

# Bacteremia among Children in Central Teaching Hospital of Pediatric in Baghdad City

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## ABSTRACT

**Introduction:** children with Occult bacteremia shows presence of fever, difficulty in breathing, tachycardia, refusal of feeds, malaise or lethargy. In such a potentially life-threatening condition, isolation of the causative pathogen in blood culture is one of the most important bacteriological examinations with important clinical and therapeutic consequences.

**Material and methods:** This prospective study was carried out in the Central Teaching of Pediatric Hospital in Baghdad. Total 300 febrile patient aged from 1 days to 11 years of age without any localizing clinical features attending central teaching hospital of pediatrics in Baghdad and who were not hospitalized 30 days prior to the initial evaluation were enrolled into the study.

**Results:** Among 300 patients, 49 were positive for different kinds of bacteria confirming OB and 235 were negative after 18 hrs of incubation. Among different age groups, OB was positive in 9.7% in age group 1day-<29 days, 4.3% in age group 1 month-<11 months, 1.0% in age group 1year-<5 years and age group 5years-10years represent (3/49) respectively and 0.3% in age groups over 11years.

**Conclusion:** Occult bacteremia is the most prevalent condition among children's less than one months. Imipenem, class of quinolone antibiotic is found to be sensitive towards bacterial isolates and thus could be effective treatment strategy for management of bacteremia.

**Keywords:** Bacteremia, Pediatric

## INTRODUCTION

Fever is a common presenting symptom in pediatric patients especially in children < 3 years of age.<sup>1</sup> Among these febrile children, finite number of patients harbors serious bacterial illnesses and clinically indistinguishable from the rest.<sup>2</sup> Such asymptomatic clinical condition with no apparent focus of infection is termed as occult bacteremia (OB). Bacteremia has been reported increasingly in pediatrics age group condition with a high mortality rate that varies between 30 and 70 per cent.<sup>3</sup> OB is defined as the presence of pathogenic bacteria in the blood stream of a febrile child with good clinical state and presents fever without a known infectious process.<sup>4</sup>

Children with OB present with fever, difficulty in breathing, tachycardia, refusal of feeds, malaise or lethargy.<sup>5</sup> Bacteremia also occur in children who have sepsis (ie, clinical evidence other than fever of a systemic response to infection). Children with sepsis generally appear ill, have an increased heart rate or respiratory rate and may have a change in temperature (typically fever, although hypothermia is often seen in very young infants and newborns). Presence of circulating bacteria

in bloodstream displays consequences like shock, multiple organ failure, disseminated intravascular coagulation, etc.<sup>6</sup> In such a potentially life-threatening condition, isolation of the causative pathogen in blood culture is one of the most important bacteriological examinations with important clinical and therapeutic consequences. The majority of bacteremia cases are caused by a number of pathogens including *Staphylococcus spp*, *Streptococcus spp*, *Escherichia coli* and *Klebsiella pneumonia*.<sup>7</sup> OB in children has different implications and different patterns than that in adults.<sup>8</sup> There is a wide variation in the incidence and clinical characteristics of OB caused by different species of bacteria. Identifying the causative species and characterizing the clinical significance in a specific age group in a community is essential for the prevention and treatment of these infections. The successful isolation of causative pathogen from blood is decisive for proper antimicrobial treatment as different organisms have different antimicrobial susceptibilities.<sup>5</sup> Administration of correct drug with antimicrobial susceptibility towards causative pathogen helps in improved prognosis. However, OB in children's residing in Baghdad region not been investigated. Thus, the present study was focused on estimation of age and gender as a risk factor of OB, identification of the focal bacterial infections and isolation of main bacterial pathogens in children's with OB aged between 3-11 years. Also, the susceptibility pattern of isolates to the commonly used antimicrobial agents in the treatment of sepsis will be determined.

## MATERIAL AND METHODS

### Subjects

This prospective study was carried out in the Central Teaching of Pediatric Hospital in Baghdad. Ethical approval was obtained from the faculty research publication committee, department of clinical laboratory science, college of medical and health technology along with official agreement of Ministry of health as well as the director of pediatrics central health hospital, Baghdad. The study was performed in between the July 2012 to October 2012. Total

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300 febrile patient aged from 1 days to 11 years of age without any localizing clinical features attending central teaching hospital of pediatrics in Baghdad and who were not hospitalized 30 days prior to the initial evaluation were enrolled into the study. Those patients with having nephrotic, rheumatologic or hematological diseases and those exposed to corticosteroid treatment for a period greater than five days or chemotherapy or radiotherapy were excluded from the study. For analysis of age and gender as a risk factor of OB, the children were divided into following groups: A-1 day-< 29 days; B- 1 month-<11 months; C- 1year-<5 years; D- 6 years-10 years and E- over 11 years.

#### Sample collection

The blood samples were collected from patients before starting antimicrobial treatment in duplicates or triplicates from two different sites at an interval at least 1-hour to check the probable chance of blood isolate contamination. For each blood culture, blood volume  $\geq 0.5$  mL for infants <1 month of age,  $\geq 1$  mL for children between 1 month and 36 months of age and  $\geq 4$  mL for children  $\geq 36$  months of age were collected.

#### Microbiology

Blood samples were cultured aseptically on aerobic (brain heart infusion) and anaerobic (thioglycolate broth) by direct inoculation of blood into culture bottles. The bottles were then incubated at 37°C. Bottles were examined daily for one week for signs of turbidity, hemolysis, or other evidence of growth. Positive samples with presence of bacteria in culture bottles were subjected to diagnostic tests by subculturing 0.1 ml of samples into blood agar plate, chocolate agar plate (3% to 10% of carbon dioxide) and MacConkey agar plate for 18 - 24 hrs at 37°C for isolation of pathogens.

Colonies were identified morphologically by Gram stain. The organisms grown on agar plates were identified by standard laboratory methods including API 20 E system, API Staph, and API 20E (Bio Merieux, France). Further identification of the clinical isolates were done by performing the biochemical

tests i.e. indole, hydrogen sulphide ( $H_2S$ ), citrate utilization, semi-solid mannitol, urease, oxidase, catalase, coagulase and mannitol salt agar. Inoculated blood culture media were discarded as negative if there was no growth after continuous incubation for 24 hours. Organisms were considered 'contaminants' if aerobic spores were observed.

#### Antimicrobial susceptibility test

Isolated microorganisms were further examined using antimicrobial susceptibility method. Antimicrobial susceptibility testing was performed for all blood culture isolates according to the criteria of the National Committee for Clinical Laboratory Standards (NCCLS) by Mueller-Hinton agar plates by Kirby-Bauer disc diffusion method. Zone diameter was measured and interpreted per the Clinical and Laboratory Standards Institute (CLSI) guidelines.<sup>9</sup> Based on zones sizes mentioned in interpretative chart, the organisms were classified as resistant, intermediate/moderately susceptible or susceptible.

#### STATISTICAL ANALYSIS

Data entry and analysis was done using SPSS version computer 19 software. Comparisons were made using Chi-square test with Fisher exact tests. A *p*-value of <0.05 was considered indicative of a statistically significant difference. Odds ratio and chi-square tests were used to determine presence of association between risk factors and culture results. Logistic regression was used to explain the dependent variable based on the independent variable.

#### RESULTS

A prospective study was performed on 300 febrile patients with fever aged 1 day to over 11 years admitted to Central Teaching Hospital of Pediatric in Baghdad from July 2012 to October 2012.

Blood culture results classified on basis of age and gender. Based on blood culture tests, among 300 patients, 16.3% (49/300) were positive for different kinds of bacteria confirming OB and 78% (235/300) were negative after 18

Blood culture / isolate	Frequency	Percent
Culture negative	235	78.3%
Occult bacteremia	49	16.3%
Contamination	16	5.3%
Total	300	100%

Table-1: Distribution of blood culture among patients

Result of growth	Age groups					Total
	(1D - <29D)	(1M - <11M)	(1Y - <5Y)	(5Y-10Y)	(11Y+)	
No growth	148 49.3%	42 14.0%	24 8.0%	14 4.7%	7 2.3%	235 78.3%
Occult bacteremia	29 9.7%	13 4.3%	3 1.0%	3 1.0%	1 0.3%	49 16.3%
Contamination	7 2.3%	8 2.7%	1 0.3%	0 0.0%	0 0.0%	16 5.3%
Total	184	63	28	28	8	300

MCP> 0.05(NS)

Table-2: Distribution of age groups according to the result of growth

Sex	Age groups					Total
	(1D - <29D)	(1M - <11M)	(1Y -<5Y)	(5Y-10Y)	(11Y+)	
Male	119 39.7%	36 12.0%	13 4.3%	6 2.0%	6 2.0%	180 60.0%
Femal	65 21.7%	27 9.0%	15 5.0%	11 3.7%	2 0.7%	120 40.0%
Total	184 61.3%	63 21.0%	28 9.3%	17 5.7%	8 2.7%	300 100.0%

MCP>0.05 (Non-significant)

**Table-3:** Distribution of age groups according to the gender

Result	First diagnosis						Total
	RDS	NNG	FIT	Fever	PUO	Jaundice	
No growth	24 8.0%	9 3.0%	48 16.0%	123 41.0%	20 6.7%	11 3.7%	235 78.3%
Occult bacteremia	4 1.3%	0 0.0%	8 2.7%	32 10.7%	4 1.3%	1 0.3%	49 16.3%
Contamination	2 0.7%	0 0.0%	1 0.3%	13 4.3%	0 0.0%	0 0.0%	16 5.3%
Total	30 10.0%	9 3.0%	57 19.0%	168 56.0%	24 8.0%	12 4.0%	300 100.0%

$\chi^2 = 10.452, P > 0.05, (NS)$

\*High fever (temperature  $\geq 39^\circ\text{C}$ ) was a predictive factor for occult bacteremia

RDS=Respiratory disease syndrome, NNJ=Neonatal jaundice, PUO=Pyroximal kunon oregon

**Table-4:** The relationship between outcome and the first diagnosis

Result of growth	Bacteria isolated									Total
	0	E.coli	Stap h.epidermidis	Klebsella	Staph.aureus	Acinetobacter	Enterobacter	Streptococcus	Pseudo	
No growth	235 78.3%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	235 78.3%
Occult bacteremia	0 .0%	15 5.0%	10 3.3%	9 3.0%	6 2.0%	4 1.3%	3 1.0%	1 .3%	1 .3%	49 16.3%
Contamination	16 5.3%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	16 5.3%
Total	251 83.7%	15 5.0%	10 3.3%	9 3.0%	6 2.0%	4 1.3%	3 1.0%	1 .3%	1 .3%	300 100%

MCP<0.01 (Highly significant)

**Table-5:** The frequency and percentage of Bacteria isolated from patient with occult bacteremia (N=49)

hrs of incubation (Table 1). Among different age groups, OB was positive in 9.7% in age group 1day-<29 days, 4.3% in age group 1 month -<11 months, 1.0% in age group 1year-<5 years and age group 5years-10years represent (3/49) respectively and 0.3% in age groups over 11years (Table 2). Based on the distribution of age groups according to the gender for patient under study found that the male represent high proportion of 60.0% (180/300) while the female represent 40% (120/300) with the male: female ratio 1.5: 1 (Table 3).

## 2. Focal source of infection and causative species of bacteremia

### 2.1 The focal bacterial infections

The focal source bacterial infections were identified in all the 300 patients included in the study. Major source of

focal infection was found to be fever in 56.0% (168/300) patients with presence of 10.7% (32/49) of isolated bacteria in positive OB cases. 19.0% (57/300) represented FIT cases with 2.7% (8/49) of isolated bacteria in positive OB cases. Other sources of focal infections were respiratory disease syndrome (RDS), 10.0% (30/300) with 1.3% (4/49) the isolated bacteria, pyroximal kunon oregon (PUO) cases, 8.0% (24/300) with 1.3% (4/94) the isolated bacteria, jaundice 4.0% (12/300) with 0.3% (1/49) bacteria isolated represent and neonatal jaundice (NNJ) cases 3.0% (9/300) with no bacterial presence (0.0%) (Table 4).

### 2.2 Causative species of bacteremia

A total of 49 isolates were collected from blood cultures, in which Gram-negative bacteria is higher in proportion representing 65.3% (32/49). Most common species

No	Antibiotic	E.coli N=15		Klebsilla Spp. N=9		Aceteobacter spp. N=4		Enterobacter Spp. N=3		Pesudomonas Spp. N=1	
		S	R	S	R	S	R	S	R	S	R
1	Cefoxitin	30	70	30	70	50	50	30	70	-	100
2	Ceftriaxon	40	60	70	30	50	50	30	70	100	-
3	Cefipim	20	80	80	20	75	25	100	-	100	-
4	Imepnem	90	10	70	30	100	-	100	-	100	-
5	Azetroneam	60	40	60	40	75	25	30	70	-	100
6	Amikacin	60	40	60	40	50	50	100	-	100	-
7	Gentamycin	80	20	70	30	75	25	100	-	100	-
8	Pipracillin	30	70	60	40	-	100	-	100	100	-
9	Ampicillin	20	80	20	80	-	100	30	70	-	100
10	Ciproflaxacin	70	30	70	30	50	50	70	30	-	100
11	Vancomycin	60	40	60	40	70	30	50	50	-	100
12	Oxacillin	40	60	60	40	-	100	50	50	-	100
13	Ticarcillin	30	70	70	30	70	30	25	75	100	-
14	Augmutin	40	60	30	70	70	30	50	50	100	-

Mcp < 0.01 (Highly significant), S=sensitive, R=resistance

**Table-6:** Antibiotic susceptibility patterns of gram negative bacterial isolates

S.N.	Antibiotic	Staphylococcus epidermidisN=10		Staphylococcus aureusN=6		Streptococcus spp N=1	
		S	R	S	R	S	R
1	Cefoxitin	50	50	60	40	-	100
2	Ceftriaxon	60	40	50	50	100	-
3	Cefipim	90	10	60	40	100	-
4	Imepnem	80	20	80	20	100	-
5	Azetroneam	40	60	60	40	100	-
6	Amikacin	80	20	80	20	-	100
7	Gentamycin	30	70	50	50	100	-
8	Pipracillin	50	50	50	50	100	-
9	Ampicillin	40	60	60	40	-	100
10	Ciproflaxacin	70	30	60	40	100	-
11	Vancomycin	80	20	80	20	100	-
12	Oxacillin	20	80	80	20	100	-
13	Ticarcillin	60	40	50	50	100	-
14	Augmutin	70	30	60	40	100	-

Mcp < 0.01 (Highly significant), S=sensitive, R=resistance

**Table-7:** Antibiotic susceptibility tests patterns of gram positive bacterial isolates

causing bacteremia in these patients were *E.coli*(5.0%), *Staphylococcus epidermidis* (3.3%), *Klebsilla spp.* (3.0%), *Staphylococcus aureus*(2.0%), *Acinetobacterspp.*(1.3%), *Enterobacter spp.*(1.0%) followed by *pseudomonas spp.* and *Streptococcus spp.* (0.3%) respectively (Table 5).

### 3. Antibiotic susceptibility of bacterial isolates

Antibiotic susceptibility tests were performed for 49 bacterial isolates obtained from positive OB cases. All 14 antibiotics showed different degrees of susceptibility towards the identified bacterial isolates (Table 6). After categorization of identified bacterial isolates based on gram staining, the results of susceptibility test of antibiotics on gram negative bacteria showed that all isolates except *Klebsiellae spp.* were sensitive to imipenem. *Klebsiellae spp.* were found to be 80% sensitive to cefipim.

*E.coli* were sensitive to imipenem (90%) followed by ciproflaxacin (70%), vancomycin, amikacin, azethronem

(60%) respectively, ceftriaxon, oxacillin, amoxcillin (40%) respectively, cefoxitin, pipracillin, ticarcillin (30%) respectively and cefipim, ampicillin (20%) respectively. *Klebsiellae spp.* were sensitive to cefipim (80%), followed by ceftriaxon, imipene, gentamicin, ciproflaxacin, ticarcillin (70%) respectively, vancomycin, amikacin, azethronem pipracillin, oxacillin (60%) respectively, amoxcillin, cefoxitin (30%) respectively and 20% to ampicillin. *Enterobacter spp.* 100% sensitive to gentamicin, imipenem, cefipim, and amikacin respectively, followed by ciproflaxacin, amoxcillin, vancomycin, ticarcillin (70%) respectively and azethronem, ampicillin, cefoxitin, ceftriaxon (30%) respectively. *Acinetobacter spp* were sensitive to imipenem (100%) followed by cefipim, azithromycin, gentamicin (75%) respectively, cefoxitin, ceftriaxon vancomycin, amikacin, ciproflaxacin amoxicillin, oxacillin (50%) and ticarcillin (25%). *Pseudomonas spp.* were sensitive

to gentamicin, imipenem, cefipim, amikacin, piperacillin, amoxicillin, ceftriaxon (100%) respectively (Table 6).

The patterns of gram-positive bacterial susceptibility to antibiotic is summarized in Table 7. *Staphylococcus epidermidis* were sensitive to ceftriaxon (90%), followed by imipenem, amikacin, vancomycin (80%), ciprofloxacin, amoxicillin (70%), ceftriaxon, ticarcillin (60%), piperacillin, cefoxitin (50%), ampicillin, azithromycin (40%), gentamicin (30%) and oxacillin (20%). *Staphylococcus aureus* were sensitive to imipenem, amikacin, vancomycin (80%), amoxicillin, ciprofloxacin, ampicillin, azithromycin, cefipim, cefoxitin (60%), ceftriaxon, gentamicin, ticarcillin, piperacillin (50%) and oxacillin (40%). *Streptococcus spp.* were sensitive to ceftriaxon, cefipim, imipenem, azithromycin, ciprofloxacin, amoxicillin, vancomycin (100%) respectively and resistant to cefoxitin, amikacin, gentamicin, ampicillin, oxacillin, ticarcillin.

## DISCUSSION

Occult bacteremia (OB) is major cause of morbidity and mortality among children's in developing countries.<sup>1</sup> Thus, identification of susceptible age group, causative organism and treatment of specific bacterial causative organism is needed for definitive treatment and proper management of disease. The goal of the present study was the evaluation of a young child with fever to identify sources of infection their antimicrobial susceptibility pattern.

### 1. Age and gender as a risk factor of occult bacteremia

Risk factors including age have been evaluated in children with occult bacteremia. In this study, distribution of children's according to the age group with fever from birth to 11 years were depicted that the rate of cases decrease with increasing age. Infants (1 day-<29 days) represented 61.3% while age group over 11 years represented 2.7% of study population. Earlier reports stated the higher incidences of bacteremia in febrile patients aged 0-1 months because of low immunoglobulin-G antibodies response to encapsulated bacteria.<sup>3,7</sup> Other study also reported greatest preponderance of bacteremia in infants younger than 1 month.<sup>10</sup> The ratio of male:female ratio in study population was 1.5: 1 slightly higher than study by Al-mousawi M. R, 2016 wherein the ratio between the male:female ratio was 1.35: 1.

### 2. Focal source of infection and causative species of bacteremia

#### 2.1 The focal bacterial infections

Focal signs and symptoms in neonates due to localized infections may be clinically imperceptible, and thus poses difficulty in differentiating generalized and blood stream infections. Often the early signs of neonatal sepsis are non-specific, such as temperature instability, difficulty in breathing, lethargy, poor feeding, and unexplained jaundice.<sup>11</sup> Clinical assessment using a combination of symptoms and signs are useful guides to provisional diagnosis of neonatal blood infection.<sup>6</sup> In present study, fever was found to be most common source of the focal bacterial infections in 56.0% followed by 19% of FIT cases in the selected

study population. Respiratory disease syndrome (RDS), 10.0% (30/300); pyroximal kunon oregon (PUO), 8.0% (24/ 300); jaundice 4.0% (12/300) and neonatal jaundice (NNJ), 3.0% (9/300) also contributed to focal bacterial infection.

#### 2.2 Causative species of bacteremia

Gram-negative bacteria were higher in proportion representing 65.3% (32/49) of bacterial isolates in accordance with study reported by Jain et al., 2015, Al-mousawi M. R, 2016. The most common gram -ve species isolated were namely *E. coli* 5.0% (15/49), most common gram -ve species isolated from blood cultures<sup>6</sup>; *Klebsiella spp.* 3.0% (9/49), earlier reported in neonatal sepsis cases in Ethiopia<sup>12</sup>; *Acinetobacter spp.* 1.3% (4/49); *Enterobacter spp.* 1.0% (3/49) and *pseudomonas spp.* 0.3% (1/49), predominant pathogen reported in case study of children undergoing transplantation.<sup>13</sup>

On the other hand, gram positive bacterial isolates constituted 34.6% (17/49) of total. *Staphylococcus epidermidis* was the commonest bacteria isolated in 3.3% of the total isolate of gram positive (10/49), *Staphylococcus aureus* 2.0% (6/49) and *Streptococci spp.* 0.3 (1/49) (p-value<0.01. *Staphylococcus epidermidis* and *Staphylococcus aureus* are reported to be present in majority of bacteremia cases because of its highly invasive nature, its virulence factors and ability to resist many antibiotics particularly Methicillin Resistant *S. aureus* (MRSA) leading to its widespread dispersal in hospitals and surrounding environment.<sup>14</sup>

#### 3. Antibiotic susceptibility of bacterial isolates

The susceptibility pattern of gram positive and gram-negative organisms to the most relevant 14 antibiotics were done for 49 bacterial isolates. Patterns of bacterial susceptibility to these antibiotic is summarized in results section. In the present study Imipenem was the most effective drug against the tested gram positive and gram-negative bacteria. Similar finding has been reported by Al-mousawi (2016). Imipenem is a relatively new class of quinolone antibiotics which has recently become very common, particularly in general practice.<sup>15</sup>

## CONCLUSION

In conclusion, occult bacteremia is the most prevalent condition among children's less than one months. Gram-negative bacteria contributes more in bacteremia with presence of bacterial species like *E. coli*, *Klebsiellae spp.*, *Acinetobacter*, *Enterobacter spp.* and *pseudomonas spp.* Among gram-positive bacteria *Staphylococcus epidermidis*, *Staphylococcus aureus* and *Streptococci spp.* are the commonest bacteria causing bacteremia. Fever without a source is found to be a focal source of bacterial infection. Imipenem, class of quinolone antibiotic is found to be sensitive towards bacterial isolates and thus could be effective treatment strategy for management of bacteremia. However, considering the frequencies of resistant bacteria in hospitals, rapid laboratory tests such as Interleukin-8 (IL-8) and/or C reactive protein (CRP) to reduce unnecessary antibiotic therapy is needed.

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