>
<td>intentional abuse</td>
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<td>Set 2</td>
<td>Keywords</td>
<td>Search Terms</td>
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<tr>
<td>abusive head trauma</td>
<td>growing skull fracture</td>
<td>intraventricular hematoma</td>
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<tr>
<td>bleeding into brain</td>
<td>haematoma</td>
<td>laceration</td>
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<td>blow to the head</td>
<td>haemorrhagic retinopathy</td>
<td>laminar necrosis</td>
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<tr>
<td>brain damage</td>
<td>head injuries</td>
<td>leptomeningeal cyst</td>
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<td>brain haemorrhages</td>
<td>head trauma</td>
<td>multiple skull fracture</td>
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<td>brain injuries</td>
<td>hematoma</td>
<td>neurologic injury in child abuse</td>
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<td>brain swelling</td>
<td>hemorrhagic retinopathy</td>
<td>neuropathology</td>
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<tr>
<td>brainstem</td>
<td>hydrocephalus</td>
<td>parafalcine</td>
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<td>central nervous system</td>
<td>hygroma</td>
<td>parenchymal contusion, laceration</td>
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<td>cerebral</td>
<td>hyoxic-ischaemic injury</td>
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<td>cerebral atrophy</td>
<td>impact injury</td>
<td>retinal haemorrhage</td>
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<td>infarction</td>
<td>retinal haemorrhage</td>
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<td>inflicted brain injury</td>
<td>sciwora</td>
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<tr>
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<td>inflicted cerebral injury</td>
<td>shaking impact syndrome</td>
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<td>cervical spine injury</td>
<td>inflicted traumatic brain injury</td>
<td>shearing injury</td>
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<td>neuropathology</td>
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<td>subarachnoid hematoma</td>
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<td>intracranial hemorrhage</td>
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<td>intracranial injuries</td>
<td>thoracic lumbar sacral</td>
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<td>craniocervical</td>
<td>intraparenchymal tear</td>
<td>traumatic effusions</td>
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<td>diagnostic triad</td>
<td>intraparenchymal haemorrhage</td>
<td>ventricular haemorrhage</td>
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<tr>
<td>diffuse axonal injury</td>
<td>intraparenchymal hemorrhage</td>
<td>ventricular hemorrhage</td>
</tr>
<tr>
<td>eggshell fracture</td>
<td>contusional tear</td>
<td>whiplash impact syndrome</td>
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<td>contusion</td>
<td>whiplash injury</td>
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<td>encephalopathy</td>
<td>hemorrhagic retinopathy</td>
<td>whiplash shaken infant</td>
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<td>extracranial CNS injury</td>
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<td>extradural hemorrhage</td>
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**Search strategy**

1. Child/
2. (child: or infant: or toddler:).af.
3. 1 or 2
4. non-accidental injur:.af.
5. non-accidental trauma.af.
6. (inflicted brain injur: or inflicted cerebral injur:).af.
7. (inflicted traumatic head injur: or inflicted traumatic brain injur:).af.
8. physical abuse.af.
9. (inflicted brain injur: or inflicted cerebral injur:).af.
10. (inflicted traumatic head injur: or inflicted traumatic brain injur:).af.
11. (or/4-10) and 3
12. (child abuse or child maltreatment or child protection).af.
13. (battered child or shaken child or battered baby).af.
14. (battered infant or shaken infant).af.
17. Caffey-Kempe syndrome.af.
18. battered child syndrome.af.
19. battered infant or shaken infant.af.
20. shaken baby.af.
21. (inflicted brain injur: or inflicted cerebral injur:).af.
22. (inflicted traumatic head injur: or inflicted traumatic brain injur:).af.
23. (or/18-21) and 12
24. screened af.
25. (child: or infant: or toddler:).af.
26. (child abuse or child maltreatment or child protection).af.
27. (battered child or shaken child or battered baby).af.
28. (battered infant or shaken infant).af.
30. shak: impact syndrome.af.
32. battered child syndrome.af.
33. battered infant or shaken infant.af.
34. shaken baby.af.
35. (inflicted brain injur: or inflicted cerebral injur:).af.
36. (inflicted traumatic head injur: or inflicted traumatic brain injur:).af.
37. (or/32-35) and 12
38. screened af.
40. (battered child or shaken child or battered baby).af.
41. battered child.af.
42. (inflicted brain injur: or inflicted cerebral injur:).af.
43. (inflicted traumatic head injur: or inflicted traumatic brain injur:).af.
44. (or/41-43) and 12
45. screened af.
46. screened af.
47. screened af.
48. screened af.
49. screened af.
50. screened af.
51. screened af.
52. screened af.
53. screened af.
54. (retinal hemorrhage or retinal haemorrhage).af.
55. skull fracture:.af.
56. (spinal cord injury adj3 radiologic abnormality).af.
57. spinal cord injur:.af.
58. (subdural haematoma or hemotoma).af.
59. (subdural hematoma or hemorrhage).af.
60. (subdural haemorrhage or subdural hemorrhage).af.
61. (ventricular hemorrhage or ventricular hemorrhage).af.
62. whiplash impact syndrome.af.
63. whiplash injur:.af.
64. whiplash shaken infant.af.
65. infarction.af.
66. (hypoxic-ischemic injur: or hypoxic-ischaemic injur:).af.
67. (contusion: or contusional tear).af.
68. (hematoma or haematoma).af.
69. laceration:.af.
70. shearing injur:.af.
71. traumatic effusion:.af.
extremely conservative imputation approach to account for this missing information. For example, if we are analysing a feature that we suspect may be associated with iBI, for instance, retinal haemorrhages: in the group of children with iBI, if only 6/10 iBI children underwent fundoscopy, we made the assumption that the four children who were not examined would not have had the feature.

By contrast, in the group of children with niBI, if an investigation for this feature was not performed, for example, if only 2/10 niBI children underwent fundoscopy, we made the assumption that the four children who were not examined would not have had the feature.

Of 320 reviewed studies, 14 met the inclusion criteria. All were published after 1995. Six were cross-sectional studies, five case series, two case–control studies and one a longitudinal cohort study. Eight studies involved prospective enrolment of cases. The six retrospective studies achieved full case ascertainment from hospital inpatient coding and/or radiology databases. Full study details are given in online appendix A.

RESULTS

Of 520 reviewed studies, 14 met the inclusion criteria. All were published after 1995. Six were cross-sectional studies, five case series, two case–control studies and one a longitudinal cohort study. Eight studies involved prospective enrolment of cases. The six retrospective studies achieved full case ascertainment from hospital inpatient coding and/or radiology databases. Full study details are given in online appendix A.

Of the 506 studies excluded, the most common reasons for exclusion were the lack of comparative data or a rank of abuse of less than 1 or 2. A small number (11 studies) were excluded...
due to study design (expert opinion/review article, etc) and a further 10 included mixed adult and child data. Many studies were excluded on more than one basis (eg, rank of abuse/non-comparative/lack of detail on features for analysis).

Studies represented combined data on 1655 children, 779 of whom had suffered iBI and 876 niBI. Eleven of 14 studies included children less than 3 years of age.14–16 19 20 22 24 25 27–29 Seven studies ascertained all children who were hospitalised with traumatic head injuries,19–22 25 26 29 six studies included all children with subdural haemorrhage of any aetiology (trauma, coagulopathy, metabolic disorder or post infection, etc)14–16 23 25 28 and one study included children with subdural or extradural haemorrhage.27 The majority (seven) were conducted in the USA,19–22 24 26 27 five were European14 15 23 25 29 (three UK14 15 29) and one each was from Australia28 and Hong Kong.16 In nine studies, children were included solely on the basis of age and confirmation of cause. However, five had specific exclusion criteria (table 3).

Gender was recorded in 980 cases and was not a distinguishing feature. More boys than girls sustained brain injuries, regardless of aetiology (PPV of iBI if the child is a boy 0.397 (95% CI 0.277 to 0.530), OR 0.697, p < 0.001).

It was not possible to undertake a formal analysis of age as a discriminating feature. More boys than girls sustained brain injuries, regardless of aetiology (PPV of iBI if the child is a boy 0.397 (95% CI 0.277 to 0.530), OR 0.697, p < 0.001).

Table 2  Abuse ranking

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Criteria used to define abuse</th>
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<tbody>
<tr>
<td>1</td>
<td>Abuse confirmed at case conference or civil, family or criminal court proceedings or admitted by the perpetrator, or independently witnessed</td>
</tr>
<tr>
<td>2</td>
<td>Abuse confirmed by stated criteria including multi-disciplinary assessment</td>
</tr>
<tr>
<td>3</td>
<td>Diagnosis of abuse defined by stated criteria</td>
</tr>
<tr>
<td>4</td>
<td>Abuse stated as occurring, but no supporting detail given as to how it was determined</td>
</tr>
<tr>
<td>5</td>
<td>Abuse stated simply as “suspected”, no details on whether it was confirmed or not</td>
</tr>
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</table>
eight studies addressing children less than 3 years of age, where mean ages were available,15 16 20 24 28 29 three studies found no significant difference between iBI and niBI.19 22 29 21 Five studies15 16 20 24 28 gave the mean ages of children with iBI as less than or equal to 6 months, while the niBI groups ranged between 7.5 and 12.4 months.15 16 24

**Combined feature analysis**

It was not possible to identify which children had specific combinations of features, as this level of detail was not given.

**Apnoea**

Apnoea appeared to be a highly discriminatory finding, with a PPV of 93% (97.5% CI 0.738 to 0.986) and an OR of 17.06 (97.5% CI 5.018 to 58.011, p = 0.001). However, it was one of the least recorded clinical features, only being analysed by two authors (405 children), perhaps reflecting that its significance has only been recognised more recently.15 16

**Retinal haemorrhage**

Although 1283 children were included in studies that considered this feature, only 998 had fundoscopy (670 iBI and 328 niBI). Many children presenting with witnessed trauma did not have formal fundoscopy, whereas the majority of children with iBI did. Therefore, to account for studies where this was not explicit,20 we used the conservative approach described above. Retinal haemorrhages were strongly associated with iBI, with a PPV of 71% (97.5% CI 0.483 to 0.868) and an OR of 3.504 (97.5% CI 0.731 to 16.799). The wide confidence interval reflects the fact that relatively few children had data recorded on this feature.

**Rib fractures**

Rib fractures were considered in studies representing 1002 children, and data were available on 905 children. Rib fractures were associated with inflicted injury, with a PPV of 73% (97.5% CI 0.500 to 0.882) and an OR of 3.027 (97.5% CI 0.716 to 12.799). The wide confidence interval reflects the fact that relatively few children had data recorded on this item. Our conservative analysis therefore results in lower significance.

**Seizures**

Seizures were considered in studies involving 760 cases, and results were documented in 758. Seizures were more associated with iBI than niBI, but not significantly so, with a PPV of 66% (97.5% CI 0.454 to 0.821) and an OR of 2.924 (97.5% CI 0.731 to 11.694, p = 0.18).

**Long bone fractures**

One of the difficulties in analysing fractures as recorded in studies, is knowing whether the author is counting individual fractures, or individual children who have sustained fractures. In studies where this was not explicit,20 we made the assumption that the number of children with fractures was recorded, a conservative approach. Studies considering long bone fractures represent 1020 children, of whom 921 underwent skeletal imaging. Overall, the PPV of long bone fractures for iBI was 59% (97.5% CI 0.48 to 0.69), OR 1.72 (97.5% CI 0.516 to 5.601, p = 0.14). Therefore a long bone fracture in association with an intracranial injury was a weak predictor for iBI, but not significantly so.

**Skull fractures and bruising to the head and neck**

Skull fractures were considered in studies representing 1014 children, and documented as present or absent in 916 children. Skull fractures were more strongly associated with niBI than iBI, with a PPV for iBI of 44% (97.5% CI 0.223 to 0.678), OR 0.811 (97.5% CI 0.316 to 2.301, p < 0.001). Likewise, bruising to the head and neck was more common in the niBI children, but it was the least recorded item, weakening its significance. Only 212 cases had this feature considered, and overall the PPV of head and/or neck bruising for iBI was 37% (97.5% CI 0.035 to 0.906), OR 0.811 (97.5% CI 0.070 to 9.410, p = 0.2). No specific mention was made of the use of 3D reconstruction techniques to define such fractures; the authors simply recorded their presence or absence when looked for.

**DISCUSSION**

Making the clinical distinction between iBI and niBI in children is always going to be challenging. By producing a multilevel logistic regression of specific clinical features on over 1600 children, we have shown that there is scientific evidence to support the distinction between iBI and niBI, and we are able to offer positive predictive values and odds ratios for individual clinical indicators in children hospitalised with brain injury. The published literature does not allow an analysis of combined features.

This review is the largest of its kind, and offers for the first time a valid statistical probability of iBI when certain key features are present (eg, retinal haemorrhages). Although in some instances, for example, rib fractures, the sample size limits our statistical power to detect the full effect of this feature, as with any systematic review, we are of course limited by the amount of high quality data available in the published literature. However, even with this limited data set, the presence of rib fractures (PPV 73%, OR 3.027) is still indicates an association with iBI rather than niBI, and emphasises how important it is to conduct appropriate imaging to determine if such fractures are present.

It appears that the younger the child, the greater the likelihood that an intracranial injury is due to abuse.
However, children as old as 10 years with severe iBI have also been described in isolated case reports.51–54 Apnoea appears to be a critical distinguishing feature (PPV for abuse 93%, OR 17.06, p < 0.001). There is increasing evidence that hypoxic ischaemic injury and its attendant complications are an integral part of the cascade in iBI. The presence or absence of apnoea must be recorded in all cases of head injury in children.

Retinal haemorrhages are a valuable discriminator, reinforcing the need for fundoscopy on any child with unexplained intracranial injury, or suspected iBI. Indirect ophthalmoscopy should be conducted by an ophthalmologist, as studies have shown that other clinicians are either unable to conduct an accurate examination, or when they do, may miss up to 15% of retinal haemorrhages present.36–38

Fractures in physical abuse are often occult.36,37 Therefore, in line with the Royal College of Paediatrics and Child Health/Royal College of Radiologists standards for the radiological investigation of suspected physical abuse, any child aged less than 2 years in whom an inflicted injury is considered should have a full skeletal survey, including oblique views of the ribs.36 Seizures were not a valuable discriminatory finding. Perhaps an analysis of specific patterns of seizures (eg, status epilepticus, complex, focal) would be more informative.

It was not possible to analyse the value of history given as a predictor, as a number of studies had used absence of a history of trauma or inconsistent explanation as part of their definition of abuse.36–39 Only one large study set out to estimate the value of the initial history in predicting whether the head injury was inflicted or non-inflicted.21 Study design ensured that the history did not contribute to the decision as to whether the child belonged to the iBI or niBI group. The study concluded that having no history of trauma had a high specificity (0.97) and high PPV (0.92) for inflicted injury.

Although many studies addressed encephalopathic features, the differing classifications that were used (altered consciousness, coma, irritability, Glasgow Coma Score (GCS)) precluded any combined analysis of this information. It is recognised that SDH documented clinical features.

This review did not address biomechanical features. It is recognised that iBI can occur as a consequence of shaking,9,40 impact,41 shaking and impact,39,42 water intoxication,43–46 suffocation54 or strangulation.46 In our review skull fracture and bruising to the head/neck were more strongly associated with iBI than niBI, suggesting blunt trauma as a common mechanism of niBI. Clinical evidence of impact may only be found on post mortem,55 so conclusions as to whether an impact injury has occurred or not in iBI cannot reliably be drawn from the clinical features alone.

It is recognised that subdural haemorrhage (SDH) can occur in infancy from other causes, and consideration must be given to possible organic disease, such as metabolic disorders (eg, glutaric aciduria),56 albeit this has characteristic MRI findings. While coagulopathy may cause intracerebral haemorrhage,58,59 it may also be secondary to an iBI,60 highlighting the need for thorough investigations in this group. It is recognised that SDH in particular, may occur as a consequence of birth, particularly following instrumental delivery.46–50 Although a neonatal SDH without skull fracture has also been described where the mother was assaulted ante-natally.51

While this review has highlighted certain clinical features that in association with intracranial injury have a high positive predictive value and odds ratio for iBI, such as retinal haemorrhage, apnoea or rib fractures, none of these features are exclusive to iBI. It is essential that the diagnosis of iBI is only made after taking into consideration full details on history (birth, medical, family, developmental, social, details of any reported trauma) and a detailed examination, and having actively excluded other relevant organic diseases. It is vital that future work should endeavour to collect data on all the features above, with detailed recording of precise abnormalities found, for example, on ophthalmology, if we are to refine these statistical correlations.

Baroness Kennedy has made it abundantly clear that clinicians must be able to cite scientific evidence to support their clinical opinions when providing evidence to the courts,52 and it is challenging for any clinician to keep up to date with all the current evidence. In the year 2007 alone 242 studies relating to iBI were published. Therefore, we feel that this unique, rigorously conducted systematic review will be a valuable resource for clinicians and other professionals in the field, providing, as it does, odds ratios of abuse for seven easily documented clinical features.

REFERENCES


22. Hettler J, Greene DS. Can the initial history predict whether a child with a head injury has been abused? Pediatrics 2003;111:602–7.