

## Etiology and Risk Factors of Bacteremia in Pediatric Intensive Care Unit

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### Abstract:

Over the study period from the first of January to the end of December 2006 a total of 102 patients were admitted to intensive care unit(ICU) in Babylon hospital for maternity and children .These patients were complaining from pneumonia, meningitis, endocarditis, osteomyelitis, urinary tract infection, gastrointestinal tract infection and sepsis. Seventy two (70.5%) patients had positive blood culture and they are diagnosed as bacteremia cases. The study showed that gram negative bacteria caused over than 52.8% of bacteremia cases, whereas gram positive cause 47.1% of total bacteremia cases. The most gram positive bacteria were *Staphylococcus aureus* cause 16.7%, followed by *Streptococcus pneumoniae* in 12.5%, While the most gram negative bacteria , *Klebsiella pneumoniae* and *Escherichia coli* representing the major isolates, 13.9% for each one, and followed by *Pseudomonas aeruginosa* in 11.1%. Other bacterial isolates were identified and less percentage in an incidence of bacteremia. Bacteremia was identified in 67.5% with bottle milk and in mixed feeding more than in breast milk feeding (32.4%).The incidence of bacteremia occurred in the second year of age groups in 34.7%.This study showed that the isolates in males were higher than those in females .The study revealed significant differences in the incidence of bacteremia among infants with low birth body weight as compared to infants with normal birth weight. The most infections among patients who have mothers with primary education.

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**Key words:** Pediatric bacteremia, Etiology, Risk factors, ICU

### الخلاصة

خلال مدة الدراسة الممتدة من اول شهر كانون الثاني الى نهاية شهر كانون الاول لسنة 2006 تم ادخال 102 طفل الى وحدة العناية المركزة في مستشفى بابل للولادة والاطفال. المرضى كانوا مصابين بعلامات خمجية مثل التهاب ذات الرئة ، التهاب السحايا، التهاب شغاف القلب، التهاب العظام، اخماج المجاري البولية، اخماج الامعاء والمعدة والانتان الدموي. اثنان وسبعون من المرضى 70.5% كانت نتيجة زرع الدم موجبة والتي مثلت نسبة تجرثم الدم لدى الاطفال .سببت البكتريا السالبة لصبغة كرام 52.8% من حالات تجرثم الدم، في حين البكتريا الموجبة لصبغة كرام سببت حوالي 47.1%. شكلت بكتريا العقنوديات نسبة 16.7% والمسبحيات الرئوية 12.5% ، اما البكتريا السالبة كانت الكلبسيلا الرئوية و الاشريشيا القولون هما السائدتان 13.9% ثم تلتهما الزوائف الزنجارية 11.1% وشملت الدراسة عوامل الخطورة ، فكانت نسبة تجرثم الدم بين الرضع من حليب الام 32.4% ومن الحليب الاصطناعي والمختلط 67.5% . اكثر حالات الاصابة 34.7% بين الاطفال بعمر سنتين، والذكور اكثر عرضة للاصابة من الاناث، وتوجد فروق معنوية لعامل وزن الطفل حديث الولادة في حدوث الاصابة .وان اغلب الاصابات كانت بين الاطفال الذين امهاتهم لديهم تحصيل دراسي ابتدائي.

### Introduction

Bacteremia is defined as the presence of viable bacteria in blood stream which is normally free of bacteria in healthy persons (Klein ,1990). Bacteria may be introduced into the circulation by physical means (e.g.: trauma), or they may be shed into the bloodstream from a focus of infection (Wagner,1990).

Invasion of blood stream by bacteria is associated with an almost uniform increase in fatality rate in comparison with the localized disease uncomplicated by bacteremia (McCabe *et al.*,1983). Isolation of bacteria from the blood of patient usually signifies serious and uncontrolled infection that may result in death (Apri *et al.*,1995). Approximately 4 millions children less than 5 years of age die annually from acute respiratory infections, most of these are pneumonia associated bacteremia (Mckenzie *et al.*, 2000).The incidence of gram negative bacteremia in the united

states is estimated at 71000-300000 cases per year (Wagner,1990; McKenzie *et al.*, 2000).

Since bacteremia frequently portends life-threatening illness, its early detection is essential. Blood culture is the single most important procedure to detect systemic infection due to bacteria (Brooks *et al.*,2004).The expeditious detection and identification of blood-borne pathogens is one of the most important functions of the microbiology laboratory. Positive blood culture may help provide a clinical diagnosis, as well as a specific etiological diagnosis (Banjee *et al.*,1991).

The aim of this study is to investigate the role of different microorganisms in causing bacteremia and also to study the risk factors that increase its incidence among children.

## **Materials and methods:**

### **Patients:**

One hundred and two children patients were admitted to intensive care unit (ICU)in Babylon hospital for maternity and children during the period from the first of January to the end of December 2006. These patients were complaining from pneumonia, meningitis, endocarditis, osteomyelitis, urinary tract infection (UTI), gastrointestinal tract (GIT) infection and sepsis. The infections were diagnosed clinically by specialist physician at the pediatric department and the bacteremia in these patients was confirmed by isolation of bacteria from blood.

### **Collection of Data:**

Informations were obtained through a questionnaire forma designed for the purpose of the study for each child included. The following informations were taken: name, age, sex, typing of feeding, mother education, and clinical features including: body weight loss, vomiting, diarrhea, fever, shaking chills, respiratory complaints, joints pain, and others.

### **Collection of specimens:**

Blood samples were collected aseptically by standard procedure as described in Baron *et al.*(1994). The site for venipuncture must be cleansed with disinfectant to prevent contamination by flora members of the skin. Three milliliters of blood was taken into EDTA tube for hematological estimation, and 5ml of blood were taken for bacteriological study.

### **Blood analysis:**

Complete blood count was done according to standard laboratory method (Sood,1995). While total proteins was measured by Biuret method (Sawhney and Singh,2000).

### **Blood culture:**

Blood cultures which used in bacteriological study were done as described in Baron *et al.*(1994).In briefly: The blood obtained (5ml) is added directly to (50ml) of a rich medium such as brain–heart infusion broth into sterile bottle .If the blood is not being inoculated into broth, it must be transported with anticoagulant agent .The blood is diluted in the broth to reduce the concentration of antibiotics to sub-effect level.

Blood culture is usually incubated at 37C for 1-7 days. They are checked daily for turbidity, gas formation (CO<sub>2</sub>) and hemolytic production. After that, subculture on different types of media such as: blood agar , chocolate agar , MacConkey agar .

### **Bacteriological study:**

Each isolate was identified by gram stain, morphological features of colonies and conventional biochemical tests (Macfaddin,2000).

### Biostatistics analysis:

Statistical analyses were done by using student t-test (Kirkwood,1988).

### Results

In present study, seventy two bacteremic children were diagnosed. The results of blood cultures of patients showed that out of 102 patients , 72 patients had positive blood cultures, whereas 30 cases had negative blood culture . All samples of patients with positive culture revealed increased number of WBCs and increased total serum proteins.

Table-1 show the type of bacteria isolated and identified in this study. The study showed that gram negative bacteria caused over than 52.8% of bacteremia cases, whereas gram positive cause 47.1% of total bacteremia cases. The major gram positive bacteria were isolated from pediatric bacteremia cases in ICU patients, *Staphylococcus aureus* in 12 cases (16.7%), followed by *Streptococcus pneumoniae* in 9 cases (12.5%), While the most gram negative bacteria, *Klebsiella pneumoniae* and *Escherichia coli* representing the major pathogens of bacteremia , cause 10 cases (13.9%) for each one, and followed by *Pseudomonas aeruginosa* in 8 cases (11.1%). Other bacterial isolates were less percentage in an infection and more details as in this table.

**Table-1: Bacterial causes of pediatric bacteremia identified in patients of ICU.**

Type of bacteria	Number of isolates	Percentage (%)
Gram positive:		16.7
<i>Staphylococcus aureus</i>	12	12.5
<i>Streptococcus pneumoniae</i>	9	9.7
<i>Streptococcus pyogenes</i>	7	5.5
<i>Staph. epidermidis</i>	4	2.7
<i>Enterococcus faecalis</i>	2	
	34	47.1
Gram negative:		
<i>Klebsiella pneumoniae</i>	10	13.9
<i>Escherichia coli</i>	10	13.9
<i>Pseudomonas aeruginosa</i>	8	11.1
<i>Proteus vulgaris</i>	5	6.9
<i>Enterobacter aerogenes</i>	3	4.1
<i>Heamophilus influenzae</i>	2	2.7
	38	52.8
Total number	72	100

Table-2 shows the pediatric bacteremia associated with other focus of infections. The most frequent of bacteremia cases were seen that in respiratory tract infections(RTI) accounted about 38.9% .In this study the major cause of RTI was gram negative such as *Klebsiella pneumoniae* (9.7%) ,followed by gram positive bacteria such as *Streptococcus pneumoniae* (8.3%) ,whereas gastrointestinal tract (GIT) infections represented (12.5% ) of type of infection in our study and most common pathogens were *E.coli* (4.2%), *Enterobacter aerogenes* (4.2%) and *S.aureus* (1.4%) . All isolates of bacteremia associated with UTI were found in

percentage (25%).The predominant isolates in infective endocarditis (IE) cases were gram positive bacteria such as *S. aureus*, *St. pneumoniae*, *E.coli* and other bacterial pathogens. Skin and other infections representing (13.9%) as clarity in the table.

**Table-2: Prevalence of bacteremia causes in patients of ICU with related diseases.**

Type and No. of bacteria	Associated with									
	RTI		GIT		UTI		IE		Skin and others	
	No.	%	No.	%	No.	%	No.	%	No.	%
Gram positive:	5	6.9	1	1.4	3	4.2	2	2.7		
<i>Staphylococcus aureus</i> (12)	6	8.3	0	0.0	0	0.0	1	1.4	1	1.4
<i>Streptococcus pneumoniae</i> (9)	3	4.2	0	0.0	2	2.7	1	1.4	2	2.7
<i>Streptococcus pyogenes</i> (7)	0	0.0	0	0.0	1	1.4	1	1.4	1	1.4
<i>Staph. epidermidis</i> (4)	0	0.0	0	0.0	1	1.4	1	1.4	2	2.7
<i>Enterococcus faecalis</i> (2)									0	0.0
Gram negative:	7	9.7	0	0.0	2	2.7	0	0.0		
<i>Klebsiella pneumoniae</i> (10)	4	5.5	3	4.2	2	2.7	1	1.4	1	1.4
<i>Escherichia coli</i> (10)	1	1.4	0	0.0	4	5.5	0	0.0	0	0.0
<i>Pseudomonas aeruginosa</i> (8)	0	0.0	2	2.7	3	4.2	0	0.0	3	4.2
<i>Proteus vulgaris</i> (5)	0	0.0	3	4.2	0	0.0	0	0.0	0	0.0
<i>Enterobacter aerogenes</i> (3)	2	2.7	0	0.0	0	0.0	0	0.0	0	0.0
<i>Heamophilus influenzae</i> (2)									0	0.0
Total number: 72(100%)	28 (38.9)		9 (12.5)		18 (25)		7 (9.7)		10 (13.9)	

Table-3 shows that distribution of bacteremia cases according to these risk factors. The risk factors of occult bacteremia include: Age groups, sex factor, body weight, nutrition nature, type of infants feeding, and mother education.

The patients were divided into two groups:

Group I : 1 day to 2 years old which included 40 patients(infants).

Group II: >2 year to five year old which included 32 patients.

The infection rate in first group representing (55.5%) and second group representing (44.4%).

The role of type of feeding in the incidence of bacteremia in these patients is monitored. Bacteremia was identified in 27 infant patients (67.5%) with bottle milk and mixed feeding more than in only mother breast milk feeding in 13 infants (32.4%).The incidence of bacteremia occurred in the age groups in the second year of children life 25 (34.7%).This study showed that the isolates in males were higher (58.3%) than those in females (41.7%).The table that there were significant differences in the incidence of bacteremia among infants with low birth body weight(less than three kilogram) as compared to infants with normal birth weight (3Kg or more). The importance of educational level of mothers in bacteremia

incidence was studied. The most infections among patients who have mothers with primary education (41.7%).

**Table-3: Some risk factors associated with pediatric bacteremia.**

Risk factors	Bacteremia cases	
	No	%
Type of feeding (in 40 infants):		
Breast	13	32.5
Bottle	18	45.0
Mixed	9	22.5
Nutrition nature:		
Normal	50	69.4
Malnutrition	22	30.6
Sex factor:		
Male	42	58.3
Female	30	41.7
Age Factor:		
1M-1Y	12	16.6
>1-2 Y	25	34.7
>2-3 Y	13	18
>3-5Y	22	30.5
Body weight:		
Normal	43	59.7
Abnormal	29	40.3
Mother education		
Primary	30	41.7
Secondary	25	34.7
College	17	23.6

## Discussion:

In this study we have shown bacteremia in patients were admitted to ICU which diagnosed by blood culture, and bacterial isolates were identified according to conventional biochemical reactions. Seventy two patients (70.5%) with bacteremia from 102 total patients during the period of the study that represented as positive blood culture, Whereas 30 patients (29.4%) had negative blood culture.

In previous studies in our country by Mahmoud (2005) and Al-Ani *et al.* (2005) the result of blood culture of children with bacteremia showed 67.1% cases had positive culture whereas 32.9% had negative blood culture.

The presence of negative results in this study were attributed to many factors , the important one is administration of antibiotic therapy before hospitalization or the diagnosis was incorrect and the clinical manifestation was due to non bacterial causes. Sometime the isolation of bacteria was difficult unless more than two samples were taken from the same patient (Reimer *et al.*,1997; Mahmoud,2005)

These results considered high if it is compared with results of other studies. In Japan reported by Wader *et al.* (1992), they found that 8.7% were blood culture

positive. In Saudi Arabia Kingdom by Shaheen *et al.*(1988), positive blood cultures were found in 14% of 709 patients .In Gambia, Hill *et al.* (2007) revealed blood stream infection in 10.6% of 871 patients. In previous study in Iraq reported by Al-Kufy *et al.*(2006) , the febrile patients aging 2 year have positive blood culture in 18%.

This discrepancy may be explained by the endemic of our country (specially in present conditions) to different types of infectious diseases and by increase susceptibility to infections because of low immunity which is due to poor socioeconomic and nutritional states which are important factors in protection against infectious diseases(Mahmoud,2005 ; Al-Kufy *et al.*,2006) .

Hematological pictures for all blood samples of patients with bacteremia were studied. In our study were all cases of bacteremia revealed high white blood cells and raised serum total proteins. In previous study in our country by Mahmoud(2005) , he found same result in bacteremia cases. The increased total WBC count greater than 15000 cell/cu.mm indicates bacterial infection and represent risk factor in bacteremic patients (Al-Kufy *et al.*,2006).

Regarding the type of bacteria isolated we did find that most common bacterial etiology have the potential to cause bacteremia, *S.aureus*,*K.pneumoniae*,*E.coli*, *St.pneumoniae* and other bacterial causes as in table-1.

These results showed similar observation reported by other authors (Mahmoud,2005; Al-Kufy *et al.*,2006). This similarity is probably due to climate condition and use of second or less choice antibiotic therapy and unavailability of vaccine against most causes, this may be due to bad health and low level of socioeconomic in our country in present time. The result which may explain the increasing incidence of the infection in our society.

Table-2 shows the pediatric bacteremia associated with other infections. The children have underlying diseases such as RTI, GIT,UTI are regarded as major precipitating factors in the development of bacteremia (Wagner,1990). Major source of infection being skin or focus of infection (Behrman *et al.*,2000). The microorganisms likely to be inhabitants of the hospital environment and thus to colonize the skin, oropharyngeal area, GIT, UTI of hospitalized patients (Wagner,1990; Mahmoud,2005). Normally, the patients' complaint from diseases, this will help in exposing them to secondary infection like bacteremia.

The result in our study showed the most predisposing factors for bacteremia incidence in table-3. The sex incidence showed significant different between male and female bacteremia.The bacteremia frequency in male patients were more than female , this may because of the social condition and the males are play out house more than female, therefore the males are more exposure to infection. This incidence due to the fact that male children are more frequently presented to medical care. The findings in present study agreed with other reports (Tseng *et al.*,2002; Mahmoud,2005) which showed that isolates in male were higher than in female.

Al-Kufy *et al.*,(2006) found the ratio male: female is 1:2 which seems to be the opposite to the theory that says the male sex is more liable to infection, but may indicate that family protection facilities for boys are more than the girls due to the social impact to that number of patients were mainly females(3:2) which may play role in this discrepancy. The other explanation is that males are generally more precious to the family and tend to get better care (Tseng *et al.*,2002).

Nutritional states are important factors in protection against infectious diseases (Al-Kufy *et al.*,2006). Berkowitz *et al.*,(1988) and Friedland (1992) identified severe malnutrition as risk factor for bacteremia and death in south Africa. In countries

where breast feeding is more common and prolonged, bacteremia is much less frequent during the first year of life and infants breast fed longer than 6 months were less likely to bacteremia disease during the second year of life (Leventhal *et al.*, 1986). These results confirmed the fact that breast feeding is one of the most effects against bacterial infections.

The incidence of bacteremia occurred in the second years of children life. These agreed with others (Berkowitz *et al.*,1988) who showed that increased occurrence of bacteremia in children less than 6 years especially in second years. The increased incidence of bacteremia among children may be due to the children in this ages become more exposure to infection especially RTI and UTI which lead to secondary infection such as bacteremia or due to immune deficiency in production of antibodies to the bacterial antigens (Berhrman *et al.*,2000).

Table-3 shows that there were significant differences in the incidence of bacteremia among infants with low birth body weight. These results agreed with other studies (Reimer *et al.*,1997,Mahmoud,2005). This explain the role of the factors contributing to initiation of such infection are low body weight, premature neonates, immunosuppressive agents, wide spread use of broad spectrum antibiotic that suppress the normal flora, invasive procedure, prolonged survival of patients (Al-Kufy *et al.*,2006).The rate of infection decreased with increasing birth weight that is the lower the birth weight the more likely the patients develops infection (Reimer *et al.*,1997;Tseng ,2002).

Other risk factor for bacteremia is mother education of patients. The culture level, personal hygiene and socioeconomic level for family of patient are very important factors in preventing the bacteremia among infants (Alla *et al.*,1996; Berhrman *et al.*,2000).

This study confirms that bacteremia is an important illness in hospital patients especially in children.

## References

- Al-Ani, S.K.; Mahmoud I.S. and Al-Rawi,A.(2005)Bacteremia in children and their antibiotic susceptibility . J. Basic Med.Sc., 5(1):99-106.
- AL-Kufy, M.;Al-Behash,F. and Abdul-Rudha,I.(2006) Blood culture positivity in febrile children aging 2 years and above without detectable focus of infection. Kufa Med.J.,9(1):182-186.
- Alla, S.; Cuunningham,M.; Derrick ,B. and Jelliffe,P.(1996) Breast feeding and health in the 1980s . J.Pediatr., 118:166-261.
- Arpi, M.; Renneberg, J. ; Anderech, H.; Nielsen, B. and Larsen, S. (1995)Bacteremia at Danish university hospital during a twenty five year period 1967-1992. J.Infect.Dis. 27:245-251.
- Banrjee, S. ; Emori,T. ;Culver,D., *et al* (1991) Secular trends in nosocomial primary blood stream infection in united states . Am. J. Med. , 91:86S-90S
- Baron, E.J.; Petrosen, L.R. and Finegold,S.M. (1994) Microorganisms encountered in the blood. In: Baily and Scott's diagnostic microbiology, Mosby, USA, 9<sup>th</sup> edition, PP.193-209.
- Behrman,R.E. ; Kliegman ,R.M. and Jenson, H.(2000) Nelson's textbook of pediatrics ,W.B Saunders Co.,Philadelphia, 16<sup>th</sup> edition, pp.328,732.
- Berkowitz, F.E.: Bacteremia in hospitalized black South Africa children. Am.J.Dis.Child; 1984;138:551-555.
- Brooks,G.F; Butel,J.S. and Morse,S.A.(2004)Principle of diagnosis medical microbiology, In: Jawetz,Melnick and Adelberge's Medical Microbiology, McGraw-Hill Co.,USA, 23<sup>rd</sup> edition, PP.703-733.

- Friedland, I.R( 1992)Bacteremia in severely malnourished children .Ann. Trop. Pediatr.,12:433-440.
- Hill,P.;Onyema,C.;Ikumapayi,U.;Secka,O.;Ameyaw,S.;Simmonds,N.;donkor,S.;How E,S.;Tapgun,M., Corrah,T. and Adegbola,R.(2007) Bacteremia in patients admitted to an urban hospital in West Africa. BMC Infectious diseases, 7(2):2334-2337.
- Kirkwood, B.R.(1988)Essentials of medical Statistics, Blackwell scientific publications, first edition, PP.41-45.
- Klein , J.O. (1990) Bacteriology of neonatal sepsis. Peadiatr. Dis. , 9:778-781.
- Leventhal,J.; Shapiro, E.;Aten, C.; Berg,A and Egerter ,S(1986) Does breast feeding protect against infection in infants less than 3 months of ages. J.Pediatr.,78:89-903.
- Macfaddin,J.F.(2000)Biochemical tests for identification of medical bacteria, Lippincott, William and Wilkins Co. ,USA. 3<sup>rd</sup> edition.
- Mahmoud, E.S.(2005) Aetiology and risk factors of bacteremia in children. J. Basic Sc.,3(4):246-250.
- McCabe, W.; Treadwell,T. and Maria, A.(1983)Pathophysiology of bacteremia. Am. J.Med., 28:8-16.
- Mckenzie, H.; Reid, N. and Dijkhuizen ,R.(2000) Clinical and microbiological epidemiology of Streptococcus pneumoniae bacteremia . J .Med. Microbiol.; 49:361-366.
- Reimer, L.G.; Wilson,M. and Weinstein ,M.(1997)Update on detection of bacteremia and fungemia. Clin. Microbiol. Rev.,10(3):444-465.
- Sawhney.S.K and Singh, R.(2000) Introductory practical biochemistry, Narosa publishing house, UK. 3<sup>rd</sup> edition.
- Shaheen, F.A; Graninger,W.; Zazgornik, J; Balcke, P.;Kopsa,H.and Stockenhuber ,F . (1988) Bacteremia in relation to the type of vascular access in patients on haemodialysis. Saudi Med.J,9(4):400-405.
- Sood, R.(1995) Practical pathology and microbiology, Jaypee Co., India, 2<sup>nd</sup> edition, PP.47-48.
- Tseng,Y.; Chiu,Y.; Wang,J.; Lin,H.; Su.B.;and Chiu,H.(2002) Nosocomial blood stream infection in a neonatal intensive care units of a medical center. J.Microbiol. Immunol. Infect. , 35:168-172.
- Wader,K; Kamashim,S; Ozaki,K.; Zasshi,K(1992) Clinical study on bacteremia in last 15 years .Pediatr. Infect. Dis.;66(5):620-627.
- Wagner, G.E.(1990) Bacteremia and septicemia, In: Kingsberg, D. and Wagner, G. Microbiology, John Wiley and sons Co., USA, 2<sup>nd</sup> edition, PP.315-323.