Study of Gram Positive Infantile bacteremia using some Physiological markers and Antibiotics Susceptibility patterns.

Ali H. Al-Marzoqi
University of Babylon, College of Science for women, Biology Department

Abstract
130 blood samples were obtained from febrile infants who admitted to Babylon Maternity and Children Hospital during the period from February \ 2008, until June\ 2008. This study investigated the distribution and the most causative agents (Gram Positive Bacteria), the elevation of (CRP, ESR and WBCs count) with the infections and antibiotic susceptibility patterns of bacterial pathogens isolated from patients with bacteremia. Results showed that *Staphylococcus aureus* formed (57%) from all bacteremia causative agents followed by *Streptococcus pneumoniae* (32.3%) and *Bacillus spp.* (10.7%).

Staphylococcus aureus showed sensitivity for Amikacin, Nitrofurantoin, Norfloxacin and Ofloxacin, while *Streptococcus pneumoniae* were sensitive to Amikacin, Amoxicillin, Cefodizime, Chloromphenicol, Clarithromycin, Gentamycin, Kanamycin, Lincomycin, Nitrofurantoin, Norfloxacin, Ofloxacin, Oxacillin, Oxytetracyclin, Penicillin and Rifampim, *Bacillus spp*. Revealed sensitivity with Amikacin, Chloromphenicol, Gentamycin, Kanamycin, Nitrofurantoin, Norfloxacin, Ofloxacin, Piperacillin, Tetracycline, Tobramycin and Vancomycin. From 130 infants with bacteremia 88 had C-Reactive Protein >24 mg/L, 82 had ESR >35 mm/hour, and 73 had WBC >15 000/mL.

الخلاصه
في هذه الدراسه تم جمع ١٣٠ عينة دم من اطفال دون السنتين مصابين بالتجرثم الدموي، ادخلو الى مستشفى بابل للولاده والاطفال للفتره من شباط/٢٠٠٨ الى حزيران/٢٠٠٨. تم التحري عن المسببات الرئيسيه للتجرثم الدموي (البكتريا الموجبه لصبغة كرام) ، ارتفاع عدد من المعايير الفسلجيه مع الاصابه (CRP, ESR, WBCs count) بالاضافه الى اختبار الحساسيه للمسببات الجرثوميه. كانت نتائج المسببات كما يلي *Staphylococcus aureus* شكلت نسب اصابه (٥٧%) ، *Streptococcus pneumoniae* (٣٢,٣%) و *Bacillus spp* (١٠,٧%).

اظهرت بكتريا الـ *Staphylococcus aureus* حساسيه تجاه المضادات Amikacin, Nitrofurantoin Norfloxacin و Ofloxacinبينما اظهرت *Streptococcus pneumoniae* حساسيه عاليه لعدد من المضادات وشملت Amikacin, Amoxicillin, Cefodizime, Chloromphenicol, Clarithromycin Gentamycin, Kanamycin, Lincomycin, Nitrofurantoin, Norfloxacin, Ofloxacin, Oxacillin, Oxytetracyclin, Penicillin and Rifampim اما لبكتريا *Bacillus spp*. فكانت المضادات التاليه Amikacin, Chloromphenicol, Gentamycin, Kanamycin, Nitrofurantoin Norfloxacin, Ofloxacin, Piperacillin, Tetracycline, Tobramycin and Vancomycin.
من ١٣٠ عينه تجرثم دموي ،كانت ٨٨ عينه (CRP >٢٤ ملغم/لتر) ، ٨٢ عينه (ESR > ٣٥ ملم/ساعه) و ٧٣ عينه (WBCs> ١٥٠٠٠ /مل).

Introduction

Fever is a common presenting symptom in pediatric outpatient practices and emergency rooms, particularly in children < 3 years of age. Approximately 20% of these children will have no identifiable source of fever after history and physical examination [1]. Although most of these children will have a

benign viral illness, children < 3 years of age are at increased risk of clinically undetectable serious bacterial infection (SBI). Approximately 2% to 3% of these children have occult bacteremia (OB) [2], while 2% to 8% have urinary tract infection (UTI), depending on the age and gender. Other causes of SBI include occult bacterial pneumonia (3%), meningitis, or less commonly bone and joint infection, deep soft tissue abscess, or bacterial enteritis [3].

Early diagnosis and treatment of infection is critical in the care of normal and immunodeficient patients. Excluding infection from the differential diagnosis avoids the use of potentially harmful antibiotics and, just as importantly, clarifies the clinical situation. Physicians are always on the alert for a method that promises to be either sensitive or specific for the early detection of infection. In the past several years, a number of investigators have concluded that measurement of the level of C-reactive protein (CRP) is a sensitive and, in certain clinical settings, specific method for the early detection of infection [4]. Blood culture remains the gold standard in detecting OB; however, the average time to detection of positive cultures is 15 to 16 hours and may be as long as 24 to 48 hours, increasing the risk of complications. Total white blood cell (WBC) is the most commonly used screening test for OB, and clinical practice guidelines suggest sing a total WBC of > 15 000 as a determining factor between patients who can be observed and those who need antibiotic therapy [5].

Some studies have suggested that acute phase reactants, including C-reactive protein (CRP) may be helpful in this clinical situation [6]. The aim of this study was to diagnostic properties of quantitative CRP in comparison with other clinical and laboratory predictors of occult SBI in young children with fever without apparent source of infection.

Materials and Methods

This prospective study was performed between February \ 2008, until June\ 2008. A total of 130 blood sample obtained from children under two years of age who presented to the Babylon Maternity and Children Hospital with temperature >38°C were evaluated by residents and pediatric emergency medicine attending. Those children who, after careful history and physical examination, had clinically undetectable source for the fever were enrolled in the study.

Demographic information, ie, age , sex, temperature, duration of fever, total WBCs, erythrocyte sedimentation rate (ESR) and semi-quantitative CRP concentration were obtained. A blood culture was carried out for each patient.

C-reactive protein test done by using latex kit from HUMATEX CRP (Germany) for qualitative and semi-quantitative determination. In this study 34 different antibiotics to estimate the sensitivity of UTI causative agents, using disk diffusion agar using Muller Hinton agar. For hemocytometer WBC counts, blood specimens were examined microscopically on a Neubauer chamber (Neubauer hemocytometer) by the same technician. Bacterial isolates were identified to the level of species using cultural characteristics and conversional biochemical test [7 and 8].

Results and Discussion

The results showed that *Staphylococcus aureus* formed (57%) from all bacteremia causative agents followed by *Streptococcus pneumoniae* (32.2%) and *Bacillus spp.* (10.7%) **(Table 1)**, these results are nearly compatible with Karin, that *Staphylococcus* was responsible for (82%) of positive blood culture [9].

Korppi in his study found that *Streptococcus pneumoniae* play important role in bacteremia infection [10].

Scott *et,al.* 2005 reported that *S. pneumoniae*, *S. aureus*, and group A streptococci predominated and that group B streptococcal infections were uncommon. They found that group B streptococcal bacteremia was the leading bacterial cause of early death in young infants [11].

Table1: Percentage of Etiological agents causes bacteremia in infants.

Etiological agents causes bacteremia	No.	%
Staphylococcus aureus	74	57
Streptococcus pneumoniae	42	32.3
Bacillus spp.	14	10.7
total	130	100

In this study, the rate of Gram-positive bacteremia in male and female was (40%) and (17 %) respectively for the *Staphylococcus aureus* infection, (20.8%) and (11.5 %) respectively for the *Streptococcus pneumoniae* infection and (3.8%) and (6.9 %) respectively for the *Bacillus spp*. infections **(Table 2)**. This result is agreeable with some other studies like Shaimaa (2006) and Al-Bass (1993), which stated that no sex based difference, exists in the prevalence of bacteremia [12 and 13].

Infants whom investigated for bacteremia were below 24 months of age. This age looks to be more infected with bacteremia because they have a low immunoglobulin G antibody (IgG) response to encapsulated bacteria [14].

Some studies pointed that infant aged 3 to 24 Months with fever and no major source of infection were at highest risk for occult bacteremia (OB) [15]. Moreover, Kuppermann concluded that all children below 24 months were at higher risk for bacteremia [16].

Table 2: Age and gender distribution and frequency of bacteremia causes isolated from infants.

Age group (**Months**)	**Gram Positive Bacteremia Causes**					
	Staphylococcus aureus		*Streptococcus pneumoniae*		*Bacillus spp.*	
	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)
< 6	10 (7.7)	2 (1.5)	2 (1.5)	-	-	-
7-12	5 (3.9)	9 (7)	2 (1.5)	-	3 (2.3)	-
13-18	22 (16.9)	-	16 (12.4)	15 (11.5)	-	2 (1.5)
19-24	15 (11.5)	11 (8.5)	7 (5.4)	-	2 (1.5)	7 (5.4)
Total	52 (40)	22 (17)	27 (20.8)	15 (11.5)	5 (3.8)	9 (6.9)
	74 (57%)		42 (32.3%)		14 (10.7)	

This study showed the distribution and antibiotic susceptibility pattern of microbial species isolated from infants with bacteremia **(Tables 3, 4 and5)**. These organisms cause a variety of infections including bacteremia [17]. Antibiotic resistance is a major clinical problem in treating infections caused by these microorganisms. The resistance to the antimicrobials has increased over the years. Resistance rates vary from country to country [18].

In present study isolates from infants with bacteremia showed sensitivity to several antibiotics; *Staphylococcus aureus* shows sensitivity for Amikacin, Nitrofurantoin, Norfloxacin and Ofloxacin, while *Streptococcus pneumoniae* sensitive to Amikacin, Amoxicillin, Cefodizime, Chloromphenicol, Clarithromycin, Gentamycin, Kanamycin, Lincomycin, Nitrofurantoin, Norfloxacin, Ofloxacin, Oxacillin, Oxytetracyclin, Penicillin and Rifampim, *Bacillus spp*. Reveals sensitivity with Amikacin, Chloromphenicol, Gentamycin, Kanamycin, Nitrofurantoin, Norfloxacin, Ofloxacin, Piperacillin, Tetracycline, Tobramycin and Vancomycin. These results are nearly consistent with the previous data of other community- based studies [19].

Table 3a: Antimicrobial potency and spectrum for 13 selected antimicrobial agents tested against most frequently occurring bacteremia pathogens.

Microorganism	**Antimicrobial agent / % sensitive strains**												
	AK	AX	AMC	AZM	B	PY	CDZ	FOX	ZOX	CL	C	CLR	DA
Staphylococcus aureus	**90**	-	1	1	15	10	50	-	10	10	10	10	-
Streptococcus pneumoniae	**88**	**90**	-	10	-	-	**100**	-	20	15	**75**	**75**	15
Bacillus spp.	**100**	-	-	-	-	-	-	-	-	-	**90**	15	10

AK \Amikacin, AX \Amoxicillin, AMC \Amoxicillin + Clavulanic acid, AZM \Azithromycin, , B \Bacitracin, PY \Carbenicillin, CDZ \Cefodizime, FOX \Cefoxitin,

ZOX \Ceftizoxime, CL \Cephalexin, C \Chloromphenicol, CLR \Clarithromycin, DA \Clindamycin

Table 3b: Antimicrobial potency and spectrum for 13 selected antimicrobial agents tested against most frequently occurring bacteremia pathogens.

Microorganism	Antimicrobial agent / % sensitive strains												
	E	CN	K	L	ME	F	NOR	OFX	OX	T	P	PRL	RA
Staphylococcus aureus	20	10	10	10	10	**90**	**95**	-	**90**	50	50	-	-
Streptococcus pneumoniae	45	**90**	**80**	**95**	10	**90**	**100**	**95**	**85**	**95**	**90**	10	**75**
Bacillus spp.	50	**70**	**85**	30	-	**100**	**100**	**90**	20	20	10	**85**	-

E \Erythromycin, CN\Gentamycin, K\Kanamycin, L\Lincomycin, ME\Methicillin, F\Nitrofurantoin, NOR\Norfloxacin, OFX \Ofloxacin, OX\Oxacillin, T\Oxytetracyclin, P\Penicillin G, PRL \Piperacillin, RA\Rifampim.

Table 3c: Antimicrobial potency and spectrum for 8 selected antimicrobial agents tested against most frequently occurring bacteremia pathogens.

Microorganism	Antimicrobial agent / % sensitive strains							
	RF	SP	S	TE	TOB	TMP	SXT	VA
Staphylococcus aureus	10	-	15	-	-	-	45	20
Streptococcus pneumoniae	**65**	**90**	-	55	**75**	55	10	**65**
Bacillus spp.	20	20	10	**65**	**75**	10	30	**75**

RF \Rifamycin, SP\Spiramycin, S\Streptomycin, TE\Tetracycline, TOB\Tobramycin, TMP\Trimethoprim, SXT\Trimethoprim + Sulphamethaxazole, VA\Vancomycin

These results were done according to performance standards for antimicrobial disk susceptibility tests, CLSI (formerly NCCLS). The antibiotic which not including in CLSI chart, FDA approved performance standars for antimicrobial discs obtained from drug manufactures [20].

CRP >20 mg/L, ESR >30 mm/hour, and WBC >15 000/mL are key findings in various studies on febrile infants [21]. CRP is an acute phase reactant which opsonises invading pathogens. Levels of CRP increase within 6 hours of an inflammatory stimulus, and may rise up to 1000-fold, measurement of CRP provide direct index of acute inflammation, in contrast to CRP, the ESR is an indirect measure of the acute phase response [22]. The diagnostic value of these parameters for predicting serious bacterial infection in febrile infants, however, is conflicting. Our investigation showed **(Table 6)** that from the 130 febrile infants with bacteremia, 88 had CRP >20 mg/L, 82 had ESR >30 mm/hour, and 73 had WBC >15 000/mL. Our results corroborate the findings Madathilparambil [23], Shaoul [24], Bircan [25] and Cuello [26] .

Table 4: The Results of Diagnostic Test in Presence of a Positive Blood Culture.

Diagnostic Test	No.	%
CRP > 24 mg/L	88	67.7
ESR > 35 mm/h	82	63.1
Peripheral WBC > 15 000/mL	73	56.2

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