Laboratory Parameters Influencing the Use of Antbiotics Amongst Paediatricians

AUTHORS-

- **Dr. Himanshu Dua,**

Associate Professor, Department of Pediatrics, NKPSIMS And Research Center Lata Mangeshkar Hospital Nagpur, Maharashtra

- **Dr. Anjali Edbor, Professor,**

Department of Pediatrics, NKPSIMS And Research Center Lata Mangeshkar Hospital Nagpur, Maharashtra

Corresponding contributor:

Dr. Anjali Edbor, Professor,

Department of Pediatrics, NKPSIMS, And Research Center Lata Mangeshkar Hospital Nagpur, Maharashtra

Abstract

Objectives: The set protocol for initiation of antibiotic therapy initiation varies in every doctor-patient-disease situation. Our objective was to identify the most common laboratory parameters advised and used for further initiation of antibiotics in a paediatric OPD and IPD setup.

Methods: A validated questionnaire was circulated among 2 groups paediatric OPD and IPD setup respectively and their responses were noted.

Results: It was observed that in OPD practice, 93.84% of practitioners prefer CBC+CRP while 96.22% of practitioners prefer CBC+CRP+Procalcitonin as a laboratory parameter of choice for assessment of fever in children. When 80% of practitioners initiated antibiotic therapy based on CBC and a positive CRP report in OPD practice, 96.22% preferred to initiate antibiotic therapy based on a positive CBC+CRP+Blood culture/Procalcitonin. It was also observed that 12.30% of practitioners initiated investigation in a fever of less than 3 days duration while 53.84% of practitioners initiated antibiotic therapy in a fever of less than 3 days.

Conclusion: This study concludes that though most practitioners prefer to investigate a fever of more than 7 days, almost 1/3rd of practitioners initiate an investigation in a fever of less than 3 days. Thus, the clinical assessment takes priority over the dictum of set protocol for initiation of antibiotics related to the duration of fever. Regulation of antibiotics and their overuse continues to be a major worry among healthcare guards. The major challenge lies in the years ahead to expand the use of antibiotics and maintain stewardship while prescribing the same.

Keywords: CBC, CRP, OPD, IPD.

1. Introduction

Dating back to the century when penicillin was isolated by Sir Alexander Fleming [1,2] and was later warned about its resistance[3], the world of antibiotics and its therapeutic advancement has now transformed clinical therapeutics[4]. However, with spurious use of antibiotics and poor stewardship antimicrobial resistance (AMR) has now become a global health crisis, exacerbated by a withered antibiotic discovery protocol [5].

Antibiotics can be a lifesaving treatment for children with bacterial infections and are the most commonly prescribed medications among children.[6] However, antibiotics have their own detrimental effects and toxicity on the gut flora[7,8] and enteric immune system.[9,10] Moreover, at the individual and community levels, overuse of antibiotics leads to the development and transmission of its resistance. Amendments to encourage rational antibiotic use is critical for preserving the effectiveness of the presently available drugs.[9-11]

In low resource setups and mass population, rationale use of the antibiotic practice is difficult and hence mass prophylaxis is practiced to avoid outbreaks even in the absence of an infection. There are differences in the practice protocols of antibiotic use on a country, region, and local setup level. Factors influencing being, poor access to care, preferences of health care workers, and parental demands being one of the common cause

The availability of antibiotics without a doctor's prescription varies[12,13] and laws to limit access to antibiotics are often poorly enforced.[13,14,15,16,17,18,19] In some settings, drug shortages may be a major limiter of antibiotic use.[20] Cultural preferences, such as high demand by mothers, also influence patterns of antibiotic use.[21,22] In situations where the healthcare workers are aware of the ideal indication for initiation of an antibiotic, there can be differences between knowledge and practice and availability of resources.[23,24]

Antibiotics are substances produced by microorganisms that selectively suppress the growth (static) of or kill (cidal) other microorganisms at very low concentrations.

Antimicrobial resistance has emerged as a major public health problem all over the world. Infections caused by microorganisms that are resistant to antibiotics fail to respond to treatment, which further results in longer periods of infectivity and an increasing number of infected people in the community.

Drug resistance is defined as the unresponsiveness of a microorganism to an antimicrobial agent and is akin to the phenomenon of tolerance seen in higher organisms.

Acquired resistance is the development of resistance by an organism (which was sensitive before) due to the use of an antimicrobial agent over a period of time. This can pose a great clinical problem.

Resistance could be due to either reduced entry of the drug into the pathogen, resistance due to drug efflux, due to destruction of antibiotics, due to altered target structure, incorporation of the drug, enhanced excision of incorporated drug, heteroresistance, and viral quasispecies, hypermutable phenotypes, and resistance by the external acquisition of genetic elements.[25]

The antibiotic treatment chosen must be based on a probable diagnosis made on some assumption regarding the nature of the disease. The treating doctor usually does not have difficulty in deciding the appropriate antibiotic to treat a disease caused by a single microorganism. – If the causative agent is not known and delaying in initiating an appropriate therapy would be life-threatening or may cause morbidity, empirically started antimicrobial therapy based on a clinically defined infection is justified. The need for antimicrobial therapy should hence be reviewed on a daily basis.

Most alarming of all the diseases are the ones that become resistant to first-line antibiotics and contribute to the post-antibiotic era.

An antibiotic stewardship program is a practice dedicated to using antibiotics only when required and when necessary to target the spectrum suspected using the appropriate dose, route, and duration of therapy. The main goals of this program are to improve patient care, and safety and reduce resistance and health care costs. Inpatient stewardship is usually protocol guided but outpatient stewardship should focus on the judicious use of antibiotics by choosing a narrow first-line antibiotic. With the use of antibiotic stewardship programs, it is possible to reduce 30% of the money spent on antibiotics.

Thus, this study was aimed at evaluating the clinician's outlook on the usage of antibiotics and tackling the upcoming demon of antibiotic resistance.

2. Objectives

Objectives:

1. To assess the most common laboratory parameters advised in OPD and IPD practice for the assessment of fever in children.
2. To evaluate laboratory parameters influencing for initiation of antibiotic therapy in OPD and IPD practice.

Secondary Objectives:

1. To determine the physician's preference to initiate investigation according to the duration of fever in OPD practice
2. To correlate initiation of antibiotic therapy and duration of fever in OPD practice
3. Observe frequently prescribed antibiotic therapy for fever with associated symptomatology in OPD practice.
4. Observe frequently prescribed antibiotic therapy in IPD practice.

Material and Methods:

In the present study, a validated questionnaire was distributed among eligible participants which consist of practicing paediatricians with a qualified degree. A questionnaire was distributed and asked to be filled out and was subsequently collected the next day. Two groups were made.

Group A consists of paediatricians having an outdoor patient facility (OPD) only.

Group B consists of paediatricians with the indoor patient facility (IPD)

Both groups consisted of 70 participants, which after scrutiny;

Group A consists of 65 eligible participants

Group B consists of 53 eligible participants

The given data was further statistically analysed on a percentage basis and the following observations were noted.

Study design: Cross-sectional study

Sample size: Group A: 65

Group B: 53

Inclusion criteria:

1. Practicing paediatricians in an OPD setup
2. Practicing paediatricians in an IPD setup

Exclusion criteria:

1. Incompletely filled questionnaire

Operational Definitions:

1. Fever of unknown origin: Fever of >38C (100.4F), for more than 3 weeks, with more than 2 visits or 1 week in the hospital
2. Antibiotic: Substance produced by microorganisms, which selectively suppresses the growth of or kills other microorganisms at very low concentrations
3. Antibiotic stewardship: A coordinated intervention designated to improve and measure the rational use of antibiotics by promoting the selection of an appropriate drug, a fixed regimen including dose, duration, and route of administration.

3. Results

Group A: 65 (Pediatricians working in OPD setup)

Group B: 53 (Pediatricians working in IPD setup)

Table 1: Laboratory parameters advised in OPD practice for assessment of fever in children.

GROUP A: n=65

LAB PARAMETER	YES	NO	NO COMMENTS
Hemoglobin	2 (3.07%)	61 (93.84%)	2 (3.07%)
CRP	55 (84.6%)	8 (12.30%)	2 (3.07%)
TLC+DLC	40 (61.53%)	10 (15.38%)	15 (23.07%)

CBC+CRP	61 (93.84%)	2 (3.07%)	2 (3.07%)
Procalcitonin	14 (21.53%)	40 (61.53%)	11 (16.92%)
Blood culture	12 (18.46%)	40 (61.53%)	13 (0.20%)

In OPD practice, 84.6% of practitioners prefer CRP while 93.84% of practitioners prefer CBC+CRP as a laboratory parameter of choice for the assessment of fever in children

Table 2: Laboratory parameters advised in IPD practice for assessment of fever in children.

GROUP B: n=53

LAB PARAMETER	YES	NO	NO COMMENTS
Hemoglobin	0 (0%)	50 (94.33%)	3 (5.66%)
CRP	40 (75.47%)	10 (18.86%)	3 (5.66%)
TLC+DLC	12 (22.64%)	22 (41.50%)	19 (35.84%)
CBC+CRP	51 (96.22%)	0 (0%)	2 (3.77%)
CBC+CRP+Procalcitonin	51 (96.22%)	0 (0%)	2 (3.77%)
CBC+CRP+Blood culture	35 (66.03%)	12 (22.64%)	6 (11.32%)

In IPD practice, 96.22% of practitioners prefer CBC+CRP+Procalcitonin as the laboratory parameter of choice for the assessment of fever in children.

Table 3: Laboratory parameters determining the initiation of antibiotic therapy in OPD practice

n=65

LABORATORY PARAMETERS	NO.OF CLINICIANS
HEMOGLOBIN LEVEL	2 (3.07%)
CRP	45 (7.50%)
TLC+DLC	30 (46.15%)
CBC + CRP	52 (80.00%)
CBC+CRP+BLOOD CULTURE	12 (18.4%)
CBC+CRP+PROCALCITONIN	14 (21.53%)

In OPD practice, 80% of practitioners initiated antibiotic therapy based on CBC and a positive CRP report

Table 4: Laboratory parameters determining the initiation of antibiotic therapy in IPD practice

n=53

LABORATORY PARAMETERS	NO.OF CLINICIANS
CRP	26 (49.05%)
CBC+CRP	41 (77.53%)
CBC+CRP+BLOOD CULTURE	51 (96.22%)
CBC+CRP+PROCALCITONIN	51 (96.22%)

In IPD practice, 96.22% of practitioners preferred to initiate antibiotic therapy based on a CBC, a positive CRP, and growth on blood culture and 96.22% of practitioners preferred to initiate antibiotic therapy on a CBC, positive CRP and raised procalcitonin level.

Table 5: Observation of physician's preference to initiate investigation according to the duration of fever in OPD practice

n=65

DAY OF FEVER	NO.OF CLINICIANS
<3	8 (12.30%)
3-5	24 (36.92%)
5-7	30 (46.15%)
>7	63 (96.92%)

In OPD practice, 96.92% initiated investigation in a fever of more than 7 days duration while 46.15% initiated investigation in a fever of 5-7 days duration. It was also observed that 12.30% of practitioners initiated investigation in a fever of less than 3 days duration and 36.92% of practitioners initiated investigation within 3-5 days of fever.

Table 6: Observation of initiation of antibiotic therapy as per the day of fever in OPD practice

n=65

DAY OF FEVER	ANTIBIOTIC THERAPY INITIATED
<3	35 (53.84%)
3-5	56 (86.15%)
5-7	65 (100%)
>7	65 (100%)

In OPD practice, 100% of the practitioners initiated antibiotic therapy in a fever of 5 to 7 days and more than 7 days duration. However, it was also noted that antibiotic therapy was initiated by 53.84% of practitioners in a fever of less than 3 days and 86.15% of practitioners initiated antibiotic therapy with a fever of 3 to 5 days duration.

Table 7: Correlation of symptomatology and preferred antibiotic therapy initiated in OPD practice

n=65

SYMPTOMATOLOGY	CEFIXIME	AMOXYCLAV	AZITHROMYCIN	QUINOLONE	CEFIXIME+ OFLOXACIN	CEFIXIME+ AZITHROMYCIN
ACUTE FEBRILE ILLNESS	32 (49.23%)	18 (27.69%)	5 (7.69%)	10 (15.38%)	10 (15.38%)	12 (18.46%)
ACUTE RESPIRATORY ILLNESS	10 (15.38%)	40 (64.53%)	12 (18.46%)	0 (0%)	0 (0%)	3 (4.61%)
DIARROHEA	20 (30.76%)	0 (0%)	0 (0%)	40 (64.53%)	5 (7.69%)	0 (0%)
OTITIS MEDIA	12 (18.46%)	35 (53.84%)	10 (15.38%)	3 (4.61%)	0 (0%)	5 (7.69%)
SUSPECTED UTI	30 (46.15%)	5 (7.69%)	0 (0%)	22 (33.84%)	8 (12.30%)	0 (0%)

In OPD practice:

- In acute febrile illness, 49.23% of practitioners preferred cefixime as the antibiotic of choice
- In acute respiratory illness, 64.53% of practitioners preferred amoxiclav as the antibiotic of choice
- In diarrhea, 64.53% of practitioners preferred quinolone as the antibiotic of choice
- In otitis media, 53.84% of practitioners preferred amoxiclav as the antibiotic of choice
- In suspected UTI, 46.15% of practitioners preferred cefixime as the antibiotic of choice

Table 8: First-line antibiotic therapy initiated in IPD practice

n=53

ANTIBIOTIC OF CHOICE	NO. OF CLINICIANS

CEFTRIAXONE	12 (22.64%)
CEFTRIAXONE+ AMINOGLYCOSIDE	15 (28.30%)
AMOXYCILLIN+CLAVULINIC ACID+AMINOGLYCOSIDE	8 (15.09%)
PIPERACILLIN+TAZOBACTUM	4 (7.54%)
PIPERACILLIN+TAZOBACTUM+AMINOGLYCOSIDE	12 (22.64%)
MEROPENEM	2 (3.77%)

In IPD practice:

- 22.64% of practitioners preferred ceftriaxone, 28.30% of practitioners preferred a combination of ceftriaxone and aminoglycoside as the first-line therapy
- 15.09% of practitioners preferred to initiate a combination of amoxycillin+clavulinic acid and aminoglycoside as first-line therapy**.**
- Piperacillin+Tazobactum is the preferred line of therapy among 7.54% of practitioners
- While 22.64% preferred to initiate a combination of Piperacillin+Tazobactum+Aminoglycoside as first-line therapy
- Meropenem alone was the antibiotic of choice among 3.77% of practitioners as first-line therapy.

4. Discussion

In a study conducted by Akhtar et al., it was found that 5.6% of drugs were prescribed per patient encounter of which 81.12% of drugs were antibiotics with an average consultation time of 7 minutes only. Hence this study was undertaken to know the appropriateness of the prescription of antibiotics among practicing pediatricians in OPD and IPD practice.

In a study conducted by Bruel et al., it was observed that CRP and Procalcitonin levels for evaluation of fever had a higher diagnostic value and positive likelihood ratio of 2.40 to 3.79 and 1.75 to 3.11. While a complete blood count had a positive likelihood ratio of 0.87 to 2.43 with a minimal diagnostic value when compared to CRP and procalcitonin levels. A combination of CRP and Procalcitonin levels increases the likelihood of a serious infection by 27 to 64%. The study also confirms that CRP and procalcitonin have comparable diagnostic accuracy to rule in bacterial infections and initiate therapy.

Similarly, in a meta-analysis, it has been shown that point-of-care CRP testing significantly reduced antibiotic prescriptions at the primary consultation.

In our study, in the OPD setup, 93.84% of practitioners preferred CBC and CRP as a combination of laboratory parameters as the investigation of choice while only 21.53% preferred to send procalcitonin. This may be contributed to the high cost of procalcitonin levels. In IPD practice, 96.22% preferred a combination of either CBC, CRP, and Procalcitonin or CBC and CRP in case of nonaffordability or inavailability of the test.

In a study conducted by Basu et al., it was observed that about 94.8% of antibiotics were started by pediatricians empirically for fever without investigations while 5.2% of pediatricians only started antibiotics empirically with requests for investigations. It was also found that 35.3% of prescriptions for antibiotics were started without any indication.

In our study, 80% of OPD practitioners started antibiotics on a positive CBC and CRP whereas 96.22% of IPD practitioners started antibiotics on a positive CBC, CRP, and Blood culture or a positive CBC, CRP, and Procalcitonin level.

In a study conducted by Elles et al., it was observed that in patients with fever without a source 71% of cases were started on antibiotics. 78% of practitioners started antibiotics after a positive inflammatory marker, 50.7% started antibiotics after a complete blood count whereas in cases of fever without a source, a blood culture was sent and 73.8% of practitioners started antibiotics. In cases of fever without a source, it was observed that 39% of prescriptions for antibiotics were given by general practitioners while 17% of antibiotic prescriptions were initiated by specialists.

In a study conducted by Amy et al., it was observed that 66.7% of children were started on antibiotics only after documented bacterial infections. When a bacterial infection was suspected, only 16.64% of children were subjected to further laboratory testing before starting antibiotics and the rest were started antibiotics empirically.

In a study conducted by Tapobrata et al., it was analysed that for evaluation of fever, in IPD practice 14.8% of practitioners started antibiotic therapy when not indicated and 11.7% of OPD practitioners started antibiotic therapy with no indication.

In our study, 12.30% of practitioners-initiated investigations within a fever of less than 3 days, while 36.92% started investigating in a fever of duration of 3-5 days. When a fever crossed a duration of 5-7 days 46.15% initiated an investigation while as high as 96.92% of practitioners investigated a fever of more than 7 days duration.

It was also seen that antibiotics were initiated without an indication with a fever of fewer than 3 days and a fever between 4 to 6 days by 8.8% of practitioners and by 55.2% of practitioners with a fever of more than 7 days.

In a study conducted by Rajesh et al., it was observed that in febrile children, an encounter with antibiotics at an index visit was as high as 32% and the most commonly prescribed antibiotic was Cefixime. In our study, antibiotic therapy was initiated by 53.84% of OPD practitioners within 3 days of fever while 86.15% of OPD practitioners initiated antibiotic therapy within 3-5 days of fever. All 100% OPD practitioners initiated antibiotic therapy for a fever of more than 5 or more than 7 days.

In a study conducted by Rajesh et al., it was found that 32% of total cases were prescribed antibiotics of which cefixime was the antibiotic of choice.

In a similar study conducted by S.Basu, it was observed that Amoxycillin was the antibiotic of choice in cases of respiratory illnesses in OPD practice while in IPD practice Ceftriaxone becomes the antibiotic of choice. In agreement with the above study, another study conducted

by Wal Pranay et al. it was observed that the most commonly prescribed antibiotic is amoxycillin+clavulunic acid. On the contrary, Pradeepkumar et al. in their study confirm that the most commonly used antibiotic in pediatric practice is cephalosporins (46.33%).

In our study, in OPD setup in acute febrile illness, 49.23% of practitioners preferred cefixime as the antibiotic of choice while in acute respiratory illness, 64.53% of practitioners preferred amoxiclav as the antibiotic of choice. In diarrhea, 64.53% of practitioners preferred quinolone as the antibiotic of choice and in otitis media, 53.84% of practitioners preferred amoxiclav as the antibiotic of choice. In suspected UTIs, 46.15% of practitioners preferred cefixime as the antibiotic of choice.

In our study, in an IPD setup, 22.64% of practitioners preferred ceftriaxone, and 28.30% of practitioners preferred a combination of ceftriaxone and aminoglycoside as the first-line therapy. 15.09% of practitioners preferred to initiate a combination of amoxycillin+clavulinic acid and aminoglycoside as first-line therapy. Piperacillin+Tazobactum is the preferred line of therapy among 7.54% of practitioners, while 22.64% preferred to initiate a combination of Piperacillin+ Tazobactum+ Aminoglycoside as the first line of therapy. Meropenem alone was the antibiotic of choice among 3.77% of practitioners as first-line therapy.

5. Conclusion:

This study concludes that though most practitioners prefer to investigate a fever of more than 7 days, almost 1/3rd of practitioners initiate an investigation in a fever of less than 3 days. Thus, the clinical assessment takes priority over the dictum of set protocol for initiation of antibiotics related to the duration of fever.

Preference for assessment of fever in children in an OPD practice is usually given to CBC+CRP while to CBC+CRP+Procalcitonin in an IPD practice by practitioners. This disparity may be attributed to the higher cost of investigation of Procalcitonin on an OPD level.

In an OPD practice, practitioners preferred to initiate antibiotics on a positive CBC+CRP report while practitioners in an IPD setup initiated antibiotics with a positive CBC+CRP+Blood culture or a positive CBC+CRP+Procalcitionin level.

It was also observed that almost all practitioners started antibiotic therapy with a fever of more than 5 days in an OPD practice, however, it was also witnessed that in a fever of duration less than 3 days, more than 50% of practitioners initiated antibiotic therapy. This scenario was where clinical assessment superseded the protocol for antibiotic initiation.

The present study enlightens the practical working aspects of a doctor-patient-prescription relationship. A number of environmental factors, geographical and economic factors affect the choice of treatment that a practitioner prefers along with his clinical judgment. It is thus difficult to regulate antibiotic protocols to be a watertight compartment.

However, the regulation of antibiotics and their overuse continues to be a major worry among healthcare guards. A collaborative effort has been undertaken with FAO and NEIVDI to regulate and keep a continuous check on the prescriptions of antibiotics and the emergence of

resistance. The major challenge lies in the years ahead to expand the usage of antibiotics and maintain stewardship while prescribing the same.

6. Limitation of The Study:

1. A small sample size is a limitation of the outcome. A widespread inclusion of practitioners of various disciplines when included would probably give a varied response as the nature of practice varies from practitioner to practitioner.
2. Demography majorly affects practitioners' choice of treatment. In this study, practitioners from an isolated demographical area were included. If the demographical area was to be expanded for the same data, there is a possibility of alteration in the outcome.

7. What Study Adds to Existing Knowledge:

Although time-consuming, blood culture is the gold standard for diagnosis of a bacterial infection and a perfect guide for an antibiotic prescription, Procalcitonin can be considered as an alternate investigation to initiate treatment with an antibiotic as a timely intervention.

8. Financial Support and Sponsorship- The authors have indicated they have no financial relationships relevant to this article to disclose.

9. Conflict of Interest- The authors declare that they have no conflict of interest.

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