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Detection of Bacteria Causing Early Onset Pneumonia among Neonates Admitted to NICU In Children Hospital, Zagazig University

Tarek Hamed Atteyah[1], Wessam Abd El monem Mokhtar[1], Mai Mohammed Malek[2], Ahmed Badawi Mohammed[1]

Departments of [1]Pediatrics and [2]Immunology and Microbiology, Faculty of Medicine – Zagazig University, Egypt

***Corresponding Author**: Ahmed Badawi Mohammed, **Mobile:** (+20)01111159254**, Email:** ahmedsanhoti3190@gmail.com

ABSTRACT

Background: Early onset pneumonia could be caused by bacteria, virus or fungi. Early identification and treatment with antibiotics is vital in reducing mortality and morbidity.

Objectives: The current study aimed for detection of organisms that cause early onset pneumonia guided by nasopharyngeal aspirate culturing, in addition to blood culturing.

Patients and methods: This study was applied on 36 neonates admitted to NICU in Zagazig University Children Hospital, during the period from October 2018 to April 2019.

Results: There was no relation between gestational age and birth weight with neonatal pneumonia (NP) incidence rates. The prevalence of confirmed early onset NP with positive blood culture was 88.9%. The hospital stays of studied subjects were 7.2 ± 3.5 days. Neonatal pneumonia caused by Gram negative bacteria (53.1%) was more common than Gram positive bacteria (46.9%). K. pneumonia (37.5%) was the most common microorganism isolated from the blood cultures. S. saprophyticus (21.8%) was the most frequently recovered CONS isolate from blood cultures, followed by S. cohnii (9.4%) and S. haemolyticus (6.3%). The most prevalent organism isolated from BAL fluid was Klebsiella (38.5%).

Conclusion: Neonatal sepsis remains a major problem in neonates. Gram-negative bacteria were the most common cause of early onset NP in Zagazig University Hospital with K. pneumonia being the most common pathogen. Regular periodic surveillance of the causative organisms of neonatal pneumonia is needed to implement the rational empirical choice of antibiotic prescription while waiting for blood culture result to come out.

Keywords: Bacteria, Early onset pneumonia, Neonates, NICU.

INTRODUCTION

Respiratory conditions are the most common cause for admission to a neonatal unit in both term and preterm infants. Early onset pneumonia "also known as congenital pneumonia" is associated with trans-placental infection and presents within 48 hours of age. Chorioamnionitis is a major contributory factor for sepsis, with infected uterine fluid being inhaled by the fetus, potentially resulting in congenital pneumonia [(1)]. Early onset pneumonia is defined as an inflammatory condition of the lungs affecting primarily the alveoli with clinical and radiological evidence present at birth. Some authors defined this condition as pneumonia that is present at birth with a positive tracheal aspirate culture obtained within 4 hours of delivery [(2)].

Early onset "congenital" pneumonia could be caused by bacteria, virus or fungi. Bacteriological study of lung tissues showed that both Gram-negative and positive bacteria could cause congenital pneumonia. Since the 1970s, Group B Streptococcus has been recognized as an important cause of early onset "congenital" pneumonia. Due to increased risk of resistance of organisms to antibiotics due to disuse of different antibiotics, early detection of organisms causing congenital pneumonia by culturing is a must [(1)].

Clinical manifestation of early onset "congenital" pneumonia may be apparent before delivery in the form of fetal distress or tachycardia, or at delivery as a low Apgar score or severe respiratory distress. In some infants, there may be a latent period of a few hours or an interval of 1-2 days before respiratory distress or shock develops. In some infants, the early signs and symptoms may be nonspecific, presenting with poor feeding, lethargy, irritability, cyanosis, temperature instability or with an overall impression that just not doing well baby [(3)].

Early identification and treatment with antibiotics is vital in reducing mortality and morbidity. This is reflected in the guidance that antibiotics must be commenced within 1 h of decision to treat. The prognosis of neonates with congenital pneumonia varies greatly and is dependent upon the organism and its virulence. However, early identification and treatment of neonates at risk of infection or with symptoms of infection reduces both morbidity and mortality. A worse prognosis is seen in infants with low birth weights and for those with intrauterine compared to those with later onset disease [(4)].

A definitive diagnosis can be made in the presence of clinical manifestation of pneumonia shortly after birth with associated chest radiograph changes, and the causative organisms cultured or isolated from nasopharyngeal aspirates or tracheal aspirates obtained aseptically within the first 8 hours of life [(1)].

The current study aimed for detection of organisms that cause early onset pneumonia guided by nasopharyngeal aspirate culturing, in addition to blood culturing. Also, the antibiotic resistance profiles of

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isolated organisms were detected, which might help in proper selection of the antibiotic strategies.

PATIENTS AND METHODS

This cross-sectional study aimed for identification of causative organisms of early onset "congenital" pneumonia in 36 neonates admitted to NICU in Zagazig University Children Hospital, during the period from October 2018 to April 2019, in order to identify the causative organism and detect the proper antibiotic.

Ethical approval:

The study was carried out after obtaining parental consents and taking approval from the Institutional Review Board (IRB) of Faculty of Medicine, Zagazig University. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Neonates within first 24-48 hours of birth. Both sexes were included. Neonates who didn't receive antibiotics at time of obtaining the sample. Full term neonates (37-41 weeks of gestation). Neonates who were delivered by either cesarean section or normal vaginal delivery. Neonates who were presented with respiratory distress in the first 24 or 48 hours of life.

Exclusion criteria: Babies who were more than 48 hours old. Babies who started treatment with empirical antibiotics. Babies who were less than 37 weeks of gestation. Babies with parents who refused to participate in the study

All patients were subjected to the following:

1- Full History.

2- Clinical examination.

Complete physical examination including Downs Respiratory Distress Syndrome Scoring System[5].

3- Laboratory Investigations:

* Complete blood count (CBC) and differential leukocytic count.
* C-reactive protein (CRP) or Procalcitonin according to policy of the unit.
* Arterial blood gases (ABG): including PH, partial pressure of carbon dioxide ($PaCO_2$), Partial pressure of oxygen (PaO_2), Bicarbonate (HCO_3) and Oxygen saturation (O_2 sat).

4- Specific tests:

A- Chest X ray (postero-anterior and lateral view): Essential in diagnosis of congenital pneumonia with clinical manifestations.

B- Bacterial culture: Conventional bacteriological culture is used most useful diagnostic test for congenital pneumonia. Aerobic incubation of cultures is sufficient for recovery of most responsible pathogens.

Source:

Specimens from endotracheal aspiration according to Koksal *et al.* [6]: Culture and Gram stain of an endotracheal aspirate obtained by aseptic technique as soon as possible after intubation (within 8-12 h of birth and before antibiotics administration) may be useful, and correlates very well with blood culture results and probably reflects aspirated infected fluid.

Specimens from Broncho-alveolar lavage (BAL) according to Heo *et al.* [7]:

The patients were all intubated, ventilated, and monitored by pulse oximeter, electrocardiogram, and intra-arterial blood pressure measurement. A pediatric bronchoscope was inserted orally to avoid nasal contamination. Breathing aliquots of saline solution (0.9%) was instilled in the lobar bronchus or diseased segment (maximum volume, 3 ml/kg of body weight).

Intracutaneous monitoring was conducted to assess oxygen saturation and heart rate, temperature, blood pressure, and supplemental oxygen was administered as necessary during the procedure. One hour after completion of the sampling, a complete clinical examination and a chest radiograph was systematically performed.

A 10 ml aliquot was transferred to a sterile container for standard Gram staining and quantitative culture. Pairs of aerobic and anaerobic blood culture bottles were inoculated with 5 ml of retrieved BAL fluid for culture.

Blood culture [8]:

Blood culture bottles were designed to accommodate the recommended blood-to-broth ratio (1:5 to 1:10) with optimal blood volume. The recommended volume of blood to collect should be based on the weight of the patient. Generally, the volume of blood collected for culture was 1 ml from peripheral venous or arterial site, collected in a paediatric blood culture bottle (BacT/ALERT®). First, tubes for aerobic pathogen was filled followed by anaerobic one, then were incubated for 5 days and were classified as positive if an organism grown during this time. This growth was sub-cultured for pathogen identification.

Cultivation and identification:

For quantitative culture, 100 µl of vortexed BAL fluid or positive blood culture specimen was inoculated onto a blood agar plate, a MacConkey agar plate, a chocolate agar plate, and a Brucella blood agar plate (Oxoid). Blood and MacConkey agar plates were incubated aerobically in 5 % CO_2 at 35 °C for 18–24 h. Chocolate and Brucella blood agar plates were anaerobically incubated for up to 48 h.

For the qualitative culture, 100 µl of vortexed specimen was transferred to the plate; each colony from this plate was 10 colony-forming units (CFU)/ml. A colony number of more than 10^4 CFU/ml was considered significant for a pathogen. The sediment

after centrifugation of the remaining fluid was used for a smear preparation for Gram staining.

A Gram stain was performed on any positive bottles and subcultures were performed on an appropriate solid media to identify the organism and perform antibiotic susceptibility testing using a disc diffusion test.

Statistical Analysis:

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures were coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for Social Sciences (SPSS version 22). According to the type of data, qualitative data were represented as number and percentage and quantitative continues groups were represented as mean ± SD. The following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X^2). Differences between parametric quantitative independent groups by t test. P value was set at **≤ 0.05** for significant results & **< 0.001** for high significant result.

RESULTS

Table (1) showed the demographic and maternal data of the studied group. Males were (58.3% and females were (41.7%), mean age was 27.2 ± 9.6 days and the majority of maternal risk factors were preterm rupture of membrane (36.1%). Regarding mode of delivery, vaginal were 33.3% and CS were 66.7%. Incidence of fever was 55.6%. The mean of GA was 38.1 ± 0.8 weeks**.**

Concerning blood culture results of the studied group, negative was 11.1% and positive was 88.9%. The majority of organism was Klebsiella pneumonia (37.5%) as shown in table (2).

Table (3) showed the broncho-alveolar culture of the studied group, negative was 63.9% and positive was 36.1%. The majority of organism was Klebsiella pneumonia (38.5%)**.**

There were no statistically significant difference between the blood and brocho-alveolar cultures results of the studied group (Table 4).

Regarding hospital stay and prognosis of the studied group, the mean of hospital stay was 7.2 ± 3.5 days. Regarding prognosis, survivals were 61.1% and deaths were 38.9% (Table 5).

There were no statistically significant difference between the studied groups regarding blood culture and isolated organisms (Table 6).

There were no statistically significant difference between the studied groups regarding the broncho-alveolar culture and isolated organisms (Table 7).

Table 1: Demographics and maternal data of the studied group

Demographics data	All patients
Neonatal demographic data	N (%) = 36 (100%)
Gender	
Male	21 (58.3%)
Female	15 (41.7%)
Age (days)	
Mean ± SD	27.2 ± 9.6
Median (Range)	25.5 (12 – 48)
Weight Kg	
Mean ± SD	2.82 ± 0.39
Median (Range)	2.80 (2.15 – 2.70)
Maternal demographic data	
Maternal risk factors	
Preterm rupture of membrane	13 (36.1%)
Pre-eclampsia	10 (27.8%)
Urinary tract infection	5 (13.9%)
Chorioamnionitis	8 (22.2%)
Mode of delivery	
Vaginal	12 (33.3%)
CS	24 (66.7%)
Incidence of fever	
No	16 (44.4%)
Yes	20 (55.6%)
Gestational age (weeks)	
Mean ± SD	38.1 ± 0.8
Median (Range)	38 (37 – 39)

Table 2: Blood culture result of the studied group

Blood culture	All patients
Count	N (%) = 36 (100%)
Result	
Negative	4 (11.1%)
Positive	**32 (88.9%)**
Organism	**N (%) = 32 (100%)**
Klebsiella pneumonia	12 (37.5%)
Staphylococcus saprophyticus	7 (21.8%)
Staphylococcus haemolyticus	2 (6.3%)
Staphylococcus cohnii	3 (9.4%)
E. coli	5 (15.6%)
Streptococcus	3 (9.4%)

Table 3: Broncho-alveolar culture result and isolated organisms of the studied group

Broncho-alveolar culture	All patients
Count	N (%) = 36 (100%)
Result	
Negative	23 (63.9%)
Positive	**13 (36.1%)**
Organism	**N=13 (100%)**
Klebsiella pneumonia	5 (38.5%)
Staphylococcus saprophyticus	3 (23.1%)
Staphylococcus haemolyticus	1 (7.7%)
Staphylococcus cohnii	3 (23.1%)
Streptococcus	1 (7.7%)

Table 4: Comparison between the blood and brocho-alveolar cultures results of the studied group

			Blood culture			Kappa	p-value
			Negative	Positive	Total		
Broncho-alveolar culture	Negative	Count	4	19	23	0.132	0.111 (NS)
		% of Total	11.1%	52.8%	63.9%		
	Positive	Count	0	13	13		
		% of Total	0.0%	36.1%	36.1%		
	Total	Count	4	32	36		
		% of Total	11.1%	88.9%	100.0%		

Table 5: Hospital stay and prognosis of the study population

Hospital stay and prognosis	All patients
Count	36 (100%)
Hospital stay (days)	
Mean ± SD	7.2 ± 3.5
Median (Range)	7 (2 – 14)
Prognosis	
Survivals	22 (61.1%)
Deaths	14 (38.9%)

Table 6: Comparison between the studied groups regarding the blood culture and organisms isolated

Blood culture	Survivals	Deaths	Test	P-value (Sig.)
Count	22	14		
Result				
Negative	3 (13.6%)	1 (7.1%)	‡F	1.000 (NS)
Positive	19 (86.4%)	13 (92.9%)		
Organism				
Klebsiella pneumonia	5 (22.7%)	7 (50%)	‡F	0.148 (NS)
Staphylococcus saprophyticus	3 (13.6%)	4 (28.6%)	‡F	0.394 (NS)
Staphylococcus haemolyticus	2 (9.1%)	0 (0%)	‡F	0.511 (NS)
Staphylococcus cohnii	3 (13.6%)	0 (0%)	‡F	0.267 (NS)
E. coli	5 (22.7%)	0 (0%)	‡F	0.134 (NS)
Streptococcus	1 (4.5%)	2 (14.3%)	‡F	0.547 (NS)

‡F Fisher's Exact test, $p < 0.05$ is significant, Sig.: significance

Table 7: Comparison between the studied groups regarding the broncho-alveolar culture and organisms isolated

Broncho-alveolar culture	Survivals	Deaths	Test	P-value (Sig.)
Count	22	14		
Result				
Negative	14 (63.6%)	9 (64.3%)	0.002 ‡	0.968 (NS)
Positive	8 (36.4%)	5 (35.7%)		
Organism				
Klebsiella pneumonia	2 (9.1%)	3 (21.4%)	‡F	0.357 (NS)
Staphylococcus saprophyticus	1 (4.5%)	2 (14.3%)	‡F	0.547 (NS)
Staphylococcus haemolyticus	1 (4.5%)	0 (0%)	‡F	1.000 (NS)
Staphylococcus cohnii	3 (13.6%)	0 (0%)	‡F	0.267 (NS)
Streptococcus	1 (4.5%)	0 (0%)	‡F	1.000 (NS)

‡ Chi-square test, ‡F Fisher's Exact test, $p < 0.05$ is significant, Sig.: significance.

DISCUSSION

Some maternal and neonatal factors were investigated in the current study to identify the predisposing factors to NP. In the current study, male predominance was found which agrees with previous reports [9].

In the current study, no relation was detected either between gestational age or birth weight with NP incidence rates, which may be related to small size of studied population and narrow median birth weight range (2.15 – 2.70), in addition, narrow median gestational age (37 – 39 week). **Awny *et al.*** [10] and **Zhu *et al.*** [11] found an inverse relation between weight and liability to NP, especially in neonates with birth weight ranged between 1:1.5 Kg. In addition, **Awny *et al.*** [10], **Petdachai** [12] and **Foglia *et al.*** [13] reported that NP incidence rates had significantly increased with decreasing gestational age. While, **Aletayeb *et al.*** [14] reported that no significant correlation between birth weight and NP.

The difficulties in diagnosis of NP have led to the development of many diagnostic techniques such as blood culture, broncho-alveolar lavage, protected specimen brush and quantitative endotracheal aspirates. The gold standard for diagnosis of NP is lung biopsy; however it is an invasive procedure [15]. Thus, blood culture is still the gold standard for definitive diagnosis of neonatal sepsis [16; 17]. The current study showed that the prevalence of confirmed early onset NP with positive blood culture was 88.9%. High

prevalence of confirmed early onset NP (64.7%) was previously reported by **Aletayeb *et al.*** [14] and (62.8%) by **Rahman *et al.*** [18]. **Aletayeb *et al.*** [14] conducted that this may be due to more referral of preterm labors and preterm newborns. Whatever, authors concluded many risk factors might be conducted to the high prevalence of NP such as ventilation mode, where 63.9% of studied samples in the current study were on ventilator mode while 36.1% on nasal mode, which might be due to that all selected subjects in the current study were suffering from respiratory stress. **Aly *et al.*** [19] and **Badr *et al.*** [20] concluded that mechanical ventilation or tracheal intubation are associated with increased risk to develop NP with 3 : 21 folds. In contrary, **Aletayeb *et al.*** [14], showed that 4.1% of the studied patients subjects, were positive blood culture

Neonatal pneumonia with Gram negative bacteria (53.1%) was more common than Gram positive bacteria (46.9%) in the current study. In accordance, Gram-negative organisms were the most common causes of NP in NICU in Jordan [2]. In contrary, **El-Din *et al.*** [16] reported in Egypt that Coagulase negative Staphylococci [21] were predominant isolates, followed by Klebsiella pneumoniae. In the current study, K. pneumonia (37.5%) was the most common microorganism isolated from the blood cultures, which was reported in Egypt [22]. Similar results were documented in other studies reported from India [23]**. Adhikari *et al.*** [24] reported in Nepal that Staphylococcus epidermidis accounted for the greatest proportion (57.3%), followed by (28.1%) of Escherichia coli, (11.2%) of Staphylococcus aureus and (1.1%) of Pseudomonas aeruginosa. By contrast, **Sharma *et al.*** [25] found that Gram-positive bacteria (S. aureus) were the most common cause (37.2%), followed by K. pneumoniae (27%) and E. coli (19.7%). S. saprophyticus was the most frequently recovered CONS isolate from blood cultures in the current study, followed by S. cohnii and S. haemolyticus. These species were present at 21.8%, 9.4% and 6.3% in blood cultures, respectively. Similar findings were reported in previous studies [26]. However, in the current study only one isolate of Streptococci was detected. In contrary, **Palazzi *et al.*** [27] concluded that the most common causes of NP were group B Streptococci (GBS), Escherichia coli (E. coli) and Listeria monocytogenes in developed countries and Gram negative bacteria and coagulase negative Staphylococci in developing countries.

In the current study, only 36.1% BAL cultures were positive. Similar result was previously (38.5%) reported in Zagazig University [20]. In the current study, the most prevalent organism isolated from BAL fluid was Klebsiella (38.5%). Similar result was previously reported in Zagazig University Hospital [20], Tanta and Benha University Hospitals [10].

Pneumonia mortality risk is strongly dependent on many risk factors [10]. The current study showed that mortality rate was 38.9%. Comparable rate was reported in Indonesia 20% [3], Tanzania 39% [28] and Cameroon 34.7% [29].

CONCLUSION

Neonatal sepsis remains a major problem in neonates. Gram-negative bacteria were the most common cause of early onset NP in Zagazig University hospital with K. pneumonia being the most common pathogen. Regular periodic surveillance of the causative organisms of neonatal pneumonia is needed to implement the rational empirical choice of antibiotic prescription while waiting for blood culture result to come out.

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