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Study on Asymptomatic Bacteriuria in Pregnancy and Comparative Study of Treated and Control Group

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ABSTRACT

Urinary tract infection (UTI) is the shorter urethra and the greater closeness of the anus to the vagina, this is a more common health condition in women than in men. Pregnant women are twice as likely to be affected as non-pregnant women of the same age. To study Asymptomatic bacteriuria in pregnancy and maternal and foetal outcome as well as the clinical efficacy of single-dose fosfomycin trometamol in the treatment of asymptomatic urinary tract infections in pregnancy. This prospective study was undertaken in 380 antenatal women, irrespective of their period of gestation were selected according to inclusion and exclusion criteria, attending OPD of Obstetrics and Gynecology at I.P.G.M.E.R and S.S.K.M Hospital, Kolkata for the first time, over a period of 18 months from February 2019 to July 2020. Women with asymptomatic bacteriuria were further divided into test group receiving treatment with fosfomycin and other control group receiving placebo. Out of 380 mother, 43 had asymptomatic bacteriuria. Incidence of asymptomatic bacteriuria during pregnancy in this study was 11.3%. *E. coli* was the predominating organism (65.11) followed by *Klebsiella* aerogenes (27.90%) and group B *streptococcus*, *Acenobacter* and *Enterococcus* (2.33%) each. Treatment with Fosfomycin significantly reduces the complication compared to untreated group. In pregnant women, asymptomatic bacteriuria is prevalent. Because of the catastrophic repercussions for both mother and foetus, all pregnant women should be screened for asymptomatic bacteriuria at their initial prenatal visit and those who are positive should be regularly monitored after treatment.

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Key Words
Asymptomatic bacteriuria, *E. coli*, pregnancy, urinary tract infection

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INTRODUCTION

Urinary tract infection (UTI) is the shorter urethra and the greater closeness of the anus to the vagina, this is a more common health condition in women than in men. It could be symptomatic or asymptomatic. Asymptomatic bacteriuria (ASB) is defined as the presence of bacteria in significant numbers inside the urine system, i.e., 100,000 bacteria per millilitre or more, without any obvious symptoms[1-3]. Pregnant women are twice as likely as non-pregnant women of the same age to be impacted[4,5]. Pregnant women's apparent decrease in immunity appears to promote the growth of both commensal and non-commensal bacteria. Several factors contribute to the increased risk of UTI during pregnancy. Because, the uterus is immediately on top of the bladder, it expands during pregnancy and its increased weight might restrict urine drainage from the bladder, resulting in infection. The ureters may get compressed as the uterus expands, making it considerably more difficult for urine to flow through them. Higher levels of progesterone reduce uterine muscular tone, causing dilation and as a result, a decrease in urine output. As a result of these changes, urine takes longer to move through the urinary tract, giving germs more opportunity to grow. It gets easier for bacteria to reach the kidneys. Urine becomes less acidic and more likely to include progestins and glucose during pregnancy, both of which increase the possibility for bacterial growth. The prevalence of asymptomatic bacteriuria (ASB) in pregnant women ranges from 2-10%, according to the western literature[6,7]. There have been studies on this topic in the Indian context and the reported prevalence rate is as high as 8%[8-12]. If asymptomatic bacteriuria is not treated, around 25% of pregnant women will develop acute infection symptoms. Asymptomatic bacteriuria that goes untreated has been associated to acute pyelonephritis, which has been connected to a number of maternal and foetal issues. Acute pyelonephritis in pregnancy is associated with anaemia (23%), septicemia (17%), transient renal failure (2%) and pulmonary insufficiency (7%). Endotoxemia and sepsis will cause multiple system dysregulation in one out of every five pregnant women with pyelonephritis. Asymptomatic urinary tract infections and their negative consequences on pregnancy continue to be common and preventive. Stenqvist *et al*.[13] reported that the risk of bacteriuria onset is greatest between the 9th and 17th gestational weeks, with the 16th gestational week indicated as the best timing for a single bacteriuria screening decided by the number of bacteriuria-free gestational weeks acquired through treatment. As a result, screening pregnant women at antenatal appointments, especially during the second trimester when asymptomatic bacteriuria is most common, is a prudent practise. The US preventive services task force recommends obtaining a urine culture between 12 and 16 weeks of gestation (an "A" recommendation). This critical topic should be revisited in order to develop more effective and faster treatment strategies to promote patient compliance. Urine culture is the gold standard screening method for ASB during pregnancy[14-16]. *Escherichia coli* is the most prevalent infecting bacteria, accounting for 75-90% of bacteriuria during pregnancy.

Antibiotic treatment is more effective than the treatment of asymptomatic bacteriuria and minimising the risk of pyelonephritis in pregnancy, placebo or no treatment was used.

Antibiotic treatment has been related to a reduction in the frequency of preterm delivery or low birth weight neonates, however the antibacterial agent used in pregnancy must be well-tolerated, empirically demonstrated to be safe for both the mother and the baby and have a low level of bacterial resistance.

The relatively high prevalence of asymptomatic bacteriuria during pregnancy, as well as its devastating consequences for women and their pregnancies and the possibility of avoiding the sequel with treatment, promote screening pregnant women for bacteraemia[8,9].

MATERIALS AND METHODS

This prospective study was undertaken in 380 antenatal women, irrespective of their period of gestation were selected according to inclusion and exclusion criteria, attending OPD of Obstetrics and Gynecology at I.P.G.M.E.R and S.S.K.M Hospital, Kolkata for the first time, over a period of 18 months from February 2019 to July 2020. Collection of "clean catch" mid stream urine sample done. A moist film of uncentrifuged urine was examined under the microscope to determine the presence of pus cells, erythrocytes, microorganisms, casts and so on. Urine samples were treated using conventional microbiological techniques within 1-2 hrs of collection. The culture was performed on 5% sheep blood agar and Mac-Conkey agar using the conventional loop method and incubated at 37 degrees Celsius for 24 hrs. If no growth was observed, the incubation period was extended for another 24 hrs. Gramme stains, motility tests, catalase tests, oxidase tests, coagulase tests and basic biochemical tests were used to identify organisms, according to Cowan and Steels Manual[16]. If no growth was obtained, the growth was considered as sterile. It was considered significant if the number of colonies corresponded 100,000 colony forming units (CFU) per millilitre.

Out of 380 women, 43 women urine report showed significant growth without any symptoms and these 43 women were further divided into test group and control group. Patients were randomly assigned to either a single dosage of fosfomycin trometamol or a placebo. A randomised mechanism was utilised to

ensure that each group had an equal number of patients. Group I was given a single dosage of 3 g fosfomycin trometamol (one sachet) in a glass of water at bedtime on an empty stomach. Group II had no antibiotics and was on routine prenatal iron and calcium supplementation.

RESULTS

Incidence of asymptomatic bacteriuria during pregnancy in this study was 11.3%. *E. coli* was the predominating organism (65.11) found in the urine of the asymptomatic bacteriurics. *Klebsiella* aerogenes was found in 27.90% and group *B. streptococcus, Acenobacter* and *Enterococcus* 2.33% each. Majority of bacteriurics were (23 out of 43) belonged to low socioeconomic group but it was evident that there was no significant difference in the percentage incidence of bacteriurics and non-bacteriurics on the basis of socioeconomic division. Majority of the bacteriurics were between age 25 and 35 years, i.e., 23 out of 43 (53.49%), 18 were between age 18 and 24 years and two were above 36 years. Asymptomatic bacteriurics was more in the primi-gravidae, i.e., 23 out of 43 (51.16%) than the multi-gravidae. Most of the bacteriurics, i.e., 28 out of 43 (65.12%) were in the second trimester of pregnancy, followed by first (20.93%) and then third (13.95%). Out of 22 treated Asymptomatic bacteriurics only one (4.55%) remained culture positive after one week of treatment. Whereas, 19 out of 21 (90.48%) untreated Asymptomatic bacteriurics remained urine culture positive ($p<0.05$). Anemia was detected in 16.64% of treated group compared to 61.90% of the untreated group. The incidence of gestational hypertension was found to be 9.1% in the treated asymptomatic bacteriurics. The incidence was more or less same (14.29%) in the untreated group of the 21 untreated asymptomatic bacteriurics 4 (19.05%) developed pyelonephritis whereas none of treated asymptomatic bacteriurics developed the pyelonephritis. Follow up study of pregnant mother showed that of the 22 treated asymptomatic bacteriurics only one (4.55%) developed symptomatic bacteriuria during late pregnancy and puerperium. In comparison of the 21 untreated bacteriurics 10 (47.62%) developed symptomatic bacteriuria later on. Of the 22 treated asymptomatic bacteriurics 4 (18.18%) had preterm delivery whereas 8 (38.1%) out of 21 untreated babteriurics had preterm delivery. None of the treated and treated asymptomatic bacteriurics had IUGR baby in comparison non bacteriurics 5.93% had IUGR baby. Out of the 22 treated asymptomatic bacteriurics 3 (13.64%) had low birth weight babies whereas 7 out of 21 (33.33%) untreated asymptomatic bacteriurics had low birth weight babies. Incidence of puerperal pyrexia was more common in untreated asymptomatic bacteriurics 7 out of 43 (16.28%). None of the treated bacteriurics was seen to develop puerperal pyrexia due to urinary tract infection. In non bacteriurics only 22 out of 315 (6.23%) develop puerperal pyrexia.

DISCUSSIONS

Although, the prevalence of asymptomatic bacteriuria in pregnant women is equivalent to that of non-pregnant women, the effects of infection are substantially more severe during pregnancy, necessitating prompt discovery and treatment[17]. Early detection and treatment of asymptomatic bacteriuria in pregnancy may be critical not only to avoid severe pyelonephritis and chronic renal failure in the mother, but also to prevent preterm and foetal mortality in the children[2]. The morphological and physiological changes that occur in the genitourinary tract during pregnancy cause urinary tract infection[7].

In my study, 380 antenatal mother were screened out of which 43 (11.3%) mother had urine culture positive. This 43 mother were divided into two groups (Group A and B). Group A were treated with single dose of Fosfomycin tometerol and the other group B did not received any treatment. All cases were screened for one year to look for any maternal complication like symptomatic UTI, gestational hypertension, anemia, pyelonephritis, puerperal pyrexia and fetal complication like preterm birth, IUGR, low birth weight. And also find relation between different variables like age, parity, gestational age and socioeconomic status with the prevalence of asymptomatic bacteriuria in pregnancy.

In my study, the prevalence of Asymptomatic bacteriuria was found to be 11.3% which was almost similar to other studies[7-9]. Overall, the incidence in various Indian studies was found to be between 5 and 17% like Rajshekhar *et al*. (11%)[11] Vaishali Jain *et al*. (16.9%)[12] and R. Sujatha *et al*. (7.3%)[17]. In other countries, the incidence ranges from 2-9% like Mohamed Abdelrazik *et al*. (8%)[18] and Shamweel Ahmad *et al*. (6.1%)[19]. In A cost evaluation study reported that screening for pyelonephritis is appropriate when the prevalence of ASB is greater than 2%[21]. So, the screening all antenatal women for ASB, especially in early pregnancy by a quantitative urine culture is recommended. In my study all women were between age 18 years and 38 years. Antenatal women aged 25-35 years had the largest percentage of culture positive cases (53.49%), followed by women aged 18-24 years (41.86%) and women aged >36 years (4.65%) (Table 1-3). According to Rajshekhar *et al*.[11] the age group of 26-35 years had the largest percentage of culture positive cases (57.57%), followed by 18-25 years (30.30%) and >36 years (12.13%). Other research such as Imade PE *et al*.[22] and Turpin *et al*.[23], found a similar age pattern. In this study, most of the asymptomatic bacteriuric cases were in second trimester (65.12%) followed by first (20.93%) and third

Table 1: Association between all parameters

	Asymptomatic bacteriuria	Late pregnancy symptoms present	Late pregnancy symptoms absent	Total
Asymptomatic bacteriurics of early pregnancy developing symptomatic bacteriuria in late pregnancy	Treated	1 (4.55%)	21 (95.45%)	22
	Untreated	10 (47.62%)	11 (52.38%)	21
	Total	11	32	43
	Asymptomatic bacteriuria	Anemia present	Anemia absent	Total
Incidence of anemia among Treated and untreated asymptomatic Bacteriuria	Treated	3 (13.64%)	19 (86.36%)	22
	Untreated	13 (61.90%)	8 (38.10%)	21
	Total	16	27	43
	Asymptomatic bacteriuria	Pyelonephritis present	Pyelonephritis absent	Total
Incidence of pyelonephritis In treated and untreated asymptomatic bacteriuria	Treated	0 (0.00%)	22 (100%)	22
	Untreated	4 (19.05%)	17 (80.95%)	21
	Total	4	39	43
	Asymptomatic bacteriuria	Puerperal pyrexia present	Puerperal pyrexia absent	Total
Frequency of puerperal pyrexia In treated and untreated asymptomatic bacteriuria	Treated	0 (0.00%)	22 (100%)	22
	Untreated	4 (19.04%)	17 (80.95%)	21
	Total	4	39	43
	Asymptomatic bacteriuria	Preterm present	Preterm absent	Total
Distribution of preterm In treated and untreated asymptomatic bacteriuria	Treated	4 (18.18%)	18 (81.82%)	22
	Untreated	8 (38.1%)	13 (61.9%)	21
	Total	12	31	43

Table 2: Causative organisms in the asymptomatic bacteriuria of pregnancy

Organisms	No. of cases	Percentage (%)
E. Coli	28	65.11
Klebsiella	12	27.90
Group *B. Streptococcus*	1	2.33
Acenobacter	1	2.33

Table 3: Incidence of IUGR in asymptomatic bacteriurics and non bacteriurics

Bactaria	IUGR present	IUGR absent	Total
ASB	0 (0.00%)	43 (100%)	43
Non Bacteriurics	20 (5.93%)	317 (94.07%)	337
Total	20	360	380

(13.95%), which is similar to Rajshekhar *et al*.[11] (54.54%) and Girish babu *et al*.[24] study. Maximum number, i.e., 22 out of 43 (51.16%) of the bacteriurics were primigravidae and rest were multigravidae (11 were 2nd gravid, 6 were 3rd gravid and 4 were 4th gravid and above). Thus in this study do not show any significant association with parity. Similar report was shown by R Sujatha *et al*.[18] (primigravidae (48.9%) and multigravidae (48.9%). But other studies says that urinary tract infection is more common in multigravidae female. In this study, most of the culture positive cases were from lower socioeconomic class, i.e., 53.44% which might correlate with personal hygiene and nutritional standard of such women. Gramme negative bacteria were primarily to blame for asymptomatic bacteriuria. In this study, the most common organism which was isolated was *E. coli* (65.11%), followed by *Klebsiella Pneumoniae* (27.90%). Rajshekhar *et al*.[11] also found *E. coli* to be common (72.72%). *E. coli* was also commonest isolates of Lavanya *et al*.[25], Kerure *et al*.[7] and Chandel *et al*.[5]. In this study out of 22 treated group 1 (4.55%) developed symptomatic bacteriuria in late pregnancy. And among the 21 untreated group 10 (47.62%) developed symptoms of urinary tract infection (p>0.05). Thus study shows that if Asymptomatic bacteriuria left untreated chance of developing symptomatic UTI increases. Connolly *et al*.[26] showed that successful treatment reduces the rate of subsequent symptomatic UTI by 80-90%. Among the 21 untreated bacteriurics 4 (19.04%) developed puerperal pyrexia, whereas none of the treated bacteriurics were found to develop the same (p>0.05). Similarly 4 (19.04%) of the untreated group developed pyelonephritis in late pregnancy and puerperal period, whereas none of the treated group developed the same the incidence of maternal complication like anemia (61.90%), pyelonephritis (19.05%) and puerperal pyrexia (19.04%) is seen higher in untreated asymptomatic bacteriuric group compared to treated group (p<0.05), whereas incidence of PIH do not show any significant difference between two group. Gratacos *et al*.[27] found a significant decrease in the annual incidence of pyelonephritis (1.8-0.6%, p = 0.001) following the implementation of a programme to screen for and treat asymptomatic bacteriuria in pregnant women in a population with a moderate to high frequency of bacteriuria.

Out of 22 treated group of asymptomatic bacteriuria 4 (18.18%) had preterm delivery and among the 21 untreated group, 8 (38.1%) had preterm delivery. The relative low incidence of preterm labour in treated bacteriurics may be due to treatment of disease and simultaneous meticulous supervision. In a study by Lavanya *et al*.[25] and Nath *et al*.[4] the incidence of low birth weight babies (50%) and preterm (75%) was higher in untreated asymptomatic bacteriuric patients.

Out of 337 non bacteriurics 20 (5.93%) intra uterine growth restriction whereas neither of the treated nor unteated asymptomatic bacteriurics had IUGR. Kerure *et al*.[7] and Cunningham *et al*.[28] showed increase incidence of IUGR among untreated bacteriurics.

Out of 22 treated aymptomatic bacteriurics 3 (13.64%) had low birth weight babies compared 7 (33.33%) out of untreated bacterurics who had low birth weight babies. In study by Kerure *et al*.[7] and Cunningham *et al*.[28] also had similar results. Wadland *et al*.[29] performed a decision and cost

analysis research to examine the utility of screening for asymptomatic bacteriuria in pregnancy on the first prenatal visit as a standard of obstetric care. Treatment of the women with positive results reduced the risk of pyelonephritis and preterm.

At the 7-day follow-up, therapeutic success (bacteriological eradication of uropathogens) was obtained in the fosfomycin trometamol-treated group, with only 1 out of 22 developing signs of urinary tract infection. Thus fosfomycin trometamol is 95.45% effective in treatment of asymptomatic bacteriuria in pregnancy. Omer Bayrak *et al*.[30] in his study found that therapeutic success after 7 days follow-up of treatment with fosfomycin trometamol is 93.2% vs cefuroxime axetyl is 95% (p = 0.912) in patient with asymptomatic bacteriuria.

Kremery *et al*.[31] discovered that a single dose of fosfomycin trometamol is as effective as a three-day course of oral ceftibuten in the treatment of acute cystitis in pregnant women. In a multicenter research, Zinner compared a single-dose fosfomycin trometamol to a 7-day course of piperamic acid, 400 mg B.I.D. in asymptomatic bacteriuric pregnant women and found the same cure outcome[32].

CONCLUSION

Asymptomatic bacteriuria was present in 11.3% in this study. The most sensitive test for its detection is urine culture with clean-catch mid stream urine. Asymptomatic bacteriuria in women can have devastating effects for both the mother and the foetus. As a result, all expectant women should be screened for Asymptomatic bacteriuria at their first prenatal appointment, ideally in the second trimester and those who are positive should be regularly monitored after treatment. This study found that treating pregnant women with asymptomatic bacteriuria with a single dosage of fosfomycin trometamol is very successful. Aside from its safety profile, the single dosage of 3 g fosfomycin trometamol may be the first drug of choice therapy in the treatment of asymptomatic urinary tract infections in pregnancy due to its reduced cost and greater patient compliance. It's time that we have a look at this strategy for improving the healthcare and for reducing the maternal and fetal morbidity and mortality.

However, further studies with large number of patients are needed to establish the definite role of fosfomycin trometamol in this context.

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