IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 13, Issue 4 Ver. V. (Apr. 2014), PP 63-67
www.iosrjournals.org

Outbreak of Methicillin Resistant *Staphylococcus aureus* in Neonatal Intensive Care Unit in a Tertiary Care Hospital in Kolkata

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Abstract : *Infection with Methicilln resistant Staphylococcus aureus (MRSA) was not very uncommon in the Neonatal Intensive Care Units(NICU) at present. In this study we report an outbreak of MRSA infection and its successful control in a tertiary care teaching hospital, Kolkata between September 2009 and June 2010. Twelve MRSA strains were isolated and identified conventionally following Clinical and Laboratory Standards Institute (CLSI) guidelines, from various clinical specimens, sent from the NICU. Subsequently, an infection control team was formed and infection control measures including isolation of infected babies, maintenance of hand hygiene , screening for colonization with MRSA, treatment of infected as well as carrier were implemented in NICU. Demographic data were collected from clinical records. Four (4) care givers were found to be colonized with MRSA strains. Antibiogram pattern of 6 infected babies matched with the MRSA strains isolated from the colonized attendant and nursing staff. Prematurity, low birth weight and gavage feeding were established risk factors for infection with MRSA in this study. Nine neonates were found to be colonized with MRSA though none was infected with the same strain. Following control measures, only one case of MRSA was detected in October 2009 thereafter no case of MRSA was reported till June 2010.MRSA outbreak acted as an alarm to the infection control committee of this tertiary care centre of eastern India for continuous monitoring and screening for MRSA in NICU.*

Keywords :*MRSA, NICU, Outbreak*

I. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of hospital acquired infection since the early 1980s [1]. Stay in the hospital for prolonged periods, admission in intensive care units, application of central lines, use of broad spectrum antibiotics, enteral feeding, extremes of age etc are considered as the risk factors for colonization and infection by MRSA[2]. In the neonatal intensive care units (NICU), the preterm neonates, critically ill full term babies and infants with congenital birth defects are admitted. They need use of prolonged invasive life supportive measures and antibiotics that increase the probability for acquiring healthcare associated infections[3]. Newborns with immature immune system are particularly liable to get infected with virulent organisms[4]. So, eradicating MRSA from NICU was quite an uphill task. Studies regarding incidence of MRSA outbreak in NICU, from India is not very common. In this study, we report an outbreak of MRSA in NICU in a tertiary care hospital in Kolkata followed by its control on instituting active surveillance and strict infection control measures.

II. Material And Methods

Setting

The NICU of the hospital is divided into two rooms – one small another large containing 8 and 12 beds respectively. There is on an average 12 admissions per day. Nearly, 90% patients in NICU are inborn. The nurse patient ratio is 1:8 to 1:6 during the study period.

Outbreak:

Routine culture send from NICU to Microbiology laboratory during September, 2009, revealed a total of 12 neonatal infections with MRSA. Among those 12 samples, 8 were pus, obtained from cases of umbilical sepsis in the neonates, 2 were endotracheal tube suction sample and 1 was blood culture sample. The 12thsample

was secretions from eye infection. After detection of these cases of MRSA infection, blood was collected from these infants for culture to detect septicemia if any.

Infection control measures

An infection control intervention was started from 2nd week of October after reporting of cluster of 12 MRSA cases from NICU in the month of September, to the Hospital Infection control committee.

Screening for MRSA colonization

Screening for MRSA carriage was done on all the departmental health workers (5 physicians, 8 nursing staff, and 4 attendants) and mothers (4) of the affected babies available at that time and all the neonates admitted at that time in the NICU.

Samples were collected from anterior nares and both hands from adult persons with a swab stick moistened with normal saline. Along with these, swabs from perineum and umbilical swabs were also collected from the neonates to detect colonization if present.

Environmental cultures were performed from different locations of NICU like baby cot, monitor, ventilator, incubator, water tap, walls of the nursery.

Identification of MRSA

The samples were inoculated on Blood agar, MacConkey's agar and Mannitol salt agar. The yellow colored colonies on Mannitol salt agar were further tested by catalase and coagulase tests and confirmed as Staphylococcus aureus. Antibiotic sensitivity was done on Muller Hinton media at 35°C for 24 hours using Cefoxitin (30µg) disc to study their MRSA status[5]. The other antibiotics used were Penicillin (10 units), Vancomycin (30 µg), Oxacillin (1µg), Netilmycin (10 µg), Linezolid (30µg), Piperacillin-Tazobactam (100/10),Ceftazidime (30 µg), Gentamicin (10 µg), Clarithromycin (15µg), Erythromycin (15 µg), Clindamycin (2µg), Cefotaxime (30µg), Fusidic acid (10 µg), Mupirocin (5 µg), Co-trimoxazole (25 µg). Quality control was performed using the *S. aureus*ATCC 29213 strain and ATCC 43300 as control for methicillin sensitive and methicillin resistance strains respectively following CLSI guidelines[6].

The strains marked as MRSA by Cefoxitin disc diffusion test were further confirmed by slidex staph latex agglutination tests (BioMerieux) to detect methicillin resistance based on the production of low affinity PBP2a encoded by mecA gene. The MRSA strains were kept for by PFGE and PCR for further strain typing and confirmation.

Control measures

NICU infants who were infected and colonized with MRSA were kept in isolation.

Outbreak control team was constituted. Appropriate hand hygienic measures, use of gloves, masks and isolation gown were strictly reinforced among all the health care workers in NICU. After proper hand washing with soap and water, Chlorhexidine 4% hand wash was used. Use of Alcohol based hand rub with 1% Chlorhexidine was also reinforced in between attending the patients which was not done previously before the outbreak.

The neonates with umbilical sepsis and colonization were given chlorhexidine bath (1: 10 dilution) and were appropriately treated with antibiotics according to the antibiogram report.

The attendant who was a nasal carrier was treated with nasal mupirocin application three times daily for 5 days.

Barrier precautions with the use of gowns, masks, gloves were instituted for all direct patient contacts.

The medical devices and baby cots, incubators, etc. were disinfected with 2% hypochlorite solution after taking swabs.

The floor was swabbed with lysol thrice daily instead of twice a day as was done earlier.

Study design

All newborns infected with MRSA were considered as Case. The neonates who stayed in the NICU, during the period before intervention strategy were implemented and were culture negative for MRSA, were selected randomly as Control.

Demographic and clinical data were collected from medical records.

Odds ratio for risk factors were determined. Chi-Square test and Fisher exact test were applied to calculate P value. P value < 0.05 was considered significant.

III. Result

Of the 12 neonates, 5 developed septicemia with the same MRSA strain as compared by antibiogram report. One of them died - may be because of extreme prematurity and very low birth weight. There was death in another neonate with MRSA infection due to respiratory distress syndrome in a case of prematurity. The neonates with MRSA isolate no. 8 and 9 were twins, placed side by side in the same cot. They developed

umbilical sepsis with the same strain, one twin followed by the other one, the next day. Probably the strain was acquired from the attendant who was a nasal carrier of MRSA. Interestingly, the blood culture report showed MRSA isolate with the same sensitivity pattern in both these neonates (Table 1).

During active surveillance MRSA was isolated from 1 physician, 1 nursing staff and 2 attendants from their hands. Of the 2 attendants, one was both nasal and hand carrier. The sensitivity pattern of 3 infected neonates matched with that of the attendant who was both hand and nasal carrier. The pattern of sensitivity of 2 neonates matched with that of 1 nursing staff and 1 neonate matched with the hand swab of the no.1 attendant (Table 2). The source of infection of the rest neonates (including the baby with eye infection) could not be determined. None of the mothers were carriers for MRSA. Colonization with MRSA was detected in 9 neonates from umbilicus. Their sensitivity pattern was similar to that of the nursing staff and the attendants. None of the 9 colonized neonates developed MRSA infection during their stay in NICU when subsequently followed up.

Staphylococcus aureus isolated from different location of NICU (baby cot, monitor, incubator, walls of the nursery) was found to be sensitive to cefoxitin i.e. MSSA.

MRSA incidence preceding outbreak

2 months preceding the outbreak, the incidence of MRSA was 2.6% (5 cases of MRSA out of total 77 cultures positive cases (Table 3).

MRSA incidence at the time of outbreak

The MRSA incidence at the time of outbreak was 19% (12 MRSA cases out of total 63 culture positive babies in the duration of 30days). 9 neonates and 4 health care personnel were found to be colonized with MRSA. The infected and colonized individuals were followed up with negative culture reports after adequate treatment.

MRSA incidence after the outbreak

After implementing the intervention strategy to control the MRSA infection, active surveillance was done for detection of infection and colonization for two months post outbreak. The MRSA incidence was found to be 1.6% (1 MRSA infection out of total 63 cases of infective etiology in next two months) of the total cases caused by other organisms. There were 2 colonized neonates during this period. The last case of MRSA colonization was detected at the end of December. Focused surveillance was continued till June, 2010 and no case of MRSA infection was identified during this period.

When potential risk factors for developing MRSA were considered, low birth weight, multiple pregnancies and Ryle's tube feeding appeared as significant risk factors for developing MRSA infection (Table 4).

IV. Discussion

The MRSA strain was present in NICU as was evident from the infections before the outbreak. If proper intervention was done at that time, this outbreak may not have occurred. One of the sources may be the Health care personnel whose antibiogram pattern was found to be similar to that of the infected neonates. Similar pattern of outbreak in NICU from the colonized care givers were reported by Albrich W C et al [7]and Saimon et al[8]. Immediate intervention was undertaken in the form of isolation, hygienic measures regarding hand washing, active surveillance, proper and strict treatment of the infected, colonized and carriers. This may have led to the control of the outbreak and reduction in the rates of MRSA colonization, infection and blood stream infection. This study confirmed prematurity and low birth weight of the neonates as significant risk factors for colonization and infection with MRSA as found by other workers[1,9]. Most of the patients had intra venous lines, and Ryle's tube feeding, which were all potential sources of infection as reported in other studies also [1, 10,11]. This further led to the exposure of the neonates to the healthcare personnel for prolonged periods; thereby increasing the chance of contracting infection. The neonates, who required prolonged stay in the NICU because of severity of their disease, prematurity etc., had more chance of contracting infection and chance of colonization. The patient and health care personnel ratio was also low in this set up, so that sometimes in case of emergency, there was a tendency for avoiding hand washing in between patients. This might be a way of introducing outbreak strain to the sick neonates. Sometimes, there is also overcrowding leading to the placement of two neonates, in the same bed like the twins in this study causing cross infection. The time period between taking a swab and receipt of the result can also be a factor in helping the spread of infection from the unknown MRSA positive infected / colonized neonate, thus acting as a source for outbreak in NICU.

Regarding the sensitivity pattern, Linezolid was 100% sensitive followed by Vancomycin which was almost 92% sensitive. One case was found to be VISA as confirmed by the E- test. The Mupirocin resistance is 25% in this study as reported elsewhere. [12] Clindamycin is 58% sensitive in this study. So, Clindamycin is proposed as effective drug as supported in other studies. [13]

Two patients died. One of them had respiratory distress, another was associated with very low birth weight and prematurity so, MRSA could not be implicated as the sole cause of death.
As MRSA outbreak in NICU is very dangerous, proper and intensive infection control measures are required for proper control of infections in NICU.Along withthis, detection of recently colonized babies should be continued for prevention of this outbreak.

V. Tables

Table 1: Sensitivity pattern of MRSA isolated from the neonates

Isolate no. / Status	Specimen	Resistance	Sensitive
MRSA 1	Blood culture	CE, CF, CN, CO, E, G, OF, OX, P, PIT	CD, FC,LZ,MU,NET, VA,
MRSA 2	Umbilical swab	CE, CF, CN, CO, E, FC, G, MU, NET, OF, OX, P, PIT,VA **	CD, LZ
MRSA 3	Respiratory secretions	CD, CE, CF, CN, CO, E, G, MU, NET, OF, OX, P, PIT	FC,LZ,VA
MRSA 4	Umbilical swab	CD, CE, CF, CN, CO, E, G, OF, OX, P, PIT	FC,LZ,MU,NET, VA,
MRSA 5	Eye swab	CD, CE, CF, CN, CO, E, FC, G, MU, NET, OF, OX, P, PIT	LZ. OF, VA
MRSA 6	Respiratory secretions	CE, CF, CN, CO, E, FC, G, NET, OF, OX, P, PIT	CD, LZ, MU, VA
MRSA 7	Umbilical swab	CE, CF, CN, CO, E, FC, G, NET, OF, OX, P, PIT	CD, LZ, MU,VA
MRSA 8	Umbilical swab	CD, CE, CF, CN, CO, E, G, NET, OF, OX, P, PIT	FC, LZ, MU, VA
MRSA 9	Umbilical swab	CD, CE, CF, CN, CO, E, G, NET, OF, OX, P, PIT	FC, LZ, MU, VA
MRSA 10	Umbilical swab	CE, CF, CN, CO, E, G, NET, OF, OX, P, PIT	CD, FC, LZ, MU, OF, VA
MRSA 11	Umbilical swab	CD, CE, CF, CN, CO, E, G, NET, OF, OX, P, PIT	FC, LZ, MU, VA
MRSA 12	Umbilical swab	CE, CF, CN, CO, E, FC, G, NET, OF, OX, P, PIT	CD, LZ, MU, VA

** The MRSA strain 2 – resistant to Vancomycin has been confirmed by E test (bioMerieux) as VISA with MIC (4mg/L).
CD= Clindamycin; CE= Cefotaxime; CF= Ciprofloxacin; CN= Cefoxitin; CO= Cotrimoxazole; E= Erythromycin; FC= Fucidin ; G= Gentamicin; LZ= Linezolid; MU= Mupirocin; NET= Netilmycin; OF= Ofloxacin; OX= Oxacillin; P= Penicillin; PIT= Piperacillin-Tazobactam; VA = Vancomycin

Table 2: Sensitivity pattern of MRSA isolated from health care staff

Isolate no.	Specimen	Resistance	Sensitive
Physician 1 (House staff)	Hand swab	CE, CF, CN, CO, E, G, NET, OF, OX, P, PIT	CD, FC,LZ,MU, NET, VA
Nursing staff	Hand swab	CE, CF, CN, CO, E, FC, G, NET, OF, OX, P, PIT	CD, LZ, MU, VA
Attendant no.1	Hand swab	CE, CF, CN, CO, E, G, NET, OF, OX, P, PIT	CD, FC, LZ, MU, OF, VA
Attendant no.2	Hand swab	CD, CE, CF, CN, CO, E, G, MU,NET, OF, OX, , P, PIT	FC,LZ,VA
Attendant no.2	Nasal swab	CD, CE, CF, CN, CO, E, G, NET, OF, OX, P, PIT	FC,LZ,MUVA

Table 3: Laboratory culture positive infections during the study period

	Before outbreak		During outbreak	After outbreak	
Month	July	August	September	October	November
MRSA	03	02	12	01	00
Staphylococcus spp. other than MRSA	20	16	26	13	14
Other Gram positive pathogens	03	04	04	02	05
Gram negative pathogens	11	14	19	08	16
Fungi	02	00	02	01	03
Positive culture	41	36	63	25	38

Table 4: Potential risk factors for MRSA infection

	MRSA+ No=12	MRSA- No=375	Statistics
Respiratory distress Present (n_1 = 39) Respiratory distress Absent (n_2 = 348)	2 10	37 338	Odds ratio 1.827 , χ^2=0.080 with 1 df, p =0.77
Birth wt < 1.5kg(n_1 = 25) Birth wt ≥1.5kg (n_2 = 362)	10 2	15 360	Odds ratio =120 , χ^2=108.339 with 1 df p =0.000
Multiple pregnancy Present(n_1 = 7) Multiple pregnancy Absent(n_2 = 380)	3 9	4 371	Odds ratio=30.917, χ^2=25.237 with 1 df p =0.000
Apgar score <3(n_1 = 53) Apgar score ≥ 3(n_2 = 334)	2 10	51 324	Odds ratio=1.271, χ^2=0.015 with 1 df p =0.903
Congenital anomaly present(n_1 = 4) Congenital anomaly absent(n_2 = 383)	1 11	3 372	Odds ratio =11.273 , χ^2=1.188 with 1 df p =0.276
Male(n_1 = 221) Female(n_2 = 166)	8 4	213 162	Odds ratio = 1.521,χ^2= 0.147 with 1 df p = 0.701
Ryle's tube feeding Present(n_1 = 27) Ryle's tube feeding Absent(n_2 = 360)	8 4	19 356	Odds ratio=37.474, χ^2= 58.826 with 1 df p =0.000
Undergone C.S(n_1 = 131) Vaginal delivery(n_2 = 256)	2 10	129 246	Odds ratio = 0.381, χ^2=0.937 with 1 df p =0.333

VI. Conclusion

The MRSA strains were present in the NICU and went unrecognized till the outbreak occurred. So, it is important to take intensive control measures even with a few cases. The increased susceptibility of the premature and very low birth weight babies to infection and presence of carriers of MRSA in NICU was responsible for the outbreak. The major intervention in the form of maintenance of hand hygiene with its strict compliance among the health care personnel, detection of carriers, and active surveillance of colonized neonates frequently combined with Mupirocin treatment has been successful in controlling such outbreaks. The health care givers should be screened at intervals for early detection and treatment of carriers. A continued education of health care personnel is also important in reducing the incidence of MRSA, so that outbreaks do not occur.

VII. Limitations

The limitation of the study is that the isolated strains could not be genetically typed on the basis of repetitive sequence PCR or pulsed field gel electrophoresis as was done by other authors [19] for epidemiological study because of the cost involved. But the strains have been preserved for future study.

Acknowledgements

We are indebted to "The West Bengal University of Health Sciences" in allowing us to publish this paper as a part of the thesis work entitled "Characterization of methicillin resistant *Staphylococcus aureus* isolated from surgical wound infection in a tertiary care hospital in Kolkata by phenotypic and genotypic methods" (PhD in Medicine) of Dr. Susmita Bhattacharya, Professor, Microbiology, NRS Medical College, Kolkata.

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