

ORIGINAL RESEARCH

Incidence, clinical profile, and risk factors for serious bacterial infections in children

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ABSTRACT

Background: Blood stream infection (BSI) is a common bacterial illness of paediatric age group. Bacteremia remains one of the most significant causes of morbidity and mortality in pediatric patients. Delaying diagnosis and treatment of bacteremia may result in increased childhood mortality.

Aim: We wanted to study the microbial profile, clinical profile and risk factors of bacterial infections in children.

Methods: This hospital based cross-sectional, observational study was conducted in the department of Paediatrics in a tertiary hospital, Indore, India. Children upto 03 years of age admitted in the department were enrolled in our study. Blood culture was done for all the patients. We compared the risk factors, clinical features, laboratory data, microbiologic results, and final outcome for patients with bacteremia and without bacteremia

Results: In the present study, out of 88 febrile children bacteremia was present in 24 (27.3%) of cases. Staphylococcus aureus was the most common pathogen isolated (25%), followed by salmonella (16%). Most common risk factors were malnutrition (wasting/stunting), low socio-economic status, incomplete vaccination and past history of hospitalization. The most common presenting symptom was cough/cold, convulsion, restlessness, not accepting feed, increased respiratory rate and excessive crying. Death rate was 8.3% in bacteraemic children whereas zero death occurs in non bacteraemic patients

Conclusions: Pediatric bacteremia remains a burdensome public health problem. Morbidity and mortality rates were higher in bacteraemic child as compared to non bacteraemic children

Key words: Bacteremia, clinical profile, risk factors, children

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Introduction

Primary bacteremia is defined as the presence of bacteria in the bloodstream without an identifiable source of infection¹. Studies conducted in the United Kingdom (2014) established the following as risk factors for bacteremia: functional or anatomical asplenia, immunosuppression, nephrotic syndrome, chronic respiratory, cardiac and/or kidney disease, diabetes, cochlear implants and children less than 5 years of age with cerebrospinal fluid fistulas²⁻³. Fever is a common clinical symptom in children and is one of the leading causes for medical consultation and hospital admissions⁴. Bacteremia and septicemia are the leading cause of children mortality and morbidity worldwide⁵. Despite the great advances in medical diagnosis and therapy over the past decades,

bloodstream infection (BSI) remains a major cause of infectious disease morbidity and mortality in both low- and middle- or high-income countries. Several studies have reported that BSI was the seventh most common cause of death and the leading cause of death caused by infections⁶⁻⁷. Bacteremia can be caused by a wide range of gram-negative and gram-positive microorganisms and can be manifested with or without a specific site of infection, such as pneumonia or meningitis. Some bacteremia is a transient self-limiting⁸. The most common microorganisms in healthy children over a month of age are pneumococcal bacteremia, Haemophilus influenzae type B, and Neisseria meningitidis, which is characterized by moderate to severe pathogenesis. Staphylococcus aureus, Salmonella and Streptococcus

They have been also reported in children⁹. Many complications are often due to bacterial infections, including blood stream infections (bacteremia) than can lead to systemic inflammatory response syndrome, septic shock, multiple organ dysfunction syndrome, and death¹⁰. To reduce the risk of death, children receiving inpatient treatment for complicated SAM should be monitored closely for any signs or symptoms suggestive of systemic infections, and infections should be treated in a timely manner with the correct antibiotic regimen¹¹⁻¹². In the state of Madhya Pradesh in India, where the present study was conducted, National Family Health Survey-4, undertaken in the year 2015-2016, reported that approximately 71% of the children less than 5 years of age were taken to a health facility for complaints of fever in 2 weeks preceding the survey¹³.

Aims and Objectives

This study aimed to determine the incidence, risk factors, microbial and clinical profile of bacteremia in febrile children upto 3 years of age, admitted in a tertiary hospital in central India.

Material and Methods

This is a cross-sectional, observational study was conducted in the department of Paediatrics in a tertiary hospital, Indore, India, during the 6 months period from January 2016 to June 2016. All the children aged upto 3 year, admitted in our department during the study period were enrolled in the study.

Inclusion criteria

- All the children aged between 0-3 year
- Children who presented with fever
- Parents of the children who provide consent for participation in the study.

Exclusion criteria

- More than 03 years age child
- Child on some immunosuppressive drugs like steroids therapy
- Children having chronic illness, malignancy, renal failure, hepatic failure, congestive cardiac failure, and bone marrow aplasia
- Parents of the children not willing for participation in the study.

The details of the study were discussed with the mother or caregiver accompanying the child fulfilling the inclusion criteria and a written consent obtained. After obtaining consent, a standardized pre-defined questionnaire containing clinical history and physical examination was done. The questionnaire also contained epidemiological, clinical, hematological and biochemical parameters of the cases. Patients were provided immediate routine or intensive care as per the department protocol. All children were examined within 24 h of admission and relevant investigations were done.

The following investigation were done for all children included in the study: complete blood count, Peripheral smear examination, C- reactive protein (CRP), serum electrolytes, Widal test, blood and cerebrospinal fluid (CSF) culture by using the automated BacT/ALERT system Urine cultures, Antimicrobial susceptibility testing of isolated microorganism was done using the Kirby Bauer disk diffusion method. All samples were subjected to smear examination after Ziehl-Neelsen staining, and Xpert MTB/ RIF assay.

Statistical analyses

All data entered into SPSS version 21 for descriptive statistical analysis. Mean and proportions were compared by Student t-test and chi-squared. $P < 0.05$ was considered to be statistically significant

Results

A total of 88 febrile children enrolled in our study, incidence of bacteremia were 24 (27.3%) [Figure:1]. *Staphylococcus aureus* was the most common (25%) bacterial agent isolated from blood culture followed by *salmonella typhi* (16%), details description of microbial profile shown in table: 1. Majority of the patients (62.5%) was residing at urban areas. Wasting, stunting, overcrowding and past history of hospitalization were the common risk factors of bacteremia [table: 2]. Most common clinical presentation was cough/cold (41.7%), restlessness (37.5%), increased Respiratory rate (29.2%), not accepting feed (29.2%) and vomiting (16.7%), detailed clinical profile shown in figure:2. Mortality rate (death) in bacteraemic patients was 8.3%, whereas no death occur in non bacteraemic patients.

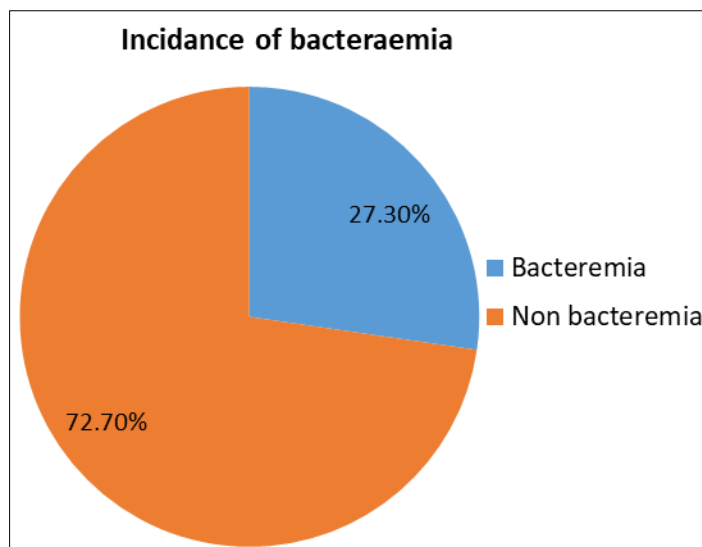


Fig 1:

Table 1: Bacterial agents isolated from bacteraemic patients by automated blood culture method (N=24)

Bacterial isolates	Frequency	Percentage (%)
Staphylococcus aureus	06	25.00
Salmonella typhi	04	16.67
Staphylococcus coagulase negative	03	12.50
Klebsiellapneumoniae	02	8.34
Staphylococcus hemolyticus	02	8.34
Citrobacterspp.	02	8.34
Pseudomonas aeruginosa	01	4.16
Salmonella paratyphiA	01	4.16
Escherichia coli	01	4.16
Staphylococcusepidermidis	01	4.16
Streptococcus Group D	01	4.16

Table 2: Association of bacteraemia with co-factors related to demographic, socioeconomic factors, and past history of hospital admission

Independent Variable		Bacteremia Yes	Bacteremia No	Total	P value
Residence	Urban	16 (66.7%)	39 (60.9%)	55 (62.5%)	0.244
	Rural	8 (33.3%)	25 (39.1%)	33 (37.5%)	
Overcrowding	Present	10 (41.7%)	24 (37.5%)	34 (38.6%)	0.128
	Absent	14 (58.3%)	40 (62.5%)	54 (61.4%)	
Past History of Hospitalization	Present	9 (37.5%)	22 (34.4%)	31 (35.2%)	0.785
	Absent	15 (62.5%)	42 (65.6%)	57 (64.8%)	
Wasting	Present	14 (58.3%)	18 (28.1%)	32 (36.4%)	0.0087
	Absent	10 (41.6%)	46 (71.8%)	56 (63.6%)	
Bipedal Edema	Present	5 (20.8%)	1 (1.6%)	6 (6.8%)	0.001
	Absent	19 (79.2%)	63 (98.4%)	82 (93.2%)	
Stunting	Present	13 (54.2%)	18 (28.1%)	31 (35.2%)	0.023
	Absent	11 (45.8%)	46 (71.9%)	57 (64.8%)	
Increased rate of respiration	Present	7 (29.2%)	28 (43.8%)	35 (39.8%)	0.213
	Absent	17 (70.8%)	36 (56.2%)	53 (60.2%)	
Excessive Cry	Present	3 (12.5%)	5 (7.8%)	8 (9.1%)	0.464
	Absent	21 (87.5%)	59 (92.2%)	80 (90.9%)	
Restlessness	Present	9 (37.5%)	7 (10.9%)	16 (18.2%)	0.004
	Absent	15 (62.5%)	57 (89.1%)	72 (81.8%)	

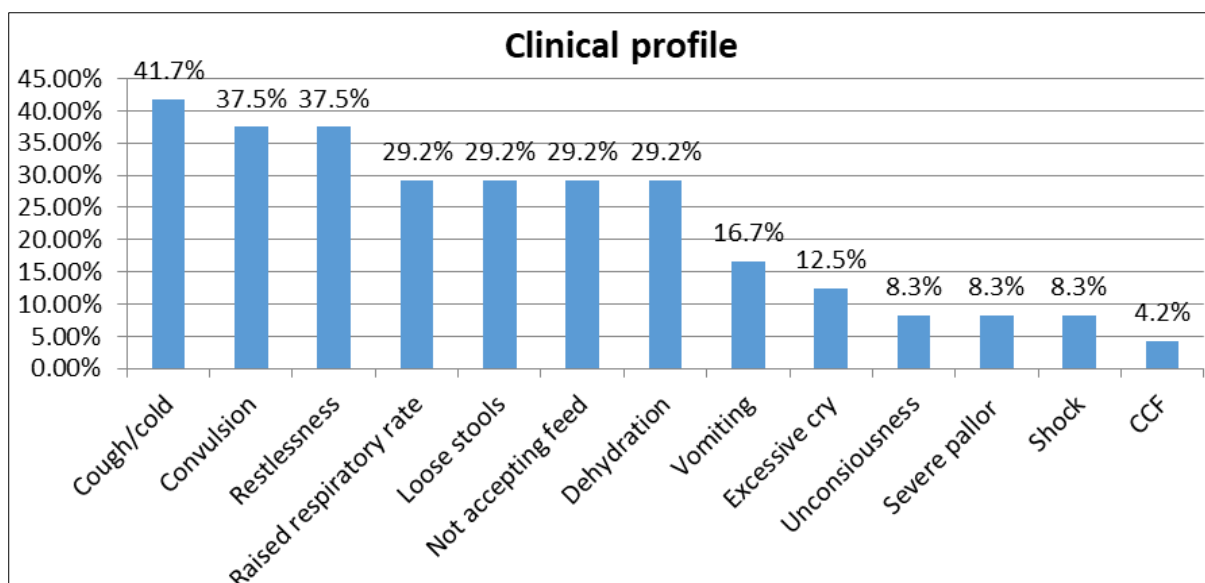


Figure 2: clinical profile of bacteraemic patients (N=24)

Table 3: Outcomes distribution among bacteraemic and non-bacteraemic patients (N=88)

Outcome	Bacteraemia		Non bacteraemia		Total	
	N	%	N	%	N	%
Discharged/DOR (discharged on request)	17	70.8	48	75.0	65	73.9
LAMA (left against medical advise)	05	20.9	16	25.0	21	23.8
Death	02	8.3	00	0.0	02	2.3
Total	24	100	64	100	88	100

Discussion

Blood stream infection is a common, potentially serious and often occult bacterial infection of childhood. Bacteremia causes acute morbidity and mortality as well as long term sequelae.

The current study found incidence of Bacteremia was 27.3%, agreement with the study of Yoon *et al.*,¹⁴ and Nielsen *et al.*,¹⁵.

Notably, in our study *Staphylococcus aureus* was the most common cause of bacteremia in children, followed by *salmonella typhi*, our findings were concordance with the study conducted by Moyo SJ *et al.*,¹⁶, Singhi S *et al.*,¹⁷ and Christopher *et al.*,¹⁸. However, the prevalence of extended-spectrum beta-lactamase and multidrug-resistant pathogens was high but should be interpreted with caution in view of the small sample size.

In our study gram positive bacterial isolates were more common than gram negative isolated from bacteremia patients through blood culture, accordance to the Boguniewicz *et al.*,¹⁹ and Harris *et al.*,²⁰.

There is no statistically significant difference between bacteremia and non bacteremia patients in terms of residential status, overcrowding and past history of hospitalization ($p > 0.05$), similar finding also reported by U.A. Memon *et al.*,²¹.

In our study, children presenting with acute malnutrition (wasting & stunting) and pedal oedema were significantly associated with the bacteremia

($p < 0.05$), our results consistent with Rao B.N *et al.*,²² and Pathak *et al.*,²³. The increased incidence and severity of infections in malnourished children is due to limited production and diminished functional capacity of B-cell and T-cell components of the immune system.

Present study observed increased rate of respiration and excessive cry were not significantly associated with the bacteremia ($p > 0.05$), our finding comparable with Kumar GV *et al.*,²⁴.

Restlessness was significantly associated with blood stream infection in children ($p < 0.05$), accordance to the Ayoola *et al.*,²⁵ and Jin L *et al.*,²⁶.

Children with bacterial infections (bacteremia) presented common symptoms, such as cough/cold, convulsion, restlessness, increased respiratory rate, not accepting feed, loose stool, dehydration, vomiting and irritability, similar clinical profile was reported by many other studies, Brent AJ *et al.*,²⁷ and Nguyen DK *et al.*,²⁸.

In the present study death ratio was certainly high in the bacteraemic group as compared to the non-bacteraemic group. It is accordance with the similar finding of Mishra *et al.*,²⁹ and Mojtahedi SY *et al.*,³⁰. Despite all the improvement in the developed world, sepsis is still a significant health care problem and is associated with high morbidity and mortality in children, mainly in developing countries.

Conclusions

The study identified multiple risk factors for bacteremia in children. Paediatricians can be made aware of these risk factors. This study should help develop clinical prediction rules that can supplement the current clinical practice guidelines. Further studies are warranted to identify age specific risk factors for bacteremia as most clinicians depend on clinical signs and symptoms to identify bacteremia. Early recognition and prompt treatment is the key to improve outcome of sepsis

Conflicts of interest: None

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References

- Diaz Pena R, Espinoza Oliva MM, Lamas Briseño MT. Abordaje del niño con fiebre sin foco infeccioso. *Enfermedades Infecc y Microbiol.* 2004;24(3):31-8.
- Aalst M Van, Lötsch F, Spijker R, Meer JTM Van Der, Langendam MW, Goorhuis A, *et al.* Incidence of invasive pneumococcal disease in immunocompromised patients: A systematic review and meta-analysis. *Travel Med Infect Dis [Internet].* 2018; 24(June):89-100. Available from: <https://doi.org/10.1016/j.tmaid.2018.05.016>.
- Cruickshank HC, Jefferies JM, Clarke SC. Lifestyle risk factors for invasive pneumococcal disease: a systematic review. *BMJ Open [Internet].* 2014 [cited 2020 Jul 12]; 4:5224. Available from: <http://dx.doi.org/10.1136/bmjopen-2014-005224>.
- NICE: Feverish Illness in Children: Assessment and Initial Management in Children Younger than 5 Years. National Institute for Health and Care Excellence Clinical guideline No. 160. 2013 NICE, London.
- Watson RS, Carcillo JA, Linde-Zwirble WT, Clermont G, Lidicker J, Angus DC. The epidemiology of severe sepsis in children in the United States. *Am J Respir Crit Care Med.* 2003;167:695-701.
- Kern WV, Rieg S. Burden of bacterial bloodstream infection-a brief update on epidemiology and significance of multidrug-resistant pathogens. *Clin Microbiol Infect.* 2020;26:151-7. DOI: 10.1016/j.cmi.2019.10.031.
- Goto M, Al-Hasan MN. Overall burden of bloodstream infection and nosocomial bloodstream infection in North America and Europe. *Clin Microbiol Infect.* 2013;19:501-9. DOI: 10.1111/1469-0691.12195.
- Norton EB, Archibald LK, Nwanyanwu OC, *et al.* Clinical predictors of bloodstream infections and mortality in hospitalised Malawian children. *The Pediatric infectious disease journal.* 2004;23:145-51. <https://doi.org/10.1097/01.inf.0000109258.82988.40> PMID: 14872181.
- Pound CM, Johnston DL, Armstrong R, Gaboury I, Menon K. The morbidity and mortality of pediatric oncology patients presenting to the intensive care unit with septic shock. *Pediatric blood & cancer.* 2008;51:584-8. <https://doi.org/10.1002/pbc.21670> PMID:18623196.
- Jones KDJ, Berkley JA. Severe acute malnutrition and infection. *Paediatrics and International Child Health.* 2014;34:1-29.
- Smith DA, Nehring SM. *Bacteremia.* StatPearls Treasure Island, Florida: StatPearls Publishing; c2020.
- Le Doare K, Bielicki J, Heath PT, Sharland M. Systematic Review of Antibiotic Resistance Rates Among Gram-Negative Bacteria in Children With Sepsis in Resource-Limited Countries. *J Pediatric Infect Dis Soc.* 2015;4(1):11-20.
- NHFS-4: National Family Health Survey-4- Ministry of Health and Family Welfare, Government of India, International Institute for Population Sciences, Mumbai. In.; 2015–16. [Available from:<http://rchiips.org/nfhs/NFHS-4Reports/India.pdf/>].
- Seo Hee Yoon, HyunDo Shin¹, Keum Hwa Lee^{1,2,3}, Moon Kyu Kim¹, Dong Soo Kim¹, Jong Gyun Ahn,*et al.* Predictive factors for bacteremia in febrile infants with urinary tract infection, *Scientific Reports | 2020;10:4469 |* <https://doi.org/10.1038/s41598-020-61421-4>.
- Nielsen MV, Sarpong N, Krumkamp R, Dekker D, Loag W. Incidence and Characteristics of Bacteraemia among Children in Rural Ghana; *Plos One.* 2012 Sep;7(9):e44063.
- Moyo SJ, Manyahi J, Blomberg B, Tellevik MG, Masoud NS, Aboud S, *et al.* Bacteraemia, Malaria, and Case Fatality Among Children Hospitalized With Fever in Dar es Salaam, Tanzania. *Front. Microbiol.* 2020;11:2118. DOI: 10.3389/fmicb.2020.02118.
- Singhi S, Kohli V, Ayyagiri A, Bacteraemia. Bacterial infections in highly febrile children without apparent focus, *Indian Pediatr.* 1992 Oct;29(10):1285-9.
- Christopher T. Andersen, Céline Langendorf, Souna Garba, Nathan Sayinzonga-Makombe, Christopher Mambula, Isabelle Mouniaman, Kerstin E. Hanson, Rebecca F. Grais, Sheila Isanaka, Risk of community- and hospital-acquired bacteremia and profile of antibiotic resistance in children hospitalized with severe acute malnutrition in Niger, *International Journal of Infectious Diseases.* 2022;119:163-171.
- Boguniewicz J, Revell PA, Scheurer ME, Hulten KG, Palazzi DL. Risk factors for microbiologic failure in children with Enterobacter species bacteremia. *PLoS ONE.* 2021;16(10):e0258114.

20. Harris PNA, Peri AM, Pelecanos AM, Hughes CM, Paterson DL, Ferguson JK. Risk factors for relapse or persistence of bacteraemia caused by *Enterobacter* spp.: a case-control study. *Antimicrob Resist Infect Control*. 2017;6:1-8.
21. Uzair Ali Memon, Abdul Rahim Ahmed, Muhammad Khalid, Karima Qadir, Naeem Jabbar, Samina Junejo, *et al.* Clinical profile and outcome of carbapenem-resistant gram negative bacteremia in children with cancer in pediatric intensive care unit of a resource-limited country, *Pediatric Hematology Oncology Journal*. 2020;5:65e68.
22. Rao BN, Rathia SK, Phuljhele S, Verma YK, Amle D. Incidence, risk factors, clinical profile, and determinants (affecting outcome) of new onset acute kidney injury developing in critically ill patients in pediatric intensive care unit of a tertiary hospital in middle India. *Int J Pediatr Res*. 2019;6(05):252-261. DOI:10.17511/ijpr.2019.i05.10
23. Ashish Pathak, Radika Upadhyay, Aditya Mathur, Sunil Rathi, Cecilia Stålsby Lundborg. Incidence, clinical profile, and risk factors for serious bacterial infections in children hospitalized with fever in Ujjain, India, *BMC Infectious Diseases*. 2020;20:162.
24. Kumar GV, George A, Viswanatha Kumar HM. Study of clinical profile and risk factors associated with febrile urinary tract infection in preschool children. *Int J Contemp Pediatr*. 2016;3:243-6.
25. Ayoola O, Adebawale A, Kikelomo O. Predictors of Bacteraemia among Febrile infants in Ibadan, Nigeria. *J Health Popular Nutr*. 2002 Sep;20(3):223-229.
26. Jin L, Zhao C, Li H, Wang R, Wang Q and Wang H (2021) Clinical Profile, Prognostic Factors, and Outcome Prediction in Hospitalized Patients With Bloodstream Infection: Results From a 10-Year Prospective Multicenter Study. *Front. Med*. 8:629671. DOI: 10.3389/fmed.2021.629671.
27. Brent AJ, Lakhnpaul M, Thompson M, Collier J, Ray S, Ninis N, *et al.* Risk score to stratify children with suspected serious bacterial infection: observational cohort study. *Arch Dis Child*. 2011;96(4):361-7.
28. Nguyen DK, Friedlander S, Fleischman RJ, Zangwill KM. Length of stay and complications associated with febrile infants <90 days of age hospitalized in the United States, 2000-2012. *Hosp Pediatr*. 2018;8(12):746-52.
29. Jyotsna Mishra, Shashikant Patidar, Chayan Chakma, Naresh Bajaj. To compare clinical profile and outcome of pediatric patients with sepsis admitted in pediatric and neonatal intensive care unit in a tertiary care hospital of central India, *European Journal of Molecular & Clinical Medicine* ISSN 2515-8260.2022;09(3).
30. Mojtahedi SY, Rahbarimanesh A, Khedmat L, Izadi A. The Prevalence of Risk Factors for the Development of Bacteraemia in Children. *Open Access Maced J Med Sci*. 2018 Nov 25;6(11):2023-2029. <https://doi.org/10.3889/oamjms.2018.41>.