ORIGINAL PROF-950

NEONATAL SEPSIS

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ABSTRACT… info@ghurkitrust.com **Objective:** To find out the bacterial pathogens in neonatal sepsis and to determine antimicrobial sensitivity patterns of these pathogens. **Place and Duration:** At the Neonatal Unit of Ghurki Trust Teaching Hospital Lahore, from February 2003 to December 2004. **Design:** It was an analytical comparative study, done in prospective fashion. **Subjects and Methods:** A total of 100 culture proven neonates of sepsis were included. Clinical data including neonatal and maternal history, physical examination and laboratory data including blood counts and cultures were recorded. The cases that have already been given antibiotics were excluded. Standard disc-diffusion method was used to assess the sensitivity pattern for the antibiotics (ampicillin, gentamicin, cefotaxime, ceftazidime, amikacin and imipenem). **Results:** Out of total of 100 cases, 64 belonged to Early onset Sepsis (EOS) and 36 belonged to Late onset Sepsis (LOS). Gram negative organisms were isolated from more than 80% of the cases. E. Coli was the commonest isolate (n=34), followed by Klebsiella (n=30) and Pseudomonas (n=13), involving both early and late onset groups. No isolate of group B streptococci (GBS) was found. Out of 34 isolates of E.Coli,14.70%(n=5),17.6%(n=6),41.17%(n=14),61.76%(n=21),79.4%(n=27) and 97.05%(n=33) were sensitive to ampicillin, gentamicin, cefotaxime, amikacin, ceftazidime and imipenem respectively. Klebsiella and Pseudomonas also showed a low sensitivity to ampicillin, gentamicin, and cefotaxime, while good sensitivity to amikacin, ceftazidime and imipenem. The mortality was significantly high ($P<0.05$) in low birth weight infants. **Conclusion:** Improvement in antenatal and natal services is mandatory to reduce incidence of neonatal sepsis and related mortality. Most of the organisms are resistant to commonly used drugs. Surveillance is required on regular basis.

Key Words: Neonatal sepsis, Bacterial isolates, Sensitivity patterns.

INTRODUCTION

Neonatal sepsis is an important and common cause of neonatal morbidity and mortality[1]. The incidence of neonatal sepsis in the developed countries is 1-10/1000

live births, where as it is roughly three times more in developing countries like Pakistan[2]. This high incidence is mainly due to poor antenatal care and lack of trained staff to conduct deliveries. There is a strong association between maternal urinary tract infection, pyrexia, vaginal discharge & unclean vaginal examination during labour and early onset neonatal sepsis[1,3].

In our set up, there is lack of proper antenatal care. In a recent study from Pakistan Institute of Medical Sciences, Islamabad, inadequate antenatal visits in even the low risk mothers have been found to be significantly associated with high chances of neonatal morbidity and mortality[4]. Furthermore, the high percentage (up to 25%) of low birth weight (LBW) deliveries in our country increases the risk of development of sepsis in these neonates[5].

Neonatal sepsis has a significant contribution in neonatal mortality rate (NNMR). In an evaluation of neonatal deaths from a community based study in and around Lahore, Jalil et al recorded an infectious etiology in almost 75% of all deaths and this was also recognized as an important factor in almost one third of all first week deaths[6]. A similar study in Northern Pakistan confirmed that vast majority of neonatal deaths was related to pneumonia or diarrhea[7]. Hospital based data indicate 30-38% overall mortality associated with neonatal sepsis[1,8].

In view of the above mentioned risk factors neonatal septicemia and related mortality can significantly be reduced by controlling maternal infections, avoiding unclean vaginal examinations, maintaining asepsis during labour and by administering the appropriate antimicrobial therapy to treat the affected babies[9].

In spite of some rapid indicators of neonatal sepsis like C-Reactive Protein (C-RP), micro ESR, Absolute Neutrophil Counts (ANC) and thrombocytopenia; isolation of the microorganism is the “gold standard” for the definite diagnosis of sepsis[10,11].

The spectrum of organisms that cause neonatal sepsis changes over times and varies from place to place. Gram negative organisms had been the most common cause of neonatal sepsis in developed countries in 1960’s. In 1970’s, group B streptococcus (GBS) was the commonest organism, while coagulase negative staphylococcus (CNS) was commonest during the 1980’s and 1990’s[12].

At present, in the developing countries, gram negative organisms remain the major etiology. These organisms have developed multi-drug resistance over the last two decades[13,14]. The reasons for this resistance are indiscriminate and irrational use of antibiotics, over the counter sale of antibiotics and ineffective infection control in maternity centers[15].

In our county pre-existing data on both early and late onset sepsis has shown great diversity in the changing pattern of the organism[5] and their sensitivity patterns[16,17]. Continued surveillance is mandatory to detect these temporal changes in spectrum and sensitivity of causative organisms, which will help in treating the septic neonates and eventually will reduce the neonatal morbidity and mortality.

OBJECTIVE

To find out the bacterial pathogens in cases of neonatal sepsis

To determine the antimicrobial sensitivity patterns of these etiological agents.

PATIENTS AND METHODS

Study Population

Total of 100 culture proven cases of neonatal sepsis were included.

Study Period & Place

From February 2003 to December 2004, at Neonatal Unit of Ghurki Trust Teaching Hospital, attached with Lahore Medical & Dental College Lahore.

Study Design

It was comparative study carried out in prospective fashion.

Inclusion Criteria

* Age range from 0 to 28 days
* Any baby suspected on clinical grounds and then proved on first blood culture was included.

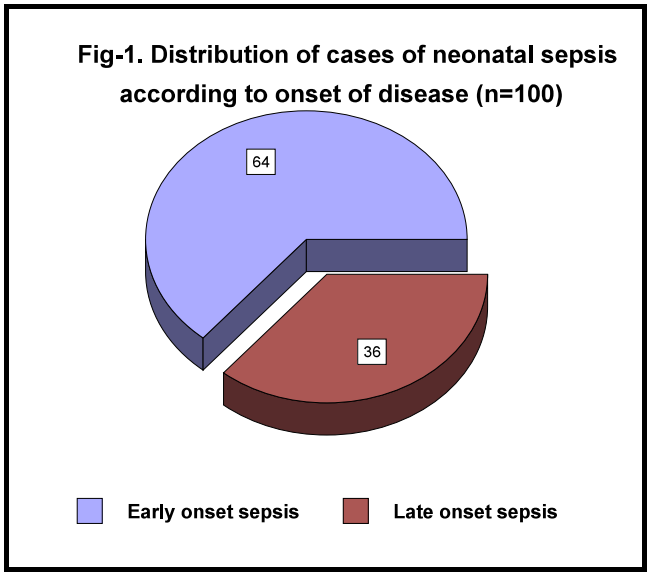
Exclusion Criteria

* Neonates who had already been given antibiotics prior to admission were excluded.

METHODS

Complete history and physical examination including obstetric history, maternal and neonatal risk factors were recorded. Complete blood counts and blood cultures were sent in all cases. Cerebrospiral fluid (CSF) examination and culture, culture of urine were sent in selected cases. Chest radiograph, arterial blood gases, serum electrolytes and renal function tests were performed where indicated. Antibiotics on empirical grounds were started and then modified accordingly. Cultures were processed by aseptic techniques, incubated onto *blood agar, chocolate agar, and Mac Conkey's Media.*

Kirby-Bauer disc-diffusion method was used to check sensitivity of the isolated organisms. The sensitivity was checked for commonly used antibiotics; ampicillin, gentamicin, cefotaxine, ceftazidime, amikacin and imipenem. Statistical analysis was done by Chi-Square test to obtain P-value where applicable.



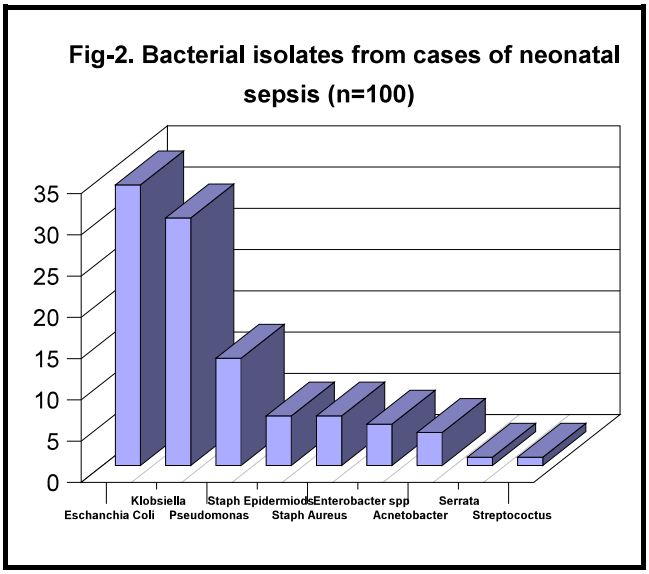
RESULTS

A total of 100 culture positive cases of neonatal sepsis were included. Sixty four percent belonged to early onset sepsis (onset of clinical features within 7 days of life) while 36% were of late onset sepsis (onset of clinical features after 7 days of life) (Fig.1).

Table I. Distribution of organism according to onset of disease.

Sr. No.	Organisms	Early Onset Sepsis (n=64)	Latest Onset Sepsis (n=36)
01	E.Coli	22(34.37%)	12(33.33%)
02	Klebsiella	22(34.37%)	8(22.22%)
03	Pseudomonas	08(12.5%)	05(13.88%)
04	Enterobacter Spp	-	05(13.88%)
05	Acinetobacter	02(3.12%)	02(5.55%)
06	Staph aureus	05(7.81%)	01(2.77%)
07	Staph epidermidis	05(7.81%)	01(2.77%)
08	Serratia	-	01(2.77%)
09	Streptococcus	-	01(2.77%)

Escherichia coli was the commonest organism isolated, followed by Klebsiella, Pseudomonas, Staph. aureus, Staph epidermidis, Enterobacter, Acinobacter, Serratia and Streptococcus (Fig-2).



E. Coli constituted 33.37% (n=22) of the early onset group (n=64), and 33.33% (n=12) of late onset group (n=36). Klebsiella constituted 34.37% and 22.22% while Pseudomonas 12.5% and 13.88% of early and late onset groups respectively. Enterobacter spp. were present only in the late, while Streptococcus in the early onset sepsis. Acinobacter, Staph. aureus and Staph. epidermidis affected both the early and late onset groups (Table I).

Generally all of the isolates were having a low sensitivity to ampicillin, gentamicin and cefotaxime, while most of the organisms were sensitive to ceftazidime, amikacin and imipenem. E. coli showed sensitivity of 14.70%, 17.6%, 41.17%, 61.76%, 79.4% and 97.05% to ampicillin, gentamicin, cefotaxime, amikacin, ceftazidime and imipenem respectively. The sensitivity of the remaining organisms has been shown in (Table-II).

The overall mortality was 37%. The mortality was significantly ($P<0.05$) associated with LBW neonates (Table III).

Table II. Sensitivity pattern of bacterial isolates to selected antibiotics

Organism	No	Ampicillin	Gentamicin	Amikacin	Cefotaxime	Ceftazimide	Imipenem
E. Coli	34	05(14.70%)	6(17.6%)	21(61.76%)	14(41.17%)	27(79.4%)	33(97.05%)
Klebsiella	30	00(00%)	6(20.00%)	21(70.00%)	13(41.9%)	22(73.3%)	30(100%)
Pseudomonas	13	02(15.38%)	4(30.7%)	5(38.4%)	4(30.7%)	7(53%)	12(92.3%)
Staph aureus	06	01(16.66%)	2(33.3%)	5(83.3%)	4(66.6%)	4(66.6%)	6(100%)
Staph epidermidis	06	03(50%)	4(66.66%)	5(83.3%)	3(50%)	3(66.3%)	6(100%)
Enterobacter	05	00(00%)	0(0%)	4(80%)	3(60%)	4(80%)	5(100%)
Acinetobacter	04	02(50%)	1(25%)	3(75%)	3(75%)	4(100%)	4(100%)
Serratia	01	00(00%)	0(0%)	1(100%)	0(0%)	1(100%)	1(100%)
Streptococcus	01	01(100%)	0(%)	0(0%)	1(100%)	1(100%)	1(100%)

DISCUSSION

Neonatal septicemia is responsible for 1.5 to 2.0 million deaths per year or between 4000 to 5000 deaths per day in the less-developed countries of the world[18]. Continued surveillance is mandatory to select the empirical therapy to reduce neonatal mortality[19].

In this study 100 cases of neonatal sepsis were distributed into early onset group (n=64) and late onset group (n=36). The high proportion of cases in EOS may be due to the fact that Ghurki Trust Teaching Hospital is surrounded by a rural community having scanty facilities for antenatal and natal care. Gram negative organisms

have been found to be responsible for about 87% of total isolates. This high predominance of gram negative organisms is consistent with most of the local data from different parts of the country[14,17,20].

E. coli, Klebsiella and Pseudomonas constituted 77% of the total. This percentage is comparable to a pooled-analyses of reports in last 30 years from different sectors in Pakistan. According to this analysis, more than 60% of the cases of both early and late onset sepsis are due to gram negative isolates[11].

Our finding of high percentage of Pseudomonas spp. even in EOS is consistent with results by Imtiaz et al[21] and Malik et al[19].

Table III. Association between neonatal Mortality & Weight at admission

Weight Categories	Total Number of Cases	Case Fatality Rate
< 2.5 kg	51	24(40.77%)
≥2.5 kg	49	13(26.53%)

Although GBS is the major isolate in the developed world, we have found no isolate of GBS, that is similar to the most of the pre-existing local data[11, 16,19,20.] Staph. epidermidis has been isolated from 6 cases, involving both early and late onset groups. Initially thought to be a contaminant, this organism has now been recognized as a considerable cause of neonatal sepsis[22].

Regarding antimicrobial sensitivity patterns, our main isolates (E. coli, Klebsiella and Pseudomonas) are having very low sensitivity to ampicillin and gentamicin. This finding is supported by 30 years data from different centers in Pakistan presented by Bhutta in 1996[11].

Recent data from developed countries also indicates increasing resistance to ampicillin[23]. Our results have not only shown the low sensitivity to ampicillin and gentamycin but also to the cefotaxime. This is supported by the data from Children's Hospital Lahore[20] and Khyber Teaching Hospital Peshawar[14].

In the present study, amikacin and ceftazidime show a reasonably good sensitivity especially for gram negative isolates. Previous data from Lahore[20], Peshawar[14] and Islamabad[24] conforms to this pattern.

Results from Jordan also support these findings and suggest amikacin combined with a third generation cephalosporin as an empiric therapy for neonatal sepsis[25]. The antimicrobial agent with a maximum sensitivity for all of the isolates was imipenem. In fact use of the imipenem is recommended for the treatment of serious bacterial infections in children[26].

Our findings of high mortality rate in LBW infants is statistically significant (P<0.05). LBW and prematurity have already been found to be the major contributory factors to the neonatal mortality[1].

CONCLUSIONS

Improvement in the antenatal services may be helpful in the preventing the early onset neonatal sepsis.
Prevention of premature/low birth weight deliveries can help in reducing neonatal mortality.

Continued surveillance is mandatory to assess the resistance pattern at a certain center, and empirical antimicrobial therapy must be tailored according to he local as well as regional data.

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