Prevalence and Profile of Device Associated Infection in Precisely Tribal Sickle Cell Disease children above 10 years of Age Admitted to ICU of a Tertiary Care Hospital of Tribal Area

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Abstract

Background: Sickle cell disease (SCD) children are more susceptible to bacterial infection due to multifactorial causewith poorimmunization status in tribal area.Device associated infections (DAIs) , due to extensive use of invasive devices in intensive care units , further increases morbidity and mortality in these patients . In the present study ,our aim is to define , the total burden and profile of DAI as presentation , spectrum of bacterial isolate and susceptibility in SCD children, in specific to, ICU of a tertiary care Hospital in Tribal area. **Methodology:**This prospective study was conducted overDevice Associated infections (DAIs) in Sickle cell disease (SCD) tribal children, having an inserted indwelling device, in the ICU of atertiary care hospital.Demographic ,clinical and date of device insertion data were recorded . Depending on the type of specimen, samples were cultured and analyzed .Antimicrobial susceptibility testing was performed on different isolates. **Result**: Out of 31 exposed SCD children to indwelling devices,the confirmed DAI cases were, 1 central line-associated bloodstream infections (CLABSI), 1 ventilator-associated pneumonia (VAP), and 3 catheter-associated urinary tract infections (CAUTI). The overall DAI rate was 16.1% with 29.7 per 1000 device days . The Organism causing infection were Gram-negative in 3(60%) cases , Gram-positive in 2 (40%), and as mixed infection with fungal organisms in 2(40%) cases. Most isolates were susceptible to Co-Trimoxazole , Ceftriaxone and Gentamycin . CONS and Klebsiella were showing multidrugresistant to more antibiotics tested.**Conclusion:**Since,In view of high DAIrate in Sickle cell Disease Tribal children in the ICU of tribal area,the preventive strategies should be plannednot only to improve immunity but also reduce morbidity ,mortality , to ensure a good quality health care in them.

Key Word - *Sickle cell disease (SCD), Device Associated infections (DAI), Central line-associated bloodstream infections (CLABSI), Ventilator-associated pneumonia (VAP), Catheter-associated urinary tract infections (CAUTI).*

Introduction

Sickle cell disease (SCD) is an autosomal recessive genetic disorder of the haemoglobin in red cells. It is particularly disastrous, mainly due to its acute and chronic complication such as painful vaso-oclusive events, acute chest syndrome and acterial infections. Bacterial infections ,the commonest etiological agent Streptococcus pneumonia have been shown to be the major cause of death in children with sickle cell disease. [1],[2],[3] The cause of increase susceptibility of SCD

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patients to Bacterial infection is multifactorial including defect in compliment activation ,functional asplenia, micronutrient deficiencies.[4] There is a predominance of invasive pneumococcal infection below the age of five and salmonella infection above five years old in SCD children.[5],[6]

Device Associated infections (DAIs) due to extensive use of invasive devices in patients, are a major cause of morbidity and mortality in intensive care units .The DAI rate in an ICU also depends upon a number of factors such as type of patient admitted, condition of patient , use of antibiotics ,protocol of using indwelling devices and infection control in these settings . In most hospitals, the ICU-acquired infections account for more than 20% of all nosocomial infections.[7] The World Health Organization (WHO) assessed the rates of DA-HAIs in the ICUs of low- and middle income countries in a systematic review , where the rate of CLABSI was 12.2 per 1,000 central line-days, CAUTI was 12.2 per 1,000 urinary catheter-days, and VAP was 23.9 per 1,000 ventilator-days .[8]

Further, DAI in infection prone sickle cell disease children will increase mortality and morbidity rate in PICUs. In a multicentre study conducted in ICUs in India, mortality due to VAP, CR-UTI, and CR-BSI were 19 0%, 11 6%, and 4 0% respectively .[9]

So, the DA-HAI surveillance played an important role in reducing the rates of DAIs and improving hospital infection control and quality assurance in developed countries.[10],[11] To our knowledge, there are no published data on the burden and spectrum of bacteria and outcome in Device associated infection , in SCD childrenin the PICU . In the present study ,our aim is to define , the total burden and profile of DAI as presentation , spectrum of bacterial isolate and susceptibility in tribal SCD children, in specific to , ICU of a tertiary care Hospital in Tribal area

Methodology

Study Design & Setting : This was a Prospective study that included all SCD children , having at least one of a placed central line, Endotracheal tube, or Foley's catheter and fulfilled the definitions of CLABSI, VAP, and/or CAUTI at any point during their stay in the ICU of SLN medical college, a tertiary care hospital , between March 2019 and February 2020 . This Study was reviewed and approved on 28th February 2019 by the ethical committee of research review board of our hospital.

Among all SCD children above 10 yearsin our 20 bedded ICU, confirmed earlier or newly diagnosed (by Sickling Test and High performance Liquid Chromatography), who fulfilled the definitions of CLABSI or VAP or CAUTI as defined by the CDC's National Nosocomial Infections Surveillance (NNIS) system criteria, at any point during their stay in the ICU were taken . The definitions of CLABSI, VAP, and CAUTI were adapted from CDC. The first CDC criterion for any of the three infections is that they must have occurred at least on the second day of placement of the respective device. Second, if the device was removed after two days of placement or more, an infection occurring, at most, on the day following the removal of the device was also considered to be associated with the respective device. **Inclusion criteria:** 1. Children who were confirmed early or newly diagnosed in ICU , 2.SCD children above the age of 10 years.3. SCD children having at least one of a placed central line, endotracheal tube, or Foley catheter in the PICU. 4. SCD children who fulfilled the definition of CLABSI, VAP, and/or CAUTI .5 . Those admitted in PICU for more than 48 hours were included in the study , 5. Tribal area SCD children.

Exclusion criteria:1.Children other than SCD admitted to ICU. 2. SCD Children below 10 years of age . 3. SCD Children neither having at least one of a placed central line, endotracheal tube, or Foley catheter in the ICU nor fulfilled the definition of CLABSI, VAP, and/or CAUTI.4. Infection other than DAI.

Sample Collection In all suspected DAI in the presence of a device cases,

The most appropriate samples for the diagnosis of a site-specific DAI were collected aseptically for microbiology analysis and sent to microbiology laboratory without delay. In case of CA-UTI, urine was collected suprapubically with a sterile needle and syringe and distal 5 cm of the aseptically removed urinary catheter was cut and sent to microbiology .Deep tracheal aspirates or distal 5 cm of used ET tube were collected aseptically for VAP. In case of CLABSI, catheter line was removed aseptically; the distal 5 cm of the IV catheter

was cut and sent to microbiology laboratory along with the blood collected for culture from the other arm. . Infection surveillance and consent form with necessary details was filled up simultaneously .Qualitative cultures were performed on peripheral or central blood, deep tracheal aspirate or from ET tube, and quantitative cultures were done on urine samples. For urine, a count of more than 10^5 colony-forming units per ml with one or two micro-organisms isolated was considered as a confirmation of UTI. Standard culture methods were used, to identify the microorganism , depending on the type of specimen to be analysed,. Antimicrobial susceptibility testing was performed on isolates .

Data Collection

In all cases , demographic data (Age ,Sex, Address,) ,vaccine status, date of admission, duration of Stay, type of devices inserted along with the time and date were recorded. Clinical data as sign, symptom at the time of admission and new symptoms after placement of central line or endotracheal tube or urethral catheter were collected .

Statistical Analysis

Microsoft Excel was used for data entry and analyzed with SPSS software version 20.0 . For quantitative variable , median and for qualitative variable ,frequency (percentage) were used to present the results.

Results

In the present study ,a total of 56 SCD tribal children treated for an aggregated duration of 518 days with different complaint, were taken. Out of these, 31 SCD tribal children were exposed to various devices for a total duration of 206 device days with a overall Device utilization rate of 0. 39 . The overall DAI rate was 16.1% with 29.7 per 1000 device days .(Table-2)

Table :1 Demographic data of SCD Tribal children.

SCD Children admitted to ICU	Total (n= 56)	Sex	Total (n)	Percentage (%)
SCD children with various Indwelling Devices (Exposed)	31(55.3%)	Male	14	45.1 %
		Female	17	54.8 %
SCD children without Indwelling Devices (Not Exposed)	25(44.6%%)	Male	18	72 %
		Female	7	28 %
SCD children with Confirmed DAI	5 (16.1%)	Male	2	40%
		Female	3	60%

Out of 56 SCD children , 31(55.3%) exposed to different indwelling devices , where 14 (45.1%)male and 17 (54.8 %) were female patients .Only 5(16.1%) cases confirmed by microbiologically as DAI . (Table-1)

Table-2 :Distribution of SCD tribal children in ICU according to Clinical presentation and Rate of DAI per specific site of Infection.

Type of DAI	Reason for ICU Admission in SCD children undergone insertion of Indwelling Devices. (Total= 31/56)							Total No of cases Exposed. (31(55.3%))	Day of ICU , Tube or catheterinserted	New signs and Symptom developed (Days)	Total No of confirmed DAI cases. N = 5(16.1%)	Total no of Device days per site (T= 206 days)	DAI per Site (%), n/1000device days
	AA (3/10)	ACS (8/10)	SS (9/9)	SP (10/10)	FUO (12/13)	PC (0/1)	SA (2/3)						
CLABSI	1	1	2	3	2	0	1	10(32.2%)	1st/2nd	> 5	1(10%)	51	19.6
VAP	0	3	1	2	0	0	0	6 (19.3 %)	2nd/3rd	>2	1 (16.6%)	34	29.4
CAUTI	2	4	6	5	10	0	1	28(90.3%)	2nd/3rd	>7	3(10.7%)	121	24.7

AA(Acute Abdomen), ACS- Acute chest syndrome , SS-Septicemia, SP- Severe Pneumonia, FUO- Fever of Unknown Origin, PC-Pain crisis, SA- Severe anaemia

The SCD tribal children admitted in ICU with cause were , Acute abdomen 3/10 (30%) , Acute chest syndrome 8/10 (80 %), Septicemia 9/9 (100 %), Severe pneumonia 10/10 (100%), Fever of Unknown Origin 12/13 (92.3 %), Pain crisis 0/9 (0%), Severe anaemia 2/3(66.6%) . A total of 31 Device exposed patients were identified with 10 (32.2%) central line-associated bloodstream infections (CLABSI), 6 (19.3%) ventilator-associated pneumonia (VAP), and 28 (90.3%) catheter-associated urinary tract infections (CAUTI). In CLABSI patients, Central line inserted on 1st or 2nd day of ICU admission and kept at least for 5 days , Where as in VAP and CAUTI patients , Endotracheal tube and urinary catheter inserted on 2nd or 3rd day of ICU admission and kept for at least for 3 and 7 days respectively. Total no of Device day was 206 days ,where for central line 51 days ,endotracheal tube 34days and urinary catheter 121 days. So the DAI rate per site of infection were CLABSI 1(10%) with 19.6 per 1000 device days ,VAP 1 (16.6%) with29.4 per 1000 device days , CAUTI 3(10.7%) with 24.7 per 1000 device days .(Table-2)

Table-3 :Distribution of microorganisms per site of(Single / Mixed infection) infection.

Microorganism	CLABSI		VAP	CAUTI		Total (n= 5)
	Single	Mixed		Single	Mixed	
Coagulase-negative Staphylococcus (CONS)	0		1	0		1 (20%)
Streptococcus Pneumonae	1		0	0		1 (20%)
Escherichia coli	0		0	1		1 (20%)
Candida albicans	0	1	0		1	2 (40%)
Pseudomonas aeruginosa	0			1		1 (20%)
Klebsiella Pneumoniae				1		1 (20%)

DAIs in Sickle cell Disease Tribal children in the ICU were caused by Coagulase-negative staphylococci (CONS) in 1 (20%) case , Streptococcus Pneumonae in 1 (20%) case , Escherichia coli in 1 (20%), Candida species 2 (40%) and Pseudomonas aeruginosa, Klebsiella Pneumoniae in 1 (20%) case each . In some sites we got mixed infection with two or more organisms. Overall ,Gram-negative pathogens in 3(60%) , Gram-positive ones in 2 (40%), and fungal organisms in 2(40%) as mixed infection , were found in these children .(Table-3)

Table-4 :Sensitivity pattern of the bacteria isolated from SCD children with DAI to some antibiotics.

Name of Organism	Isolates susceptible to different antibiotics											
	GMN	AMX	VAN	COT	CZM	CTZ	CPZ	IMP	CTX	NF	LZ	CFX
Coagulase-negative Staphylococcus	0	0	1	0	0	0	0	0	1	0	0	0
Streptococcus Pneumonae	0	1	1	1	0	1	0	0	1	0	1	1
Escherichia coli	1	1	0	1	1	1	0	1	1	1	1	1
Klebsiella Pneumoniae	1	0	0	0	1	0	0	1	0	1		0
Pseudomonas aeruginosa	0	0	0	1	1	1	0	1	1	0	0	0

GMN-Gentamycin,AMX-Amoxycillin,VAN-Vancomycin,COT-Co-Trimoxazole,CZM-Ceftazidim,CTX-Cefotaxime ,AMK- Amikacin ,CPZ – Cefoperazone ,IMP- Imipenem , CTZ-Ceftriazone, NF-Nitrofurantoin, LZ-Linezolide, CFX-Cefuroxime

In the present study, most of the isolates were found susceptible to Co-Trimoxazole , Ceftriaxone ,cefotaxime, imipenem and Gentamycin. The susceptibility rate of Enterobacteriaceae members (Escherichia coli and Klebsiella pneumoniae) were found to be more with Gentamycin, Imipenem and Ceftazidime. Overall susceptibility of Escherichia coli isolates was better than Klebsiella isolates for most of the antibiotics tested. Klebsiella isolates were resistant to Vancomycin and Co-Trimoxazole. Among the gram positive bacteria Streptococcus Pneumonae was susceptible to most of the antibiotic as compared to CONS., where as CONS was resistant to Gentamycin and Co trimoxazole ,Amoxycillin . Pseudomonas aeruginosa wassusceptible to ceftazidime, ceftriaxone, Imipenem and resistant to gentamycin.. For Candida species we have not done any susceptibility test. (Table-4)

Discussion

The place of study is a tertiary care hospital in the tribal area ,covering a large population and the border of another state , where Consanguineous marriage at second degree is more. . These people are also migrated to this place , hence genetic diseases are expected more . Again. because of unawareness ,and lack of health consciousness , the immunization status of these SCD children is poor , which make them more prone for infection leading to more ICU admission .So we decided to do study over these children for better outcome in the ICU . Out of 56 SCD tribal children, only 31(55.3%) were exposed to different invasive devices, where females 17(54.8%) and male 14(45.1 %) cases . (Table-1)

In the present study ,out of 31 exposed SCD children, 5 patients were microbiologically confirmed

cases as DAI. . The overall DAI rate was 16.1% with 29.7 per 1000 device days (Table-1) , which was more as compared to a study in Thai PICU, where the rate of DAIs was 28.3 per 1,000 patient-days, [12] and to an another study in Egypt from two PICUs by INICC ,were 22.8 DAHAIs per 1,000 ICU-days .[13] For DAI in ICU setting , the findings of the International Nosocomial Infection Control Consortium (INICC) in ICUs of seven Indian cities had found overall infection rate of 4.4%. [14] It showed that ,even if the device utilization rate was less ,the device infection rate in our study in SCD children was high. This high DAI rate in SCD children , might be due to all are improperly immunized ,sick and referral cases . Again the sample size was small as compared to utilization of indwelling devices in our ICU .

To determine the CLABSI in ICU ,a total of 10(32.2%) were exposed to the central line over a period of 51 Device days , from where only 1 (10%) case was confirmed as DAI ,resulting in an infection rate of 10% with 19.6 per 1000 device days . It was more in comparison to a study by INICC in Egypt from two PICUs, reported 18.8 CLABSIs per 1,000 line-days, and 31.8 VAPs per 1,000 ventilator-days[13] and quite high to a study in US and Turkish rates of 3.2 and 9.69 infections per 1000 device days [15] and less to peripheral line related blood stream infection rates of 0.3 to 31.1% .[16],[17],

In order to know the CAUTI, 28 patients were undergone urinary catheterization, with a total of 121 Device days . Only 3 cases were confirmed as DAI microbiologically ensuing a rate of 10.7 % with 24.7 per 1000 device days. This was more as compared to 6.8 CA-UTI per 1000 device days in one study by Vonberg et al. [18] High CAUTI rate may be due to more female patient as compared to male , even after the high risk of infection in SCD children .

In our study , We studied 6 intubated patients kept on ventilators, for 34 device days in order to determine the VAP . Out of which , only 1 patients was confirmed VAP with an infection rate of 16.6% with 29.4 per 1000 device days; which was high or near to that of a Turkish study, reporting a rate of 20.8% with 24.1 infections per 1000 device days, [19],[20] and same to other different studies ,where the rates of VAP had ranged from 10.5 to 34.8% .[14],[16],[19],[21] But it was less as compared to another study by Priyanka et al ,where VAP rate was 31.74 per 1000 ventilator-days with 0.46 DUR .[22]

In the present study, CAUTI was the most common type of DAI in our ICU, followed by CLABSI and VAP (Table-2). These results are against to those found in other developing countries, where VAP is the most common cause of DAIs, and similar to the high-income countries, where CAUTI is the most common type in PICU in children .[8] .

All DAI rate of specific site in our study were more to a study on children other than SCD in PICU in Egypt by INICC reported 18.8 CLABSIs per 1,000 line-days, and 31.8 VAPs per 1,000 ventilator-days .[13] It revealed that the DAI (CAUTI &CLABSI) in SCD tribal children in our ICU was more than non SCD children in the ICU , because of infection prone poorly immunized children and also not following properly the protocol to prevent DAI or delay in using antibiotics therapeutically and prophylactically . VAP is less due to frequent changing of endotracheal tube prophylactically because of tube block .

The organisms isolated in the present study were Coagulase-negative staphylococci,Streptococcus Pneumoniae, Candida albican, Escherichia coli , Klebsiella Pneumoniae .(Table-3) Which was similar to findings in other studies .[14],[23] Staphylococcus aureus(1 CLABSI and 1 VAP) was the most common cause of DAIs, followed by Candida species (1CLABSI and 1 CAUTI) as mixed infection followed by Escherichia coli (1 CAUTI), which was different from the nosocomial infections among PICU patients in an another study in Alexandria, Egypt , [24] where Klebsiella species were the most commonly isolated pathogens (46.7%), but having some similarity to a study done in the Arab region of Tunis ,[25] showed Staphylococcus aureus to be the most common cause (26.8%) of nosocomial bloodstream infections, followed by coagulase-negative staphylococci (17%).

Most of the isolates were found susceptible to Co-Trimoxazole , Ceftriaxone and Gentamycin. The susceptibility rate of Enterobacteriaceae members (Escherichia coli and Klebsiella pneumoniae) were found to be more with Gentamycin, Imipenem and Ceftazidime. Among the gram positive bacteria ,Staph aureus were susceptible to most of the antibiotic as

compared to CONS. All the organisms isolated in the present study were showing some resistant to more than two different classes of antibiotics .Mostly CONS and Klebsiella were showing multidrug resistant to more antibiotics tested. (Table-4)

However ,our study had some limitations, we did not search for viral and sensitivity pattern for Fungal agent in these SCD tribal children . we have not followed up of DAI patients to find out DAI associated morbidity and mortality .

Conclusion

To reduce mortality and morbidity in Tribal Sickle Cell Disease children with DAI in the ICU, a preventive strategies such as antibiotic policy, protocol for using device , proper immunisation and at the same time better quality of life to improve immunity and quality health care in ICU of any hospital in Tribal area should be planned . Hence regular surveillance of device-associated infections in ICU is therefore highly informative not only to clinicians but also to administration, specifically for these children in the tribal area , in determining the burden and type of infection , rateand risk factor.

Recommendation

Keeping in mind the chance of DAI rate in Sickle Cell Disease children, more surveillance studywith large sample size over tribal children should be done in the ICU of hospital in tribal area .

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