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Original Research Article

The trends of isolation and antimicrobial susceptibility of group B *Streptococcus* in urine culture: a 7-years cross sectional study

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ABSTRACT

Background: Group B Streptococcus (GBS)/*Streptococcus agalactiae (S. agalactiae)* is a common rectovaginal colonizer, thereby a potential agent of neonatal and maternal infection. This study estimates the trends of isolation of GBS, its antimicrobial profile in urine culture and the demographic characteristics of these patients over a 7-year period.
Methods: A record-based study was conducted, which included all the urine culture reports of GBS/*S. agalactiae* from January 2014 to December 2020. The trend of occurrence of GBS bacteriuria, demographic characteristics and antimicrobial susceptibility pattern were analyzed.
Results: Out of 137 urine samples which grew GBS/*S. agalactiae,* 55(40.15%) were from antenatal women. Most of the isolates were from females (72.26%), with a male preponderance noted among the elderly population (age>60 years). The predominant age group affected were adults between 20 to 59 years. The majority of the isolates (60.58%) were susceptible to all the four tested antibiotics, namely, ciprofloxacin, nitrofurantoin, ampicillin and vancomycin. Ciprofloxacin resistance was observed in 32.85% (45/137) isolates, 5.84% (8/137) isolates were resistant to ampicillin and 2.92% (4/137) were resistant to nitrofurantoin.
Conclusions: All the isolates were susceptible to vancomycin. GBS/*S. agalactiae* is an important agent of bacteriuria in antenatal women as well as in non-pregnant population, especially the elderly males. Emerging resistance to various group of antibiotics warrants routine susceptibility testing.

Keywords: Antimicrobial susceptibility testing, *Streptococcus agalactiae*, Urine, Urinary tract infection

INTRODUCTION

Streptococcus agalactiae/Group B *Streptococcus (GBS)* was first isolated from milk and cows with bovine mastitis.[1] GBS colonization of the vaginal tract of asymptomatic women and reports of fatal post-partum infection have been reported since 1938.[2] It has a significant role in antenatal woman, either as a colonizer or as an agent of infection of the genitourinary tract, thereby posing tremendous risk for neonatal invasive infections.[3,4] GBS bacteriuria is common when there is a heavy rectovaginal colonization,[4] though its role in causing urinary tract infection remains obscure. This cross-sectional study intends to bring to fore the trend of occurrence of significant bacteriuria due to GBS in antenatal women and a cause of urinary tract infection (UTI) in non-pregnant population for 7 years from a single center. The demographic characteristics of these patients and the antimicrobial susceptibility profile of these isolates were also analyzed.

METHODS

A cross sectional study was conducted in the department of Microbiology in liasing with the Obstetrics and Gynecology department of a tertiary care health center, Puducherry. All culture reports of urine samples from which *Streptococcus agalactiae*/GBS was isolated, over seven years (January 2014 to December 2020) were included in the study. The culture was done on cysteine lactose electrolyte deficient agar for all the samples. GBS was identified using conventional biochemical tests as well as Streptococcal grouping targeting the "C" carbohydrate antigen by latex agglutination test during the years 2014 to 2017. For all the isolates obtained from 2018 to 2020, in addition to the conventional methods, MALDI TOF MS (VITEK MS V3/KB V3.2.0) was used to confirm the identification. GBS was reported as a significant pathogen from all antenatal women irrespective of the colony count or presence of symptoms as per the guidelines of American college of Obstetricians and Gynecologists.[5] In nonpregnant patients, significant bacteriuria was reported considering various factors like-colony count, age of the patient, gender, presence of symptoms, type of the sample, urine microscopy findings etc. Antimicrobial susceptibility testing was performed by disk diffusion method and interpreted according to the clinical laboratory standard infection guidelines of the respective years.

RESULTS

The total number of GBS isolated from urine culture during the study period (2014 January-2020 December) was 137, of which 55(40.15%) were from antenatal women. The year wise distribution of the total number of GBS isolated from the general population as well as among the antenatal women is enlisted in Table 1.

Table 1: Year wise distribution of isolation of GBS in study population and antenatal women.

Year	Total number of isolates (n)	Number of isolates from antenatal women -n(%)
2020	16	5 (31.25)
2019	28	15 (53.57%)
2018	7	4 (57.14%)
2017	9	1 (11.11%)
2016	19	4 (21.05%)
2015	27	15 (55.56%)
2014	31	11 (35.48%)
Total	137	55 (40.15%)

Predominant isolation was from females (72.26%), with a female to male ratio of 2.61. The commonest age group affected was adults between 20 to 59 years (72.26%), followed by the elderly age ≥60 years (16.06%). Among the elderly, male (63.64%) predominance was noted. Overall, among the adult patients, females were commonly affected, with 68.75% (55/80) being antenatal. When considering the nonpregnant adult population, there was not much difference in the proportion of males and females affected (males=19.19%, nonpregnant females=25.25%). The yearly trend of isolation of GBS based on age and gender and the gender distribution across various age groups are depicted in Table 2.

Table 2: Age and gender distribution among the study population.

Age and gender distribution across the years							
Year	**Female n (%)**	**Male n (%)**	**Child (0-9 years) n (%)**	**Adolescent (10-19 years) n (%)**	**Adult (20-59 years) n (%)**	**Elderly (≥60 years) n (%)**	**Total n**
2020	13 (81.2)	3 (18.7)	1 (6.2)	2 (12.5)	7 (43.7)	6 (37.5)	16
2019	23 (82.1)	5 (17.9)	0	3 (10.7)	23 (82.1)	2 (7.1)	28
2018	7 (100)	0	0	0	5 (71.4)	2 (28.6)	7
2017	5 (55.6)	4 (44.4)	2 (22.2)	0	5 (55.6)	2 (22.2)	9
2016	12 (63.2)	7 (36.8)	2 (10.5)	0	14 (73.7)	3 (15.8)	19
2015	21 (77.8)	6 (22.2)	1 (3.7)	0	25 (92.6)	1 (3.7)	27
2014	18 (58.1)	13 (41.9)	2 (6.4)	3 (9.7)	20 (64.5)	6 (19.3)	31
Total	99 (72.3)	38 (27.7)	8 (5.8)	8 (5.8)	99 (72.3)	22 (16.1)	137
Gender distribution across different age groups							
Age group				**Gender**			
				Male n (%)	**Female n (%)**	**Total n (%)**	
Child (0-9 years)				3 (37.5)	5 (62.5)	8 (5.8)	
Adolescent (10-19 years)				2 (25)	6 (75)	8 (5.5)	
Adult (20-59 years)				19 (19.2)	80 (80.8)	99 (72.3)	
Elderly (≥60 years)				14 (63.6)	8 (36.4)	22 (16.1)	
Total				38 (27.7)	99 (72.3)	137 (100)	

The antimicrobial susceptibility pattern of the individual antibiotic tested for the isolates of GBS were analyzed. The susceptibility profile of the antibiotics tested among the overall population and the antenatal women in each year is listed in Table 3. Overall, the majority of the isolates (60.58%) were susceptible to all the four tested antibiotics-ciprofloxacin, nitrofurantoin, ampicillin and vancomycin. Ciprofloxacin resistance was observed in 32.85% (45/137) isolates, 3.65% (5/155) were intermediate to ciprofloxacin, 5.84% (8/137) isolates were resistant to ampicillin, 2.92% (4/137) were resistant to nitrofurantoin. All the isolates were susceptible to vancomycin.

Table 3: Antimicrobial susceptibility pattern of GBS.

Year	Susceptible isolates in the total population					Susceptible isolates in the antenatal women				
	Total n	Cf n (%)	F n (%)	A n (%)	Va n (%)	Total No (n)	Cf n (%)	F n (%)	A n (%)	Va n (%)
2020	16	11 (68.7)	16 (100)	16 (100)	16 (100)	5	2 (40)	5 (100)	5 (100)	5 (100)
2019	28	22 (78.6)	28 (100)	28 (100)	28 (100)	15	12 (80)	15 (100)	15 (100)	15 (100)
2018	7	5 (71.4)	7 (100)	7 (100)	7 (100)	4	3 (75)	4 (100)	4 (100)	4 (100)
2017	9	3 (33.3)	9 (100)	6 (66.7)	9 (100)	1	1 (100)	1 (100)	1 (100)	1 (100)
2016	19	8 (42.1)	18 (94.7)	14 (73.7)	19 (100)	4	2 (50)	3 (75)	2 (50)	4 (100)
2015	27	16 (59.4)	27 (100)	27 (100)	27 (100)	15	9 (60)	15 (100)	15 (100)	15 (100)
2014	31	21 (67.7)	28 (90.3)	31 (100)	31 (100)	11	10 (90.9)	10 (90.9)	11 (100)	11 (100)
Total	137	86 (62.8)	133 (97.1)	129 (94.2)	137 (100)	55	39 (70.9)	53 (96.4)	53 (96.4)	55 (100)

Cf-Ciprofloxacin, F- Nitrofurantoin, A-Ampicillin, Va-Vancomycin

DISCUSSION

S. agalactiae is a Gram-positive coccus belonging to the Group B according to Lancefield's classification. They are well-known colonizers of the gastrointestinal tract and female genital tract, especially in the reproductive age group.[6,7] They are known to cause variety of invasive as well as non-invasive infections in neonates, pregnant woman and elderly with underlying comorbidities.[8] The role of GBS as a causative agent of UTI is not well defined.[9] GBS bacteriuria during pregnancy accounts for a prevalence of 1-3.5%, though most of the episodes are asymptomatic.[10] Globally around 18% of pregnant woman are found to be colonized with GBS, with wide regional variations.[4] This could result in an ascending route of colonization or infection of the urinary tract from the vagina in antenatal women. Though, majority of the pregnant woman remain as asymptomatic colonizers, 10% of cases of pyelonephritis in pregnant women accounts to GBS.[10] They are also prone to develop various obstetric complications such as preterm labour, premature rupture of membrane and chorioamnionitis, as well as puerperal infections.[11] Moreover, neonates born to these mothers are at high risk of developing invasive neonatal infections such as neonatal meningitis, pneumonia, bacteremia and bone/joint infections.[4] Several guidelines are in place to identify these antenatal colonizers and recommend appropriate intrapartum prophylaxis to prevent the neonatal infections and maternal complications. The recent guidelines by American College of Obstetricians and Gynecologists recommend rectovaginal screening of antenatal women at 36 to 37 weeks of gestation for GBS and intrapartum prophylaxis to prevent vertical transmission.[12] Similarly, GBS bacteriuria detected during any time of the current pregnancy in any colony count represents heavy rectovaginal colonization and therefore is an indication for intrapartum antibiotic prophylaxis, even without a subsequent rectovaginal screening.[12] Significant reduction of neonatal mortality and obstetric complications related to GBS has been observed in the USA, after implementing universal screening of antepartum women followed by intrapartum prophylaxis. Guidelines of Royal College of Obstetricians and Gynecologists from the United Kingdom in 2017 and Queensland, Australia in 2020 recommends a risk-based screening protocol rather than a universal approach.[12] But in developing countries like India, such policies are still preliminary and are yet to be standardized, possibly due to scarcity of studies and data on the prevalence of infection.[13] There are many studies conducted worldwide, exploring the prevalence of GBS among pregnant and non-pregnant groups of people, their implications, and the risk factors associated with it. However, limited data is available from developing countries on this aspect. The existing literature from India shows a varying prevalence ranging from 2.3 to 15%.[13,14] Through this observational study, we intend to implore the trend of isolation of GBS from the urine sample over the past seven years and its proportion present in pregnant and non-pregnant population.

In this study, the isolation of GBS from the urine did not show a consistent trend over the years. Similarly, proportion of pregnant woman with GBS bacteriuria/UTI also had a fluctuating trend over the years. The emergence of COVID 19 pandemic and subsequent lock down in 2020, could have contributed to an underestimation of the actual burden in recent times. A significant proportion of the cases belonged to non-pregnant group, pointing the significance of GBS as an agent of UTI. GBS was reported from the urinary samples of nonpregnant cases, only when there was a significant count (>10^5 colony forming units/ml) or other indicated scenario where even a lesser count has to be considered significant (e.g. symptomatic patients, samples obtained from suprapubic aspirate etc.). Previous studies showed that among the invasive GBS disease in non-pregnant individuals, 5- 23% causes urinary tract infection and were often associated with other comorbidities such as diabetes mellitus, neurogenic bladder, anatomical abnormalities of the urinary tract, prostate disease, catheterization etc.[15-17] A prospective study conducted in Madrid showed an incidence of 2% GBS UTI in nonpregnant adults, with 95% among them having an underlying disease, the majority being abnormalities of the urinary tract followed by chronic renal failure and diabetes mellitus.[9] Unfortunately, the association of such risk factors could not be explored further. Many other reports of GBS bacteremia had identified urinary tract as the source of infection, which emphasizes the role of GBS as a significant agent of UTI in non-obstetric setting.[9,17,18] A study conducted to explore the pathogenic mechanism of GBS UTI using a murine cystitis model had shown that GBS can bind directly to human bladder uroepithelial cells, thereby facilitating its colonization. This leads to upregulation of host interleukin 1α, which constitutes the initial pathogenic mechanisms of GBS UTI.[8]

On analyzing the gender distribution of GBS bacteriuria/UTI, the majority were females as expected. However, when considering the nonpregnant population, the proportion of UTI in males and females were almost equal in the adult population, thus its role in causing UTI in males cannot be undermined. In a population-based survey conducted in the USA, for the epidemiological characters of invasive GBS among nonpregnant adults for 8 years showed a consistently high number of males affected compared to females.[19] In this study, the reproductive age group was predominantly involved among which 52.1% were antenatal women. The following common age group was the elderly (>60 years), which constituted 18.34%, and among them, males were predominantly affected compared to females.

Antimicrobial susceptibility pattern observed among the majority of the isolates showed that they were susceptible to ampicillin, nitrofurantoin, vancomycin and variably susceptible to ciprofloxacin (susceptible in only 62.77% isolates). Overall resistance observed to ciprofloxacin was 32.85%. Resistance to fluoroquinolones in GBS is indicative of an increasing trend in Japan, China, USA and several European countries.[19] The most common mechanism detected was due to mutation in the gyr A and Par C region of the quinolone resistance determining region.[20] Majority of the isolates in this study were susceptible to ampicillin, with resistance observed in 5.84% isolates. Penicillin is considered to be the drug of choice for the treatment of clinical infections by GBS as well as for intrapartum prophylaxis in pregnant women.[12] GBS was considered to be universally susceptible to penicillin until a few reports of decreased susceptibility emerged, and was referred to as penicillin resistant group B Streptococcus (PR-GBS).[20] In a study conducted in Japan between 2012 to 2013, a prevalence of 14.7% of PR-GBS was observed among the clinical isolates obtained from various clinical specimens.[21] However, when they compared this with a previous study from same region which was conducted 10 years ago, there was a significant increase in the resistance in later years emphasizing an increasing resistance trend. The most common mechanism of resistance detected by them was a mutation of pbp2x gene.[22] In this study, all the isolates which showed resistance to ampicillin were also resistant to ciprofloxacin. A similar observation was also noted in the study mentioned above from Japan, where 95.6% of the PR-GBS were harboring mutations in the quinolone resistance determining region of the gyr A, gyr B, par C and par E genes.[22] Recent studies have revealed that there is an increase in resistance to other antibiotics as well in PR-GBS, such as macrolides, cefotaxime, ceftriaxone and levofloxacin.[22,23] Strains which are susceptible to penicillin, but with reduced susceptibility to other beta lactam agents such as cephalosporins are also emerging and these are termed as GBS with reduced beta-lactam susceptibility (GBS-RBS).[20] In this study, all the isolates were sensitive to vancomycin. Though vancomycin was considered to be the last resort antibiotic for GBS, it is currently the drug of choice for intrapartum antibiotic prophylaxis in patients with penicillin allergy and if the isolate is resistant to clindamycin.[12] Till now there are two well characterized reports of vancomycin resistance reported from the USA, and the mechanism of resistance detected was the presence of Van G gene in both the isolates.[20,24] There could be an under recognition of vancomycin resistance in GBS as many of the laboratories do not perform antimicrobial testing routinely on isolation of GBS, considering its universal susceptibility to penicillin. The trend of the antimicrobial resistance in our study has shown a fluctuating pattern, with a higher resistance observed in the mid years (2016-17). The antimicrobial susceptibility of the isolates from antenatal women was consistent with the pattern in the total population.

CONCLUSION

In this study, the trend of isolation of GBS from urine culture showed a fluctuating course over the years. Though predominant isolates were from females, especially antenatal women, it is also an important agent of UTI in elderly males. Routine antimicrobial susceptibility testing should be implemented upon isolation, owing to the emergence of antimicrobial resistance to various groups of antibiotics.

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