Clinico-demographic Profile and coinfections among hospitalized children with chikungunya in a tertiary care hospital of North India: lessons learnt

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ABSTRACT

Background: Chikungunya is a vector-borne arboviral disease. Children are known to have atypical manifestations. Overlapping features with other infections can make the diagnosis difficult. **Objective:** The objective was to study the clinicodemographic and laboratory profile of chikungunya and the impact of coinfections on the course and outcome among hospitalized children. We conducted the study during a large outbreak of chikungunya in the national capital. **Materials and Methods:** A retrospective analytical study was conducted on children admitted from July to November 2016 at a tertiary care hospital in North India. Case records of all hospitalized children (1 month–14 years) with immunoglobulin M positive chikungunya serology were reviewed. Children were categorized into Group A (isolated chikungunya infection) or Group B (coinfection) after entering baseline data, clinical, laboratory, and management details in a pre-designed case record pro forma. Groups A and B were compared to see any statistically significant difference in the clinical and laboratory parameters using appropriate statistical tests. **Results:** Of 102 children, 45 (44.1%) had isolated chikungunya and 57 (55.9%) had chikungunya with other coinfections. In the coinfection group, 37 (36.3%) had dengue, 7 (6.8%) enteric, 6 (5.9%) malaria, 5 (4.9%) pyomeningitis, and 2 (2%) viral hepatitis-A. Vomiting and splenomegaly ($p<0.05$) were significantly more in the coinfection group. The classic triad of chikungunya was present in only three cases of isolated chikungunya. **Conclusion:** Children lack the classical triad of chikungunya and coinfections are very common in children.

Key words: *Atypical, Chikungunya, Children, Coinfections, Dengue, Epidemic, Isolated*

Arboviral diseases (dengue, chikungunya, zika, and yellow fever) are emerging as a major threat worldwide. Chikungunya derives its name from the Makonde term kungunyala, meaning "that which bends up" [1]. It has resurfaced in India over the past 10 years (2005–2006) [1]. Resurgence of chikungunya has been attributed to the various factors including urbanization, absence of herd immunity, and mutation in the E1 gene causing a significant upsurge in chikungunya virus infectivity. As per the annual report (2016–2017) of the Ministry of Health and Family Welfare, 49,659 cases of chikungunya were reported across India, with national capital reporting as many as 11,915 cases until November 2016. There are a limited number of studies among children with chikungunya and associated coinfections from India [2,3]. We conducted a retrospective analysis among a cohort of chikungunya-positive hospitalized children to elicit the clinicodemographic profile of chikungunya and to understand the impact of coinfections.

MATERIALS AND METHODS

After getting approval from the Institutional Ethical Committee, we conducted this single-centered retrospective analytical study in the Department of Pediatrics from July 1, 2016, to November 30, 2016. The patient identification details such as name, age, sex, and central record number of all children (1 month to 14 years) with immunoglobulin M-positive chikungunya serology by MAC-ELISA kit (developed by National Institute of Virology, Pune, India) were collected from the microbiology laboratory record book.

Through proper channel, patient particular matched case sheets of shortlisted patients were released from Medical Record Section (Fig. 1). Patients with incomplete case record sheets and those leaving against medical advice were excluded.

Pre-designed case record forms were used to enter baseline data such as age, sex, residence, month of admission, presenting symptoms and its duration, details of examination, laboratory parameters at admission (hematocrit, total leukocyte count [TLC], differential leukocyte count, platelet count at admission, and the lowest platelet count; liver function parameters such as serum bilirubin, aspartate transaminase [AST], and alanine transaminase [ALT]), and radiological parameters [chest X-ray and ultrasound findings]). The details of any coinfection mentioned in the case record were also noted. The cutoffs for various clinical and laboratory parameters were taken

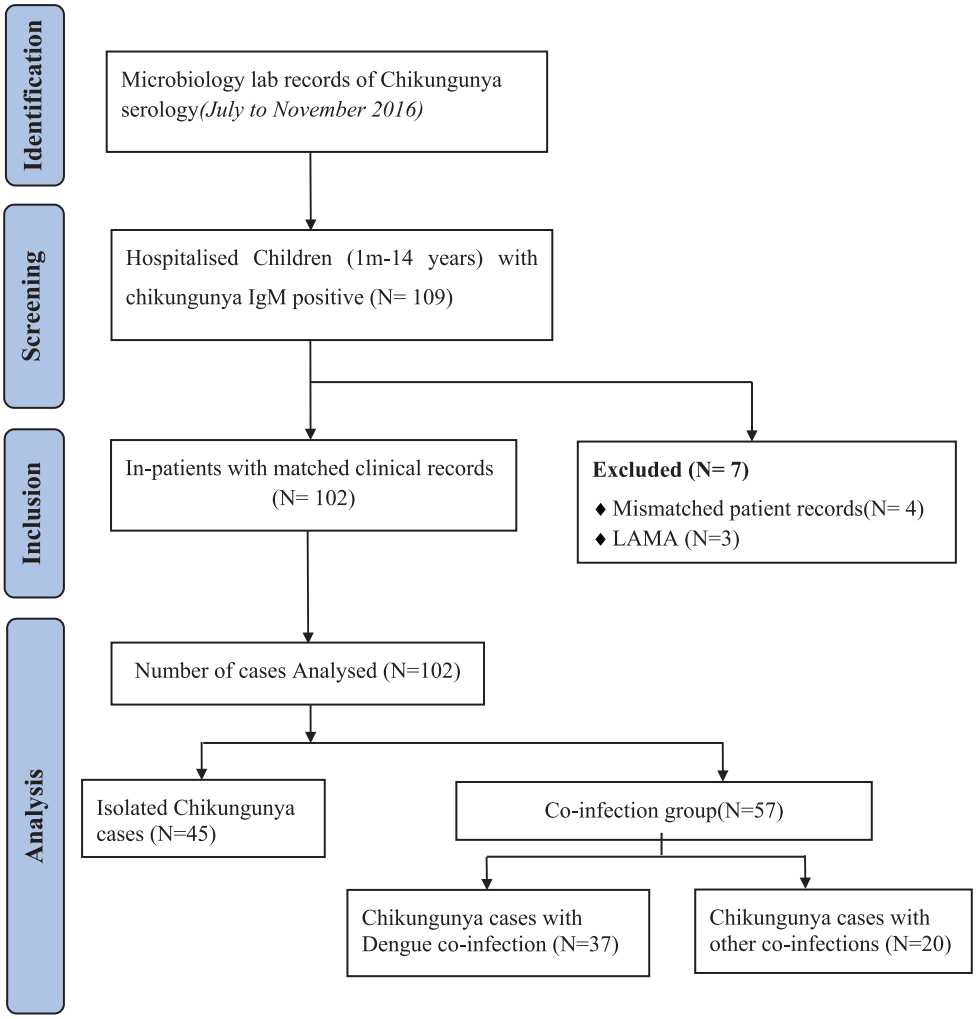

Figure 1: Flow chart of study participants

as per standard age-dependent references in children. Details of treatment (duration of intravenous fluids, vasopressors, and blood component therapy), condition at discharge, and mortality were noted. All children were categorized into either Group A (isolated chikungunya infection) or Group B (coinfection). Groups A and B were compared to see any statistically significant difference in the clinical and laboratory parameters.

The data collected in a predesigned pro forma were entered into MS Excel 2007 and analyzed using software Stat 12.0. Mean±standard deviation and median (p25–p75) were calculated for the quantitative variables following normal distribution and non-normal distribution, respectively, while all qualitative variables were expressed in number (%). All quantitative variables were compared between two group using t-test if underlying distribution was normal otherwise counterpart of t-test, i.e., rank-sum test was used. Chi-square test/Fisher exact test was used to see an association between all qualitative variables with our grouping variable. The significance level was considered at p=0.05.

RESULTS

Of 102 children, 44.1% (45) of children had isolated chikungunya infection, 36.3% (37) had dengue coinfection, and 19.6% (20) had other coinfections with chikungunya. After dengue, the most common coinfection was enteric fever (6.8%, 7), followed by malaria in 5.9% of cases (*Plasmodium vivax* - 5 and *P. vivax*+ *Plasmodium falciparum* - 1), pyomeningitis in 4.9% (5) of cases, and viral hepatitis A in 2% of cases. The age- and month-wise distributions of cases are depicted in Fig. 2. Of 102 children, 62.7% (64) were boys and 37.3% (38) were girls. 90.1% (92) were residents from Delhi and NCR, while 9.8% (10) were from the neighboring states of Delhi (Uttar Pradesh, Haryana, and Rajasthan).

Clinical presentation, physical examination findings, and laboratory parameters in both groups were comparable (Table 1) except for the vomiting and splenomegaly, which were significantly more in the coinfection group ($p<0.05$).

The morbidity profile in both the groups was comparable except that the highest axillary temperature recorded was significantly higher in coinfection group than in the isolated chikungunya group (101.84±1.99°F vs. 100.93±1.91°F; p=0.04) and the duration of intravenous antibiotics was significantly higher in the coinfection group (Table 2). There was only one death in the coinfection group due to dengue shock syndrome.

Table 1: Comparative analysis of clinical and laboratory profile of isolated chikungunya (Group A) and coinfection (Group B)

Variables	Isolated chikungunya n=45 (%)	Coinfection n=57 (%)	p value
Clinical presentation			
Fever	43 (95.55)	56 (98.25)	0.42
Vomiting	21 (46.67)	38 (66.67)	0.04
Abdominal pain	17 (37.78)	23 (40.35)	0.76
Poor oral intake	18 (40.00)	17 (29.82)	0.24
Headache	14 (31.11)	18 (31.58)	0.91
Rash	15 (33.33)	11 (19.30)	0.09
Generalized body ache	7 (15.55)	14 (24.56)	0.38
Seizures	8 (17.78)	8 (14.04)	0.60
Altered sensorium	5 (11.11)	9 (15.79)	0.49
Backache	5 (11.11)	9 (15.79)	0.49
Cough	6 (13.33)	8 (14.04)	0.95
Joint pain	6 (13.33)	7 (12.28)	0.84
Loose stools	3 (6.67)	9 (15.79	0.15
Irritability	4 (8.89)	6 (10.53)	0.78
Dizziness	2 (4.44)	5 (8.77)	0.39
Jaundice	4 (8.89)	1 (1.75)	0.09
Physical examination			
Hepatomegaly	18 (40.00)	32 (56.14)	0.08
Muscle tenderness	16 (35.55)	27 (47.36)	0.81
Abdominal tenderness	4 (8.89)	14 (24.56)	0.67
Splenomegaly	3 (6.67)	14 (24.56)	0.01
Arthritis	3 (6.67)	3 (5.26)	0.41
Petechiae	0 (0.00)	4 (7.02)	0.06
Laboratory values ⋆			
TLC (cell/mm^3)	8000 (4300–12000)	7000 (5600–9500)	0.85
Hematocrit (%)	30.50±10.07	30.49±7.05	0.49
Platelet count (cells/mm^3)	1.6 (1–2.5)	1.2 (0.5–1.2)	0.09
SGOT (IU/L)	51 (37–119)	78 (45–125)	0.19
SGPT (IU/L)	33 (23–62)	49 (25–80)	0.31

Data expressed as number (%), §Age expressed as mean±SD, and ⋆Lab values expressed as Median (p25–p75). SD: Standard deviation, SGPT: Serum glutamate pyruvate transaminase, SGOT: Serum glutamic oxaloacetic transaminase, TLC: Total leukocyte count

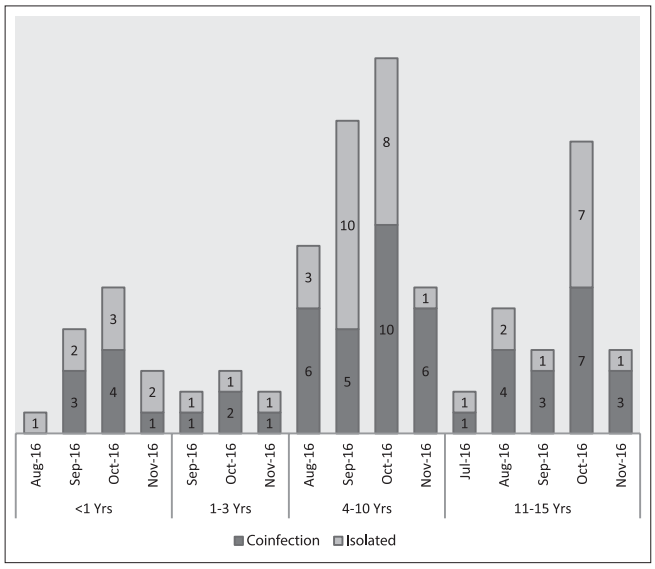

Figure 2: Distribution of a number of patients in different age groups admitted in various months of study period

DISCUSSION

Chikungunya is an epidemic vector-borne arboviral disease. The first case in India was reported in 1963 from West Bengal followed by several outbreaks in southern, western, and eastern India between 1964 and 1973 [1-3]. This single-center study from Delhi retrospectively analyzed chikungunya outbreak among children in the national capital during 2016 and the impact of coinfections during the same period. During the period from July to November, i.e., monsoon and post-monsoon season, 47.6% (102/214) of the seropositive chikungunya children were hospitalized. The most common age group in our study was 4–10 years of age with maximum cases seen in October. This was in concordance with a study from another tertiary care hospital of Delhi where the post-monsoon month of November was reported as the peak month unlike summer months as reported from South India. However, the earlier studies conducted in the national capital on patients of chikungunya have included all age

Table 2: Morbidity profile

Variable	Isolated chikungunya (n=45)	Coinfection (n=57)	p-value
Maximum axillary temperature (°F)[§]	100.93±1.91	101.84±1.99	0.04
Duration of IV fluids (days)[★]	6 (0–10)	7 (5–15)	0.3710
Duration of IV antibiotics (days)[★]	5 (5–15)	6 (0–10)	0.06
Duration of hospital stay (days)[★]	8 (5–15)	7 (4–11)	0.2331
Lowest platelets (in lakhs) (cells/mm^3)[★]	1.50 (0.60–2.30)	1.00 (0.40–2.00)	0.1076
Total duration of fever (days)[§]	8.05±6.64	9.78±9.06	0.323
Shock[α] (%)	11 (24.44)	18 (31.58)	0.428
Fluid leak[α] (%)	3 (6.67)	10 (17.54)	0.614
Bleeding[α] (%)			
Epistaxis	2 (4.44)	3 (5.26)	0.818
Gum bleed	1 (2.22)	3 (5.26)	0.458

Values are expressed as [§]mean±SD, [α]number (%) and [★]median (p25–p75). SD: Standard deviation

groups as opposed to the exclusivity of pediatric patients in our study [4,5].

Of 102 cases with chikungunya infection, 56% (57/102) had evidence of coinfections and dengue was the most common coinfection seen in 36.2% (37) of cases. The prevalence of coinfection with dengue using serological tests has been previously reported to be 2.7–12.4% [6,7]. Artificial collection of water in June–September rains and Aedes being the common vector may be the possible explanation for the high incidence of this coinfection.

The most common symptoms were fever, vomiting, poor oral intake, and abdominal pain across both the groups. The classic triad of fever, rash, and joint pains was present in only 3/45 cases of isolated chikungunya infection. This was in contrast to most of the studies done earlier. The study done in children during the Caribbean epidemic showed that the predominant complaints in confirmed cases of chikungunya were joint pains (98.6%) and skin rash (46.4%) [8]. Similarly, severe arthralgia and joint swelling were the dominant features in chikungunya in another study from West Bengal, and abdominal pain was dominant in cases of dengue. Diarrhea was seen only in cases of dual infection [7].

Sahadeo *et al*. had shown that a combination of joint pain, rash, and TLC <7000/mm^3 was able to differentiate chikungunya from other acute undifferentiated febrile illnesses [9]. Our study highlighted the fact that, apart from the common mosquito-borne coinfections such as malaria and dengue, non-mosquito-borne endemic infections such as enteric fever, pyomeningitis, and viral hepatitis may also coexist with chikungunya infection. This may explain the significantly higher preponderance of vomiting and splenomegaly in the coinfection group ($p<0.05$). Hepatomegaly, muscle tenderness, and abdominal tenderness were also more common though not statistically significant.

Rash is a predominant feature of arboviral infections; however, it was found only in 25% (26/102) of the patients in our study. It was maculopapular in 58% (15/26), flushing in 27% (6/26), vesiculobullous in 15.4% (4/26), and hyperpigmented rash in 3.8% (1/26) of cases. In most of the patients, it was a generalized type of rash seen in 42% (11/26) of cases. In a previous study from South India on 52 children, the pigmented rash was the most common (27/52) type, followed by vesicobullous rash (16/52) and maculopapular rash (14/52) [10].

Only 13 (12.7%) children presented with joint pains, of which six were in the isolated chikungunya group and seven in the coinfections group. Restriction of movement was noted in 9/13 (69.2%) patients and knee joint being the most common joint involved. However, any joint can be involved in chikungunya, but most commonly reported joints are the wrist, metacarpophalangeal, interphalangeal, ankle, and metatarsophalangeal joints [11]. This above phenomenon might highlight a changing pattern of infectivity of the virus and the fact that clinicians must be adept enough to suspect chikungunya infection in children, during the mosquito-breeding season, even without the classical presenting features.

Among the alarming laboratory parameters, leukopenia, because of lymphopenia, has been most commonly been reported. There have been reports of increased transaminases, raised hematocrit, and occasionally thrombocytopenia in chikungunya. The mean platelet count was lower in the coinfection group (1.2 vs. 1.6 lakhs), whereas the mean AST/ALT was found to be higher in the coinfection group [12,13].

Complications such as fluid leak, shock, and bleeding were present in both the groups. However, their presence in the isolated chikungunya group reflects that chikungunya which is generally a benign disease can be potentially fatal as well. In concordance with our data, a retrospective pediatric intensive care unit study of nine children with chikungunya showed the presence of extensive skin blisters in 5 children, encephalopathy in 4, myocarditis and hemodynamic disorders in 5, and bleeding in 1 [14]. Strength of our study was exclusive pediatric study during a large outbreak of chikungunya in a tertiary care hospital of North India. However, limitations were that only indoor patients were enrolled and outpatients were excluded. There were no long-term follow-up of cases. The data from these patients could have given us additional valuable insight into milder presentations of chikungunya and any significant long-term morbidity.

CONCLUSION

Typical presentation of fever, rash, and joint pains is rare among children with chikungunya. A high index of suspicion in monsoon and post-monsoon season is necessary due to the potential risk

of complications such as bleeding and shock. High-rise of temperature, presence of vomiting, and splenomegaly can be the clues to investigate other coinfections.

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