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Clinical Pattern of Viral Fever in Children: Is Rational Antibiotic Use Possible in Non-Critical Hospitalized Children in Resource Limited Setting?

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ABSTRACT

Introduction: Most of Viral infections in non-critical children are self-limiting. Yet, many times, due to lack of clinical knowledge, antibiotics are prescribed which leads to antimicrobial resistance. Aim is to study the demographic and clinical profile and outcome in non-critical children admitted with suspected viral infection.

Materials and method: It was a prospective observational study carried out in the pediatric ward of Shardaben Hospital between November 2014 and August 2015.

Results: Out of the total 3143 patients, 1760(56%) were non-critical with suspected viral infection on admission. The fever was regular in 89% patients, while 88% patients got better on 3rd day of admission. 82% children were not sick in the inter-febrile period. The fever was high grade at onset in 75% patients and 91% responded to paracetamol. In 4.6% of patients fever found to be non-viral but none of the patients required PICU care. There was no mortality.

Conclusion: Viral fever is usually high grade at onset, with non-sick inter-febrile period and natural improvement by 3rd or 4th day of illness. With these clues, viral infection can be suspected and antibiotic misuse can be avoided even in hospitalized children.

Key words: Rational antibiotic use, viral fever, antimicrobial resistance, non-critical.

INTRODUCTION

Fever is one of the commonest complaints with which children present to the pediatrician in the OPD. Not only that, it is the commonest cause of hospitalization in children.[1]

It is a known fact that fever is not a disease in itself, but is a manifestation of an underlying cause, most of the times, an infection. Such an infection could be viral, bacterial or parasitic, commonest in children being viral. Common viral infections are usually self-limiting and fever usually subsides on its own in a few days, till that time one has to use general measures only to control fever.[2]

Despite this, many a times, antibiotics are indiscriminately used in clinically suspected viral infections without waiting for a proper diagnosis. In absence of risk factors in a febrile child, it is rational to wait and observe progress without antibiotic therapy. Periodic clinical examination is necessary over a few days to pick up any clues to diagnosis, impending complication or any improvement or worsening of illness. Every attempt must be made to differentiate bacterial infection from viral infection, let the bacterial infection localize (which takes about 2-3 days), so that we can know which organism is probably involved and which antibiotic needs to be used.

The data regarding clinical patterns of suspected viral infections in hospitalized patients in India are particularly lacking. In resource limited settings like ours where viral PCR or viral culture are not available, such clinical clues can go a long way in restricting the use of antibiotics to prevent antimicrobial abuse and resistance.[3]

OBJECTIVES

The present study was conducted with objectives to know the percentage of clinically suspected viral infection in non-critical hospitalized children and to study the clinical and laboratory patterns of viral infection in non-critical hospitalized children.

MATERIALS AND METHODS

It was a prospective observational study carried out in the pediatric ward of Shardaben Hospital affiliated to NHL Medical College, Ahmedabad. The study period was November 2014 to August 2015.(10 mnths).

Inclusion Criteria: Non critical children with clinically suspected viral infections between age group of 3 months to 12 years admitted in the pediatric ward for associated morbidity like vomiting, fever, loss of appetite etc. during the study period were enrolled in study.

A) Criteria for non-critical children:

History	Examination
No altered behavior/sensorium	No disproportionate rise in heart rate & respiratory rate (age wise)
Normal urine output	Normal capillary refill time
No history of convulsions except febrile convulsion	No purpuric skin lesions
No bleeding from any site	No differential body temperature
	No chest retractions
	No meningeal signs
	No membrane in throat
	Maintaining spo_2>95% without oxygen

Out of all admissions, patients with all of the above criteria were considered as non-critical children and included in the study.

B) Criteria for viral infection[19]:

Fever	Bacterial	Viral	Malarial
Degree at onset	Moderate	**High**	High
Rhythm	Regular	**Regular**	Irregular
Response to paracetamol	Poor	**Fair**	Fair
Inter febrile state	Sick	**Normal**	Normal
Extent of disease	Localized	**Generalized**	--

Out of all non-critical admissions, patients matching with any 2or more of the above criteria were considered as clinically suspected viral infections and were enrolled in the study and rest were excluded.

Exclusion criteria: Children with long duration of fever (fever for more than 7 days) were excluded. Those children with obvious diagnosis of acute infective viral hepatitis (jaundice), measles, mumps and chicken pox were also excluded.

In our study following definitions were used-

Fever[4] (axillary temperature recorded by digital thermometry) was graded in to Low grade fever (99˚- 101˚ F), Moderate grade fever (101.1˚ – 103˚ F) and High grade fever (103.1˚ – 106.5˚ F).

Laboratory parameters[5,6]: Normal leucocyte count was considered to be 4.0-12.0 cells/mm^3 while in differential count Normal neutrophil count was taken between 54-62% and Normal lymphocyte count between 25-33%. ≤1% eosinophil count was considered as eosinopenia. Normal platelet count (thrombocyte count) was taken as 1.5-4 Lakh/mm^3.

After taking consent from parents, all the details with demographic profile, presenting complaints, detailed history, clinical features were recorded as per proforma. The patient's progress in ward was closely monitored for improvement or deterioration or localization as bacterial infection. Clinical improvement was considered as decrease in intensity, frequency and duration of fever, subjective wellbeing and improved appetite. Daily detailed physical examination was performed by an expert pediatrician and necessary investigations were sent as and when required.

All these patients were treated as per institute's protocol without the use of antimicrobials on admission.

RESULTS

A total of 1760 patients were included in the study based on inclusion and exclusion criteria. Out of the total 3143 patients hospitalized during the study period, 1760(56%) were non-critical with suspected viral infection on admission.

Table 1: Demographic profile of study population

Age	Male (n=1103)	Female (n=657)	Total (n=1760)
3m-1 yr	267 (24.2)	138 (21)	405 (23)
1-5 yr	666 (60.4)	355 (54)	1021 (58)
5-12 yr	170 (15.4)	164 (25)	334 (19)

Figure in parenthesis indicate percentage.

Out of the total 1760 admitted patients, 1103 patients were male (62%) while 657 patients were female (38%). Also, the age wise distribution of the study population was 23%, 58% and 19% amongst age groups 3-12 months, 1-5 years and 5 to 12 years respectively.

The rhythm of fever was regular in 89% patients, while 88% patients got better on 3rd day of admission. 82% children were not sick in the inter-febrile period. The fever was high grade at onset in 75% patients while 91% responded to paracetamol.

Table 2: Pattern of fever in study population

Fever pattern (viral fever)	Cases (n=1760)(%)
Grade at Onset	
High grade	1320 (75)
Moderate/low grade	440 (25)
Rhythm	
Regular	1566 (89)
Irregular	194 (11)
Inter-febrile period	
Sick	317 (18)
Non-sick	1443 (82)
Response to paracetamol	
Fair/Good	1602 (91)
Poor	158 (9)

Table 3: Complete blood count in children with clinically suspected viral infections (n=1760)

Complete blood count	Cases (%)
Total leukocyte count	
High (>12,000/mm3)	357 (20)
Low (<4,000/mm3)	158 (9)
Normal (4,000/mm3-12,000/mm3)	1245 (71)
Differential leukocyte count	
Lymphocytosis (>33%)	704 (40)
Neutrophilia (>62%)	206 (12)
Eosinopenia (<=1%)	1760 (100)
Platelet count (thrombocyte count)	
Thrombocytopenia (<1.5 lakh/mm3)	212 (12)
Thrombocytosis >4.0 lakh/mm3)	397 (22)

Table 4: Final diagnosis on discharge of children admitted with clinically suspected viral infections (n=1760)

Diagnosis	Cases (%)
Viral	1668
Acute Gastroenteritis	686 (39)
Viral fever without focus	333 (19)
LRTI(WALRI/Bronchiolitis)	281 (16)
Viral fever without focus with febrile convulsion	158 (9)
Acute gastroenteritis + WALRI/ Bronchiolitis (two system involved)	97 (5.5)
Viral URTI	79 (4.4)
Dengue fever (clinically and/or serology) without warning signs	44 (2.5)
Non Viral	82
Enteric fever (clinically and/or serology)	33 (1.9)
Malaria	25 (1.4)
Urinary tract infection	15 (0.8)
Bacterial (pustulartonsilopharyngitis)	9 (0.5)

Table 5: Outcome of children with clinically suspected viral infections without the use of antimicrobials

Outcome	Cases (n=1760)(%)
Discharge	1652 (99)
DAMA	13 (0.8)
Abscond	5 (0.3)
Expiry	0

In the present study, out of the 1760 clinically suspected viral infections, 71% showed total leukocyte counts within normal range, all the patients had eosinopenia and 66% had normal platelet counts and 12% had thrombocytopenia.

Out of the total clinically suspected viral infection cases, 82 (4.6%) turned out to be non viral- bacterial infection (3.2%) or malaria (1.4%) and they required specific treatment. These patients were followed up till discharge. None of them required shift to PICU, or recorded any mortality.

Out of 1760 cases of clinically suspected viral fever and treated without antimicrobials in the hospital, 99% children were eventually discharged, 0.75% took DAMA, 0.25% absconded.

DISCUSSION

More than half of the total admitted patients during the study period had suspected viral fever. It is known that fever is the most common reason for a sick child visit and most fevers are the result of self-limiting viral infections.[7,8]. A study by Joshua M Colvin et al found that one or more viruses were detected in 76% of 75 children with fever without an apparent source.[8]

The higher number of male patients in the study could be because of more number of male children being brought to the hospital as compared to female children in the lower socioeconomic group. Also, the higher incidence of viral infections in the 1-5 years age group could be attributed to increased exposure to surroundings.

In the present study rhythm of fever was regular in 89% patients which show a high rate of predictability for viral infection.[9]

This was closely followed by the next parameter i.e. progress on 3rd day of admission, where 88% patients got better. This correlates with the fact that fever due to viral infection peaks over a day or two and gradually declines in 3-4 days while bacterial fever worsens if left untreated.[10]

In 82% cases in the study population, the interfebrile period was non-sick. It is known thatif the child continues to look sick even when the fever is relatively less under the effect of paracetamol, it suggests an acute bacterial infection. In most other febrile illnesses, this is not true.[11]

The fever at onset was high grade in only 75% of the total patients in the study. Children 1-5 years of age may have exaggerated febrile response to viral infections as well as severe bacterial infections.[7]

Response to paracetamol was fair in 91% of patients which correlated with the fact that viral in-

fections have fair/good response to paracetamol.[9] A study done by Weisse et al has shown no difference in response to paracetamol between viral and bacterial infections.[12]Antipyretic agents have the same effect on fever of either viral or bacterial origin.[6]

Despite all this it is important to realize that exceptions do exist –in cases of low virulence, immune-compromised state, severe malnutrition, the typical pattern of fever may not be observed.[11]The therapeutic response to antipyretics and the length of the fever may not allow the physician to predict the aetiology and seriousness of the infection.[2,12,13]Few studies have shown that pattern of fever has limited value in prediction of aetiology of fever because of interference with use of paracetamol.[10]

Here, 71% patients had normal total leukocyte count and 20% had high total leukocyte count. The cut off for leukocytosis was kept at 12,000 in our study. In the study done by Weisse et al keeping the limit of leukocytosis as 20,000 a significant difference ($P<0.05$) was found between leucocyte count in viral infections versus bacterial infections with a definite leukocytosis in bacterial infections.[10]Bacterial infections are more likely than viral infections to have a leukocyte count of 15,000/mm^3 or more, but because viral infections are much more frequent than bacterial infections, the majority of febrile children with a high leukocytosis have viral infection as a possibility.[2,14]

40% of patients in the study had lymphocytosis. Louise in 2012 described that rising neutrophils in general is consistent with a bacterial infection and lymphocytosis indicates viral infection (most common).[15]

All the patients in the present study had eosinopenia (eosinophils ≤1%). According to literature, eosinopenia is a feature of acute infection (both viral & bacterial) & a normal eosinophil count in an acute infection may suggest a non-viral, non-bacterial infection or a recovering acute infection.[16]

12% of the patients in this study showed thrombocytopenia. In a study done by PrithvirajPatil et al which studied the clinical evaluation and outcome of patients with febrile thrombocytopenia, out of the 100 patients studied, 32% patients had viral fever/dengue and 54% had malaria.[17] 22% patients of acute viral fever had thrombocytosis but in an automated cell counter, thrombocyte count may be falsely reported as higher than what it actually is, as in microcytic anemia, small RBCs are erroneously counted & reported as thrombocytes.

White blood cell count results can be confusing for physicians when there is an obvious discrepancy between the number of leukocytes and the child's general condition. In such cases, the clinical aspect is more important than a simple laboratory result.[2]

Out of the total clinically suspected viral infection cases, 82 (4.6%) turned out to be bacterial infection (3.2%)/malaria (1.4%) and they required specific treatment. The definitive diagnosis of acute bacterial infection is generally not possible for the first 2-3 days; hence antibiotic prescription for the fever of acute onset is not justified except in cases of serious infections or early localization.[11]

In a study done by Greenes DS et al titled 'Low risk of bacteremia in febrile children with recognizable viral syndromes', it has been documented that highly febrile children 3-36 months of age with uncomplicated recognizable viral syndrome have a very low rate of bacteremia-2 out of 876 patients (0.2%)(95% CI0.01,0.8%) whereas in the present study only 3.2% turned out be bacterial infection.[14]

Of the study population, none required PICU care eventually. There were no expiries. It has not been formally proven that the absence of specific treatment in viral infections has ever been the direct cause of a serious accident.[2,18]

CONCLUSION

Viral infection is a common cause of hospitalization in non-critical febrile illness in children, most of the times it is self-limiting and harmless.

It is not difficult each time to clinically suspect viral infections in most non-critical febrile hospitalizations (serious bacterial infections must be ruled out), if few general principles are strictly followed , classical being clinical fever pattern and complete blood count findings.

Fever is being high grade at onset, non-sick inter-febrile period, regular rhythm, good response to paracetamol and natural improvement by 3rd or 4th day of illness with or without localization.

Complete blood count indicates Leucopenia with lymphocytosis and eosinopenia with or without thrombocytopenia which may point towards a viral etiology. However total leucocyte count & differential leucocyte count should not be interpreted in isolation without analyzing the clinical profile.

There is no increase in mortality or morbidity if antibiotics are not started on admission in febrile non-critical children with no obvious bacterial focus of infection. Hence, even in hospitalized children rational use of antibiotics is possible in resource limited settings where viral culture/PCR is not available.

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