

Paediatric practice: an approach to a child with fever

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Nearly seventy percent of all children between the ages of one week and two-years-of-age are brought to Kanti Children's Hospital for some Type of febrile episode. And 50% of these visits are for temperatures greater than or equal to 39 degrees celsius. These children may have significant bacterial infection. In 35% of these children there's no definable source for the fever on clinical examination. So the child that don't have identifiable sources could be either bacteremic, meningitis or could have a bone or joint infection in evolution. Simple clinical observation to differentiate a well looking infant from a toxic infant helps to differentiate children who needs admission or out patient follow-up.

Introduction

Children are smaller, their surface area is greater in comparing with the body weight therefore they tend to have higher metabolic rates and because of that their core temperatures are higher than that of an adult. So for a child, a rectal temperature of greater than or equal to 38C degrees, or 100.4F degrees is considered a fever. Anything below that is acceptable as normal. Fever documented at home by a reliable adult should be treated the same way as reported by a nurse or a colleague. The Integrated Management of Childhood Illnesses (IMCI) includes fever even if reported by mother although there may not be fever during examination by a health worker.¹

Fever in children:

- 65% of children <2 years will visit a physician for an acute febrile illness
- 60-80% of encounters in clinical practice
- Most commonly caused by self-limited viral illness and localized bacterial infection, but may be presenting feature of something more serious infection e.g. meningitis

It is important to find out the common cause of fever in that area. This will help to formulate a set of questions necessary for the OPD settings. The causes of fever could be infective or noninfective. In developing countries infective causes are the primary one and it could be viral or bacterial. The best guide to distinguishing bacterial from viral is clinical acumen.² It is always important to question about recent immunizations in this age group because some vaccines

tend to give fever. DPT, the pertussis component, can give a fever 24 hours or so after the vaccine. MMR can cause fever in about 40% anywhere from 5 to 7 days after the vaccine. It can be as high as 38C or 39C degrees.³ So if this question is not asked, an infant may get a sepsis work-up. It is important to ask specific symptoms that can help to localize the infections.

Fever, for the management purpose could be classified under three headings: fever of less than three days duration; fever of four to one week duration and fever of more than one week duration. This classification is based on the clinical signs seen during fever and the prevalent diseases in Kathmandu. Within the first three days if there are no any localizing symptoms or signs the probable cause is unlikely to be diagnosed and needs further observation with antipyretics. If the fever persists beyond one week without localizing signs then the most common causes are non infective in origin.

Associated symptoms with fever that helps to localize the infection

Convulsion- meningitis, acute encephalitic syndrome, sepsis

Headache-sinusitis, otitis media, meningitis, acute encephalitis syndrome

Vomiting, pain in abdomen-Hepatitis, appendicitis, enteric fever, amoebiasis.

Red eye-

Bulbar conjunctivitis-Kawasaki's disease, leptospirosis

Palpebral conjunctivitis-measles, infectious mononucleosis..

Cough, cold, breathlessness -URTI, bronchitis,

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pneumonia, empyema, sinusitis, lung abscess, otitis media, pharyngitis.

Difficult to swallow/ excessive salivation- Herpangina, gingivostomatitis, tonsillitis, pharyngitis, epiglottitis.

Noisy breathing- Croup syndromes

Projectile vomiting - Meningitis.

Jaundice- hepatitis.

Increased frequency of urination or cry – Urinary tract infection

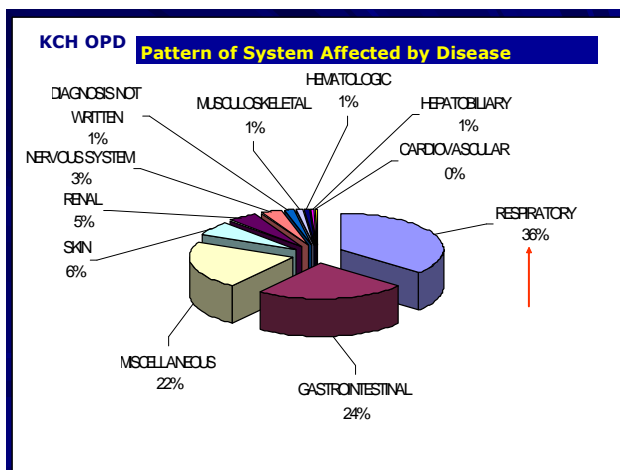
Skin rash- measles, chickenpox, rubella, meningococemia, fifth disease, rickettsia.

Joint swelling- septic arthritis.

Swelling in the neck- Tuberculosis, Toxoplasmosis, Infectious mononucleosis, Brucellosis,

Palpable mass in abdomen-splenomegaly- malaria, kala-azar, infectious mononucleosis, lymphoma, enteric fever, bacterial endocarditis.

As many cases are seen in OPD it is essential to find a set of questions that will try to triage for the severe cases so that they can be treated urgently. These questions will also try to find out the cause of the fever quickly saving time in the heavily numbered OPD. The following set of questions when asked to parent or the guardian will fulfill the above objectives. These questions are based on the IMCI.¹



Important questions for the history in OPD setting

Does your child has convulsion or unconsciousness? Meningitis/encephalitis/ febrile seizure

Is the child able to swallow? Tonsillitis/herpangina/

Does he vomits every thing? Raised intracranial pressure/hepatitis/gastritis

How long your child has fever? Prolonged fever: kalazar/ tuberculosis/malignancy/ malaria

Is this fever associated with

Cough or difficulty breathing? Respiratory problem

Diarrhoea? Dysentery

Rash? Viral/meningococcal/ sepsis

Ear problem? Otitis media/mastoiditis

Swelling? Abscess/lymphadenopathy/ cellulites/urticaria

Salivation? Herpangina/ herpetic gingivostomatitis/ tonsillitis

Joint pain? Rheumatoid/rheumatoid/ septic/osteomyelitis

Urine problem? UTI

Are other members of family having similar problem?

Viral

Has your child traveled within one month? Malaria/ kalazar

Is your child on treatment? Drug induced/ inappropriate therapy

Any history of allergy? Drug or other

Young infant (up to the age of two months) are different from older children when related with cause and management of fever. Therefore they need special consideration and the above mentioned symptoms, signs, and historical questions will not be valid. The need special considerations.

The young infant (up to two months)

Serious bacterial infections can present with normal or subnormal temperatures.⁴ So an absence of a fever does not rule out a serious bacterial illness in a child. An issue that we are seeing right now, summer time of year, is over-bundling.⁵ Even in summer young infants are over-bundled specially in Tarai and their temperature rises significantly. One way to deal with that and try to figure out if that's really a fever or over-bundling is summarized here: unbundled the patient and recheck the temperature 15 to 30 minutes later, prior to giving any type of antipyretic, and see if the child's temperature is down and the patient looks good, then it's probably a fever related to over-bundling. Again, it depends on how the patient is doing and what the history is, but it's one way to look this type of a problem. The response to antipyretics does not predict the presence of bacteremia.

Fever and serious bacterial infection:

The prevalence of serious bacterial infections in infants less than or equal to 2 months of age who come in with fevers of 39C degrees or greater is high.⁶ We are defining serious bacterial infections as these: severe pneumonia, meningitis, sepsis, bone and joint infections, urinary tract

infections, and enterocolitis. Otitis media except in young infants and sinusitis are not listed as serious bacterial infection because they are not considered serious bacterial infections.⁷

The bacterial pathogen in this age group are *B* beta streptococcus, *E. coli*, *Listeria monocytogenes* occasionally, staphylococcus, streptococcus, staphylococcus species and primarily staphylococcus aureus. Streptococcus pneumoniae and Hemophilus influenzae are starting to be seen more frequently. In developed countries Hemophilus influenzae Type B disease are not seen commonly in children greater than two or three months of age. That's because of Hib vaccine coverage. We do not have enough data for the Hib or Pneumococcal burden of the disease for this country.

Two months to up to five years

In this age group the incidence of occult bacteremia, which is a frequent cause of fever of undetermined origin, seems to have decreased over time in developed countries because of vaccine against Haemophilus influenzae and Streptococcus pneumoniae.

The common causes of fever in this age group are:

Respiratory:	nasopharyngitis / pneumonia/ tonsillitis/ otitis media/ tubercular
Viral:	measles/ chicken pox/ mumps/ herpangina/ hepatitis/
GI infection:	dysentery/ acute watery diarrhoea/ typhoid
CNS infection:	meningitis/ encephalitis/ brain abscess
Skin infections:	abscess/ cellulites
Urinary infections:	pyelonephritis/ cystitis
Protozoal infections:	malaria/ kalazar/ amoebiasis
Collagen disease:	rheumatoid/ rheumatic

The evaluation of nontoxic-appearing, young, febrile children has been a subject of considerable debate. Of young, nontoxic-appearing children aged 2 to 36 months with temperatures of 39 degrees C or more and no clear source of infection is identified, approximately 25% of untreated patients have persistent bacteremia or develop new focal infections, including 3% to 6% who develop meningitis and occult meningococcal bacteremia, although rare, has frequent complications, including meningitis in approximately 40% and death in approximately 4%.⁹ But in developing countries we do not have enough data to observe these facts. It is believed that Hemophilus influenzae Type B and Streptococcus Pneumoniae constitutes probably 95% to 98% of all cases of occult bacteremia. Regardless where we see children in this country, that's the major pathogen. The common pathogens isolated

in these children are Streptococcus pneumoniae, Hemophilus influenzae and Neisseria meningitidis.¹⁰ The incidence of penicillin resistant pneumococcus has gone up in the last five to six years.

Occult bacteraemia

In the study done by Alpern ER et al the overall rate of occult bacteremia was 1.9% (95% confidence interval [CI]: 1.5-2.3). *S* pneumoniae accounted for 92 of 111 isolates (82.9%; 95% CI: 74.6-89.4) in children with occult bacteremia.¹¹ The risk of a child with occult pneumococcal bacteremia later having meningitis is approximately 3%.¹² Persistence of bacteremia, depending on the studies, anywhere from 7% to 50% and meningitis in 27%.¹³ Hemophilus influenzae was the commonest cause in the past in developing countries but its incidence has been reduced remarkably with the introduction of the Hib vaccine. Depending upon the study, from 7% to 22%, probably about 17% or 15% or so are going to be persistently bacteremic 24 to 48 hours later.¹⁴ Meningitis is going to be seen in about 6%. Longer the bacteria is in the circulation, greater the possibility of having meningitis.

Serious bacterial infection

A child who appears ill, respiratory rate of equal or more than 60 per minute, chest indrawing, grunting, cyanosis, wheezing, lethargic, too hot, too cold or distended abdomen may have possible serious bacterial infection.¹⁵ If any one of these criterias are present then that child is going to be in a high risk for serious bacterial infection. When these clinical criteria are not present we may call low risk clinical criteria, and using this coupled with some laboratory data one can follow-up those children that are lowest risk for serious bacterial infections. In other words, when we look these children, they are relatively happy? If we bring the fever down they smile. Do they try to interact with us? If they try to interact with us, then they are low risk children. Otherwise they are probably falling out of the low risk group and may be at high risk for serious bacterial infection. On physical examination there should be no focal bacterial infection identifiable, other than possibly an otitis media. And lastly, the child should come from a good social situation and can be easily followed up.

Laboratory investigations

When compared with "no work-up," the strategy of "CBC + selective blood culture and treatment" using a white blood cell (WBC) cutoff of $15 \times 10^9/L$ prevents 48 cases of meningitis, saves 86 life-years per 100 000 patients, and is less costly at the current rate of bacteremia (1.5%).¹¹ The

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other issue is the absolute band count. It's simple; take that percentage of bands in the report e.g. 15% and multiply it times the total white count. So if we have got a white count of 10,000 and our band count is 15%, then the absolute band count is 1,500 cells. So what most authorities are recommending is that if the absolute band count is above 1,500 then that child might be infected and probably needs to be worked up. If the white count is below 2000 there may be overwhelming sepsis.

A urine analysis should be obtained in these children and should be normal; as defined by less than 5 WBC's per high power field. Or should have a negative gram stain by smear. If the child has diarrhea there should be less than 5 WBC's per high power field because that correlates with an absence of a bacterial pathogen. If all those criteria plus the previous criteria are met, that child is in the low risk group and that's the child that's going to have that 1% risk for serious bacterial infection, 1% risk for bacteremia, and less than a percent, less than 0.5% for meningitis. That child can usually be managed as an out-patient.

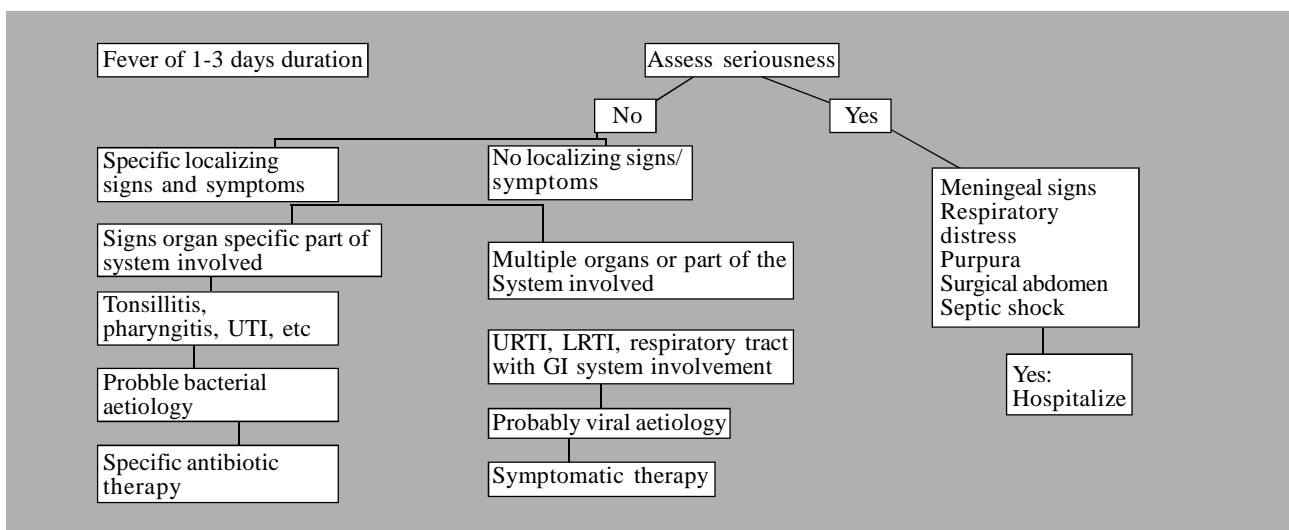
The Kernig's and Brudzinski's sign, those classic signs of meningitis, do not become fully developed until the child is about a year to 15 months of age. So a negative Kernig's and Brudzinski's in a child less than 15 months of age, doesn't rule out meningitis. We can make them to look up and down and move their head and if they can they probably don't have meningitis provided there are no other signs involved.. Paracetamol for control of pain and fever and then of course, the all important follow-up in 24 to 48 hours. Bring them back and look them over. If there is history of convulsion and no other specific signs, lumbar puncture should be done and the result of CSF should be available within 30 minutes. This helps to differentiate the first episode of febrile seizure with meningitis.

Algorithm

Here are the options for children less than 28 days of age – this is very much similar as outlined in the IMCI guidelines developed by WHO for young infant.¹⁶ Option number one: for a child less than 28 days of age we are recommending hospitalization and a substance evaluation for all children with a fever greater than 100.4F. That's because the pathogens that they are subjected to at this age group are particularly virulent and as we all know, they have a relative immaturity in their immune system. The substance evaluation should include a CBC with differential, the serum glucose, a lumbar puncture which should include a cell count with differential, protein and glucose determination, and a bacterial culture at minimum.

Next algorithm for old children: The first question we are going to ask ourselves here is, is this a non-toxic appearing previously healthy child? If the answer is no, if they look sick, they probably have to be admitted in the hospital. And we need to do our complete sepsis work-up and parenteral antibiotics. That is, either cefotaxime or ceftriaxone empirically. Now, if the child meets this first cut off, or first break point, and the answer is yes, then the next break point is temperature. If we have a temperature that is less than 39C degrees, there really isn't much to do. We don't have to do any diagnostic tests or give antibiotics. Just examine the child and make sure there is nothing that we are missing. Antipyretics should be given. Generally paracetamol is sufficient. The patient should be instructed to return or given an appointment to return in 24 to 48 hours, or sooner if the patient is getting worse or not better. On the other hand, if the temperature is greater than 38C degrees then we should proceed with some Type of an outpatient's work-up and that depends on what the constellation of

Algorithm for fever (less than three days)



symptoms are for each child. So in general, if the child is a male and less than six months of age, or a female less than two years of age, a urine culture should be obtained to rule out a urinary tract infection. Stool culture is there is blood or mucus in the stool, or if there's greater than 5 WBC's on stool smear.

If the patient has respiratory symptoms the guidelines therefore emphasise the importance of tachypnoea in the diagnosis of childhood pneumonia, defined according to the usual WHO criteria: In children <2 months: >60 breaths/minute, in children 2-12 months: >50 breaths/minute and in children >12 months: >40 breaths/minute.

The best guide to distinguishing bacterial from viral pneumonia is clinical acumen, and the Guidelines present two well validated clinical observations that should reduce inappropriate antibiotic use in toddlers, while identifying those children who do need antibiotics: in the preschool child, if wheeze is present, primary bacterial pneumonia is unlikely. Bacterial pneumonia tends to be associated with pyrexia, dyspnoea, and tachypnoea; bacterial pneumonia should be considered in children up to 3 years of age with a temperature >38.5°C along with chest recession and respiratory rate >50 per minute.¹⁷

The case for performing a chest x ray as part of the investigation of a febrile child with no respiratory signs is dubious. The Guidelines suggest: if clinical signs are present, x ray examination is not necessary to diagnose pneumonia and in children in whom clinical recovery has been satisfactory, repeat x ray examination serves no useful purpose.¹⁸ Here the advice is simple and to the point: there is no indication for any tests in a child with suspected pneumonia in the community.

Blood culture should also be obtained if the white count is greater than 15,000. And that's because we know that when the white count is greater than 15,000 we have a higher rate of bacteremia. It's one way of being cost effective. Empiric antibiotic therapy again can be linked with the issue of white count and temperature. So that if the white count is greater than 15,000 and the temperature is greater than 39°C degrees give the antibiotic.

Some of us advocate initiating empiric antibiotics until we have the results of the 48 or 72-hour blood culture. It seems that the interval from the time of the blood draw to the time that we can consider them negative has decreased in time over the last few years. That probably has to do with the fact that we have better culture systems than we did in the past. It now appears that with the newer systems they are so accurate that we get a good idea by 48 hours. And if the blood cultures are negative at 48 hours we can stop the antibiotics, and if the child is doing well, consider sending him home. Or treat them longer if they are not doing well yet.

Further investigations if fever persists

Blood culture

Widal test

Liver function tests

Serological tests to antibodies such as for Hepatitis virus, EBV, CMV, Brucellosis, HIV etc.

Paul Bunnell test for infection mononucleosis

Mantoux test

Sputum examination

Auto antibody tests such as RA factor, ANA, ds DNA.

USG Abdomen

Biopsy of affected organ -liver, lymphnodes, bone marrow.

Total body CT or MRI scanning.

Antibiotics

Fever of unknown origin (FUO) is best defined as fever without obvious source on initial clinical examination and then classified into acute (illness of < or =1 week's duration) and prolonged (>7 to 10 days' duration). Aetiologically, there is a marked overlap between acute and prolonged FUO, and infections are major players in both. Age, climate, local epidemiology and host factors are the major aetiological factors that should be considered in the choice of definitive tests. Depending on age, serious bacterial infections (including bacteraemia, meningitis and urinary tract infection) occur in 3 to 20% of cases of acute FUO. Prevention of mortality and sequelae from these infections, particularly bacteraemia and meningitis, is of particular concern in acute FUO. An individualised approach, based on clinical evaluation supplemented with screening and definitive laboratory tests to determine the need for empiric antibiotic therapy and hospitalisation, seems to be the best approach to acute FUO (although this may be less applicable to neonates and infants younger than 90 days, particularly those aged 0 to 7 days). The place of laboratory tests, empiric antibiotic therapy and hospitalisation are important issues that are likely to remain so for some time.¹⁹ The appropriate antibiotics for a child less than 30 days of age is ampicillin plus gentamicin. The ampicillin/gentamicin should cover most of the pathogens at this age group. Newer regimens include things using like cefotaxime and ampicillin. The common denominator in both of these is the ampicillin component and that's because that component offers coverage for *Listeria monocytogenes*. *Listeria* is not covered

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by the cephalosporins alone. Ceftriaxone is not used in this age group, because it displaces bilirubin from its albumin-binding sites, and so it can lead to kernicterus or jaundice.

Conclusion

There are ample evidences to suggest that investigations and antibiotics are not indicated in children under the age of 36 months if they do not have signs of serious bacterial infection. Surveys also indicate that many physicians do not agree with recommendations for venipuncture and bladder catheterization in nontoxic febrile children, and that many employ watchful waiting rather than empiric antibiotic therapy. Surveys of parents note a preference for less testing and treatment. More aggressive management may be appropriate in febrile infants younger than three months old; however, criteria have been proposed to identify infants older than one month who are at low risk for serious bacterial infection. Because of widespread vaccination against *Haemophilus influenzae* infection, *Streptococcus pneumoniae* has become the cause of most cases of bacteremia in western countries. However in developing countries these bacteria are the major cause of serious bacterial infection and it should be remembered in choosing the antibiotics. The risk of serious bacterial infection is greater in younger children and in those with higher temperatures and white blood cell counts. These variations affect both cost and standard of care. Future studies assessing whether these strategies affect patient outcomes would further elucidate their clinical implication. Pediatric health care providers have a unique opportunity to make an impact on parental understanding of fever and its role in illness. There is poor compliance with published practice guidelines in the management of febrile infants and children among medical professionals. Future studies are needed to evaluate educational interventions and to identify the Types of medical care practices for fever.

References

1. Sandy Gove Integrated Management of Childhood Illness. In Strickland GT(Ed) Hunter's Tropical Medicine and Emerging Infectious Diseases. 8th Ed. WB Saunders Co. 2000.125-140.
2. Russel G. Community acquired pneumonia, *Arch Dis Child* 2001;**85**:444-446.
3. Peltola H, Heinonen OP. Frequency of true adverse reactions to measles-mumps-rubella vaccine. A double-blind placebo-controlled trial in twins. *Lancet* 1986;**1**:939-942
4. Pulliam PN, Attia MW, Cronan KM. C-reactive protein in febrile children 1 to 36 months of age with clinically undetectable serious bacterial infection. *Pediatrics* 2001;**108**:1275-9
5. Cheng TL, Partridge JC. Effect of bundling and high environmental temperature on neonatal body temperature. *Pediatrics* 1993; **92**:238-40
6. Luszczak M Evaluation and management of infants and young children with fever. *Am Fam Physician* 2001; **64**:1219-26
7. Buckingham SC, McCullers JA, Lujan-Zilbermann J, Knapp KM, Orman KL, English BK. Pneumococcal meningitis in children: relationship of antibiotic resistance to clinical characteristics and outcomes. *Pediatr Infect Dis J* 200; **20**: 837-843
8. Kamalaratnam CN, Kang G, Kirubakaran C, Rajan DP, Daniel DJ, Mathan MM, Mathan VI. A prospective study of nosocomial enteric pathogen acquisition in hospitalized children in South India. *J Trop Pediatr* 2001; **47** : 46-9.
9. Kuppermann N. Occult bacteremia in young febrile children. : *Pediatr Clin North Am*; 1999; **46**: 1073-109.
10. Jamuna R, Srinivasan S, Harish BN. Factors predicting occult bacteremia in young children. *Indian J Pediatr* 2000; **67**: 709-11
11. Alpern ER, Alessandrini EA, McGowan KL, Bell LM, Shaw KN. SeroType prevalence of occult pneumococcal bacteremia. *Pediatrics* 2001; **108**:E23
12. Baraff LJ. Management of fever without source in infants and children. *Ann Emerg Med* 2000; **36**:602-14
13. Di Troglia J. Occult bacteremia from a pediatric emergency department. *Pediatrics* 2001; **108**:520-1.
14. Greenes DS, Harper MB. Low risk of bacteremia in febrile children with recognizable viral syndromes. *Pediatr Infect Dis J* 1999; **18**:258-61.
15. Brady JP, Awan FB, Wafula EM, Onyango FE. Recognition of illness in very young infants by inexperienced health workers. *Ann Trop Paediatr* 1993; **13**:401-7.
16. Gupta R, Sachdev HP, Shah D. Evaluation of the WHO/UNICEF algorithm for integrated management of childhood illness between the ages of one week to two months. *Indian Pediatr* 2000; **37**:383-90.
17. Cherian T, John TJ, Simoes E, et al. Evaluation of simple clinical signs for the diagnosis of acute lower respiratory tract infection. *Lancet* 1988; **2**:125-128
18. Swingle GH, Hussey GD, Zwarenstein M. Randomised controlled trial of clinical outcome after chest radiography in ambulatory acute lower-respiratory infection in children. *Lancet* 1998; **351**: 404-408
19. Akpede GO, Akenzua GI. Aetiology and management of children with acute fever of unknown origin. *Paediatr Drugs* 200; **3**:169-93.