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Original Article

Community Versus Nosocomial *Staphylococcus aureus* Septicemia in Children Admitted to Aliasghar Children Hospital, Tehran, Iran

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ABSTRACT

Background and Objectives: **The aim of the study was to determine the role and characteristics of nosocomial and community acquired *Staphylococcus* sepsis in admitted children in tertiary centers in Iran.**

Patients and Methods: **A cross sectional descriptive-analytic study was performed since March 2008 to March 2009 in which all blood cultures from various admitted patients were checked for *Staphylococcu aurues* in Aliasghar Children Hospital, Tehran, Iran. Upon diagnosis by appropriate microbiologic tests, antimicrobial testing was done according to CLSI methods.**

Results: **Overall, 2647 blood culture samples from 5197 admitted children were sent from which, 25 cases of *S. aurues* septicemia were isolated; the rate was 4.8 in 1000 admissions;1.3 in 1000 admissions were nosocomial and 3.5 in 1000 admissions were community acquired sepsis. Ten cases were neonates and remainder was older. Eighteen cases were CA and 28% were NI septicemia with mean age of 38.8 months and 8.2 months, respectively. Mean duration of admission in NI group was 20.5 days, however it was 12.6 days in CA group; they also had higher mortality rate.**

Conclusion: **The rate of *Staphylococcus* sepsis in this study was higher than developed countries for both CA and NI cases, both groups had high rate of resistance. Although most cases were CA in which significant proportion had underlying malignancy, NI group had a longer duration of admission and mortality.**

Keywords: *Staphylococcus aureus*, Septicemia, Community Acquired Infections, Nosocomial Infection, Children

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Introduction

Although *Staphylococcus aureus* septicemia is not considered a common community or nosocomial septicemia in pediatric age group, but it is a very important cause of sepsis in adults (1). In a 5 year retrospective study in Royal Alexandra Hospital in Asuralia on children,140 cases of *Staphylococcus* bacteremia was diagnosed which indicated a rate of 3 positive out of 1000 blood culture requested in this age group(2);community acquired sepsis had a rate of 0.5 in 1000 admitted child while nosocomial *S. aureus* sepsis had a rate of 1.6 in 1000 admission in this study; despite the improvement of living standards this organism has remained an important pathogen and seems to remain a problematic pathogen in the future as well (2).

Some studies in Iran have also shown that *S. aurues* sepsis has not been a common blood isolate there. In a retrospective study in Ahvaz for example, 2790 blood cultures were analyzed during a 28 months period and from those positive cultures, about 87% were gram negative organisms and among gram positive organisms coagulase negative *Staphylococcus* infection was the most predominant organism.

This study was done in a general hospital and almost half of cases were in pediatric age group(3). However, study of *Staphylococcus* sepsis is still very important due to increasing rate of resistance even to vancomycin among these organisms and very dangerous complications of *S. aureus* septicemia. *Staphylococcus aureus* frequently colonizes and infects hospitalized patients with decreased host defenses, chronic diseases and indwelling medical devices so study on specific risk factors in pediatric age group for both community and hospital acquired sepsis is important(4).

Since this organism commonly colonize children with chronic diseases, those with altered immune function and cases with various indwelling catheters(5),such a study in a pediatric tertiary and teaching center is more important as such patients are usually admitted in these centers and the rate of nosocomial infections are usually higher in these hospitals(6).

Some studies have criticized present classification of community versus hospital acquired sepsis for *S. aureus* as the later one should be more predictive of methicillin resistant *S. aureus* (MRSA)(6). On the other hand, clinical course and manifestation of *S. aurues* septicemia in pediatric age group differs from adult cases and there might be some differences also between those septicemias acquired from community from nosocomial cases as the later group usually is caused by more resistant organisms and needs more aggressive empiric therapy and may have a worse prognosis and course.

Therefore, we performed this study to compare the rates in our setting and to clarify the differences between these two types of sepsis from both clinical and health care associated burden views.

Material and Methods

We studied the *S. aurues* septicemia during one year period in Aliasghar Children Hospital, a 140 bed tertiary educational hospital in Tehran, Iran. A cross sectional descriptive-analytic study was performed since March 2008 to March 2009 in which all blood cultures from various admitted patients were checked for *S. aureus*. Only one sample was taken from each patient.

Blood cultures were kept for at least one week at 37˚C, subcultures were performed every 24,48 and 72 hours on blood and chocolate agar. After observing any bacterial growth, the colonies were isolated and subjected to bacterial identification schemes such as gram staining, catalase and coagulase tests.

Then antimicrobial sensitivity test was done by disk diffusion method (Padtan Teb disks made by a home made company)and was interpreted according CLSI method. Immediately upon diagnosis of *S. aureus* at the lab, patients were visited daily and

questionnaire including demographic, underlying disorders, clinical and treatment parameters were gathered and national nosocomial surveillance system criteria was used to classify cases as nosocomial sepsis versus community acquired cases(7).

For acceptance of *S. aureus* as a nosocomial pathogen, we followed the criteria in national manual of infection control based on national nosocomial surveillance system(NNIS) definition of nosocomial infections; so a code of "laboratory confirmed blood stream infection " was labeled if one of following criteria was present:1)Growth of a pathogen from one or more blood samples in a patient who has an intravenous line and has developed fever, chills and /or hypotension at least 48 hours after admission at hospital. 2)For patients below one years of age, fever, hypothermia, apnea and /or hypotension can be substituted as clinical findings.

Data were analyzed by student *t*-test for quantitative parameters by SPSS software in these two groups; *P* value of 0.05 or less considered significant. Other parameters were shown in percentages in all patients separately in two groups[newborns(first 30 days of life) and after neonatal period]and also in nosocomial(NI)and community acquired (CA) groups, respectively. Patient's names kept secret and no intervention was done, so there was no ethical issue for this study.

Results

Overall, 2647 blood culture samples from 5197 admitted children were sent during this period from which, 25 cases of *S. aureus* septicemia including 18 males (72%) and 7 females (28%) were isolated;i.e,0.9% of all blood cultures were positive for this organism and the rate of *S. aureus* bacteremia was 4.8 in 1000 admissions;1.3 in 1000 admissions were nosocomial and 3.5 in 1000 admissions were community acquired sepsis.

Ten cases (40%) were neonates and remainder (60%) was older than 1 month of age. Mean age for all cases was 30 months (from 1 day of life to 12 years of age); 18 cases (72%) were CA and 28% were NI septicemia with mean age of 38.8 months (SD=43 months) and 8.2 months (SD=18months), respectively. The proportion of NI sepsis to CA sepsis in newborns was 4 to 10(40%) and for older children was 3 to 15(20%). The two-tailed *P* value was equal to 0.6690 (95% confidence interval :from -176.8712 to 115.6312,df=23). So by conventional criteria, this difference was considered not statistically significant.

Mean duration of admission in NI group (up to discharge or death) was 20.5 days (SD=14.8 days), however it was 12.6 days (SD=13.2 days) in CA group. The two-tailed *P* value was less than 0.0001(95% confidence interval: from 40257.359 to 40353.441,df=23), so this difference was considered to be extremely statistically significant.

For NI cases, the underlying or triggering problems for such an infection were metabolic disorder in 1(14%), acute lymphoblastic leukemia and chemotherapy in 1(14%) and mechanical ventilation in 1(14%). In CA group, acute lymphoblastic leukemia and chemotherapy was found as an important underlying disease in 7 cases(39%), other problems was severe failure to thrive in one case(6%).

Overall, clinical manifestations of *S. aureus* sepsis during neonatal period in order of frequency were: poor feeding(100%),respiratory distress(50%), icter(40%), fever(10%) and bollous skin lesions(10%). In older children, fever (67%), respiratory distress (40%), convulsion (20%) and sore throat(7%) were the presenting manifestation. Table 1 shows the clinical manifestations in each group.

Table 1: Clinical manifestations and outcome of Community acquired and nosocomial *Staphylococcus aureus* septicemia in 25 cases in Aliasghar Children Hospital, 2008-2009,Tehran (n,%)

groups	Age groups No. (%)	Poor feeding No. (%)	Fever No. (%)	Respiratory distress No. (%)	Icter No. (%)	Skin lesion No. (%)	Convulsion No. (%)€	Sore throat No. (%)	outcome
CA group 18(72%)	Newborn 6(33)	6(100)	1(17)	1(17)	3(50)	1(17)	-	-	Death:2 cases(11%),others were discharged
	Older 12(67)	12(100)	8(67)	6(50)	-	-	-	1(8)	
NI group 7(28%)	Newborn 4(57)	4(100)	-	4(100)	1(25)	-	-	-	Death:4(57),transfer to other hospital by the family:2(29), discharge:1(14)
	Older 3(43)	3(100)	3(100)	-	-	1(33)	1(33) ¥	-	

€:vesicular and bollous lesions ¥:petechia and purpura

Table 2 indicates the in vitro susceptibility tests in isolates. For CA group, no *S. aureus* coverage had been started on admission in 7(39%) of cases, empiric therapy with vancomycin had been used for 9 cases (50%) and clindamycin for 2 cases(11%). In NI group, anti *S. aurues* drug were started for 5 cases (71%) ;4 cases had got vancomycin and one case got cloxacillin as empiric therapy, for two cases(29%) no initial *Staphylococcus* coverage had been used.

Table 2: Resistance rates by in vitro susceptibility tests in Community acquired and nosocomial *Staphylococcus aurues* septicemia for 25 cases in Aliasghar Children Hospital,2008-2009,Tehran (n,%)

Groups	Cloxacillin No. (%)	Cephalothin No. (%)	Vancomycin No. (%)	Cotrimoxazole No. (%)	Ceftriaxone No. (%)	Imipenem No. (%)
NI cases 7(28%)	6(86)	6(86)	0	4(57)	6(86)	3(43)
CA cases 18(72%)	10(56)	10(56)	0	7(39)	9(50)	4(22)
total	16(64)	16(64)	0	11(44)	15(60)	7(28)

Discussion

Staphylococcus aureus is known to be a leading cause of bacteremia in childhood, and is associated with severe morbidity and increased mortality (8). The rates of both NI and CA sepsis in the present study were quite more than Australian study(2); the total rate of *Staphylococcus* sepsis was more than twice of their rate and interestingly, the proportion of NI to CA sepsis was reverse in our study; most cases were apparently community acquired but given the high rate of malignancy as underlying disorder in CA group in our study, it seems that this difference might be due to our hospital setting in which large number of leukemic cases are admitted in oncology ward. Various chemotherapy regimens are being used for these patients with various myelosuppression effects, so the observed result might also be due to chemotherapy that is more aggressive and needs to be investigated more.

Our previous study for nosocomial infections at Aliasghar Children Hospital had shown that *S. aureus* is the leading cause of nosocomial infections; it was causative agent for 10 episodes of nosocomial sepsis,5 cases with surgical site infections and 3 episodes of *Staphylococcus pneumonia*. After *S. aureus*, *Klebsiella pneumonia* and *E. coli* were the next common organisms for nosocomial sepsis during the period of study (9).

The observed rate of community acquired *S. aureus* sepsis in a multicentric study from Argentina in children was 44 cases during one year period of study in 2006-2007(10), which shows that there is similar high rate for CA infection due to this organism in developing countries. In this study, the mean age of patients was 30 months, which is similar to our study and in both of aforementioned studies, males were more affected; the finding, which is again consistent with our findings.

In contrast, *S. aureus* bacteremia in children and neonates in a 10 year retrospective review from 1993 to 2003 in England showed that thirty-three were neonates and all of their bacteremia were hospital acquired; these newborns usually (87%) had non-specific presentation and three (10%) infants died. However, in pediatric unit, 64 episodes were found with median age 2 years; 20% of bacteremia was hospital acquired. Presentations were with skin infection 18, bone/joint infection 13, non-specific 13, and respiratory 8. One (2%) child died, from an unrelated cause (11). So just 97 cases during a 10 years study had been found which again shows that the observed rate of SA bacteremia in our setting is unacceptably high. Although there are similarities in terms of CA sepsis group manifestation, but they had much less cases of NI cases after neonatal period; hence comparing to this study in UK, the more aggressive and fulminant presentation of SA sepsis is seen more frequently in our setting after neonatal period. This might be again due to large number of underlying problems in our CA group.

It is important to note that the rate and clinical picture of SAB in children seems to change over time; for example, another study in Denmark was done to determine developments in incidence and mortality rates, as well as risk factors associated with outcome in *S. aurues* sepsis in children. Data from 1971 through 2000 in a nationwide registration of *S. aureus* bacteremia (SAB) among children and adolescents from birth to 20 years of age was performed. During the 30-year study period, 2648 cases of SAB were reported. Incidence increased from 4.6 to 8.4 cases per 100,000 population and case-mortality rates decreased from 19.6% to 2.5% (8) .Therefore, the observed rate of mortality in our study seems to be high. Hospital-acquired infections dominated the infant group in this study, accounting for 73.9%-91.0% versus 39.2%-50.5% in the other age groups. These figures are in contrast to our study in which although the proportion of NI sepsis by SA was higher in newborns but still most cases were diagnosed as community-acquired infection. Previous colonization and invasive procedures for patients with malignancy or in NICU setting with intravascular catheters might have a role to colonize our apparently CA cases by *S. aurues* and must be better studies.

Concerning risk factors of death, some studies have shown that by multivariate analysis, pulmonary infection and endocarditic for all age groups, comorbidity for the older than 1 year, and hospital-acquired infections for the oldest group were independently associated with an increased risk of death (8), so higher mortality rates in our study can be partially explained.

Over two third of isolates from NI group and more than half of isolates in CA group in our study were resistant to penicillinase resistant penicillin and first generation of cephalosporin. This shows a very high rate of MRSA in both groups. Given the fact that Fatality rates for patients with clinically significant bacteremia are higher than MSSA (11) treatment of MRSA bacteremia with vancomycin is recommended for most cases, provided it is begun early. At hospitals with endemic MRSA it may be necessary to use vancomycin in the initial treatment of nosocomial bacteremia in high risk patients until the identity and antimicrobial susceptibility of the bloodstream pathogen can be determined (12).

The increase in duration of admission in NI

group compared with CA group in this study was not surprising as the former groups were admitted for unrelated cause and *Staphylococcus* sepsis occurred unexpectedly during their admission; it has also been shown previously that nosocomial infections extend the duration of admission in PICU admitted cases (13).

Most cases of CA sepsis in this study were older than 1 month of age, were resistant to cloxacillin and significant number (39%) had cancer as the underlying disease; the increase in CA-MRSA sepsis in children with cancer was also recently shown in a study in Hawaii in which 10 cases out of 52 cases of staphylococcusbacteremia were due to MRSA during a seven years period; one third of cases developed complications (hypotension, port abscess, embolic skin lesions, lung abscess vein thrombosis and meningitis),73% of bacteremia episodes were catheter associated (14). Risk factors of *S. aureus* bacteremia in a recent study in Australia in adults were injectable drug use, haemodialysis, indwelling vascular catheters and immunosuppression. Metastatic infection developed in up to one-third of patients, with joints and heart valves being the most commonly affected sites (15). It is therefore very important to differentiate complicated from uncomplicated *S. aureus* bacteremia as the treatment, prognosis and investigations are different(16). Studies have shown that in approximately one-half of patients with *S. aureus* bacteremia, no portal of entry can be documented. This group of patients as well as patients receiving haemodialysis, injection drug users, patients with diabetes, and patients with preexisting cardiac conditions or other comorbidities are especially prone to septic metastases. Nasal carriage has been identified as the most important source of CA sepsis. So, better eradication and control strategies, including nasal decolonization and more-active antibiotics, are needed to combat *S. aureus* bacteremia (17).

Concerning the limitations of study, we did not look at MRSA rate in these two groups; it should be done as a complementary study to define the exact role of empiric treatment of cases who are suspicious to *S. aureus* bacteremia in various settings.

Conclusion

Staphylococcus sepsis in this study was an important cause of sepsis both in CA and NI cases suspicious to bacteremia, although most cases were community acquired in which significant proportion had underlying malignancy, NI group had a longer duration of admission and mortality; isolates in both groups had high rate of resistance to penicillinase resistant penicillin and first generation of cephalosporins but the more reliable methods for antimicrobial sensitivity tests are needed if better empiric protocols for CA and NI suspicious cases are to be developed.

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