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RESEARCH ARTICLE

Overview Regarding Microbial etiologies incriminated with infections among newly born infants

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Abstract

Background:
In the past decades, term as sepsis had been used extensively to denote a variety of illness occurring in neonatal period. In many developing countries, neonatal mortality rates (death in the first 28 days of life) are as high as (40-50) per 1000 live birth with infections, being the major cause of death.

Patients and Methods: The current prospective cohort study had been carried out in Al-Yarmouk teaching hospital in Baghdad - Iraq, which has been initiated on (130) from the total 286 newborn infants aged (3-28) days after birth who were admitted to neonatal intensive care units (NICUs) in the same hospital, and their staying time was more than 72 hours and not transferred to another unit through the time of study, from August 2011 through April 2012 by culturing blood and swab samples from neonates, who were suspected of having nosocomial infections.

Results:
Through ongoing the present study the most frequent etiological agent, which were gram-negative bacteria, and; Enterobacter aerogenes (31.5%), Enterobacter cloacae (20%), Serratia marcescens (19.2%), Pseudomonas aeruginosa and Klebsiella pneumoniae (7.7%), Acinetobacter baumannii, Citrobacter koseri ,Escherichia coli (1.5%). The gram-positive bacteria were; Staphylococcus aureus (6.9%), Staphylococcus epidermidis (1.5%), and Streptococcus agalactiae (0.8%).

Conclusions: gram-negative bacteria were the most common organisms isolated from neonates infected with nosocomial infections.

INTRODUCTION

In many developing countries, neonatal mortality rates (death in the first 28 days of life) are as high as (40-50) per 1000 live birth with infections, being the major cause of death (Stoll, 2007). Different studies on newborn infants were conducted and reported that different types of bacteria were isolated from septic cases such Proteus species, Escherichia coli, pneumococci. Over the past five decades there have been several shifts in the predominant organisms responsible for neonatal bacteremia, through the causative agents may vary among different situation (Condat, 1917).

Historical review as in (1930-1940), the predominant organism was β-hemolytic Streptococcus pyogenes (Wilson et al., 1974). In the late (1940), gram-negative organisms, chiefly Escherichia coli replaced the former microbe (McCracken, 1976). This pattern changed, temporarily in the late (1950), when hemolytic-Staphylococci became the predominant pathogen. At the period from 1954 through 1958, the predominant role of Staphylococcus aureus was noted (Shinefield et al., 1966).

Thereafter in the early 70th they emphasized that an increase in the incidence of group-β-Hemolytic Streptococcus sepsis (Franciosi et al.,1972), and Escherichia coli together accounted for approximately 60-70% of neonatal sepsis and meningitis (McCracken ,1976). Klebsiella represented at Johns Hopkins hospital, a substantial cause of neonatal nosocomial sepsis in parallel with Pseudomonas aeruginosa (Crosson et al., 1977). In Saudi Arabia, Ohlsson et al., (1981) noted a very high incidence of Salmonella enteritidis as a cause of sepsis. Coagulase-negative Staphylococcus may cause hospital acquired bacteremia (Martin et al., 1989).

Enterobacter bacteremia outbreaks in a NICUs, and analyzed the major risk factors for development of bacteremia. Enterobacter species that isolated from the cases were E. aerogenes and E. gergoviae, and the most frequently described Enterobacter isolates have been E. cloacae and E. aerogenes (Moore 1996). Also bacteremia may be transmitted to neonates through feeding (Oie et al., 1993), use soaps (Archibald et al., 1997), contaminated antiseptics (Bosi et al., 1996), and breast pumps (Gransder et al., 1986). The skin and umbilical cord becomes an important alternative route for the entrance of bacteria into systemic circulation of the neonate.

Tallur et al., 2000, reported that at NICUs of Kims hospital at India indicated that, gram-negative bacilli were more common in neonatal nosocomial bacteremia than gram-positive cocci.

Colonization of the newborn infants can take place very quickly, after they have initially been colonized by flora of low pathogenicity, and along stay in an intensive care unit; that will lead to a greater number of colonization with potentially pathogenic organism such as Klebsiella -Enterobacter group and S. aureus. The development of the infection depends on the condition of the infant and on the virulence of the colonizing organism (Malik et al., 2001).

Patients and Methods:

A prospective cohort study was carried out at the NICU of Al-Yarmouk teaching hospital in Baghdad-Iraq, over a period from August 2011 to April 2012. The NICU consist of a single room, average of 4-6 nurses, and followed by two neonatologists for each 24 hours duty.

Any neonate proved to be infected at the time of admission and any neonate died or discharged before 48 hour. From total 286 neonates admitted to hospital NICU during the study period, 80 neonates were discharged from the NICU in the first 48 hour, 16 neonates died and 60 neonates have the signs of infections at the time of admission; so the final total sample that met inclusion and exclusion criteria included 130 neonates who were admitted without infection at the time of admission and remained more than 48 hour. Blood and swab samples were taken from infants in NICU and swabs then taken from the environment and instruments of the NICU and delivery rooms, for assessment the microbial isolates; then the chosen specimens was cultivated onto the appropriate media aerobically and anaerobically and the microbial growth were identified via the proper assisting identification kits.

Results:

The bacterial isolates (Table-1) from blood and swab aerobic cultures were in the following order; most common Enterobacter aerogenes 41(31.5%), followed by Enterobacter cloacae 26 (20.0%), Serratia marcescens 25(19.2%), Klebsiella pneumoniae and Pseudomonas aeruginosa 10 (7.7%) for each, Staphylococcus aureus 9 (6.9%); and each of Acinetobacter baumannii, Citrobacter koseri, Escherichia coli and Staphylococcus epidermidis 2 (1.5%) equally and Streptococcus agalactiae 1 (0.8%). Concerning the anaerobic culture, no bacteria were isolated.

All bacteria isolated	Number of isolates (%)
Enterobacter aerogenes	41 (31.5)
Enterobacter cloacae	26 (20.0)
Serratia marcescens	25 (19.2)
Klebsiella pneumoniae	10 (7.7)
Pseudomonas aeruginosa	10 (7.7)
Staphylococcus aureus	9 (6.9)
Acinetobacter baumannii	2 (1.5)
Citrobacter koseri	2 (1.5)
Escherichia coli	2 (1.5)
Staphylococcus epidermidis	2 (1.5)
Streptococcus agalactiae	1 (0.8)
Total	130 (100)

In coincide also relation of neonate gender with the causative agent (Table-2) was reviewed as follows: 21 (30.9%) of male neonates were infected with E.aerogenes, followed by 15(22.1%) with E. cloacae, 9(13.2%) with S. marcescens, 6 (8.8%) with K. pneumoniae and S. aureus each one equally, 5(7.4%) with P.aeruginosa, followed A.

baumannii and E.coli 2(2.9%) for each one, and S.epidermidis, S.agalactiae 1(1.5%) each one equally. While the most frequent microorganism causes an infection in female neonates were E.aerogenes 20(32.3%) neonates followed by S. marcescens 16(25.8%), E.cloacae 11 (17.7%), P.aeruginosa 5 (8.1%), K. pneumoniae 4(6.5%), S. aureus 3 (4.8%), C. koseri 2 (3.2%) and S.epidermidis 1(1.6%).

Microorganisms	Male No. (%)	Female No. (%)	No. of Cases
E.aerogenes	21 (30.9)	20 (32.3)	41
E.cloacae	15 (22.1)	11 (17.7)	26
S.marcescens	9 (13.2)	16 (25.8)	25
S.pneumoniae	6 (8.8)	4 (6.5)	10
P.aeruginosa	5 (7.4)	5 (8.1)	10
S.aureus	6 (8.8)	3 (4.8)	9
A.baumannii	2 (2.9)	0 (0.0)	2
C.koseri	0 (0.0)	2 (3.2)	2
E.coli	2 (2.9)	0 (0.0)	2
S.epidermidis	1 (1.5)	1 (1.6)	2
S.agalactiae	1 (1.5)	0 (0.0)	1
Total	68 (100)	62 (100)	130

Additional data (Table-3) were investigated in the present work; the distribution of blood and swab culture microorganisms causing neonatal nosocomial infections in relation to gestational age as follows; 31 (33.7%) of preterm babies were infected with E.aerogenes, followed by E.cloacae 18(19.7%), S. marcescens 16 (17.4%), S.aureus and K. pneumoniae 7(7.6%) for each one, P.aeruginosa 6 (6.5%), A.baumannii and S. epidermidis 2 (2.2%) equally, and each of C. koseri, E. coli and S. agalactiae 1(1.1%).
While in full term babies; 10 (26.3%) were infected by E. aerogenes. Followed by S. marcescens 9 (23.7%), E.cloacae 8 (21.1%), P. aeruginosa 4 (10.5%), K. pneumoniae 3 (7.9%), S. aureus 2 (5.3%) and C. koseri and E. coli 1 (2.6%) for each one.

Microorganisms	Preterm NO. (%)	Full Term NO. (%)	NO. of cases
E.aerogenes	31 (33.7)	10(26.3)	41
E.cloacae	18 (19.7)	8 (21.1)	26
S. marcescens	16 (17.4)	9 (23.7)	25
K. pneumoniae	7 (7.6)	3 (7.9)	10
P.aeruginosa	6 (6.5)	4 (10.5)	10
S.aureus	7 (7.6)	2 (5.3)	9
A.baumannii	2 (2.2)	0 (0.0)	2
C.koseri	1 (1.1)	1 (2.6)	2
E.coli	1 (1.1)	1 (2.6)	2
S.epidermidis	2 (2.2)	0 (0.0))	2
S.agalactiae	1 (1.1)	0 (0.0)	1
Total	92 (100)	38 (100)	130

Another prospect analyzed in this study (Table-4) is the distribution of blood and swab culture microorganisms causing neonatal nosocomial infections in relation to birth weight. As had been clarified below: 20 (32.3%) of the neonates with birth weight between (1000 – 1499 gm) were infected with E. aerogenes, followed by S. marcescens 15 (24.2%), E.cloacae 10 (16.1%), K. pneumoniae 5(8.1%), P.aeruginosa 4 (6.5%), and S. aureus and C. koseri 2 (3.2%) for each one, and each of A. baumannii, E. coli, S. epidermidis, and S. agalactiae were 1 (1.6%). Also the same table shows that 14 (32.6%) of the neonates with birth weight (1500-2499gm) were infected with E. aerogenes, followed by E. cloacae 12 (27.9%), S. marcescens 6(13.9%), P. aeruginosa 4 (9.3%), S. aureus 3 (7.0%) , K. pneumoniae 2 (4.7%) and each of E. coli and S. epidermidis 1 (2.3%) equally; While neonates with birth

weight (≥2500gm), it shows that 7 (28%) of the neonates were infected with E. aerogenes, followed by each of E. cloacae, S. marcescens, and S. aureus 4 (16%) equally, K. pneumoniae 3 (12%), P. aeruginosa 2 (8%) and A. baumannii 1 (4%).

Microorganisms	Birth weight (gm) (1000-1499) NO. (%)	Birth weight (gm) (1500-2499) NO. (%)	Birth weight (gm) (≥2500) NO. (%)	No. of Cases
E.aerogenes	20 (32.3)	14 (32.6)	7 (28)	41
E.cloacae	10 (16.1)	12 (27.9)	4 (16)	26
S. marcescens	15 (24.2)	6 (13.9)	4 (16)	25
K. pneumoniae	5 (8.1)	2 (4.7)	3 (12)	10
P. aeruginosa	4 (6.5)	4 (9.3)	2 (8)	10
S.aureus	2 (3.2)	3 (7.0)	4 (16)	9
A.baumannii	1 (1.6)	0 (0.0)	1 (4)	2
C.koseri	2 (3.2)	0 (0.0)	0 (0.0)	2
E.coli	1 (1.6)	1 (2.3)	0 (0.0)	2
S.epidermidis	1 (1.6)	1 (2.3)	0 (0.0)	2
S.agalactiae	1 (1.6)	0 (0.0)	0 (0.0)	1
Total	62 (100)	43 (100)	25 (100)	130

Discussion:

A bloodstream infection is one of the most important infections and the more frequent among newborns who were born in hospitals especially in developing countries. Neonatal sepsis is a clinical syndrome resulting from pathophysiologic effect of systemic infection in the first month of life (Bas et al., 2010).

The susceptibility of the human neonate to overwhelming bacterial infection is well established and is commonly attributed to immaturity of the neonatal host defenses (Natasha et al., 2011).

The causative agents of neonatal nosocomial infection especially neonatal nosocomial septicemia in Baghdad neonatal intensive care units were different from those in other countries. The obtained results regarding this aspect were agreed with other studies obtained by (Tallur et al., 2000; Rebecca et al., 2010; Natasha et al., 2011). In our country there was a difference in the general appearance of bacterial isolates twenty six years ago as compared with Baqir (1986) and seven years ago as compared with Yassmen (2005).

Eleven different organisms were responsible for nosocomial infections among our involved patients during the present study period, as we recognized that E.aerogenes was the most predominant pathogen isolated (31.5%).

These data were similar to analogue data reported by Salamti et al., 2006, it shows that most common pathogenic organisms which isolated were Enterobacter (27%); however, such data may not pass parallel with other data gained by Bas et al., (2010) as it shows that the most commonly isolated microorganism was Klebsiella species (39.6%).

Gram negative bacilli constituted the largest number (90.8%) of the total isolates. Such results were similar to that recorded in Iraq by Yassmen (2005); plus in India by Salamati et al., (2006); and in Turkey by Bas et al., (2010). On the contrary; in South Korea a work was carried out via Ihn et al.,(2006); beside in Saudi Arabia by Mahfouz et al.,(2010), they were obtained that gram positive bacteria were the most predominance.

This phenomenon could be explained by the high occurrence and virulence factors for the gram negative bacteria in our country and also due to new strains may be formed. Natasha et al., (2011), discussed that increased colonization with gram negative microorganisms, probably could be due to prolong staying in neonatal intensive care unit.

In the current work bacteremia was caused by E.aerogenes (31.5%), E.cloacae (20%), and S. marcescens (19.2%) respectively. Here our data is higher than the data gained by Yassmen (2005) and Mahfouz et al., (2010), were S. marcescens constitute (6.5%, 5.3%) respectively. This high difference might focus upon the high source of contamination in the delivery rooms.

The percent of infection by K. pneumoniae (7.7%) in the current work is lower than Yassmen (2005), Salamati et al., (2006), Mahfouz et al., (2010), and Bas et al., (2010). This variance between results may be due to the area of the study performance and the time in where the study carried out.

Many reports mentioned that P. aeruginosa were more commonly associated with hospital acquired infections mainly in patients with compromised immune system (Adams et al.,2005; Valeria et al.,2009; Bas et al.,2010). P. aeruginosa bacteremia occurrence was low (7.7%); and this result if compatible with the results of studies carried

out by; Yassmen (2005), Mahfouz et al.,(2010) and Bas et al.,(2010), they will were agreed with us (9.2%, 6.5%, 10.1%,) respectively. A.baumannii also constitute low occurrence (1.5%) among the total isolates, and this will agreed with Makhoul et al.,(2001) and Yassmen(2005), but such results disagreed with Ahmed et al., (2002) and Stoll (2007).

Citrobacter species are primary invaders in early infancy; they have a propensity for producing a necrotizing meningo-encephalitis (Crosson et al., 1977). Citrobacter species are found as a normal human gastrointestinal flora, and its transmission either endogenous or from person to person, especially in hospitalized patients (Forbes et al., 2002). Citrobacter koseri constitute low occurrence (1.5%) of the total isolates in our study. It was similar or near to other studies reported by: Tallur et al., (2000), Ahmed et al.,(2002), Yassmen (2005) and Mahfouz et al.,(2010). This low occurrence of C.koseri due to unique ability to penetrate, survive and replicate into vascular endothelial cells and macrophages. Also C.koseri is often associated with brain abscesses or meningitis only (Prais et al., 2003).

Escherichia coli were also commonly associated with hospital acquired infections. It is commonly found as part of vaginal flora and gastrointestinal tract flora; it can cause vertical septicemia infection (Sarah et al., 2010). In the present study, E. coli was also with low occurrence (1.5%). It was lower than the finding by Yassmen (2005), Salamati et al.,(2006) and Mahfouz et al., (2010) were (13.2%, 14%, 7.8%) respectively. Staphylococcus aureus is also concern for most nurseries around the world. The main reservoir of this bacterium is the hospital staff and contamination, usually occurs through the hand (Zaidi et al., 2005).

In our study S. aureus constitute (6.9%) in occurrence of the total isolates. These results were less than the finding of Yassmen (2005) and Salamati et al., (2006) were (21.1%, 21 %) respectively. This difference may be due to the number of newborn infants with low birth weight.

Yalaz et al. reported that S. aureus infections increased due to the survival increase of very low birth weight infants and as a result of increased of using invasive devices and broad spectrum antibiotics (Yalaz et al., 2006).

S. epidermidis can cause serious morbidity but not mortality mainly in preterm infants and low birth weight infants, and this is due to its lower virulence. It causes hospital acquired bacteremia mainly if remained in the hospital for a long time. Different studies had been carried out to clarify its pathogenicity (Eva et al., 2003; Nejjari 2003; Valverde et al., 2004; Yalaz et al., 2006).

The transition of these organisms from commensals to true pathogenic associated with the creation of a highly susceptible population of very low birth weight premature infants, who now survive due to neonatal intensive care unit. The presence of centrally placed vascular lines, use of intravenous lipid emulsions and ventilation, which are integral parts of modern neonatal intensive care have been identified as major risk factor for the development of infection with these opportunistic pathogens (Rodrigo, 2002).

In the current work S. agalactiae constitute low occurrence (0.8%) from the total isolates. This finding was similar with other report by Yassmen (2005). While in other studies by; Tallur et al., (2000), Ahmed et al., (2002) and Mahfouz et al., (2010) they did not isolate this bacteria. However, this organism is one of the most common causative of neonatal sepsis in the western and developed countries.

Anaerobic organisms such as Bacteroides, Peptococcus, and Peptostreptococcus were not isolated, this situation was similar to others like Makhoul et al., (2001), Yassmen (2005) and Stoll et al.,(2007), and it might be due to the low virulence of these organisms and the difficulty in isolating and identifying these organisms.

Ihn et al., (2006), Mahfouz et al., (2010) and Natasha et al., (2011), noted that nosocomial infections (especially neonatal blood stream infections) among male newborn infants were more frequently than females, the ratio was a bout 2:1; they suggested that this difference was according to genetic hypothesis that concerns agene locus on X-chromosome of human beings, which involved in the synthesis of immunoglobulines. This agrees with the current work as it shows that nosocomial infections in male neonate (52.3%) were higher than in female neonates (47.7%).This result is similar to other results obtained by Ohlsson et al., (1987) in USA and Al-Gabban et al., (2001) in Iraq.

previous studies done by Khalid et al., (2005), Mahfouz et al.,(2010) and Natasha et al (2011) were coincide that the most important predisposing factor to neonatal nosocomial infections, especially neonatal blood stream infections was prematurity (< 37 weeks), and that was a direct correlation between the degree of prematurity and the risk of infection. The authors reported that such infants have 2 -10 folds higher incidence of infection and bacteremia than do full term.

In the ongoing work; shows that two third (70.8%) of total neonatal nosocomial infections were preterm and one third (29.2%) were full term (about 3 folds) higher than full term. The explanation for these results is that premature infants were under high risk factor for infection because of their lack of protective maternal antibodies. The serum concentration of IgG at birth is low in premature infants in comparison with the full term baby. The fetus produces very few antibodies before birth, after (20 to 22) weeks of gestation, an accelerated active transport of IgG across the placenta begins. The most vulnerable infants in the neonatal intensive care unit were those with gestational ages (<

37 weeks) that have acquired very few maternal antibodies benefit of protection against infections (McKenney, 2001; Natasha et al., 2011).

Mahfouz et al., and Natasha et al., indicated that the most important neonatal factors predisposing to infection is low birth weight; the lower birth weight, the greater the susceptibility of the newborn to bloodstream infection by 3 - 10 fold, as such patients were expected to be debilitated and their immunity could be immature. It is clear that with decreasing weight, more numbers of neonates with nosocomial infections especially bloodstream infections were occurred. The morbidity was observed more in neonates with low birth weight (1000-1499 gm) (47.7 %), and the association between the microorganisms causing neonatal nosocomial septicemia and mortality / morbidity was gram-negative bacteria, which were isolated from cases of neonatal intensive care unit.

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