

## A RURAL BASED STUDY ON GESTATIONAL SYMPTOMLESS BACTERIURIA (GSB)

Monalisa Subudhi<sup>1</sup>, Sudhanshu Kumar Dash<sup>2</sup>, Khetrabasi Subudhi<sup>3</sup>, Sitansu Kumar Satapathy<sup>4</sup>, Pramoda Kumar Sahoo<sup>5</sup>, Asutosh Subudhi<sup>6</sup>

<sup>1</sup>Assistant Professor, Department of Microbiology, Gayatri Vidya Parisad Institute of Health Care and Medical Technology, Visakhapatnam, Andhra Pradesh.

<sup>2</sup>Associate Professor, Department of Paediatrics, Gayatri Vidya Parisad Institute of Health Care and Medical Technology, Visakhapatnam, Andhra Pradesh.

<sup>3</sup>Professor, Department of Obstetrics and Gynaecology, MKCG Medical College and Hospital, Berhampur, Odisha.

<sup>4</sup>Specialist, Department of Obstetrics and Gynaecology, Gayatri Medical College, Visakhapatnam, Andhra Pradesh.

<sup>5</sup>Postgraduate Student, Department of Obstetrics and Gynaecology, MKCG Medical College and Hospital, Berhampur, Odisha.

<sup>6</sup>Student, KIIMS, Bhubaneswar, Odisha.

### ABSTRACT

#### BACKGROUND

Gestational Symptomless Bacteriuria (GSB) or Gestational Asymptomatic Bacteriuria (GASB) is one of the commonly encountered renal infections during pregnancy. The incidence of GSB varies between 2% - 13% of all pregnant women. It is a hidden, undiagnosed, unexpected bad obstetric factor which may have serious, preventable adverse effects if untreated with many debatable controversial issues. Hence, the study was undertaken.

The objectives of the study were to find the incidence of GSB, maternal and foetal outcomes and different causative organisms in GSB.

#### MATERIALS AND METHODS

This study of Gestational Symptomless Bacteriuria (GSB) was undertaken in a remote rural area, Pathara in the District of Ganjam, Odisha. It included randomly selected 200 pregnant women as study group and 200 non-pregnant women as control group. After fully history taking, the cases were studied for symptomless bacteriuria by 2 consecutive urine cultures.

#### RESULTS

In our study, the following results were obtained. The incidence of GSB was 8.5%. It was mostly in less than 20 years of age (7.6%), in low socio-economic status (76.4%), in literacy of upto 7<sup>th</sup> standard (58.8%) in primigravida (G1) (53%), in gestational age (13-28 weeks). The commonest organism isolated was *Escherichia coli* (64.8%). The most common maternal complication during pregnancy was anaemia (41.1%) and foetal complication was prematurity (17.6%).

In control group, gestational symptomless bacteriuria was more common in married non-pregnant women (2%). The isolated *Escherichia coli* was found more commonly in married non-pregnant women (66.7%).

#### CONCLUSION

Since Gestational Symptomless Bacteriuria (GSB), is an important silent bad obstetric factor, having many dilemmas, associated with obstetric and neonatal complications, universal screening in early pregnancy and its management is essential to prevent unexpected preventable obstetric disorders.

#### KEYWORDS

Gestational, Symptomless, Bacteriuria, Infection, Pyelonephritis, Urinary Bad Obstetric Factor.

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#### BACKGROUND

Gestational Symptomless Bacteriuria (GSB) is the most common type (about 70%) of urinary tract infection (2-13%),<sup>1,2,3,4</sup> which is commonest renal bacterial infection

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*Corresponding Author:*

*Dr. Sudhanshu Kumar Dash,*

*Associate Professor, Department of Paediatrics,*

*Gayatri Medical College, Vishakhapatnam,*

*Andhra Pradesh.*

*E-mail: swayam.dr007@gmail.com*

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during pregnancy, a unique state.<sup>1,2,3,4</sup> As a result of pressure of the gravid uterus and altered physiological hormonal milieu, there occurs many anatomic and physiologic hormonal changes of urinary system during pregnancy. There occurs decrease of ureteral peristalsis and ureteral dilatation, especially of the right side mostly during the last trimester of pregnancy, other causes of hydronephrosis is the effect of progesterone on smooth muscle tone and compression of ureter by the gravid uterus. There is also affection of renal functions. The net result is the alternation of the natural history of bacteriuria during gestation. The renal pelvis and ureters begin to dilate as early as the 8<sup>th</sup> week of gestation<sup>5</sup> and there is displacement of bladder

superiorly and anteriorly. Smooth muscle relaxation results in decreased peristalsis of the ureters, increased bladder capacity and urinary stasis. There may be facilitation of growth of bacteria due to differences in urine pH and osmolality and pregnancy induced glycosuria. There is decreased ureteral and bladder tones due to increased levels of progesterone and oestrogen. There is decrease of urine concentration and increase of bladder volume due to increase of plasma volume during pregnancy. The kidneys increase in length and filtration rate by 30% to 50% increasing renal clearance of drugs and possibly decreasing the duration a drug stays in the urine.<sup>6</sup>

Many adverse maternal and perinatal conditions are associated with the cases of untreated and even some cases of treated symptomless bacteriuria in pregnancy. Gestational symptomless bacteriuria is the biggest risk factor for symptomatic urinary tract infection during gestation. If symptomless bacteriuria is untreated, there is risk of development of symptomatic UTI (25-40%) and acute pyelonephritis upto 30% during pregnancy. There may be maternal outcomes like anaemia, preterm labour, prelabour rupture of membranes, pyelonephritis, septicaemia and perinatal outcomes like prematurity, foetal growth restriction, low birth weight and increased perinatal morbidity and mortality.

The incidence of gestational symptomless bacteriuria occurs in about 2%-13% of all pregnant women. It is defined as the presence of a single pathogenic significant bacteriuria ( $\geq 10^5$  CFU/ml) on two consecutive clean catch midstream voided urine cultures without any acute urinary symptoms.

Though it is cost-effective, screening of GSB with culture and sensitivity of urine is strongly recommended at 12 to 16 weeks of pregnancy by the US preventive task force, 2008 and NICE guidelines, by which at least some of major complications can be prevented. Bacteriuria is a cause of serious complications like acute pyelonephritis, preterm delivery, foetal growth restriction, low birth-weight babies as well as risk to concerned health personnel, family and society. There also exists controversy about the duration of gestation (either first visit or first trimester, or at 12 weeks, or at 16 weeks, or each trimester) or frequency of screening (once or twice). Early screening is definitely better than the late screening as far as prevention of later complications. Screening for twice is better than once as far as diagnosis is concerned. Even if screening is done twice there is about 90% of diagnosis made and still about 10% of cases remained undiagnosed. Hence, there is need of increase of frequency i.e. thrice for diagnosis of still more cases and treatment can be done.

### Aims and Objective

- To find the incidence of GSB.
- To find the maternal and foetal outcomes.
- To find different causative organisms in GSB.

### MATERIALS AND METHODS

The study was undertaken in a rural area, Pathara in the Ganjam district, Odisha from October 2015 to October 2017. The cases were selected randomly. The study group included 200 pregnant women and 200 non-pregnant women as control group. The history regarding age, socioeconomic status, literacy, gravidity, gestational age, past risk factors of all the cases were taken. The cases were followed up and maternal and fetal complications of GSB were noted. Cultures of 2 consecutive clean catch midstream urine were done with the treatment of positive cases by suitable antibiotics after sensitive tests.

### RESULTS

In our study, the following results were obtained. Out of 200 cases of study group, gestational symptomless bacteriuria was present in 17 cases with the incidence of 8.5%.

Age Group in Years	Positive Cases	
	Number	Percentage
<20 Yrs.	12	70.6
20-30 Yrs.	03	17.6
>30 Yrs.	02	11.8
<b>Total</b>	<b>17</b>	<b>100.0</b>

**Table 1. Distribution of Age in GSB Positive Cases of Study Group (n=17)**

Most of cases (70.6%) of Gestational symptomless bacteriuria belonged to the age group of <20 years.

Socio-Economic Status	Positive Cases	
	Number	Percentage
Low	13	76.4
Medium	02	11.8
High	02	11.8
<b>Total</b>	<b>17</b>	<b>100.0</b>

**Table 2. Socio-Economic Status in GSB Positive Cases of Study Group (n=17)**

Majority of cases (76.4%) were from the low socio-economic status, one of the important predisposing factors of GSB.

Literacy (Education)	Positive Cases	
	Number	Percentage
Upto 7 <sup>th</sup> standard	10	58.8
> 7 <sup>th</sup> to 10 <sup>th</sup> Standard	05	29.4
> 10 Standard	02	11.8
<b>Total</b>	<b>17</b>	<b>100.0</b>

**Table 3. Literacy of GSB Positive Cases of Study Group (n=17)**

It was most common in low literacy condition i.e. upto 7<sup>th</sup> standard of education (58.8%).

Gravidity (G)	Positive Cases	
	Number	Percentage
G1	09	53.0
G2	02	11.8
G3	03	17.6
≥G4	03	17.6
<b>Total</b>	<b>17</b>	<b>100.0</b>

**Table 4. Gravidity of GSB Positive Cases of Study Group (n-17)**

Majority cases were seen in primigravida (53%).

Gestational Age	Positive Cases	
	Number	Percentage
Upto 12 weeks	06	35.3
13 - 28 weeks	08	47.1
> 28 weeks	03	17.6
<b>Total</b>	<b>17</b>	<b>100.0</b>

**Table 5. Gestational Age of GSB Positive Cases of Study Group (n-17)**

It was most commonly found in the gestational age of >12-28 weeks (47.1%).

Complications	Positive Cases	
	Number	Percentage
Anaemia	07	41.1
Hypertensive disorders of pregnancy	01	5.9
Preterm labour	02	11.8
Prelabour rupture of membranes	01	5.9
Urinary tract infection	01	5.9
No complications	5	29.4
<b>Total</b>	<b>17</b>	<b>100</b>

**Table 6. Maternal Complications During Pregnancy of GSB Positive Cases of Study Group (n-17)**

The commonest maternal complication occurred during pregnancy was anaemia (41.1%, followed by preterm labour (11.1%).

Complications	Positive Cases	
	Number	Percentage
Foetal growth restriction (FGR)	02	11.8
Low-birth foetuses	02	11.8
Prematurity	03	17.6
No complications	10	58.8
<b>Total</b>	<b>17</b>	<b>100</b>

**Table 7. Foetal Complications During Pregnancy of GSB Positive Cases of Study Group (n-7 which was 41.2% out of 17)**

The commonest foetal complication occurred during pregnancy was prematurity (17.6%).

Complications	Positive Cases	
	Number	Percentage
Urinary tract Infection	02	11.8
Gestational diabetes	01	5.8
<b>Total</b>	<b>3</b>	<b>17.6</b>

**Table 8. History of Previous Risk Factors of GSB Positive Cases of Study Group (n-17)**

Previous risk factors of GSB was present in 17.6% of cases including 11.8% of urinary tract infection and 5.8% of gestational diabetes.

Organisms	Positive Cases	
	Number	Percentage
E.coli	11	64.8
Klebsiella	03	17.6
Staphylococcus aureus	02	11.8
Proteus	01	5.8
<b>Total</b>	<b>17</b>	<b>100.0</b>

**Table 9. Isolated Organisms of GSB Positive Cases of Study Group (n-17)**

The most common organism isolated was Escherichia Coli (64.7%), followed by Klebsiella (17.6%), staphylococcus aureus (11.8%), and proteus (5.9%).

Control Group	Number	Positive Culture	Percentage
Unmarried women	100	02	1.0
Married non-pregnant women	100	04	2.0
<b>Total</b>	<b>100</b>	<b>06</b>	<b>3.0</b>

**Table 10. GSB Positive Cases of Control Group (n-200)**

In control group, the incidence of gestational symptomless bacteriuria was 3% in non-pregnant women including 1% of unmarried women and 2% of married non-pregnant women.

Control Group	No. of Positive Group	Organisms isolated	Percentage
Unmarried women	01	E. Coli	33.3
Married non-pregnant women	02	E. Coli	66.7
<b>Total</b>	<b>03</b>	<b>E. Coli</b>	<b>100.0</b>

**Table 11. Isolated Organisms of Positive Cases of Control Group (n-3)**

Organism isolated in control group was Escherichia coli which was found more commonly in married non-pregnant women (66.7%) than in unmarried women (33.3%).

GSB Positive Cases	Number	Percentage
Study Group	17	8.5
Control Group	06	3.0
Total	23	11.5
<b>Table 12. Comparison Between Study Group and Control Group</b>		

The incidences of GSB positive cases were 8.5% in study group and 3% in control group.

## DISCUSSION

Gestational symptomless bacteriuria is defined as the presence of a single bacterial strain in quantitative counts of at least 100,000 colony-forming units/ml ( $\geq 10^5$  CFU/ml) on two consecutive clean catch midstream voided urine cultures without any acute urinary symptoms with diagnostic accuracy of 80% to 95% in compared to culture of urine collected via bladder catheterisation with diagnostic value of 100 CFU/ml with accuracy of 96% (Gunito 2010).<sup>1,2</sup> But according to Kass (1962) gestational symptomless bacteriuria is diagnosed when a routine midstream urine culture of a clean-voided specimen contains more than 10,000 organisms per ml.

The urine specimen should be collected in a manner that minimizes contamination and should be transported to the laboratory in a timely fashion to limit bacterial growth. Catheterization increases complication risk in pregnant women and is only indicated if repeated contaminated clean catch urines are obtained. In catheterized urine sample, bacterial count as low as 100 colony forming units / ml are also considered significant bacteriuria.<sup>7</sup> It indicates actively multiplying bacteria within the urinary tract. Apart from urine culture, less expensive poor accuracy, rapid urine testing methods like dipstick test or nitrite or dipslide for leukocyte esterase or by urinary microscopy can be used for purpose of screening in case of population of low prevalence. Dipsticks are less sensitive and less specific alternative to dipslides in a study of urine culture (sensitivity 98% compared to 92%) (Mignini 2009). The diagnostic odds ratio of dipsticks is 165 and gestational symptomless bacteriuria is excluded with the negative results of both nitrites and leukocyte esterase and are to be confirmed of the positive results. There may be false negative results which are to be confirmed by urine cultures. There may be also false positive dipsticks and dipslide tests, to be confirmed by cultures of urine. At last no single or combination of tests is having accuracy of 100%.

The incidence of gestational symptomless bacteriuria in the study group was 8.5%, which was almost similar to other studies. If the incidence of gestational symptomless bacteriuria is  $\geq 2\%$ , the screening and treatment is not cost-effective. But if it is  $< 2\%$ , the screening is cost effective.<sup>7</sup> Screening techniques have a definite space when the incidence is 2% or more.

The gold standard is the 2 consecutive voided urine cultures with accuracy of 80-95%.<sup>7</sup> A single voided urine cultures detect 80% of cases and it is more permissive,

practical and cost effective than that of multiple culture.<sup>7</sup> If two consecutive voided specimens had positive tests, a third consecutive specimen of restrictive criteria yielded consistent result in better results.

Majority of cases (70.6%) of gestational symptomless bacteria were in the age group of less than 20 years (Table 1). Most of cases (76.4%) belonged to low socio-economic status, which is the important predisposing factors of GSB (Table 2), and most common in low literacy condition i.e. upto 7<sup>th</sup> standard of education (58.8%) (Table 3), might be due to lack of cleanliness. Majority cases (53%) were found in primigravidae (GI) Table-4.

The commonest gestational age of diagnosis of gestational symptomless bacteria was between more than 12 weeks and 28 weeks of gestation (47.1) (Table 5). The incidences of gestational symptomless bacteriuria gradually increase from early trimester to late trimester of pregnancy i.e. 0.8% in the 12<sup>th</sup> gestational week and 1.93% at the end of gestation. The highest incidence of GSB is observed between the 9<sup>th</sup> and 17<sup>th</sup> week. The optimal time of screening is the 16<sup>th</sup> gestational week because it provides the maximum number of bacteria free gestational period after management at that time. There is maximum detection of GSB cases by a single urine specimen collected between 12 and 16 weeks of gestation. According to others, each trimester urine samples collections have increased diagnostic rates, though it is cost effective.<sup>6,7,8</sup> Screening by culture of urine and microscopy on the first antenatal visit is recommended. The US preventive task force and NICE guidelines strongly recommend routine screening of antenatal women with culture of urine and sensitivity at 12 to 16 weeks gestation (USPSTF 2008).<sup>7</sup> Early detection of GSB is an established factor for prevention of some serious complications.

Out of maternal complications (70.6%) of GSB in study group, anaemia (41.1%) and preterm labour (11.1%), occurred more commonly (Table 6), which may result in adverse obstetric outcomes. GSB is the biggest risk factor for symptomatic urinary tract infection during gestation. If GSB is untreated, there is risk of development of symptomatic urinary tract infection in 25%-40% of cases and acute pyelonephritis in 30% of cases during pregnancy. GSB is an important risk factor for serious complications such as symptomatic urinary tract infection acute pyelonephritis, anaemia, pre-eclampsia, preterm delivery, fetal growth restriction, and low birth weight. According to a case control study, untreated group B streptococcus bacteriuria was associated with chorioamnionitis or premature rupture of membranes or infection in the placental tissues and amniotic fluid (adjusted odds ratio 7.2, 95% confidence interval (CI) 2.4 to 21.2.<sup>7</sup> The increased association of premature labour and growth restricted babies is probably related with the underlying chronic renal lesions. Recurrent GSB is associated with high incidence of urinary tract abnormality (20%) congenital or acquired. There is more risk of development of chronic renal disease in later life.

Out of all foetal complications (41.2%) of GSB, the commonest foetal complication, occurred in study group of

GSB was prematurity (17.6%) (Table 7). The cause of preterm labour is the association of microorganism production of phospholipase A2 and resultant activation of prostaglandin. There is presence of significant correlation between bacteriuria and medically indicated preterm labour but not between spontaneous preterm labour (10%).

There is increased risk of urinary tract infection in pregnancy as a result of different physiological, anatomical and hormonal changes occurred in the excretory system which starts from 6<sup>th</sup> week and peaks during 22 to 26 weeks of pregnancy lasting still delivery.

In the study group, there was presence of previous risk factors in GSB was 17.6%, out of which the incidence of urinary tract infection and gestational diabetes were 11.8% and 5.8% respectively (Table 8).

The commonest organism isolated was *Escherichia coli* (64.8%) followed by *klebsiella* (17.6%), *staphylococcus aureus* (11.8%) and *proteus* (5.9%) table 9 which was similar to other studies. According to Gladys Dodd (1931), intestinal stasis resulting from insufficient fluid intake causing constipation leading to urinary stasis, especially during pregnancy and at least resulting in GSB with adverse effects and *E. coli* proliferates better in higher pH. Particularly in the presence of structural abnormalities of the urinary tract, the following organisms are associated with urinary tract infection *proteus*, *klebsiella*, *pseudomonas*, *enterobacter* spp. and *enterococci* and *staphylococcus*. The causative bacteria of bacteriuria are almost similar both in non-gestational and gestational women. The most important and common cause of bacteriuria in females is short urethra in compared to males, because of commonly colonized organisms arising from the gastrointestinal tract.

*Escherichia coli* is the commonest involved organism of bacteria accounting about 70-80% of organisms<sup>9,10,11</sup> and 90% or more in about one report. Other causative organisms are other gram-negative bacteria and group B streptococcus. About 22% of strains of *E.coli* causing symptomless bacteriuria had the ability of adherence to the uroepithelial cells compared to about 75% of strains of *E. coli* causing pyelonephritis. Group B streptococcus (*streptococcus agalactiae*) is more associated with prelabour rupture of membranes, premature labour and early onset of neonatal sepsis. The value of B streptococcus is lower than the usual value of symptomless bacteriuria (105 CFU/ml) and is the significant factor. The cause of gestational group B streptococcal bacteriuria is the heavy vaginal colonization. Therefore, also other anaerobic organisms and fastidious microorganism causing gestational symptomless bacteriuria. But at present, there is no evidence of routine screening of these organisms.

In the control group, gestational symptomless bacteriuria was more common in married non-pregnant women (2%) in comparison to unmarried non-pregnant women (1%) out of 3% of non-pregnant women, probably due to sexual intercourse in marital life, predisposing factors for development of GSB (Table-11). In the control group, *Escherichia coli* was found more commonly in married non-

pregnant women (66.7%) than in unmarried non-pregnant women (33.3%) (Table 2), again which might be due to sexual act in married women. The GSB positive cases were more in study group in compared to control group (Table-12).

The positive cases of GSB were treated with appropriate antibiotics after culture and sensitivity report. The antimicrobial agents should be appropriate and safe for the mother, fetus and neonates with excellent efficacy. The most common aetiological agent of the GSB is *E. coli*, which usually responds well to broad spectrum antibiotics such as Ampicillin, Amoxicillin and Cephalosporins and Nitrofurantoin. Fosfomycin is a bactericidal antibiotic in both gram positive and gram-negative bacteria. A single dose of fosfomycin tromethamine produces a therapeutic concentration in the urine for 1-3 days reaching a peak concentration in the urine with 1053-4415 mg/L and the fosfomycin concentration in the urine is maintained at levels more than 12 mg/L for 24-48 hours, sufficient for treatment of many pathogenic bacteria in the urinary tract.<sup>7</sup> Nitrofurantoin is very effective drug against organism found in the urinary tract and is found in very low levels in maternal serum and tissues and the foetal compartment. Sulfonamides are best avoided in the third trimester of gestation because of risk of neonatal jaundice. Antibiotics, safe during pregnancy and after sensitivity should be prescribed usually for 5-7 days, but it varies all bacteriuria in pregnancy requires treatment to prevent pyelonephritis and preterm delivery (Cochrane guideline level 1 A evidence). Blood culture and sensitivity is indicated when the patient does not respond to antibiotic treatment. Most clinical practical guidelines recommend screening and antibiotic treatment for GSB.<sup>7</sup>

## CONCLUSION

As gestational symptomless bacteriuria is an important, hidden bad obstetric factor, universal screening in early pregnancy and proper management should be advised for prevention of adverse effects. It may be better to treat the patients with colony counts less than the 105 CFU/ml. Though the gold standard diagnostic method of gestational symptomless bacteriuria (GSB) is midstream clean catch urine cultures by 2 consecutive times. This requires further research and evaluation.

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