Clinical Cancer Investigation Journal-ISSN: 2278-0513

Investigating the bacterial causes of fever in 2-month to 14-year-old febrile children admitted to Afzalipour Hospital of Kerman

Abstract

Fever is one of the most common reasons for admission to the emergency department, especially at the age of under 3 years. In some cases, there are no localizing clinical signs in febrile children, and in some cases, children suffer from bacteremia, which has severe consequences. The present study aims to investigate the cause of bacteremia in 2-month to 14-year-old febrile children without any other clinical symptoms.

The present study was carried out on 2-month to 168-month-old children hospitalized due to non-localizing fever in the pediatric wards of Afzalipour Hospital in Kerman. The blood samples of the patients were sent to the hospital laboratory in a BACTEC culture medium, and the interpretation of the results was expressed as sensitivity and resistance to antibiotics.

In this study, 93 children were investigated, 62 of which were male, and 31 (33.3%) were female. Their mean age was 3 years, and the mean hospitalization time was 5 days. Also, 18.3% had an underlying disease, and 37.6% had a history of receiving antibiotics. Additionally, 26.9% had a positive blood culture, 6.5% had a positive urine culture, and 3.2% had positive CSF cultures. Based on this study's results, bacteremia's prevalence differs in different regions and times. Our patients' most common diagnosis was pneumonia, followed by pyelonephritis. The most common causes of bacteremia were pneumococcus, Klebsiella, and Staph epidermidis. One of the limitations of our study is the negative blood culture in a great number of the patients, which may be due to the history of previous antibiotic use or other causes. In general, a quick diagnosis of bacterial infection in febrile children can be helpful in prognosis and selecting an appropriate antibiotic. Also, lack of diagnosis causes serious complications, and unnecessary treatment causes antibiotic resistance.

Keywords: Fever, bacteremia, Children, Antibiotic

Ali Hosseininasab
The infectious and tropical research center, Kerman University of medical sciences, Kerman, Iran

Maryam Ebrahinpour*
Assistant Professor of Neonatal-perinatal Medicine, Pediatric Department, School of Medicine Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran
Dr.mebrahimpour66@gmail.com

Maryam yavarzadeh
Pediatrician, Kerman University of Medical Sciences, Kerman, Iran

Niousha Ebadirad
Dentistry student, Department of dentistry, University of Debrecen medical school Hungary

Fatemeh Sabzevari
Assistant Professor of Neonatal-Perinatal Medicine Department of Pediatrics, School of Medicine Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran

Introduction

Fever is one of the most common reasons for admission to the emergency department in children under 3 years of age. It accounts for 10-35% of hospitalizations in children (1). In some cases, there are no localizing clinical signs in febrile children, called FWLS (Fever without Localizing Sign) (2). Early studies have reported the prevalence of bacteremia at 1.6% to12.9% (3). Small children with fever, in some cases, have bacteremia, which results in severe consequences. Differentiating the presence of bacteremia from simple viral infections in the clinic practically provides diagnostic and treatment problems for emergency physicians. Quickly diagnosing bacterial infections in hospitalized children with fever results in correct and early treatment. It provides important information about patients' prognosis and the appropriate antibiotic choice. However, failure to diagnose and treat children with bacteremia quickly and properly causes serious complications, and sometimes it leads to death, and unnecessary antibiotic treatments cause antibiotic resistance (4).

Organisms that are responsible for bacteremia are Streptococcus group B, Listeria monocytogenes (late neonatal sepsis and meningitis), community-acquired pathogens including Salmonella (enteritis), Escherichia coli (urinary tract infections), Neisseria meningitides, Streptococcus pneumoniae, Haemophilus influenzae type B (sepsis and meningitis) and Staphylococcus aureus (bone-joint infections) (5). Therefore, knowing the common organisms helps to select the appropriate antibiotic, shorten the hospitalization period, and reduce antibiotic side effects (6). Complete blood count (CBC) has been widely studied as a potential tool in diagnosing acute bacteremia. Some studies have indicated that the ability to predict bacteremia in febrile children using the erythrocyte sedimentation rate (ESR) is less useful than CBC. However, other studies have shown that the serum concentration of C-reactive protein (CRP) may be more accurate in distinguishing viral from bacterial infections than CBC. In some studies, increasing serum prolactin levels is more appropriate for diagnosing bacteremia (7). Currently, the guidelines for dealing with 3 to 36-month-old children with high fever and without any localizing signs is to take a sample for blood culture and start intramuscular antibiotics until the result of the blood culture is reported if there is no indication for hospitalization (8). Thus, early diagnosis of bacteremia helps in early treatment, reduces the mortality rate caused by bacteremia, and prevents the development of antibiotic resistance. Given what was stated above, the present study aims to investigate the causes of bacteremia in 2-month to 14-year-old febrile children admitted to Afzalipour Hospital in Kerman.

Methods:

This cross-sectional study was carried out in 2019 on 2 to 168-month-old children hospitalized due to non-localizing fever in the pediatric department of Afzalipour Hospital of Kerman. The patients only had fever without any other clinical symptoms. Patients with viral symptoms such as coryza, conjunctivitis, typical viral skin rashes and those with underlying diseases such as malignancy, weak immune system, neutropenia and those who were unwilling to cooperate were excluded from the study. To collect blood from children, delicate needle tops or scalp veins were used. The sampling area was cleaned with gauze soaked in isopropyl alcohol or 70% ethyl alcohol in a circular motion from the inside to the outside. After drying the area in the air, 5 cc blood samples were taken from children at an angle of 30 degrees or less while the diagonal part of the needle tip was upwards by the laboratory personnel of Afzalipour Hospital to prevent hemolysis and reduce the irritation caused by the contact of the needle tip with alcohol and the skin. Then, the samples were sent to the Afzalipour hospital laboratory in a BACTEC culture medium. The interpretation of culture results was expressed as sensitivity and resistance to antibiotics. Other information (including age, gender, antibiotic history, WBC, ESR, CRP, blood culture results, fever, and clinical diagnosis) was collected by referring to the patient's medical records. After collecting the data, the data were statistically analyzed using SPSS-14 software.

Results:

In this study, 93 children with asymptomatic fever were investigated. The patients were referred only because of fever and had no other clinical symptoms except for the fever. Among them, 62 people (66.7%) were male and 31 33.3%) were female. The mean age of the patients was 3.10 years with a standard deviation of 0.09. The duration of hospitalization was 5.71 days, with a standard deviation of 0.33. In the course of hospitalization and disease, the diagnoses were determined, and the type of antibiotic used was investigated (Tables 1 and 2). Fifty-six people (60.2%) had a fever for less than 5 days, and 37 people (39.8%) had a fever for more than 5 days. Seventeen people (18.3%) had a history of an underlying disease, and 35 people (37.6%) had taken injectable antibiotics. Twenty-five people (26.9%) were positive for B/C culture, which type of bacteria is shown in Chart 1. Six people (6.5%) were positive for U/A culture, and 3 people (3.2%) were positive for CSF culture. The mean CRP was 34.65±3.57, the mean ESR was 39.19±6.92, the mean WBC was 18751.72±68.82, the mean hemoglobin was 10.7±1.70, and the mean poly was 55.51±19.21.

Discussion and Conclusion:

Bacteremia is considered one of the most serious and threatening infectious diseases in children and may be caused by a wide range of Gram-positive and Gram-negative microorganisms (9). Diagnostic cultures positively affect antibiotic treatment and should be prepared before antimicrobial treatment (10). The prevalence of bacteremia infection varies in different regions and at different times. The prevalence of bacteremia in hospitalized children in Bandar Abbas (6.46%) (11), Tehran (6.53%) (12), Turkey (11.18%) (13), Malawi (17.2%) (14), Kenya (15), Mozambique (16) and Tanzania (17), admitted to the hospital with fever, was reported in the range of 4.9% to 5.8%. This difference in the prevalence of different regions is because the bacteremia agents are different in different regions.

In our study, the prevalence of asymptomatic fever was higher in males than females. In general, the mean age of the patients was 3.10 years, and the duration of hospitalization was 5.71 days. Most disease diagnoses were related to pneumonia (30 people), viral infection (9 people) and pyelonephritis (8 people). Almost all patients had a history of taking antibiotics, and 35 had also taken injectable antibiotics.

In our study, the frequency of asymptomatic fever in males was higher than in males. As in our study, in Nemati et al., asymptomatic fever was higher in males than females (11). In the study conducted by Jafari et al. (2018), males also had the highest number of asymptomatic fever cases. Among them, one patient died, and the rest of the patients had limited fever during hospitalization or follow-up visits (18). In our study, 25 people were positive for B/C culture, 6 were positive for U/A culture, and 3 were positive for CSF culture out of 93 people. In the study conducted by Chitsaz et al. in Tehran Children's Medical Center, the rate of positive blood culture was reported at 53.6% (12), which is almost similar to the study conducted by Nemati et al. in Bandar Abbas (6.46%) (11).

In the study conducted in Turkey, among 8942 blood culture samples, 1000 cases were positive.

In the study conducted by Blomberg et al. in Tanzania, 13.9% of blood cultures were positive (13). In the study by Walsh et al. in Malawi, among 2123 blood culture samples taken from patients with fever without a specific cause, 365 cases (17.2%) were positive (14). In the study conducted by Curson, using the PCR technique, out of a total of 101 samples, 25 cases were positive, of which 10 people had negative blood cultures, and 15 people had positive blood cultures, of which 6 cases were caused by Gram-positive organisms (19). In the study by Jordan and Durso, out of 548 blood samples of newborns hospitalized in NICU who were suspected of sepsis, PCR was positive in 27 cases, of which only 1 had negative PCR. However, the blood sample of 520 other patients had no detectable level of bacteria by PCR and culture methods (20).

In our study, the most diagnosed disease was related to pneumonia, with 30 cases (33.6%). Data from Kenya (21) and Gambia (22) show the fight against pneumonia outbreaks in children. In 2000, the main cause of bacteremia in children worldwide was pneumonia (23), and in a recent meta-analysis, it has been identified as the most common cause of bacteremia (24). In a study in Kumasi in 2004, only one case (2%) of pneumonia was identified (25). The authors explained the low prevalence rate due to laboratory problems and previous antimicrobial therapy of the patients. Other studies emphasized the importance of the invasiveness of pneumonia in children and supported vaccination (26, 27). It is necessary to examine antibiotic resistance in different societies. In this regard, the SENTRY antibiotic control program started in North America, Latin America and Europe in 1997. In their studies, a total of 81213 pathogens were investigated during the years of 1997 to 2002. Staphylococcus aureus, Escherichia coli and coagulase-negative Staphylococcus were the 3 most common organisms in these areas (28).

In our study, pneumococcus, Klebsiella and Staphylococcus epidermidis was the most common bacteremia causes. In a retrospective study on pediatric blood cultures of a training hospital in Tehran, 118 positive samples were analyzed over 6 months. In that study, Gram-negative organisms were the most common causes; among them, Pseudomonas and Enterobacter were at the top (29). In another study in Sari, staphylococcus saprophyticus, Escherichia coli, and Klebsiella were the most common microbes isolated in this training center (30). In the study conducted by Nemati et al., the most frequent isolated bacteria were coagulase-negative staphylococci (70.16%), and Klebsiella pneumoniae, Staphylococcus aureus and Escherichia coli were placed in the next ranks with a big difference (11). In the study conducted by Chitsaz et al., the common bacteria were Staphylococcus aureus, Pseudomonas aeruginosa and related types, and Streptococcus viridans, respectively (12).

In the study of Hajizadeh and Daneshjoo at Imam Khomeini Hospital, the most common isolated microorganisms were coagulase-negative Staphylococcus, followed by Staphylococcus aureus and Klebsiella, respectively (31). In the study by Mojtabaei and Nursalehi, the most common causes of bacteremia in infancy were Escherichia coli and Klebsiella. Still, Pseudomonas and Salmonella were the most common post-infant period (32). In the study conducted by Kara in Turkey, the highest frequency was related to coagulase-negative staphylococci, Staphylococcus aureus, Pseudomonas and Klebsiella, respectively (13). This difference is due to the pattern of previous antibiotic use.

One of the limitations of this study was that many patients' blood cultures were negative, which may be due to previous antibiotic treatment, insufficient blood sample volume, unknown bacteriostatic factors in serum, or organisms with delayed growth. Another limitation of the study was that diagnosing bacterial agents is often a problem in critically-ill and febrile patients. In this study, the most diagnosed diseases were related to pneumonia (30 people), viral infection (9 people) and pyelonephritis (8 people). Twenty-five people were positive for B/C culture, 6 were positive for urine culture, and 3 were positive for CSF culture out of 93 people. In this regard, pneumococcus, Klebsiella, and Staphylococcus epidermidis were the most common causes of bacteremia. In general, the quick diagnosis of bacterial infections in hospitalized children with fever leads to correct and early treatment and provides the conditions to select the appropriate antibiotics, resulting in a reduction in the rate of morbidity and mortality in the patients. It is necessary to record and publish the specific results of each region, especially in the area of serious infections, to compare the results in different centers and different age groups.

Acknowledgments

None.

Conflict of interest

None.

Financial support

None.

Ethics statement

None.

References

1.Azzari C,Moriondo M, Pi Pietro P, Di Bari C, Resti M, Mannelli F, et al .The burden of bacteremia and invasive diseases in children aged less than five years with fever in Italy. Ital J Pediatr 2015; 41(1): 92.

2. Gaeta GB, Fusco FM, Nardiello S. Fever of unknown origin: a systematic review of the literature for 1995-2004. Nucl Med Commun. 2006;27(3):205-11.

3. Bleeker-Rovers CP, Vos FJ, de Kleijn EM, Mudde AH, Dofferhoff TS, Richter C, et al. A prospective multicenter study on the fever of unknown origin: the yield of a structured diagnostic protocol. Medicine (Baltimore). 2007;86(1):26-38.

4.Bordelon JR, Abbas SU, Shabbir AQ, Ross AL. Rewriting history: Fever of unknown origin. Am J Med. 2015;128(9):956-8.

5. Rantakokko-Jalava K, Nikkari S, Jalava J, Eerola E, Skurnik M, Meurman O, et al. Direct amplification of rRNA genes in the diagnosis of bacterial infections. J Clin Microbiol 2000; 38: 32-9.

6. Kuppermann N. Occult bacteremia in young febrile children. Pediatr Clin North Am 1999; 46(6): 1073-109.

7.Khosravi N, Arab Mohammad Hosseini A. The Prevalence of bacteremia and determination of the most common organism after exchange transfusion in the newborn in Akbar abadi hospital (1996-1999). RJMS 2002; 9(29): 205-208.

8. Afsharpaiman Sh, Mamishi S. Diagnosis of bacteremia in febrile patients: PCR versus other routine methods. TUMJ 2008; 66(3): 169-175.

9.Jamuna R, Srinivasan S, Harish BN. Factors predicting occult bacteremia in young children. Indian J Pediatric 2000; 67: 709–711.

10. CIA: CIA factbook 2012 (2012) Available: https://www.cia.gov/library/publications/the-world-factbook/geos/gh.html. Accessed 2012 June 17.

11. Nemati N, Javadpour S, Nazemi A. Antibiogram pattern of isolated bacteria from bacteremia in hospitalized children – Bandar Abbas, Iran. Journal of Hormozgan medical university 2010; 14(4): 297-304.
12. Chitsaz M, Khotaei Gh, Shahcheraraghi F, Poorheydari N. Blood culture contamination in children's edical center of Tehran from April to July 2004. The Journal of Tehran Faculty of Medicine. 2005;63:108- 15. Persian]
13. Kara A, Kanra G, Cengiz AB, Apis M, Gür D. Pediatric Blood Culture, time to positivity. Turkish Journal of Pediatric. 2004;46:251-255.
14. Walsh AL, Phiri AJ, Graham SM, Molyneux ME. Bacteremia in febrile Malawian Children: clinical and microbiologic features. Pediatr Infect Dis J. 2000;19:312-318.
15. Berkley JA, Bejon P, Mwangi T, Gwer S, Maitland K, et al. HIV infection, malnutrition, and invasive bacterial infection among children with severe malaria. Clin Infect Dis 2009; 49: 336–343.
16. Sigauque B, Roca A, Mandomando I, Morais L, Quinto L, et al. Community-acquired bacteremia among children admitted to a rural hospital in Mozambique. Pediatr Infect Dis J 2009; 28: 108–113.
17. Nadjm B, Amos B, Mtove G, Ostermann J, Chonya S, et al. WHO guidelines for antimicrobial treatment in children admitted to hospital in an area of intense Plasmodium falciparum transmission: a prospective study. BMJ 2010; 340: c1350.
18. Jafari S, Fatollahzadeh A, Ghiasvand F, Seifi A. Epidemiology of Causes of Fever of Unknown Origin in an Academic Center: A Five-Year Evaluation from 2009 to 2014, Arch Clin Infect Dis. 2018; 13(5):e69608. doi: 10.5812/archcid.69608.
19. Cursons RT, Jeyerajah E, Sleigh JW. The use of polymerase chain reaction to detect septicemia in critically ill patients. Crit Care Med 1999; 27: 937-40.
20. Jordan JA, Durso MB. Comparison of 16S rRNA gene PCR and BACTEC 9240 for detection of neonatal bacteremia. J Clin Microbiol 2000; 38: 2574-8.
21. Berkley JA, Lowe BS, Mwangi I, Williams T, Bauni E. Bacteremia among children admitted to a rural hospital in Kenya. N Engl J Med 2005; 352: 39– 47.
22. Hill PC, Onyeama CO, Ikumapayi UN, Secka O, Ameyaw S, et al. Bacteraemia in patients admitted to an urban hospital in West Africa. BMC Infect Dis 2007; 7: 2.
23. O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet 2009; 374: 893–902.
24. Reddy EA, Shaw AV, Crump JA. Community-acquired bloodstream infections in Africa: a systematic review and meta-analysis. Lancet Infect Dis 2010; 10: 417–432.
25.Evans JA, Adusei A, Timmann C, May J, Mack D, et al. High mortality of infant bacteraemia clinically indistinguishable from severe malaria. QJM 2004; 97: 591–597.
26. Holliman RE, Liddy H, Johnson JD, Adjei O. Epidemiology of invasive pneumococcal disease in Kumasi, Ghana. Trans R Soc Trop Med Hyg 2007; 101: 405–413.
27. Donkor ES, Newman MJ, Oliver-Commey J, Bannerman E, Dayie NT, et al. Invasive disease and pediatric carriage of Streptococcus pneumoniae in Ghana. Scand J Infect Dis 2010; 42: 254–259.
28. Biedenbach DJ, Moet GJ, Jones RN. Occurrence and antimicrobial resistance pattern comparisons among bloodstream infection isolates from the SENTRY Antimicrobial surveillance program (1997-2002). Diag Microbiol Infect Dis; 2004. 50:59-69.
29. Riahi-fard A. Evaluation of blood and urine cultures in Mofid children hospital in Tehran. A thesis supervised by Dr Abdollah Karimi, in Shahid Beheshti university of medical sciences; 2003. p.1. Pediatr; 2004. 163:530-535.
30. Nasrolahei M, Sharif M. Evaluation of blood cultures in Sari hospitals. Med J Iran Red Crescent; 2005. 5:24-29.
31. Hajizadeh N, Daneshjoo Kh. Evaluation of in-vitro antimicrobial drug resistance in Imam Khomeini Hospital. Iranian Journal of Pediatrics. 2003;13:133-139. [Persian]
32. Mojtabaei Sh, Noorsalehi E. Survey of efficacy of antibiotics in Gram-negative septicemia in neonates and children. Journal of Medical Faculty Guilan University of Medical Sciences. 2004;13:39-44. [Persian]

Table 1: Determining the frequency of disease diagnosis in the examined samples

	f	%
pharyngitis	2	2.2
Systemic JIA	1	1.1
Sinusitis	4	3.4
sepsis	4	3.4
Pyelonephritis	8	7.8
Viral infection	9	8.9
Rickettsia infection	1	1.1
pneumonia	30	6.33
Septic arthritis	2	2.2

Preseptal cellulitis	1	1.1
Viral gastroenteritis	5	4.5
Post-infectious arthritis	3	3.3
Shigella	2	2.2
scarlatina	1	1.1
meningitis	5	4.5
Visceral leishmaniasis	1	1.1
Mesenteric lymphadenitis	5	4.5
Lupus	1	1.1
S4	2	2.2
peritonitis	1	1.1
Hydatid cyst	1	1.1
leukemia	1	1.1
Lymphadenitis	1	1.1

Table 2: Determining the frequency of the type of antibiotics used in the examined samples

	f	%
Clindamycin	32	4.34
ceftriaxone	41	1.44
Azithromycin	1	1.1
Cephalexin	3	2.3
Metronidazole	2	2.2
amikacin	6	5.6
Doxycycline	1	1.1
Vancomycin	15	1.16
Meropenem	11	8.11
Cefotaxime	7	5.7
Ampicillin	3	2.3
Gentamicin	4	3.4
Penicillin	1	1.1
Ceftazidime	4	3.4
Cefazolin	1	1.1
Ampicillin Sulbactam	2	2.2
Ciprofloxacin	1	1.1
Amoxicillin	1	1.1
Linezolid	1	1.1

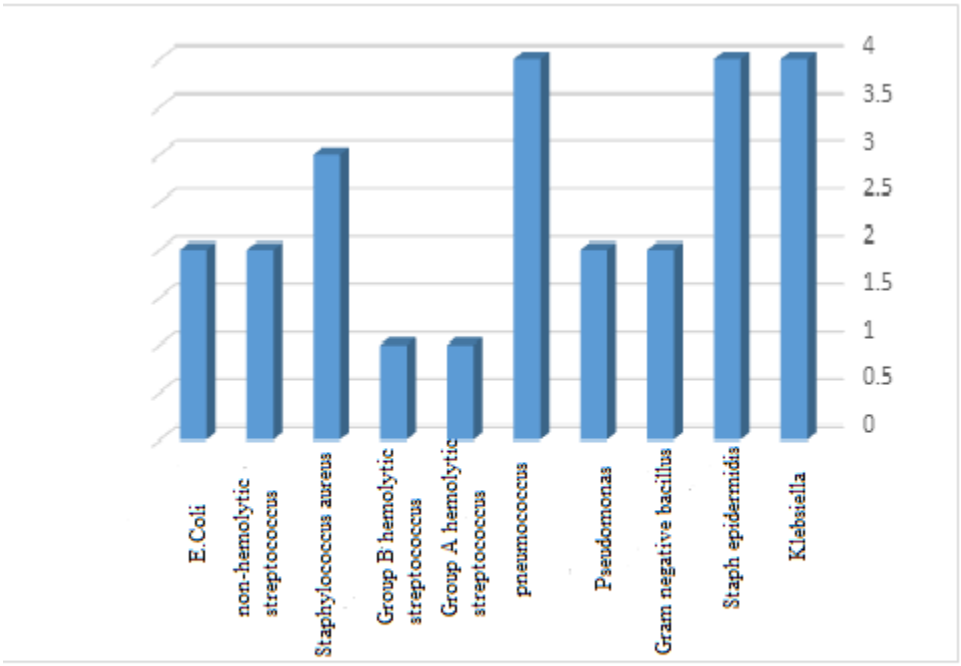

Chart 1: Determining the frequency of blood culture type in the examined samples