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Clinical Profile and Outcome of Dengue Fever in Children Admitted to a Tertiary Care Centre

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ABSTRACT

Dengue is the most widespread mosquito-borne viral illness of children, and hospital series describing its clinical profile and outcome are common in the literature. This narrative review addresses the topic as it appears in published work and reports no data from any single centre. It brings together evidence on the virus and its spread, the immune and vascular events that make a minority of infections severe, the clinical course and its classification, the particular position of infants, diagnostic testing, supportive management and the few specific treatments and preventive tools that have been tested. The central message is that most paediatric dengue is self-limited, that the risk lies in a short critical phase around defervescence when plasma leakage may occur, and that outcome in well-resourced care depends far more on timely recognition and careful fluid management than on any drug. Early clinical and laboratory indicators of severity are only moderately useful, the 2009 classification has both supporters and critics, and trials of antivirals, corticosteroids, statins and platelet transfusion have not shown benefit, although most enrolled adults. Vaccine evidence depends on prior infection status and on serotype. Differences in case definitions, referral patterns and age groups limit comparison between hospital series, and the review closes with the information a comparable series should report.

Keywords: Dengue; Children; Plasma leakage; Warning signs; Fluid resuscitation; Dengue vaccine; Narrative review

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Article Class: Narrative Review

1. Introduction

Dengue has become one of the commonest reasons for a febrile child to be brought to hospital in tropical and subtropical countries. The virus is carried by *Aedes*

mosquitoes that breed around houses, and its range has grown as cities have grown (1, 2). Estimates of global burden vary with method, but they agree that infections number in the hundreds of millions each



year and that most are mild or never noticed (1, 3). The economic cost of the illness is also large, borne by health systems and by households that lose wages while a child is sick (4).

Hospital series describing the clinical profile and outcome of children admitted with dengue are among the most frequently published documents in the field, and the title of this article describes exactly that kind of report. We have not conducted one. No local data are reported here, and no figure in this review comes from a particular ward, district or season. What follows is a narrative account of what the published literature says about the clinical profile and outcome of dengue in childhood, and about how much of that literature can be compared from one hospital to the next.

The topic repays a careful look because a hospital series is only as informative as its definitions. Whether a child counts as having severe disease depends on the classification used; whether dengue was confirmed depends on the day of illness and the test; and whether the outcome looks good depends partly on who was referred in the first place. We set out how these choices shape what is reported, summarise the biology that makes children vulnerable to a particular pattern of illness, and ask which clinical interventions have been tested rather than assumed. The aim is a fair account of what is known and what is only repeated.

The article follows a conventional order. A literature review covers the virus, the pathophysiology, the clinical course and classification, infants, and diagnosis. A short methods section states plainly how the sources were assembled. The results section gathers the evidence on presentation, fluid management, specific treatments and prevention, and on the quality of that evidence, and the discussion

turns to limitations and to what a future series should report.

2. Literature Review

2.1 The Virus, the Vector and the Burden in Children

Dengue virus is a flavivirus with four antigenically distinct serotypes, and infection with one gives lasting protection against that serotype but only brief protection against the others (5, 6). Transmission depends on the mosquito population, and the mapped distribution of *Aedes aegypti* and *Ae. albopictus* now covers much of the tropics and a growing part of temperate regions (2). Where all four serotypes circulate, children are exposed repeatedly over a lifetime, and the first infections often fall in childhood.

Studies in ten countries across Asia and Latin America found that symptomatic dengue in children was common and that its incidence differed by site and by year (7). Long surveillance series, such as the Thai experience over a decade or more, show the same thing: dengue rises and falls in waves, with the age of those affected shifting as population immunity changes (8). A hospital that sees mostly children is therefore looking at the exposed fraction of a larger and largely hidden epidemic. A clinician reading a series needs one answer above all: would these children resemble the ones in my ward?

2.2 Pathophysiology of Severe Disease

Most children infected with dengue recover without complications. In a minority, the illness takes a different turn as fever settles, when capillaries leak plasma into the pleural and peritoneal spaces and the circulating volume falls. Why this happens is only partly understood. A second infection with a different serotype carries a higher risk than a first, a pattern first documented in a prospective study in Thailand and later



supported by work linking intermediate levels of pre-existing antibody to severe disease (9, 10).

The immune response is part of the story. T cells that recognise the earlier serotype may dominate the response to the later one, and the resulting cytokine release is thought to contribute to vascular dysfunction (11, 12). The viral protein NS1 is also implicated: high circulating levels early in illness have been associated with more severe disease, and experimental work shows that NS1 can disturb endothelial barriers directly (13, 14). Studies of the protein leak in shock found that it was selective for molecular size, which fits a functional change in the vascular barrier rather than gross structural damage (15). None of these mechanisms has yet produced a treatment. This is why the same finding can look decisive in one report and unremarkable in the next.

2.3 Clinical Course and Classification

Textbook descriptions divide illness into a febrile phase, a critical phase and a recovery phase (16, 17). The febrile phase brings high fever, headache, myalgia, vomiting and often a rash, and it can look like many other childhood fevers. The critical phase, typically around the time the fever falls, is when plasma leakage may become apparent through a rising haematocrit, a falling platelet count and signs of poor perfusion. In recovery, reabsorbed fluid can overload a child who has been given too much, a reminder that the same intervention can help or harm depending on timing (Figure 1).

Two classification schemes sit side by side in the literature. The 1997 scheme graded dengue haemorrhagic fever and shock syndrome by defined criteria, whereas the 2009 scheme groups patients by warning signs and by severe manifestations (Table 1). Comparisons of the two have generally found that the older scheme

missed children who needed intensive care, while the newer one captures them more sensitively but is harder to apply uniformly (18, 19). Critics of both schemes have argued that a classification built for triage should not also serve as a research definition (20).

Table 1. Two ways of grouping symptomatic dengue.

Scheme	Groups	Main criticism
1997	Dengue fever; dengue haemorrhagic fever grades I–IV, grades III–IV being shock syndrome (21, 22)	Many severe cases fit no group (18, 22)
2009	Dengue without warning signs; with warning signs; severe dengue (19, 20)	Warning signs are broad and partly subjective (19)
Use	Triage and monitoring (2009); epidemiological comparison with older series (1997)	Mixed use blurs comparison (18, 20)

Note: Summary of the published WHO schemes; the 2009 scheme is based on warning signs and severe manifestations rather than on thresholds alone.

2.4 Infants and Age-Related Differences

Infants occupy a distinctive place. Maternal antibody passed across the placenta protects at first, and as it wanes to levels that no longer neutralise but still bind virus, infection may be enhanced rather than prevented (23, 24). This is the proposed reason why severe disease clusters in the second half of the first year in endemic areas. Clinical and cytokine profiles in infants with dengue haemorrhagic fever have been described in detail, and they differ in places from those of older children (25).

Beyond infancy, the picture is less clear. Detailed paediatric series, such as ten years of children with shock syndrome in a single Vietnamese hospital, describe the clinical features well but cannot say how



the same illness would look in a different age group or setting (26, 27). Comparisons between age bands are clouded by differences in how each group is referred and defined, and we do not draw a firm conclusion about them.

2.5 Diagnostic Testing

Laboratory confirmation depends on timing. In the first days, the virus or its NS1 antigen can be detected in blood; later, IgM antibody becomes the more useful marker. Reviews of commercial tests found that NS1 detection alone and IgM alone each miss a meaningful share of cases, and that using them together improves detection (28, 29). Evaluations of rapid point-of-care kits reached the same conclusion, and recommended that antigen and antibody be read together (30).

Clinical features alone cannot reliably separate dengue from other fevers, although leucopenia, rash and a low platelet count shift the probability (31). An observational study of Thai children tried to predict later severity from early laboratory findings, and the indicators it identified were helpful but far from definitive (32). That is a recurring theme: easy tests that are available on the first or second day of illness do not settle who will deteriorate. Such differences look small on paper and are anything but small at the bedside.

3. Materials and Methods

3.1 Scope and Question

This is a narrative synthesis. The question was what published work says about the clinical profile and outcome of dengue in children, and which management and prevention strategies have evidence behind them. Adult studies were included only where they informed a paediatric question and are labelled as such. No patient data were collected and no new analysis was done. None of these steps is difficult, but

each one is easy to skip.

3.2 Literature Assembly

Sources were gathered informally from the authors' knowledge of the field and from the reference lists of major reviews. No formal systematic search protocol, registered strategy or dual screening was used, and no claim of completeness is made. Only works published up to the year of this issue were considered. Evidence of several kinds was used, including trials, large observational series, laboratory studies and authoritative reviews, and each is described for what it is.

3.3 Appraisal Framework

Each body of evidence was read against a short set of questions, listed in Table 2: how the case was defined, who was studied, whether there was a comparison, how the outcome was measured and whether the findings could be carried to another setting. The questions were applied informally and no scores were assigned. Where the sources disagreed we state it, and where they were silent we say so. Reviews of this kind are more useful when they say where the evidence stops than when they smooth it over.

Table 2. Appraisal questions applied to each body of evidence.

Question	What was looked for	Common problem
Case definition	Which classification, which tests	Mixed or unstated
Population	Age band, setting, referral level	Hospital cases only
Comparison	Control group or none	Descriptive series
Outcome	Shock, bleeding, death, length of stay	Differing definitions
Transfer	Whether findings apply elsewhere	Single site or serotype

Note: The framework is qualitative and was applied informally; it is not a scoring tool.



4. Results

4.1 Presentation and Early Recognition

Across the literature, the early illness is described as an undifferentiated fever, and what distinguishes the children who go on to develop complications is largely what happens after the third or fourth day. Warning signs in the 2009 scheme include abdominal pain, persistent vomiting, mucosal bleeding, lethargy or restlessness, liver enlargement and a rising haematocrit alongside a falling platelet count (17, 19). The course across the three phases is sketched in Figure 1, and the sketch is deliberately qualitative: the timing of each phase varies from child to child.

Evidence that any single sign predicts severe disease is limited. In Thai children, combinations of early laboratory findings were informative but did not replace clinical judgement (32). A ten-year Vietnamese hospital series of children with shock syndrome gives one of the fullest paediatric descriptions of how the illness unfolds, though it describes one hospital and one era (26). Cardiac involvement, including myocarditis and rhythm disturbance, has been reported in a minority of patients and is probably under-recognised (33).

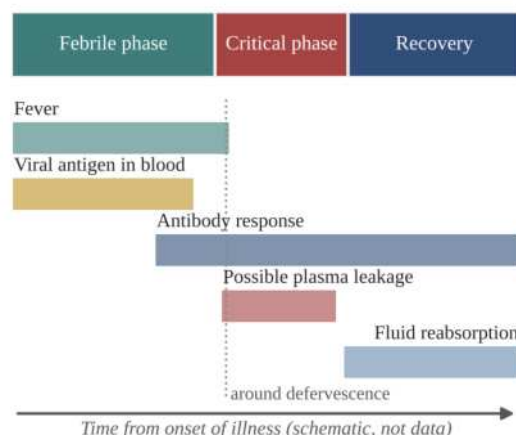


Figure 1. Course of a typical dengue illness in a child and where monitoring matters (schematic, not data).

What the literature supports, in short, is a principle rather than a rule: a child with suspected dengue should be reassessed over time rather than judged once, because the risk moves with the phase of illness. A child who is observed closely through this window is in a different position from one who is not. Figure 1 is meant to make that point visible, not to give times.

4.2 Fluid Management and Supportive Care

Fluid is the intervention with the strongest evidence in children. Trials in Vietnamese children with shock compared crystalloid and colloid solutions and found that children could be resuscitated with crystalloid or colloid, with no clear difference in the main outcomes, although in one of them colloids restored pulse pressure faster in the most severe cases (34, 35). In experienced centres most children with shock syndrome survived, which says more about prompt recognition and close monitoring than about any particular fluid (26).

A decision sketch of how the literature frames the problem is given in Figure 2. It is organised around reassessment rather than around fixed volumes, in keeping with published reviews that stress giving the least fluid needed for perfusion and stopping when leakage reverses (27, 36). Fluid overload in the recovery phase, and the complications that follow, such as respiratory distress, are widely discussed, although trials designed specifically to compare restrictive and liberal strategies in children are scarce.

Transfusion deserves separate mention. A randomised trial in adults found that prophylactic platelet transfusion did not prevent bleeding and was associated with more adverse events (37). Whether the finding applies to children is not known, since the trial did not enrol them, but it has changed practice in some centres by



weakening the case for correcting a platelet count for its own sake. It is a habit worth keeping even when the answer seems obvious.

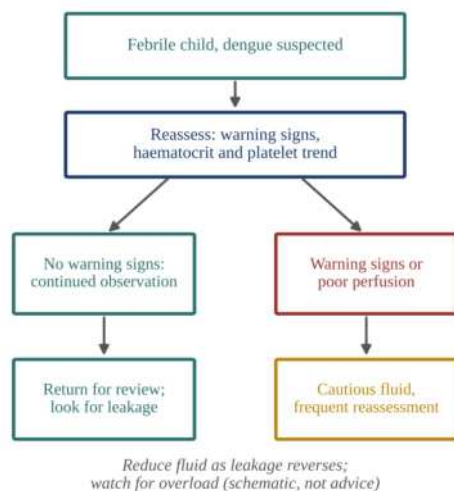


Figure 2. Conceptual flow of assessment and fluid decisions in a child with suspected dengue (schematic, not clinical advice).

4.3 Specific Treatments and Prevention

No antiviral drug has been shown to help. Chloroquine did not alter viraemia in Vietnamese adults, and celgosivir did not change viral load or fever curves in a small proof-of-concept trial (38, 39). A placebo-controlled trial of a short course of oral corticosteroid in early illness found no clear benefit (40). These studies are summarised in Table 3, which also shows how little of the therapeutic evidence comes from children.

Vaccination is a different story, but a conditional one. The first licensed vaccine protected children who had been infected before, and it raised the risk of hospitalised dengue in children who had not, so that serostatus before vaccination became decisive (41, 42). A second tetravalent vaccine showed efficacy against symptomatic dengue in children aged four to sixteen years, with the strength of protection differing by serotype (43). Both findings describe a tool whose value

depends on who receives it.

Vector control reaches children without relying on them. Releases of *Wolbachia*-infected mosquitoes in a cluster-randomised trial in an Indonesian city were followed by a clear fall in symptomatic dengue (44). This is encouraging, though it shows efficacy in one setting and has not been tested everywhere dengue is endemic.

Table 3. Specific interventions tested in dengue and what the trials reported.

Intervention	Who was studied	Finding
Intravenous fluids	Children with shock (34, 35)	No clear difference in main outcomes between solutions in moderate shock
Prophylactic platelets	Adults (37)	No benefit; more adverse events
Oral corticosteroid	Early illness, Vietnam (40)	No clear benefit
Chloroquine; celgosivir	Adults (38, 39)	No effect on viral measures or fever
Tetravalent vaccines	Children, several regions (41, 43)	Protection depends on serostatus and serotype (42)

Note: Most trials enrolled adults or mixed ages; the table describes direction of findings only and gives no effect sizes.

4.4 Quality of the Evidence

Stepping back, the strength of evidence differs sharply from one question to the next. The biology of enhancement, the clinical phases and the value of careful fluid management are fairly secure. Prediction of severity, the best classification and the benefit of particular drugs are not, and prevention is conditional on circumstances. Figure 3 arranges these questions in a qualitative grid, and it should be read as the authors' judgement of the literature rather than as a measured quantity.

Four weaknesses recur. First, case definitions differ: older series used the



1997 scheme, newer ones the 2009 scheme, and some mix the two (20, 22). Second, hospital series reflect referral patterns, so the share of children with severe disease is inflated compared with the community. Third, laboratory confirmation is incomplete in many reports. Fourth, outcomes such as shock and death are defined differently, which makes pooling hazardous. The point is not that a study is poor, only that its result travels less far than its abstract suggests.

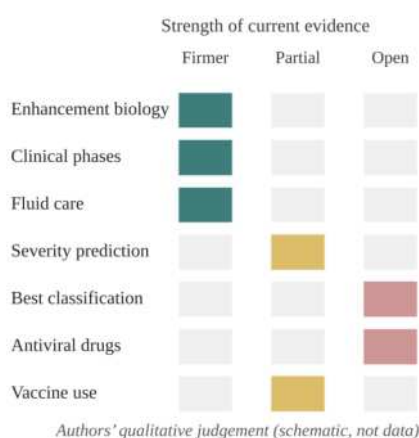


Figure 3. Qualitative judgement matrix of how firmly each question is answered by current evidence (schematic, not data).

Another source of confusion is the choice of comparator. A trial that compares a drug with placebo in uncomplicated dengue can show no effect on severe outcomes simply because few children become severe, and a trial of fluids in shock is by definition restricted to those already in trouble. The same illness, studied at two different points of its course, can give opposite impressions of what matters. A null result from a trial that enrolled few children is not evidence that no effect exists.

5. Discussion

5.1 Interpretation

Taken as a whole, the literature gives a consistent account of the typical pattern in children: a febrile illness that usually resolves, a critical window around

defervescence in which plasma leakage may develop, and good outcomes when the window is anticipated. The clinical profile reported by any one hospital will depend on which children reach it and when, so that a high proportion of severe cases is as likely to reflect referral as to reflect the virus (6, 45).

Outcome, in published series from experienced centres, is overwhelmingly favourable, and mortality is low when care is early and monitoring close (26, 34). Reviews commonly attribute avoidable deaths to late recognition and to fluid decisions that do not track the child's state (21, 45). This is the most actionable finding of the literature, and it is a finding about systems of care rather than about patients. Nothing in this reading argues against careful hospital care; it argues for measuring what that care achieves.

5.2 Limitations

This review has several limitations. The search was not systematic, so relevant work may have been missed and selection may have favoured widely cited studies. Most trials of specific therapies enrolled adults, and extending the results to children is an inference. The literature is also weighted toward a few well-studied sites, notably in Thailand, Vietnam and Nicaragua, so that regional variation in serotype and in care is represented unevenly. Publication bias is a further worry, since series with striking findings are more likely to be written up. Findings from a single tertiary hospital cannot be treated as general.

Because no local data are presented, nothing here describes any one centre's outcomes, and readers should not use this article to benchmark a ward. It offers a framework for reading such reports, which is a narrower thing. It is a modest aim, but



it is one this article can honestly meet.

5.3 Future Work

A useful paediatric series would state which classification it used and would report the same result under both schemes. It would give the day of illness at admission and at testing, the tests used, the referral route and the definition of each outcome. It would also say how fluid was chosen and reassessed. Trials in children are needed on fluid strategy, on prevention, and on anything that might address vascular leak directly. Registries that collect these items in a common format would let hospitals learn from one another without arguing about definitions. These points apply with equal force to many other infections of childhood, not only to dengue.

6. Conclusion

The published literature on the clinical profile and outcome of dengue in children shows a disease that is mostly mild, with a defined window of risk, and with outcomes that depend on recognition and careful supportive care more than on any specific drug. Warning signs and early laboratory findings help but do not decide, and the choice of classification changes the picture.

For a hospital preparing its own series, the advice from this review is to define terms, report timing and say who was referred. For readers of published series, the advice is to ask what the denominators are before comparing outcomes. Prevention through vaccination and vector control is promising but conditional, and it will need to be evaluated in children where dengue is actually found. Above all, a series that states its definitions and denominators can be read, compared and learned from whatever its size, and that is a more reachable goal than a larger series that

does not.

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9. Conflict of Interest

The authors declare no conflict of interest.

10. Author Contributions

P.W. conceived the review and wrote the sections on clinical course and management. F.P. wrote the sections on epidemiology and prevention. J.C. wrote the sections on pathophysiology and diagnostics. All authors revised the manuscript and approved the final version.

11. Ethics Statement

This is a review of published literature. No patients were involved and no ethical approval was required.

12. Data Availability

No new data were generated. All sources are cited in the reference list.

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