

# Clinical Response to Amoxicillin among Children with Acute Suppurative Otitis Media

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## ABSTRACT

**Background:** Acute Suppurative Otitis Media (ASOM) is a very common disease of childhood caused by various bacteria and viruses. Amoxicillin is used as first line antibiotics in the community setting as well as hospital setting.

**Methods:** This is a hospital based prospective observational cross-sectional study. All cases of ASOM of patients under 14 years presenting to the Patan Hospital with duration of less than 6 weeks were included in the study. Ear discharge was collected using sterile cotton swab using aseptic precautions and sent to the Department of Microbiology for further processing. The children were treated with amoxicillin (80mg/kg/day) with maximum dose not exceeding 3g/day and follow up was done after 1 week of antibiotic therapy for clinical responsiveness.

**Results:** Out of 32 cases, 13 cases showed no growth of organism in the culture sensitivity reports. Among remaining 19 cases, 9 were sensitive and 10 were resistant to amoxicillin. Coagulase negative Staphylococcus (7) was the most common organism grown in the laboratory followed by Staphylococcus aureus (4) and Klebsiella pneumoniae (4). Chloramphenicol, linezolid, clindamycin and trimethoprim-sulphamethoxazole were the most common antibiotics sensitive to the organisms grown besides amoxicillin. Out of total 32 patients, 31 were responsive to high dose amoxicillin at the end of 1 week.

**Conclusions:** Oral amoxicillin in high doses is effective in the treatment of ASOM in children.

**Keywords:** ASOM; clinical response; high dose amoxicillin.

## INTRODUCTION

Acute suppurative otitis media (ASOM) or Acute Otitis Media (AOM) is a very common disease of childhood. Approximately 80% of children are affected by AOM during their first 5 years of life.<sup>1</sup> Global AOM incidence rate is 10.85%.<sup>2</sup> A study showed even higher incidence in Nepal i.e. 13% of children under 16 years of age and 23.19% of children under 5 years of age.<sup>3</sup>

Amoxicillin is recommended as first line drug for the treatment of the condition in Nepal.<sup>4,5</sup> Though amoxicillin is widely used to treat ASOM, studies regarding efficacy and clinical response are not done in Nepal. Adequate treatment of ASOM is as necessary as preventing irrational use of antibiotics.

The objective of this study is to observe clinical response to amoxicillin in children <14 years with ASOM and to determine if it is time to change the antibiotic of choice.

## METHODS

This is a hospital based prospective observational cross-sectional study done in Department of ENT and HNS, Patan Academy of Health Sciences (PAHS) from September 2020 to September 2021. Children under 14 years of age with ear discharge of less than 6 weeks with congestion of tympanic membrane with perforation of tympanic membrane were included in the study not having otitis externa and who had not used topical and/or systemic antibiotics and not known allergy to amoxicillin. After

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confirming the diagnosis, informed and written consent was obtained from the patient's guardian.

Sterile swab sticks were used to collect the specimen from external auditory canal. The pinna was pulled upward, backward and laterally in children older than 3 years whereas downwards and backwards in children less than 3 years then sterile swab stick was introduced into the external auditory canal after cleaning with normal saline, gently rotated and taken out. The procedure was carried out under direct vision using light source. The swab was then sent to the Department of Microbiology. The swabbed sample from external auditory canal was inoculated onto Blood agar, Chocolate agar and MacConkey agar plates. The plates were incubated aerobically at  $35\pm 2^{\circ}\text{C}$  with 5%  $\text{CO}_2$  supplement for blood agar. Organisms were identified by Gram staining and different biochemical testing. Antibiotic sensitivity testing was done as per standard CLSI 2019 guideline. The reports were collected by the researcher after 72 hours.

The children were treated with amoxicillin (80mg/kg/day) with maximum dose not exceeding 3g/day and follow up was done after 1 week of antibiotic therapy for clinical responsiveness i.e. no ear discharge and normal tympanic membrane and/or middle ear mucosa. In case of patients not responding to amoxicillin after 1 week i.e., having ear discharge or congested tympanic membrane and/or middle ear mucosa, second line antibiotics was used as per culture sensitivity reports. However, patients were advised to come earlier on follow up if symptoms worsen or general condition of the child deteriorates. Paracetamol was given to the children having pain and/or fever.

Follow up was done after one week and clinical response was evaluated. On otoscopy, dry ear i.e. absence of ear discharge with normal tympanic membrane and in case of perforated tympanic membrane, dry ear with healthy middle ear mucosa was taken as clinically responsive case.

The sample size was 20 considering 10% loss to follow-up.

Calculation was done on the basis of following:

Clinical response rate at the end of amoxicillin therapy(p): 93%<sup>6</sup>

Confidence limit: 10%

Confidence level taken 90%

It is calculated on the basis of following formula from openepi.com

$$n = Z^2(pq)/d^2$$

The data was entered into the computer using Epi Info and Microsoft Excel software and analysed in Epi info and Easy R software. Frequencies and percentage were calculated for study variables. Results were presented in tables and diagrams. P value of less than 0.05 was taken as significant.

## RESULTS

Thirty-two children with ASOM were included in the study from September 2020 to September 2021. Twenty-two (68.75%) were male and 10(31.25%) were female. Out of 32, 13 (40.63%) cases had no growth of organism after 48hours of incubation at  $37^{\circ}\text{C}$ , 19 (59.37%) had growth of bacteria. Dual organism seen in 1 case whereas single organism was seen in rest. Sensitivity to amoxicillin is seen in 9 (47.37%) cases and resistance in 10 (52.63%) cases. Clinically responsive and non-responsive groups and corresponding culture is presented in the figure 2. Fisher exact test was used to see the relation between culture positive cases and clinical responsiveness. It is not statistically significant (p value=1). Only 1 case was clinically non responsive to amoxicillin. In vitro resistance pattern is shown in table 2 and other antibiotics sensitive to Gram positive and Gram-negative isolates is shown in table 3 and 4.

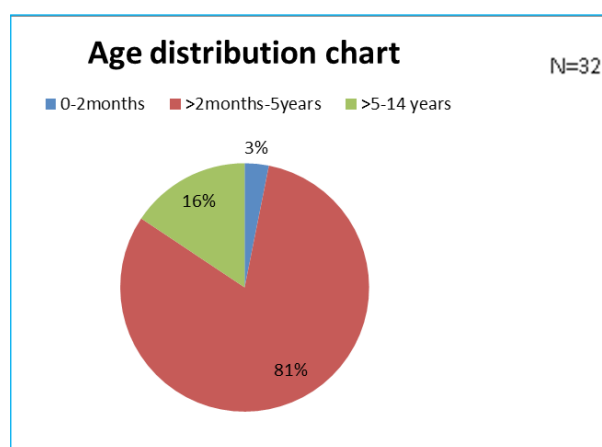
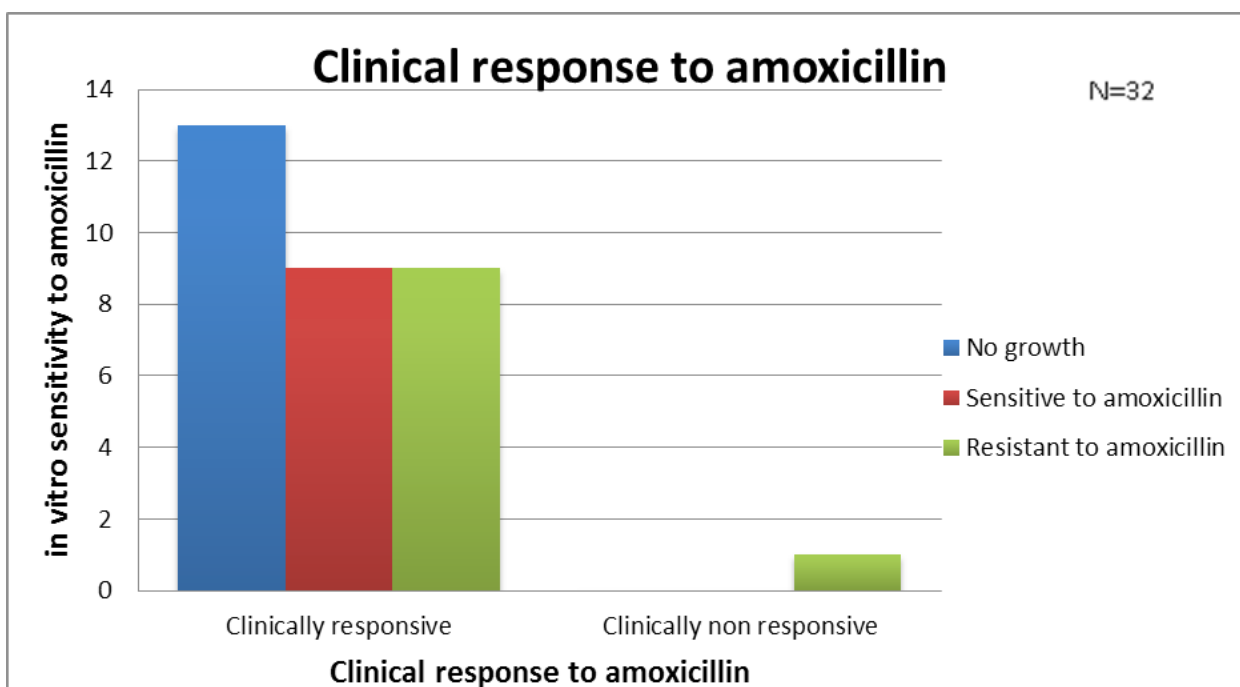


Figure 1. Age distribution chart.

**Table 1. Growth of organism.**

Growth of organism	No. of children	%
No growth	13	40.63
Coagulase negative Staphylococcus	7	21.21
Staphylococcus aureus	4	12.12
Klebsiella pneumonia	4	12.12
Escherichia coli	2	6
Others	3	9
Total	33	100



**Figure 2. Clinical response to amoxicillin.**

**Table 2. In vitro resistance to amoxicillin.**

Isolated organism	Total number of growth	Sensitive		Resistant	
		No. of patients	%	No. of patients	%
Coagulase negative Staphylococcus	7	4	57	3	43
Staphylococcus aureus	4	4	100	0	0
Klebsiella pneumoniae	4	0	0	4	100
Escherichia coli	2	0	0	2	100
Methicillin resistant Staphylococcus aureus	1	0	0	1	100
Klebsiella oxytoca	1	0	0	1	100
Enterococcus spp	1	1	100	0	0
Total	20	9		11	

**Table 3. Most sensitive drugs for Gram positive isolates.**

Antibiotic	Sensitive %	Sensitive	Tested
Vancomycin	100	7	7
Linezolid	92	12	13
Amoxicillin	69	9	13
Chloramphenicol	67	8	12
Clindamycin	50	6	12
Erythromycin	42	5	12
Trimethoprim-sulphamethoxazole	42	5	12
Doxycycline	42	5	12
Gentamicin	42	5	12
Ofloxacin	38	5	13
Ciprofloxacin	25	3	12

**Table 4. Most sensitive drugs for Gram negative isolates.**

Antibiotic	Sensitive %	Sensitive	Tested
Chloramphenicol	100	7	7
Imipenem	100	6	6
Ofloxacin	86	6	7
Amikacin	86	6	7
Meropenem	86	6	7
Ciprofloxacin	71	5	7
Trimethoprim-sulphamethoxazole	57	4	7
Piperacillin tazobactam	57	4	7
Gentamicin	57	4	7
Amoxicillin	0	0	7

## DISCUSSION

AOM is a very common childhood condition. AOM refers to the inflammation of middle ear cleft with rapid onset of signs and symptoms. Various guidelines have recommended treatment of AOM with either watchful waiting or use of antibiotics. Signs and symptoms of AOM usually improve within 24 hours of onset of symptoms regardless of treatment. However use of antibiotics is recommended in case of children under 6 months of age, recurrent AOM, AOM with discharge or with complications and AOM in high risk children including those with Down syndrome, craniofacial abnormalities, congenital inner ear abnormalities, immunodeficiencies.<sup>7</sup> High dose

amoxicillin is recommended in our national guidelines as first line antibiotics for various childhood infections including AOM.<sup>4,5</sup> Amoxicillin at dosage of 40-50mg/kg is found to be effective for the eradication of penicillin-susceptible *Streptococcus pneumoniae* but may be insufficient for the eradication of many drug-resistant *S. pneumoniae* isolates.<sup>8</sup>

Different studies have shown different gender predisposition of AOM. However most studies have shown that it is more prevalent in males and our study also supports so. Though various risk factors for AOM have been identified but gender of the child is not a risk factor. AOM is more prevalent in males than females (68.75% Vs 31.25%) in our study which is similar to study by Sigdel et al.<sup>3</sup> (57% vs. 43%), Mustafa et al.<sup>9</sup> (55% vs. 45%), Kumari et al.<sup>10</sup> (64% vs. 36%) but contrasting to findings by Akinjogunla et al.<sup>11</sup> (46% vs. 54%).

It was more prevalent in the age group >2 months to 5 years, similar to global prevalence in a study by Monasta et al. in which 60.99% were in the age group 1-4 years and 45.28% in the first year of life.<sup>2</sup> The high prevalence in this age group may be due to increased incidence of URTI in this age group and exposure of developing immune system to daycare and environmental allergens. Anatomically, the Eustachian tube in children is shorter and more horizontal hence, infection from nasopharynx can readily spread to middle ear via Eustachian tube.<sup>11</sup> In the study done by Sigdel et al. in tertiary care centre, Pokhara, Nepal; it was more prevalent in the age group 0-5 years (36.5%) and then similar prevalence in the age group 6-10 years and 11-16 years i.e.; 31.7%.<sup>3</sup> The differences in the findings may be due to decreased hospital visit during the pandemic, treatment of AOM according to guidelines in the pediatrics OPD or under 14 clinic by general practitioners, increasing trend of over the counter prescription of medicines including antibiotics; more so during pandemic and differences in case selection.

In our study, 59.37% were culture positive while in a similar study by Piglansky et al., 64% were culture positive<sup>6</sup>, 86% in a study by Kumari et al.<sup>10</sup>, 96.7% in a study by Akinjogunla et al.<sup>11</sup> and 67% in a systematic review and meta analysis by Mather et al.<sup>12</sup> Piglansky et al. evaluated the middle ear aspirate whereas Kumari et al. and Akinjogunla et al. evaluated ear discharge using aseptic precautions. Negative culture implies towards non-bacterial aetiology of the disease or presence of anaerobic bacteria or may be due to unavailability of transport media. Common viruses causing AOM are respiratory syncytial virus, influenza

A virus, parainfluenzae viruses, human rhino and adeno viruses.<sup>13</sup> In a study by Akinjogunla et al, 50.5% of the isolates were Gram positive, 49.5% were Gram negative while 98.5% of the isolates were aerobes while 1.5% were anaerobes whereas in our study 65% isolates were Gram positive and 35% Gram negative. Besides Staphylococcus aureus, other bacteria isolated were Haemophilus influenzae, Moraxella Catarrhalis, Streptococcus pneumoniae, Streptococcus pyogenes, Coagulase negative Staphylococcus spp., Pseudomonas aeruginosa, E. coli, Proteus mirabilis, Proteus vulgaris, Klebsiella pneumoniae and Bacteriodes fragilis.<sup>11</sup>

Coagulase negative Staphylococcus (CoNS) was the most common bacteria isolated in our study. CoNS was also isolated in case of AOM in other studies by Akinjogunla.<sup>11,14</sup> It was present in 10% of cases and amoxicillin resistance was observed in 52% whereas in our study it was present in 35% of isolates and amoxicillin resistance in 43% cases. So we can conclude that coagulase negative Staphylococcus may not just be contamination in our study, as we have thoroughly cleaned the EAC with normal saline before taking the swab for c/s and the procedure was performed in an aseptic technique. Contrary to our findings most other studies suggest Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis as common bacteria causing AOM.<sup>6,7,12,15</sup> Differences in the findings may be due to low sample size in our study or due to change in causative organism over years. Introduction of Haemophilus influenzae type b vaccine in 2009 and Pneumococcal conjugate vaccine in 2015 in the national immunization programme by Government of Nepal can be the possible factor for such finding.<sup>16,17</sup> Cochrane review of 2020 showed that administration of PCV vaccine in early infancy is associated with large relative risk reductions in pneumococcal AOM.<sup>18</sup>

Sensitivity to amoxicillin was 47.37% in our study while it was 71.4% in the study by Kumari et al.<sup>10</sup> Despite majority of culture positive cases (52.63%) were resistant to amoxicillin in vitro; only 1 case (3.12%) was non-responsive clinically. In this case culture showed dual growth of organism i.e. Escherichia coli and Klebsiella pneumoniae, both resistant to amoxicillin. It was in a 2 years old female child who was later treated with syrup chloramphenicol which was sensitive in both Escherichia coli and Klebsiella pneumoniae and she was cured after one week of culture directed antibiotics.

Clinical response was 97% at the end of 1 week for amoxicillin therapy in our study. Clinical success with high dose amoxicillin was 93% in the study done by Piglansky et al.<sup>6</sup> and 85% in a meta analysis by Mather et al.<sup>19</sup>

Adverse effects associated with use of high dose amoxicillin in acute otitis media in children are diarrhoea and generalized rash in a systematic meta analysis by Hum et al.<sup>20</sup> However, no any adverse effects of drug or allergy were seen in our study.

Limitation of our study are limited sample size, decreased hospital visit during COVID pandemic, transport media not used during transport of sample to microbiology laboratory and unavailability of anaerobic culture in our setting and possible viral cause of the disease. Viral PCR may have further proved the viral etiology.

Hence, high dose amoxicillin was found to be effective in treating ASOM in children at the end of 1 week therapy in our study though in vitro resistance was seen 31.24% cases.

## CONCLUSIONS

From our study we observed that high dose amoxicillin was effective in treating ASOM in 31 out of 32 children. Though resistance to amoxicillin was seen in 10 cases, 9 responded to high dose amoxicillin (@80mg/kg/day) treatment. Though the causative organism isolated were totally different than expected but high dose amoxicillin being clinically responsive in all except one case, can still be used as first line antibiotics for ASOM. Other oral antibiotics that can be used as second line agents are chloramphenicol, linezolid, clindamycin and trimethoprim-sulphamethoxazole.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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