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# Resistant Bacteria in Children with Prolonged Tracheostomy (> 2 Weeks): A Cross-Sectional Study in Tehran, Iran

**Mohammad Vafaee-Shahi[1], Samileh Noorbakhsh[2]*, Leila Tahernia[3] and Aina Riahi[4]**

[1]*Associate Professor of Pediatric Neurology, Pediatric Growth and Development Research center, Iran University of Medical Sciences, Tehran, Iran*

[2]*Professor of Pediatric Infectious Disease, Department and Research Center of Pediatric Infectious Diseases, Iran University of Medical Sciences, Tehran, Iran*

[3]*Fellowship of Pediatric Intensive Care, Children Medical Center, Tehran University of Medical Sciences, Tehran, Iran*

[4]*Pediatrician, Iran University of Medical Sciences, Tehran, Iran*

***Corresponding Author:** Samileh Noorbakhsh, Professor of Pediatric Infectious Disease, Department and Research Center of Pediatric Infectious Diseases, Iran University of Medical Sciences, Tehran, Iran.

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## Abstract

**Objective:** To determine the resistant bacteria in children with prolonged tracheostomy (> 2 weeks).

**Methods:** This observational cross-sectional study was performed on all PICU admitted children with prolonged (> 2 weeks) tracheostomy during 4 years. After initial exams, the culture was taken and transported in the transport medium. The organisms were identified and antibiotic susceptibility first by disc method and E test method in resistant cases had done. Chi-square values were calculated for all categories. P value < 0.05 was considered significant.

**Results:** From 51 samples (18 cases); 94% of cases had at least one positive culture. *A. baumannii* (47%) was the most common of samples. The frequency of *K. pneumonia, P. aeruginosa* and MRSA was 26%, 12%, and 7%, respectively. All *S. aureus* (100%) were sensitive to linezolid but just 33% were sensitive to trimethoprim. *Acinetobacter, E. coli* and *K. pneumonia* were 100% sensitive to colistin. *P. aeruginosa* was resistant (85%) to ceftazidime. The highest resistance rate (100%) were observed for ciprofloxacin, clindamycin, erythromycin, oxacillin and penicillin. Determination the MIC level (E-test) had done for 7 grams negative organisms (colistin) and 2 MRSA (vancomycin). Duration of tracheostomy and previous antibiotic usage had a good correlation with positive culture and presence of high antibiotic resistance organisms. But no correlation observed between duration of tracheostomy and underlying disease.

**Conclusion:** Given the long-term of tracheostomy with complications such as infection and their antibiotic resistance pattern, care should be taken during hospitalization in preventing these patients to infection. The rational use of antibiotics would prevent the antibiotic resistance in children with prolonged tracheostomy.

***Keywords:*** *Bacterial Strains; Antibiotic; Resistance; Children; Long-Term Tracheostomy*

## Introduction

Tracheostomy is one of major treatments for problem in upper airway. If an airway is needed for a long-term period, the tracheostomy is the best choice [1,2]. Children are more vulnerable than adults due to physiology and premature structure of airways, lower respiratory reserve and smaller airways compared to adults [3-5]. More than 50% of tracheostomy cases has been for the establishment of long-term ventilation and 40% has been carried out for management of upper airway obstruction (usually due to respiratory infections) and neurological disorders [4,5]. The use of tracheostomy in treatment of obstructive infectious causes decreased from 7/6% to 1/1%. Tracheostomy often was indicated after long-term intubation (prolonged intubation) and in the next level to fix airway obstruction and establishment of pulmonary toilet [7,8]. Due to the underdeveloped physiology and structure of the airways in children and the different causes and complications of tracheostomy in them, obstructions and problems associated with these pathways are of particular importance. Broncho-pulmonary dysplasia and neurological disorders have been mentioned as the major causes of tracheostomy in children [9-11] in pediatric group, tracheostomies were mainly performed electively. The overall complication rate was 29%. Mortality was 59% and there was one death related to the tracheostomy procedure [10]. The early complications (in early hours): bleeding, pneumothorax, surgical damage on esophagus and recurrent laryngeal nerve, the late complications: trachea-cutaneous fistula, tracheal constriction, trachea-esophageal fistula, tracheomalacia and delayed bleeding [12-15]. The total complications of tracheostomy and mortality rate have been reported 49% and 2%, respectively [10,11]. Nosocomial infections are one of the most common causes of increased length of hospital stay, hospital costs and mortality Thus, obtaining an organism does not necessarily mean pneumonia, but because choosing the appropriate initial antibiotic is effective in the survival of the patient with VAP [10-12]. The microbial resistance is one of the major problems in the healthcare sector, which is more evident in developing [13,14]. The antimicrobial resistance or drug resistance is to reduce the effect of a drug in treatment of a disease or to reduce its effect on the improvement of clinical symptoms. The microbial resistance occurs naturally, but the abuse of antibiotics in humans and animals significantly speeds up the process of microbial resistance. In fact, microbial resistance means the resistance of a microorganism to one or more antimicrobial drugs which have been susceptible to these drugs before [10,14]. Therefore, the results of microbiology and resistance pattern of microorganisms are very important in the choice of treatment regimen [15,16]. McCaleb., *et al*. reported the respiratory microbiology of children with long-term tracheostomies [17]. The prevalence of pneumonia in tracheostomy patients is 21 times more than other patients and the risk of illness is increased by 1 - 3% per every one day of endotracheal tracheostomy and mechanical ventilation [13,14]. Lower respiratory tract colonization is common following endotracheal intubation [15-17].

Nosocomial infections have been reported in up to 30% in developing countries, like Iran [18,19]. In recent years, we have seen a significant increase in bacterial isolates with multiple resistance patterns in our field, which by definition refers to bacteria that are resistant to at least one of three classes of antibiotics, including beta-lactamase, aminoglycosides and fluoroquinolones [18]. According to the recent studies, the highest rate of gram-negative bacterial infections is reported in hospital PICUs. Patients with serious condition, prolonged hospitalization in this ward, the use of invasive devices such as catheter, tracheal tube, broad-spectrum antibiotic use in these patients are influential factors in high infection rates in this ward [19,20,22]. The microbial resistance to a variety of pathogens, including bacteria, parasites, viruses, fungi, and cancer cells, can be life-threatening at any age and in our country like others [20,22].

Hospitalization of children in PICU ward of Rasool Akram Complex (3$^{rd}$ level of care) from various hospitals is due to presence of active ENT ward and other related specialties especially pediatric, neurology, infectious and neurosurgery which related patients require long-term tracheostomy. All data for prolonged tracheostomy in children (different causes; complications, obstructions) are of particular importance which may not be addressed in our country which may not be addressed in our country. Moreover, physicians and medical professionals are not informative enough about specific data about this age category. Indeed, one of the problems of these patients was recurrent infection of the tracheostomy site. The use of multiple antibiotics in these patients often resulted in antibiotic resistance and would increase the length of hospital stay and antibiotic use.

## Aim of the Study

The aim of this study was to determine the bacterial strains and antibiotic susceptibility pattern of these strains in patients admitted to PICU with long-term tracheostomy (> 2 weeks) in 3rd level referral hospital (Rasoul Akram) in Tehran, Iran.

## Materials and Methods

This description/cross-sectional study was performed upon 18 children with prolonged tracheostomy (> 2 weeks) admitted to the pediatric intensive care unit (PICU) of Rasoul-e-Akram (2015-2019); Tehran, Iran.

This study was approved by the Ethical Committee in Research Center of Pediatric Infectious Diseases affiliated by Iran. The reference number with ethical committee approval was…. University of Medical Sciences. The study was committed to the principles of Helsinki and written informed consent was obtained from the parents of all children enrolled in the study. Performing all clinical examinations and diagnostic tests will be at the expense of the plan.

Initially, a check list was completed for each case by an authorized physician. The culture was taken from the tracheostomy site by sterile method and sent to the Research Laboratory of Rasool Akram Hospital in a bacterial transport medium containing nutrients. The organisms were identified by standard laboratory methods. In order to determine antibiotic susceptibility, the disc method first determined the susceptibility and resistance of each microorganism to the prescribed antibiotic types. For the types of microorganisms that were likely to be antibiotic resistant, E test method determined the MIC level for each type of antibiotic. Referring to the standard tables available, the types of refractory and susceptible webinars will be identified.

**Data collection:** Check list covering different aspects: personal information (e.g. sex, age, type of underlying disease, previous antibiotic intake, physical examination), lab tests (type of microorganism isolated by laboratory expert approval, determination of antibiotic susceptibility by disc diffusion, determination of specific MIC of for resistant organisms (sensitive, intermediate, resistant).

**Statistical analysis:** All analyses were conducted by SPSS-22. Descriptive statistical techniques were used to analyze the descriptive data. Mean and SD were used for quantitative variables and percentage was used for qualitative variables. Pearson and Spearman correlate on tests were also used to analyze the data. Chi-square were calculated for all categories. The Student's t test was used to determine significant differences in means of all continuous variables. Chi-square values (CI 95%, $p < 0.05$) were calculated for all categories. P value $< 0.05$ was considered significant.

## Results

During this study, 18 patients (range of age = 1 month - 11 years; mean age = 5.6 ± 3 years); 44% (n = 8) were male, 56% (n = 10) were female. Five cases (28%) had no underlying disease; but, 13 cases (72%) were reported with Down syndrome, nephrotic syndrome, atrial septal defect, Werdnig Hoffman, pneumonia, seizure, cerebral pulse, Subglottic stenosis, laryngeal web, laryngomalacia, cerebral teratoma, cerebellar medulloblastoma, brain tumor, cerebral medulloblastoma, and astrocytoma.

Causes of tracheostomy (n = 18): the most frequent cause for prolonged intubation was Brain Mass (Cerebral teratoma, astrocytoma, medulloblastoma, unidentified) in 26% [5]; laryngeal anomalies (laryngeal web, laryngomalacia, subglottic stenosis) 17% [3]; cerebral damage (Epilepsy/seizure, head trauma, cerebral palsy, electrical injury, decreased level of conscientious due to metabolic, intoxication etc.) 28% [5]; respiratory distress (aspiration pneumonia, swallowing disorder, respiratory distress despite intubation) 17% [3]; Tracheal papillomatosis 6% [1]; Prolonged intubation 6% [1].

Total 51 tracheal samples were studied during the study period;94% of cases had at least one positive culture (Table 1).

| First culture result | Number | Percentage | Further culture results | Number | Percentage |
|---|---|---|---|---|---|
| Positive | 12 | 67% | Positive | 10 | 56% |
| | | | Negative | 2 | 11 |
| Negative | 6 | 33% | Positive | 5 | 28% |
| | | | Negative | 1 | 6 |
| Total | 18 | 100% | Total | 18 | 100% |

***Table 1****: The frequency of positive cultures from tracheostomy site in PICU patients.*

From 51 cultured samples, 43 cases were positive. *A. baumannii* isolated from 47% of cases, *K. pneumonia, P. aeruginosa* and methicillin-resistant *S. aureus* were isolated in 26%, 12%, and 7%, respectively (Figure 1).

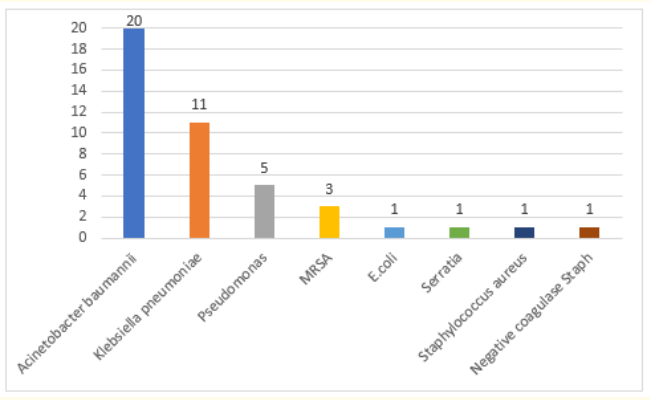


***Figure 1:*** *The types of organisms isolated from patients.*

The susceptibility and resistance of the *A. baumannii* determined, 100% of isolate were sensitive to colistin, the highest resistance (95%) observed for piperacillin (Figure 2).

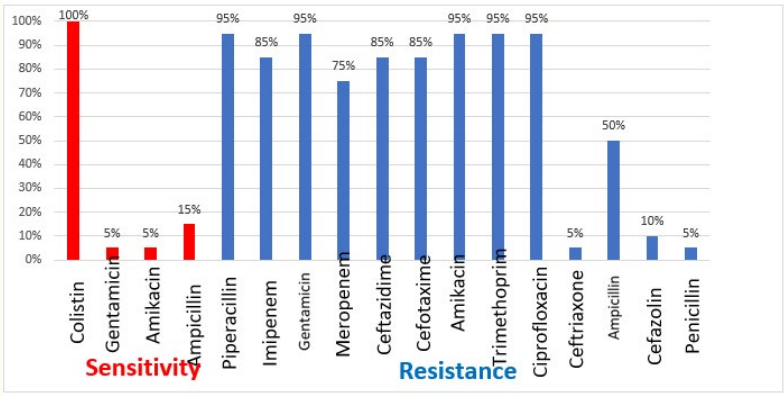


***Figure 2:*** *Sensitivity and resistance of isolated A. baumannii to antibiotics.*

*Serratia* had 100% sensitivity to trimethoprim; amikacin, meropenem, imipenem and ceftazidime, piperacillin, ciprofloxacin and the most resistant observed for colistin (100%).

*E. coli* were highly sensitive to piperacillin, imipenem, meropenem, ciprofloxacin, colistin. *P. aeruginosa* were 100% sensitive to gentamicin and amikacin, piperacillin, ciprofloxacin, but was resistant (40%) to cefotaxime. *K. pneumonia* was 100% susceptible to colistin but resistant (36%) to amikacin. The highest resistance was also observed to ceftazidime (100%).

All *S. aureus* isolates (100%) were sensitive to linezolid. But just 33% were sensitive to trimethoprim.

MIC level were measured by E-test method in 9 samples; 7 for colistin and 2 samples for vancomycin. The antibiotic MIC level (E-test method) for different microorganisms showed in table 2.

| Antibiotic | Mean MIC | Standard Deviation | Minimum | Maximum |
|---|---|---|---|---|
| Colistin | 1.04 | 0.27 | 0.75 | 1.5 |
| Vancomycin | 1.25 | 1.06 | 0.5 | 2 |
| Total | 1.09 | 0.45 | 0.5 | 2 |

***Table 2:*** *The antibiotic MIC level (E-test method) for different microorganisms.*

According to the result of Pearson's test, totally there was no significant relationship between previous antibiotic use and positive culture (P-value > 0.05). But a significant correlation between the duration of tracheostomy and positive culture were seen (P-value = 0.000). In this way, increasing the duration of the patient's tracheostomy increases the chances of positive culture.

There was no positive relation between underlying disease and positive culture (P-value = 0.067). There was a significant inverse relationship between previous antibiotic use and gentamicin sensitivity (P-value < 0.05). However, prior antibiotic use reduced the susceptibility of microorganism to gentamicin antibiotic. No significant relationship was observed in other antibiotics (P-value > 0.05).

The antibiotic resistance was not related to duration of tracheostomy duration for imipenem and meropenem, ceftriaxone ampicillin, cefazoline, clindamycin, erythromycin oxacillin, penicillin and colistin (P-value = 0.241, 0.297, 0.772, 0.366, 0.529, 0.473, 0.473, 0.473, 0.588, 0.919); but a good relation were seen for other antibiotic resistance: Piperacillin, gentamycin, ceftazidime, cefotaxime, amikacin, trimethoprim, ciprofloxacin (p value: 0.001, 0.009, 0.001, 0.013, 0.009, 0.042, 0.004) (Table 3). Thus, increasing the duration of tracheostomy has increased the resistance of the isolated microorganisms to some antibiotics.

| Resistance | Piperacillin | Imipenem | Gentamycin | Meropenem | Ceftazidime | Cefotaxime | Amikacin | Trimethoprim | Ciprofloxacin |
|---|---|---|---|---|---|---|---|---|---|
| Correlation coefficient | .446** | 0.241 | .362** | 0.149 | .453** | .346* | .362** | .286* | .400** |
| P-value | 0.001 | 0.095 | 0.009 | 0.297 | 0.001 | 0.013 | 0.009 | 0.042 | 0.004 |
| Number of cultures | 51 | 49 | 51 | 51 | 51 | 51 | 51 | 51 | 51 |
| Resistance | Ceftriaxone | Ampicillin | Cefazoline | Clindamycin | Erythromycin | Oxacillin | Penicillin | Colistin | |
| Correlation coefficient | -0.042 | 0.135 | -0.090 | -0.103 | -0.103 | -0.103 | 0.078 | 0.015 | |
| P-value | 0.772 | 0.366 | 0.529 | 0.473 | 0.473 | 0.473 | 0.588 | 0.919 | |
| Number of cultures | 50 | 47 | 51 | 51 | 51 | 51 | 51 | 51 | |

***Table 3:*** *The relationship between tracheostomy duration and microbial resistance.*

## Discussion

Eighty children (mean age- 5.3 years) with prolonged tracheostomy (> 2 weeks) were studied in the current study. Among the causes leading to tracheostomy, the most common causes was brain masses (28%) and brain injury (26%), laryngeal anomalies (17%) Non-infectious causes (88%), infectious causes (6%) and unknown causes (6%) resulted in tracheostomy. The mean age of studied cases (with prolonged intubation > 2 weeks) is very close to Yazdi., *et al*. and Car MM., *et al*. (mean age = 2.6 years).

In the last decade due to some reasons (increasing the NICU and PICU; increased prolonged mechanical ventilation) admission insertion the tracheotomy tube increased in pediatric group [1-5].

The most common causes of tracheostomy in studied children with prolonged intubation resulted by neurologic disorders and airway obstruction in form of subglottic stenosis which were similar to the studies by some authors [9-11]. According to Kremer., *et al*. report (25 children < 6 years); long-term intubation and congenital anomalies of the upper respiratory tract was the most causes for prolonged tracheostomy [10].

İlçe., *et al*. published his experience in pediatric tracheostomy in 14 children (mean age = 30.3 months; range = 1 week-13 years) [9]. Causes for tracheostomy: prolonged intubation (n = 5), subglottic stenosis (n = 3), general body trauma (n = 2), tracheomalacia (n = 2), tracheoesophageal cleft (n = 1), cervical tumor pressing trachea and larynx (n = 1), congenital myotonic dystrophy plus respiratory failure (n = 1), burn injury of trachea and esophagus (n = 1), and foreign body aspiration (n = 1). Tracheostomy was performed after prolonged intubation, in later stages to remove upper airway obstruction and finally pulmonary drainage. But it was contrary to the study of Izadi., *et al*. which the most common causes leading to tracheostomy were the non-infectious causes of larynx and brain masses.

Mc Caleb el also described the respiratory microbiology in 93 children (mean age = 0.84, range = 0.36 - 3.25y), with long-term tracheostomies. The results was different from us. *P. aeruginosa* (90.3%) was the most common and MRSA (55.9%) was the second common organisms [17].

Here, the previous use of antibiotics has increased the resistance of the microorganism to the antibiotics of gentamicin and ceftazidime. Although there was no significant relationship between underlying disease and positive culture, a significant correlation was reported between tracheostomy duration and positive culture (P-value < 0.05); A considerable relation was reported between duration of tracheostomy and resistance to antibiotics including piperacillin, gentamicin, ceftazidime, cefotaxime, amikacin, trimethoprim and ciprofloxacin. There was a meaningful correlation between previous antibiotic use and gentamicin; ceftazidime resistance. Therefore, according to the findings of the present study, previous antibiotic use increased resistance and decreased susceptibility of microorganisms to antibiotics.

Like the Grosse-Onnebrink., *et al*. study, *A. baumannii* defined as a risk factor for lower respiratory tract infections in cases with tracheostomy [12]. They studied 51 tracheal samples; 94% of cases had at least one positive culture. Out of 3 cases (84.3%) were positive with the highest frequency of *A. baumannii* (47%), *K. pneumonia* (26%), *P. aeruginosa* (12%) and MRSA (7%). Amini., *et al*. showed the bacterial colonization in tracheal tubes of ICU patients [20] Like us, Peimanni., *et al*. [19] reported the multidrug-resistant *A. baumannii* in Tabriz (northwest of Iran).

Saiman., *et al*. study is very close to present study [16]. Out of 717 cases in PICU residents (mean age = 2.6; range = 0.4 - 9.1 years); 215 (30.0%) had tracheostomies [16].

In the study of Aminzadeh., *et al*. the most common microorganism was Coagulase positive *Staphylococcus* which was inconsistent with the present study. The most common gram-negative bacteria found in Aminzadeh [18] were *Klebsiella* and *Acinetobacter*, similar to the present study.

Here, *A. baumannii, E. coli* and *K. pneumonia* were 100% sensitive to colistin. *Serratia* had 100% sensitivity to trimethoprim.

The current study showed that MRSA was 100% susceptible to linezolid but just 33% were sensitive to trimethoprim. The highest resistance was to ciprofloxacin, clindamycin, erythromycin, oxacillin and penicillin (100%).

Thus, similar to other studies confirming rapidly developing drug resistance and ineffectiveness of antibiotics [22,23] many factors promoted infection among hospitalized patients, such as increasing the age of patients, chronic diseases in patients, use of potentially self-infectious invasive diagnostic therapies, the spread of drug-resistant bacteria in hospitals and the lack of proper adherence to the principles of personal and public health in hospitals could be considered as major contributors [15,16,22]. Drug resistant isolates are also reported today in other hospital wards, indicating their high importance in causing different clinical infections in hospitalized patients [25]. The high rates of complications, particularly respiratory tract infection (RTI), have been reported in patients with chronic tracheostomy (CT). However, past CT studies have been more relevant to hospitalized patients. This study followed colonization patterns of upper and lower respiratory tract bacteria and recorded all upper respiratory tract infections in 39 patients with chronic tracheostomy over a 12-month period. In 95% and 83% of patients, one or more potential pathogens were formed at the site of ostomy and in the trachea, respectively. *S. aureus*, gram negative *Enterobacteriaceae* and *P. aeruginosa* were the most common colonized bacteria in these areas. Only 18 of 39 patients (46%) were treated with antibiotics due to RTI. Of these patients, only five episodes of pneumonia were recorded in 4 patients, corresponding to approximately 10 patients per 100 years. They concluded that patients with chronic tracheostomy did not cause severe problems [11].

In critical parts of the hospital, including ICU ward, due to the existence of multiple intrinsic and acquired drug resistance mechanisms towards antimicrobial agents, physicians and infectious specialists have faced serious problems in choosing the appropriate medication for the treatment of infections. This bacteria causing infection in different parts of the hospital often exhibits wide drug resistance patterns and causes mortality especially in ICU ward [20-22].

## Research Limitation

Prior antibiotic use by the patient reduces the likelihood of cultures and inoculating microorganisms on admission. Using BACTEC culture method instead of the usual method compensated this defect. The time of study increased to adequately evaluate the number of each type of microorganism, to evaluate more precisely for the determination of drug resistance and limitations in the preparation of standard microbial strains required for susceptibility testing (due to difficulty in preparation, economic sanctions or loss of germs during transport and...).

## Conclusion

Given the long-term of tracheostomy with complications such as infection and their antibiotic resistance pattern, care should be taken during hospitalization in preventing these patients to infection. The rational use of antibiotics would prevent the antibiotic resistance in children with prolonged tracheostomy.

## Ethics Approval and Consent to Participate

This study was accredited by Ethical Committee of Iran University of Medical Sciences. Helsinki Declaration was respected across the study and the informed consent form was signed by the parents.

## Competing Interests

The authors declare no conflict of interest in preparing this study.

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## Authors' Contributions

NS designed and supervised the study, writing the initial report.

VM visited and interpreted the patients data; AS and RA analyzed data.

TL were major contributors in rewriting and English editing the manuscript.

All of authors read and approved the final manuscript.

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