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"Tracheal Aspirate Culture ForEarly Prediction Of Ventilator Associated Pneumonia In Neonates In A Tertiary Care Centre, Dhaka, Bangladesh"

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ABSTRACT: Background: Ventilator-associated pneumonia(VAP) is the second most common nosocomial infection and one of the most common reason for antibiotic use in the neonatal intensive care unit (NICU). VAP is associated with significant morbidity and mortality. An early isolation of pathogen from tracheal aspirates (TA) will be helpful for early initiation of treatment and better outcome.**Objective:**To evaluate the utility of tracheal aspirate culture for early prediction of ventilator-associated pneumonia in neonates.**Methodology:**This was a prospective observational study conducted in the department of neonatology, BangabandhuSheikh MujibMedical University (BSMMU), Dhaka, Bangladesh over a period of one year from January 2018 to December 2018. Neonates who were mechanically ventilated for more than 48 hrs.were included in this study. Tracheal aspirate culture of all mechanically ventilated neonates was done except those who were diagnosed already as a case of pneumonia. All neonates were followed up for 7 days after sending sample (TA) – to observe whether VAP developed or not. VAP was diagnosed as defined by CDC (centre for disease control and prevention criteria of nosocomial pneumonia for patients younger than 12 months of age). **Results:**Ventilator-associated pneumonia occurred in 23/37 (62.2%) neonates as per CDC criteria. Sensitivity, Specificity, positive predictive value and negative predictive value of tracheal aspirate culture for detection of VAP wasfound 82.6%,71.4%, 82.6% and 71.4% respectively.**Conclusion:** Tracheal aspirate culture can be used as an investigation to diagnose VAP along with CDC criteria with an added advantage of earlier prediction of VAP in neonates.

Key words: Ventilator-associated pneumonia (VAP), bacterial culture of tracheal aspirate (TA), CDC criteria for diagnosis of VAP.

I INTRODUCTION

Mechanical ventilation refers to various artificial means to support oxygenation and ventilation and has become an indispensable part of neonatal intensive care.[1,2] Bangladesh is a resource limited developing country in south east Asia with neonatal mortality rate 30per 1,000 live birth (BDHS, 2017-18).Bangladesh has made tremendous progress towards millennium development goal 4. Sustainable development goal - target to reduce neonatal mortality to at least as low as 12 per 1,000 live birth by 2030 (World health statistics, 2017). Improving intensive care facilities for the neonate in the country could be one of the effective intervention to achieve this.There has been a dramatic fall in neonatal mortality in developed countries with the advent of mechanical ventilation and the concept of neonatal intensive care.[3, 4]Critically ill patients who require mechanical ventilation are at risk for Ventilator-associated pneumonia (VAP). Ventilator-associated

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pneumonia is the second most common nosocomial infection and one of the most common reason for antibiotic use in the pediatric & neonatal intensive care unit. Attributable mortality is uncertain but ventilator-associated pneumonia is associated with significant morbidity and cost. If early diagnosis can be possible by culture & sensitivity of tracheal aspirates, it will be helpful for early initiation of treatment and better outcome and may contribute in decreasing neonatal mortality rate.

II MATERIALS AND METHODS

This prospective observational study conducted in Department of Neonatology, BSMMU, Dhaka, Bangladesh after approval by Institutional review board of BSMMU over a period of one year (January, 2018 to December, 2018). Study population was 37 mechanically ventilated neonates. After taking informed written consent from the parents/ guardians of eligible newborn, face-to-face interview was taken from mother or caregivers and related information were recorded in a data collection form.All ventilated patient after 48 hrs. Of intubation were enrolled in this study except those before diagnosed as a case of pneumonia. All ventilated babies were nursed in the supine position, and routine care as per NICU protocol were provided. After enrolment sample (Tracheal aspirate) was collected after 48 hrs. Of intubation by an open suction using Hagedorn method (Suctioning was performed by using sterile feeding tube (5/6 Fr) or suction catheter (6Fr) and 3cc syringe through endo-tracheal tube). Minimum 0.5 ml aspirate was needed for culture.

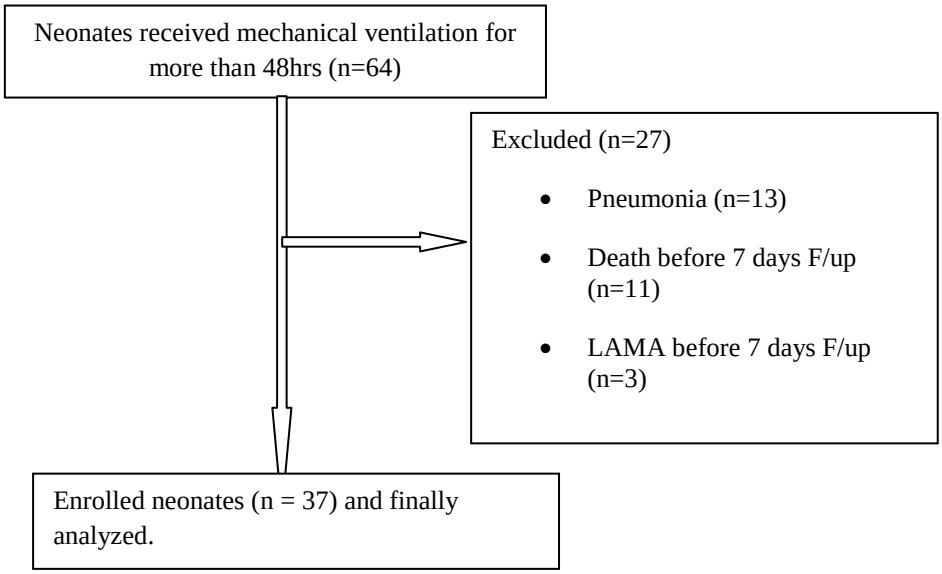

Figure 1: Flow chart of participants in the study.

Sample was collected aseptically by researcher in a sterile test tube/sterile vial supplied by microbiology department and was sent immediately for quantitative culture to microbiology department of BSMMU. Culture of tracheal aspirates were done on Blood agar, Mac-Conkey agar and Chocolate agar media. Studied infants were carefully followed up for 7 days after sending sample. During this period enrolled infants were observed for any sign of Ventilator Associated Pneumonia (VAP) according to CDC criteria (gold standard for diagnosis of VAP).[5]

Clinical follow up was done (2hourly up to stabilization then 4-6 hourly), recording of body temperature (4 hourly), Changes of ventilator parameter (peak inspiratory pressure, positive end expiratory pressure and fraction of inspired oxygen (FiO2)) according to arterial blood gas analysis (ABG). Leukocyte count and C-reactive protein, blood culture were done according to unit protocol as a part of sepsis work up and chest radiographs (just after intubation & thereafter when indicated). Indications are - any clinical deterioration of respiratory status, after re-intubation. Routinely ABG was done 12hrly and more frequently can be done if indicated (any acute deterioration).

Data were analyzed using the statistical package for social sciences (SPSS) version 20. Quantitative data were expressed as mean ± SD and categorical data were presented as proportion. For data analysis used t-test for continuous data and chi-square test/Fisher exact test for categorical data. Standard formula were used to see sensitivity and specificity of tracheal aspirate culture.

III RESULTS

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During the study period, total 64 neonates received mechanical ventilation for more than 48 hours. Among them total 27 neonates were excluded [13neonates were excluded due to pneumonia, 11 neonates were excluded due to death before 7days of F/up, 3 neonates were excluded due to left against medical advice (LAMA) before 7 days of F/up]. Finally 37 neonates were analyzed. [Figure 1]. Baseline characteristics of the studied infants are presented in [Table 1]. Majority (43.2%) of neonates were 30-34 weeks of gestation. According to birth weight classification, highest percentage (45.9%) of neonates were low birth weight (1500-2500g). Gender distribution reflected male preponderance among enrolled neonates. Delivery by LUCS (64.9%) was twice of delivery by NVD (35.1%). Among the enrolled neonates, inborn babies were more in no. (54.1%).

Table 1: Distribution of demographic characteristics among the enrolled neonates (n=37).

Characteristics	No of Neonates (n=37)	Percentage (%)
Gestational age(week)		
<30weeks	03	8.1
30-34 weeks	16	43.2
>34-37 weeks	07	18.9
>37 weeks	11	29.7
Birth weight(g)		
<1500 g	09	24.3
1500-2500 g	17	45.9
>2500 g	11	29.7
Sex		
Male	28	75.7
Female	09	24.3
Place of delivery		
Inborn	20	54.1
Outborn	17	45.9
Mode of delivery		
NVD	13	35.1
LUCS	24	64.9

Categorical data are presented as number and percentage (%)

Table 2 Shows about two third (62.2%) of mechanically ventilated neonates developed Ventilator Associated Pneumonia (VAP).

Table 2: Frequency of VAP among the enrolled mechanically ventilated neonates.

Outcome	N	Percentage (%)
VAP	23	62.2
No VAP	14	37.8
Total	37	100

Data are presented as number and percentage (%)

Table 3 shows the outcome of enrolled mechanically ventilated neonates in relation to baseline characteristics. There was no significant difference between VAP and non VAP group in relation to place of delivery, Mode of delivery and sex distribution, Gestational age, and birth weight of the enrolled neonates.

Table 3: Comparison of baseline characteristics among the VAP and non VAP group.

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Characteristics	VAP(n=23)	Non VAP(n=14)	p-Value
Gestational age (wks) Mean ± SD	34.43 ± 3.94	34.14 ± 3.20	0.817^{ns}
Birth wt (g) Mean±SD	2096 ± 777.59	1922 ± 583.94	0.474^{ns}
Place of delivery Inborn Outborn	12(60%) 11(64.7%)	8(40%) 6(35.3%)	0.769 ^{ns}
MOD NVD LUCS	7(53.8%) 16(66.7%)	18(46.2%) 8(33.3%)	0.443^{ns}
Sex Male Female	19(67.9%) 4(44.4%)	9(32.1%) 5(55.6%)	0.208 ^{ns}

Continuous data are presented as mean ± SD and categorical data as number &percentage (%)
Statistical test: Chi square test/fisher exact test
s: significant , ns: not significant

Figure 2 shows that culture (Tracheal Aspirate) positivity is more in VAP group (82.6%) than non-VAP group (28.5%)group (P value is 0.001).

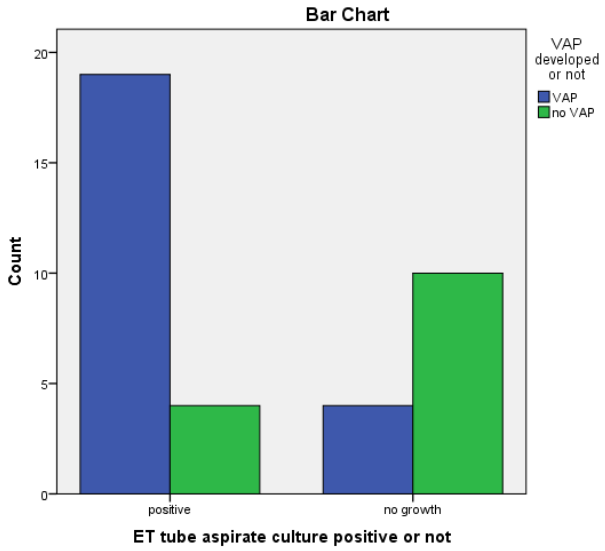

Figure 2: Distribution of enrolled mechanically ventilated neonate according to ET tube aspirate culture positivity (comparison chart between VAP and non VAP group).

Table 4 shows Comparison of ET tube aspirate culture positivity among the VAP and non VAP group among the enrolled mechanically ventilated neonates .There was significant (p value– 0.0017) difference between VAP and non VAP group in relation to ET tube aspirate culture positivity of the enrolled neonates.

Table 4: Comparison of ET tube aspirate culture positivity among the VAP and non VAP group.

Characteristics	**VAP(n=23)**	**Non VAP(n=14)**	**Odds ratio**	**95% CI**	**p-Value**
Culture positive	19(82.6%)	04(28.5%)	11.875	2.438 to 57.849	0.0017^{s}
No growth	04(17.4%)	10(71.5%)			

Categorical data as number & percentage (%) Statistical test: Fisher exact test

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s: significant, ns: not significant

Table 5 ShowsSensitivity, Specificity, PPV(Positive predictive value) and NPV(Negative predictive value) pattern of Tracheal Aspirate culture among enrolled infants for VAP detection. Tracheal Aspirate Culture is 82.6% sensitive & 71.4% specific for VAP detection. It has also 82.6% PPV and 71.4% NPV as well.

Table 5: Sensitivity, Specificity, PPV and NPV pattern of Tracheal Aspirate culture among enrolled infants.

Name of investigation	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Tracheal aspirate culture	82.6	71.4	82.6	71.4

PPV: Positive predictive value
NPV: Negative predictive value

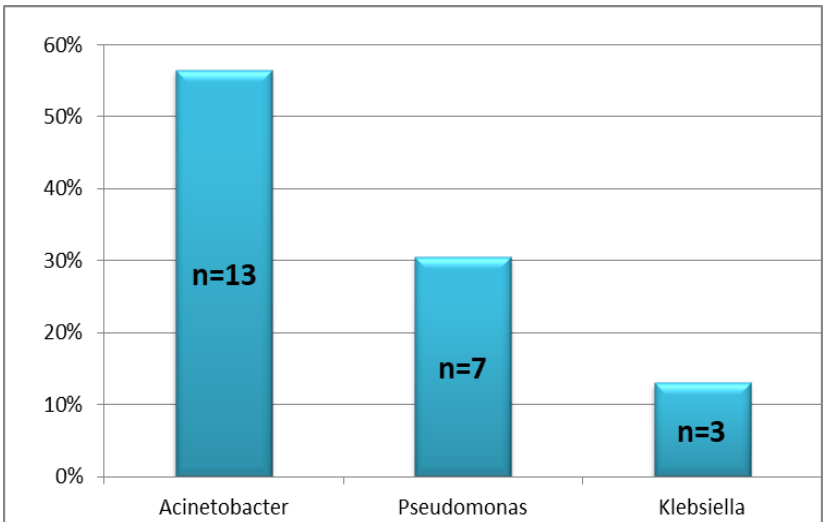

Figure 3: Pattern of organism found in trachael aspirate culture (TA) among enrolled mechanically ventilated neonates.

Among 37 enrolled mechanically ventilated neonates highest percentage 62.2% (n-23) of neonates were TA culture positive. And among 23 TA culture positive cases most of the organism were Acinetobacter (n = 13), followed by Pseudomonas (n = 07), rest of (n = 03) were Klebsiella [**Figure 3**]

IV DISCUSSION

This study revealed that Ventilator-associated pneumonia (VAP) occurred in 62.2% neonates. Another study also done in Bangladesh also found that ventilator-associated pneumonia (VAP) observed 79.2% neonates among enrolled babies, which is much higher than our study.[6] Where as some other studies showed that Ventilator-associated pneumonia occurred in 41%, 33%, 39% ventilated neonates respectively.[5, 7, 8] More VAP observed in our study compared with other country's study, this higher incidence of VAP is most probably due to higher patient load, poor infection control strategies. In this study, efficiency of bacterial culture of tracheal aspirate for detection of ventilator-associated pneumonia (VAP) is expressed by sensitivity, specificity, positive predictive value and negative predictive value. Tracheal aspirate culture had 82.6% sensitivity, 71.4% specificity, positive predictive value (PPV) of 82.6% and negative predictive (NPV) value of 71.4%. Sensitivity, specificity, PPV and NPVin our study were similar with other study.[5, 7, 8, 9]One study showed that Endo-tracheal aspirate (ETA) culture had 75% sensitivity, 90%specificity, positive predictive value of 84%, and negative predictive value of 83.72%.[5]Another study showed that bacterial index of >5 in broncho-alveolar secretions showed the best concordance compared with the reference standard (concordance, 83%; kappa, 0.61), Bacterial index of >5 also showed the best validity (sensitivity-78%; specificity-86%; positive

predictive value-70%; negative predictive value-90%; global value-90%).[7]Another study alsoshowed that tracheal aspirate samples were useful for predicting Staphylococcus sp. in ET bio-films with a sensitivity of 85.7% and a specificity of 83.3%. The sensitivity for the combination of tracheal aspirate and throat swab samples to detect Staphylococcus spp. in ET bio-films was 100%. The detection of Pseudomonas spp. in throat swabs assisted its identification in ET bio-films (sensitivity 33.3% and specificity 100%).[9]Another study done in Maastricht University Medical Centre, Netherlands showed that ventilator associated pneumonia (VAP) incidences varied from 15% to 68%. For the diagnosis of ventilator associated pneumonia (VAP), the most accurate threshold for positivity of endo-tracheal aspirate (ETA) semi-quantitative cultures was moderate or heavy growth.[8]In this study most of the babies were preterm 70.2%. Some other study also found most of the enrolled infants were preterm.[1,2,5,10]Among enrolled neonates most of the neonates were within 30-34 weeks 16 (43.2%), followed by >37 weeks 11(29.7%), >34-37 weeks 07 (18.9%), <30 weeks only 03(8.1%).Another study done in 2012 found that most the enrolled neonates were within 28-32 weeks 51.8 %, followed by < 27 weeks 22.2%, 33-37 weeks 14.8 %, >37 weeks 11.1%.[10]Ghosh UK et al. also found that more than half (51.4%) neonates were of gestational age 34 to <37 weeks.[6]In this study most of the enrolled neonates were between 1500-2500 grams 17 (45.9%), followed by >2500 grams 11 (29.7%), then <1500 grams 09 (24.3%).Another study also found most of the enrolled babies were between 1500-2500 grams 42 (58.3%).[6]A study found that most of the enrolled neonates were <1500 grams 61.7%, followed by between 1500-2500 grams 19.7%, >2500 grams 18.5%.[10]Among enrolled neonates most of the neonates were male 75.7%. Some otheralso found that most of the enrolled neonates were male.[1,5,6,10,11]In this study most of the enrolled neonates were Inborn 54.1%. Another study also found that most of the enrolled neonates were inborn 58.3%.[2]Among enrolled neonates most of the neonates were delivered by Lower Uterine Caesarian Section (LUCS) 64.9%. Another study also found that most of the enrolled neonates were delivered by Lower uterine caesarian section (LUCS) 65.2%.[10]Regarding demographic characteristics no significant difference was observed between VAP and non-VAP group of enrolled neonates. In this study Mean gestational age of VAP group was 34.43 ± 3.94 weeks and Mean gestational age of non-VAP group was 34.14 ± 3.20 weeks, mean birth weight of VAP group was 2096 ± 777.59 grams, mean birth weight of non-VAP group was 1922 ± 583.94 grams.Another study also found the same findings there was no significant difference of demographic characteristics between VAP and non-VAP group, mean gestational age of VAP group was 36.9 ± 1.8 weeks, Mean gestational age of non-VAP group was 38 ± 1.7 weeks, mean birth weight of VAP group was 2300 ± 600 grams, mean birth weight of VAP group was 2700 ± 500 grams.[5]This study shows more culture (tracheal aspirate) positivity in VAP group (82.6%) than non-VAP group (28.5%) and this findings is statistically significant (P value is 0.0017). Another study also shows the similar findings – they also found 75% ETA culture positivity in VAP group and 10% ETA culture positivity in non-VAP group.[5]In this study most of the organism found in culture of tracheal aspirates were Acinetobacter 56.5% (13/23), followed by Pseudomonas 30.5% (7/23) and Klebsiella 13.0% (3/23). This findings are similar to the following studies –A study found the similar organism responsible for VAP in their study, they showed that micro-organism associated with VAP and resistance to antibiotics in NICU patients are Klebsiella, Acinetobacter and Pseudomonas at the top of the list[12],Another study also found organisms cultured in ETA were Acinetobacter (29.4%), Klebsella (4.4%), Pseudomonas (3%), MRSA (3%), mixed growth was seen in one case,[5]Another study also found Pseudomonas aeruginosa, S. aureus, Escherichia coli, Klebsiellaspp. and H. influenza were the most frequently identified VAP-causing microorganism.[8]

V LIMITATIONS OF THE STUDY

- Single centered study
- small sample size
- study duration was too short to fulfill the calculated sample size
- Resource limited research center.

VI CONCLUSION

Tracheal aspirate culture is 82.6% sensitive and 71.4% specific for detection ofVAP in neonates. So tracheal aspirate culture can be used as an investigation to diagnose VAP along with CDC criteria with an added advantage of earlier prediction of VAP in neonates.

VII RECOMMENDATION

Further large scale (Large sample size, long duration, multi-centered) study is needed to support the findings of this study.

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