The Journal of Obstetrics and Gynecology of India (January–February 2020) 70(1):36–43
https://doi.org/10.1007/s13224-019-01287-3

ORIGINAL ARTICLE

Multimodality Screening for Lower Genital Tract Infections Between 18 and 24 Weeks of Pregnancy and its Efficacy in Predicting Spontaneous Preterm Delivery

Vidyashree Ganesh Poojari[1] · Samantha Dawson[1] · Akhila Vasudeva[1] · Nivedita Hegde[1] · Geetha Kaipa[2] · Vandana Eshwara[2] · Chaitanya Tellapragada[3] · Pratap Kumar[1]

Received: 22 July 2019 / Accepted: 28 September 2019 / Published online: 15 October 2019

Abstract

Background Predicting spontaneous preterm birth (SPTB) during mid-trimester would be very useful. We used a multimodality screening approach mainly focusing on urogenital infections among unselected obstetric population between 18 and 24 weeks in a tertiary center.

Method Diagnosis of lower genital tract infection (LGTI) was attempted among 228 pregnant women using several factors—symptom of vaginal discharge, characteristic appearance of discharge on speculum, point of care tests using Amsel's criteria and gram staining of vaginal swab. Nugent's scoring was taken as gold standard. Urine microscopy/culture was obtained. Serum inflammatory markers were done. Total leukocyte count, neutrophil/lymphocyte ratio and C-reactive protein were obtained. Data on cervical length were obtained from mid-trimester scan.

Results Thirty patients complained of vaginal discharge. Speculum examination revealed discharge in 221 (96.92%), appearing pathological in 192 (86.87%). Amsel's criteria showed poor sensitivity to detect full (57%) and partial (24%) bacterial vaginosis (BV). On gram staining, 104 (45.61%) showed evidence of LGTI; 14 full BV (6.1%); 45 partial BV (19.5%); 40 candidiasis (17.5%); and two each of trichomoniasis and aerobic vaginitis. Appearance of vaginal discharge and microscopic diagnosis of LGTI were poorly correlated. Forty women (17.5%) had SPTB, 24 following membrane rupture and 16 following spontaneous labor. The presence of BV (specifically partial) increased the likelihood of SPTB with OR of 3.347 (CI 1.642, 6.823). Three of seven women with short cervix delivered preterm. No other screening modality was associated with SPTB.

Conclusion Active screening for LGTI between 18 and 24 weeks shows high prevalence of BV in Indian setting. There is a strong link between partial BV and SPTB.

Vidyashree Ganesh Poojari is an Associate Professor in Department of Obstetrics and Gynecology at Kasturba Medical College, MAHE, Manipal, Karnataka, India. Samantha Dawson is an Junior Resident in Department of Obstetrics and Gynecology at Kasturba Medical College, MAHE, Manipal, Karnataka, India. Akhila Vasudeva is an Professor in Department of Obstetrics and Gynecology at Kasturba Medical College, MAHE, Manipal, Karnataka, India. Nivedita Hegde is an Assistant Professor in Department of Obstetrics and Gynecology at Kasturba Medical College, MAHE, Manipal, Karnataka, India. Geetha Kaipa is an Junior Resident in Department of Microbiology at Kasturba Medical College, MAHE, Manipal, Karnataka, India. Vandana Eshwara is an Professor in Department of Microbiology at Kasturba Medical College, MAHE, Manipal, Karnataka, India. Chaitanya Tellapragada is an Post Doctorate, Department of Laboratory, Medicine, Karolinska institute, Sweden. Pratap Kumar is an Professor in Department of Obstetrics and Gynecology at Kasturba Medical College, MAHE, Manipal, Karnataka, India.

Extended author information available on the last page of the article

Keywords Screening for preterm delivery · Lower genital tract infection · Bacterial vaginosis · Vaginal discharge · Screening · Amsel's criteria · Nugent's criteria

Introduction

Lower genital tract infections account for nearly 30–40% of spontaneous preterm birth (SPTB) [1, 2]. Spontaneous preterm labor (SPTL) due to infection is refractory to tocolytics as irreversible inflammatory changes would have already occurred in the uterus by 22 weeks [3]. However, early diagnosis is still a challenge, as most infections are asymptomatic. The ascent of organisms causing lower genital tract infection (LGTI) is known to be a cause of infection-related SPTB [1, 3]. No international guidelines are supporting routine mid-trimester screening for urogenital infection, as the data from the west have not shown a clear benefit of such a practice, in terms of reducing the burden of SPTB. Such guidelines should be formulated based on the local prevalence of the problem. In addition, the strength of association between screen positivity and SPTB needs to be understood, as relevant to the local obstetric community.

Not enough Indian data is available on the prevalence of urogenital infection in unselected obstetric population in the mid-trimester. Also, the best way to identify LGTI in our population is unknown. Very few Indian studies have directly correlated patient's symptoms, speculum findings, and point of care tests as against the gold standard of gram staining. In this study, we analyzed the diagnostic accuracy of the above methods, in addition to know about the prevalence of LGTI among all pregnant women visiting the antenatal clinic in the mid-trimester. We have also attempted to correlate microbiologically diagnosed LGTI with spontaneous preterm birth in the screened population. Serum inflammatory markers, urine analysis, and cervical lengths were added upon as screening parameters to predict SPTB. Mid-trimester was chosen as this screening exercise can be easily combined with the routine antenatal visit around the time of anomaly scan, leading to timely prediction and prevention of SPTB.

Study Design and Methodology

The present study was a prospective observational study conducted in a tertiary care hospital of Southern India over two years. Kasturba Medical College and Kasturba Hospital, Manipal—Institutional ethics committee clearance was obtained (IEC Number–403/2015). Informed written consent was taken from the patients. Considering an exposure rate of 30% for bacterial vaginosis (BV) [3], relative precision of 25%, 225 was the required sample size. Two hundred and twenty-eight pregnant women attending the antenatal clinic between 18–24 weeks of gestation with a singleton pregnancy were included. The symptom of vaginal discharge was noted. After the obstetric examination, patients underwent a speculum examination during which:

(a) The presence/absence of discharge and quantity noted.
(b) Type of discharge studied (thick homogenous white discharge that correlates with physiological discharge seen in pregnancy; homogenous thin white correlating with bacterial vaginosis (BV); thick curdy white correlating with candidiasis, yellow frothy correlating with trichomoniasis)
(c) Three high vaginal swabs were collected from the posterior fornix:

- One smeared on a litmus paper for pH
- Another swab was applied to a glass slide. Few drops of potassium hydroxide (KOH) [4] were put over it. Whiff's test was considered positive (for BV) if amine-like/"fishy" odor was noted.
- The last swab was smeared on a glass slide for gram staining.

Amsel's Bedside Test

Amsel's criteria are the point of care diagnostic test for BV, considered positive when three out of four criteria are met.

- Homogeneous, thin white discharge smoothly coating the vaginal walls.
- Whiff Test—amine odor with potassium hydroxide.
- Microscopy—Presence of 20% or more clue cells
- Litmus paper—pH more than 4.5

Microscopy/Gram Staining of High Vaginal Swabs

In the present study, we used gram-stained smear examination of the high vaginal swabs as the reference method for diagnosis of LGTIs such as bacterial vaginosis, aerobic vaginitis, and vulvovaginal candidiasis. Wet mount examination of the high vaginal swab was used for diagnosis of trichomoniasis. In the absence of all the above infections, women were considered as not having LGTI.

Bacterial Vaginosis (Full)

Diagnosis of "full" BV was made when the Gram's stained smear of the high vaginal swab had a Nugent's score within

7–10, less than 5 lactobacillary forms and predominance (> 30/Oil Immersion field) of Gardnerella vaginalis and/or anaerobic/curved gram-negative bacillary forms consistently throughout the smear.

Partial BV

Women harboring Nugent's intermediate vaginal flora have reduced vaginal lactobacilli (5–10 bacilli/oil immersion field) and the presence of streaks of anaerobic gram-negative bacilli and/or thin gram-variable coccobacillary forms with occasional clue cells (< 20% clue cells).

Candidiasis

Microscopically visualizing hyphae/pseudo-hyphae after application of KOH.

Trichomoniasis

Wet mount showing motile flagellated trichomonads.

Urinary tract infection was diagnosed based on urine microscopy and culture/sensitivity. Serum inflammatory markers were assessed at the same visit, including total leukocyte count (TLC), neutrophil/lymphocyte ratio (NLR), and C-reactive protein (CRP). Data on cervical length (done as a part of mid-trimester anomaly scan) were also taken into consideration.

Pregnancies were followed up till delivery. The occurrence of SPTL and/or preterm premature rupture of membranes (PPROM) leading to spontaneous preterm delivery (SPTD) was recorded along with their gestational age at delivery.

Results

Demographic data of the study population are shown in Table 1. Of the 228 women, 30 (13.1%) complained of vaginal discharge. On speculum examination (which was done on symptomatic and asymptomatic women), 221 (96.92%) women had some form of vaginal discharge. It appeared homogenous thin white (correlating with BV) in 158 (69%) followed by curdy white (correlating with candidiasis) in 31 (14%), and thick homogenous (thought to be physiological) in 29 women (13%). Thus, 192 (86.87%) had pathological looking discharge, as the only thick homogenous discharge is likely to be physiological. The discharge was scanty in 168 (76.1%), while moderate in an amount in 53 (23.9%).

Table 1 Baseline characteristics of the study population ($N = 228$)

Parameters	*n* (%)	
Maternal age		
20–24 years	39 (17.1%)	Mean age—29.01 years
25–29 years	94 (41.2%)	
30–34 years	59 (25.9%)	
More than 35 years	36 (15.8%)	
BMI (Body mass index)		
Less than 18.5 (Underweight)	40 (17.5%)	Mean BMI—22.39
18.5–22.9 (Normal)	96 (42.10%)	
23–24.9 (Overweight)	30 (13.15%)	
25–29.9 (Pre-obese)	49 (21.5%)	
More than 30 (Obese)	13 (5.7%)	
Gestational Age at the recruitment for the study		
18–19 weeks	150 (65.8%)	Mean gestational age at recruitment 18 weeks
20–21 weeks	45 (19.7%)	
22–24 weeks	33 (14.5%)	
Parity		
Primigravida	117 (51.3%)	
Multigravida	111 (48.7%)	
Type of conception		
Spontaneous conception	186 (81.6%)	
Ovulation induction	5 (2.2%)	
Ovulation induction + intrauterine insemination	16 (7%)	
Invitro fertilization	21 (9%)	

Accuracy of Point of Care Tests

Taking gram stain/Nugent's scoring as the gold standard, only eight out of 14 (57.14%) patients with full BV were Amsel's positive. Only 11 out of 45 (24%) patients with partial BV were Amsel's positive. Diagnostic accuracy of individual Amsel's criteria for bacterial vaginosis is shown in Table 2.

Gram Staining

Taking gram staining as the gold standard, 104 (45.61% of the screened population) women showed evidence of LGTI in the mid-trimester. Out of them, 45 (19.7%) had partial BV, 14 (6.1%) had full BV (thus giving an overall BV prevalence of 25%), 40 (17.5%) had candidiasis, two (0.9%) had trichomoniasis, two (0.9%) had aerobic vaginitis, and one (0.4%) had gram-negative bacilli.

In our study, 13 out of 30 symptomatic (43.33%) and 91 out of 198 asymptomatic women (45.95%) had LGTI. Among 30 symptomatic women, 17(56.67%) women had normal vaginal flora (NVF), while the remaining had some form of LGTI. Table 3 shows the poor correlation between speculum examination appearance of vaginal discharge, and the gram stain-based diagnosis of LGTI.

Out of 228, 15 (7%) had neutrophil lymphocyte ratio (NLR) more than 6.4 of whom three (20%) had LGTI, 23 (11%) had leukocyte count > 15,000/mm out of whom ten (43%) had LGTI (nine being BV), and 69 (31%) had CRP > 7.4 mg/L of whom 34 (49%) had LGTI (24 being BV). These cut-offs were taken from the relevant published literature, linking the serum inflammatory markers to preterm labor [5]

Out of 228, 79 (35%) of women had pyuria (Urine pus cells > 10/HPF); 13 (5.7%) were culture proven of whom E.coli was the commonest pathogen.

Correlation of these Screening Tools with Preterm Labor

Forty women (17.5%) had SPTD, of whom 24 (60%) followed preterm prelabor rupture of membrane (PPROM) and 16 (40%) followed SPTL. White discharge, as a complaint, was not predictive of SPTB (Table 4). There was a

Table 2 Diagnostic accuracy of individual Amsel's criteria, taking Nugent's criteria as the gold standard ($N = 228$)

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Amsel's criteria for full bacterial vaginosis				
pH > 4.5	37	69	8	93
Whiff test	57	77	14	95
Clue cells	56	93	37	96
Homogenous thin white discharge	78	31	8	95
Amsel's criteria for partial bacterial vaginosis				
pH > 4.5	44	72	26	84
Whiff test	46	80	37	86
Clue cells	35	95	66	85
Homogenous thin white discharge	75	32	21	84

Table 3 Correlation of type of discharge vs gram stain diagnosis ($N = 228$)

Type of discharge	Gram staining						
	Normal flora ($n = 124$)	BV (Full) ($n = 14$)	BV (Partial) ($n = 45$)	Candidiasis ($n = 40$)	Trichomoniasis ($n = 2$)	Aerobic vaginitis ($n = 2$)	Gram-negative bacilli ($n = 1$)
Thin homogenous ($n = 158$)	81 (51.3%)	**11 (7%)**	**38 (24.1%)**	27 (17.7%)	0	0	1 (0.6%)
Thick homogenous ($n = 29$)	18 (62.1%)	**2 (6.9%)**	**6 (20.7%)**	2 (6.9%)	0	1 (3.4%)	0
Curdy white ($n = 31$)	19 (61.3%)	0	0	**11 (35.5%)**	1 (3.3%)	0	0
Yellow frothy ($n = 3$)	0	0	1 (33.3%)	0	1 (33.3%)	1 (33.3%)	0
No discharge ($n = 7$)	6 (85.7%)	1 (14.3%)	0	0	0	0	0

Bold values are the percentage of Bacterial vaginosis/candidiasis among cases with various types of discharges

Table 4 Association between mid-trimester screening parameters and spontaneous preterm birth ($N=228$)

Parameters	Outcomes								
	Spontaneous preterm delivery			Spontaneous preterm labor			PPROM		
	Yes ($n=40$)	No ($n=188$)	p value	Yes ($n=16$)	No ($n=212$)	p value	Yes ($n=24$)	No ($n=204$)	p value
WDPV as symptom($n=30$)	4 (13.8%)	26 (86.7%)	0.360	2 (6.7%)	28 (93.3)	0.647	2 (6.7%)	28 (93.3%)	0.358
Bacterial vaginosis (full + Partial) ($n=59$)	19 (32.2%)	40 (67.8%)	0.001	10 (16.9%)	49 (83.1%)	0.001	9 (15.2%)	50 (84.8%)	0.216
Full bacterial vaginosis ($n=14$)	4 (28.6%)	10 (72.4%)	0.215	2 (14.3%)	12 (86.7%)	0.256	2 (14.3%)	12 (86.7%)	0.448
Partial bacterial vaginosis, ($n=45$)	15 (33.3%)	30 (66.7%)	0.003	8 (17.8%)	37 (82.2%)	0.005	7 (16.5%)	38 (84.5%)	0.023
Candida ($n=40$)	8 (20%)	32 (80%)	0.423	1 (2.5%)	39 (97.5%)	0.191	7 (17.1%)	33 (83.9%)	0.104
NLR > 6.4 ($n=15$)	3 (20%)	12 (80%)	0.532	0	15 (100%)	0.647	3 (20%)	12 (80%)	0.220
Total counts > 15,000 ($n=23$)	2 (8.7%)	21 (91.7%)	0.670	2 (8.7%)	21 (91.7%)	0.440	0	23 (100%)	0.140
CRP > 7.4 ($n=69$)	13 (18.4%)	56 (82.6%)	0.440	7 (10.7%)	62 (81.3%)	0.170	6 (8.7%)	63 (91.3%)	0.360
Urine microscopy pus cells > 10/mm ($n=79$)	3 (3.79%)	76 (96.2%)	0.345	5 (6.3%)	74 (94.7%)	0.143	2 (2.5%)	77 (97.5%)	0.231
Urine culture ($n=13$)	1 (7.7%)	12 (92.3%)	0.299	0	13 (100%)	0.838	1 (7.7%)	12 (92.3%)	0.593
Cervical length < 25 mm ($n=7$)	3 (42.9%)	4 (58.1%)	0.050	1 (14.3%)	6 (85.7%)	0.401	2 (28.6%)	5 (72.4%)	0.008

p values refer to incidence of preterm delivery, among the group found to have positive mid-trimester screening parameter versus those with negative mid-trimester screening parameter. Two-tailed p value using Fisher's exact test

statistically significant association between microbiologically proven BV and SPTD (Table 4). The presence of BV increased the odds of going into SPTL by 3.3. However, analyzing full and partial BV separately, the association between partial BV and SPTD was statistically significant, and that of full BV with SPTD was not, probably due to the smaller number. BV was significantly associated with SPTL and not PPROM in our study. There was no significant association between candidiasis and spontaneous preterm delivery. There were two patients with aerobic vaginitis; both delivered preterm. However, the incidence of LGTI other than BV was too small to comment on their association with SPTD. Neither raised serum inflammatory markers nor urinary infection was independently predictive of SPTD (Table 4). Routine targeted scan performed at this visit showed short cervix (< 2.5 cm) in seven, of whom three (42.9%) delivered preterm.

We considered screen-positive women at mid-trimester if any of the study parameters were abnormal. Screen positivity was associated with SPTL (Table 5). However, this association was weaker when compared to the strong association between BV as a single predictive factor for SPTD.

Among the 228 women in the study population, 174 (76%) delivered at term, whereas 54 (24%) women delivered preterm. Out of these 54 women, 14 pregnancies were terminated preterm due to iatrogenic causes, i.e., either due to maternal or fetal indication, e.g., fetal distress/imminent eclampsia, etc. The remaining 40 had a spontaneous preterm delivery, out of which 40% was preceded by spontaneous preterm labor and the remaining 60% by preterm prelabor rupture of membranes (PPROM). Analyzing the gestational age at SPTD, out of the 40 who had SPTD, there were 28 screen-positive and 12 screen-negative women. Interestingly, 11 out of 12 screen-negative women delivered at or beyond 34 weeks (Fig. 1). Thus, women who were screen-negative in the mid-trimester were very unlikely to go into SPTL before 34 weeks. None of the screen-negative women delivered before 32 weeks.

Table 5 Association of overall screen positivity with pregnancy outcomes ($n=228$)

Screen positivity	Outcomes					
	Spontaneous preterm delivery		Spontaneous preterm labor		PPROM	
	Yes ($n=40$)	No ($n=188$)	Yes ($n=16$)	No ($n=212$)	Yes ($n=24$)	No ($n=204$)
Present ($n=144$)	28 (19.4%)	116 (80.6%)	14 (9.7%)	130 (90.3%)	14 (9.7%)	130 (90.3%)
Absent ($n=84$)	12 (14.3%)	72 (85.7%)	2 (2.4%)	82 (97.6%)	10 (11.9%)	74 (88.1%)
p value	0.370		0.057		0.657	

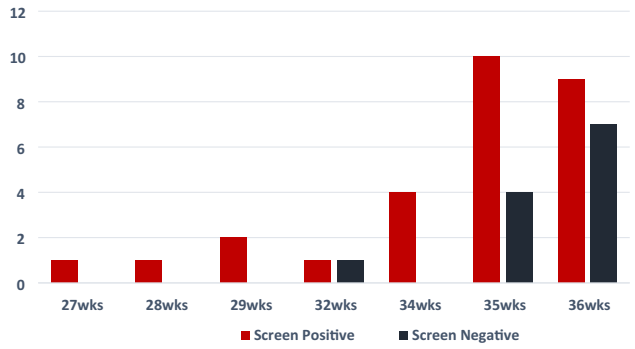

Fig. 1 Gestational age at preterm labor/delivery/PPROM among the mid-trimester screen-positive and screen-negative women ($n=40$)

Discussion

Our study aimed at screening women in the mid-trimester (18–24 weeks), using multiple available gadgets, mainly focusing on infection, thus attempting to predict SPTD. We chose this time in pregnancy, as screen positivity can be dealt with appropriately timed specific intervention, thus hoping to reduce the burden of SPTD.

LGTI in pregnancy is routinely diagnosed and treated based either on the symptom of vaginal discharge or on the appearance of vaginal discharge, on speculum examination (performed only prompted by the symptoms). Our study suggests that neither methods are accurate in diagnosis, taking gram staining of vaginal swab as the gold standard. Vaginal discharge as a complaint is neither sensitive enough to pick up LGTI nor specific to always suggest LGTI. Mengistie et al. [6] reported that 63.3% of pregnant women who were diagnosed with BV by gram stain were asymptomatic. Relying on the appearance of vaginal discharge may lead to the erroneous treatment of LGTI. There was gross disparity between clinician's impression of the cause of discharge (based on appearance) versus specific LGTI as diagnosed by gram staining. Bedside (point of care tests) did not perform well in screening for LGTI. Amsel's criteria showed poor sensitivity to diagnose BV—both full (57%) and partial BV (24%)—taking gram staining (Nugent's criteria) as the gold standard. However, point of care tests have performed well with a high negative predictive value in some observational studies [7, 8]. The literature suggests that a single pH measurement is unlikely to reflect true vaginal microbiota to guide antibiotic therapy in pregnancy [9, 10]. Systematic reviews have highlighted the possible inaccuracies in treating LGTI based on the syndromic approach, specifically in pregnancy [4, 11, 12]. Inadequate treatment leads to treatment failure, relapses, and SPTD, whereas antibiotic overtreatment leads to unnecessary side effects, antibiotic resistance, as well as the abolishment of normal vaginal ecoflora, all of which may prove harmful in pregnancy.

Indian studies have reported varying prevalence of bacterial vaginosis among asymptomatic pregnant women before 28 weeks of gestation; ranging from 6 to 20% [13–15]. Our study reports one of the highest such BV prevalence's at 25%. The literature from all over the world also shows varying prevalences of BV in the similar cohort—28% LGTI mainly constituted by BV in Sudan [16]; 28% full BV and 12% partial BV in Brazil [17]; and 40% BV in a mixed ethnic population of New York [18].

Significant association of BV/LGTI and SPTB is well-documented uniformly in the literature from India [13–15]. Such an association has also been documented in the literature from across the world [17, 19, 20], although the strength of such an association has been variable. Specifically, the significant association of partial BV with SPTD among Indian women was first observed by Tellapragada C [15], which is strongly supported by our results. Gupta A from Uttar Pradesh [13] reported a high prevalence of BV (19.5%) among asymptomatic pregnant women before 28 weeks, and 23.5% of the BV positive women delivered preterm; whereas in our study population, 32% of BV positive women had SPTD with an odds ratio of 3.3, which is one of the highest reported from India and across the world. Gupta A et al. demonstrated a strong link between PPROM and BV, which was not clear in our study. However, such a link was seen between PPROM and partial (not full) BV in our study.

There is some evidence supporting active screening + treatment policy of LGTI in asymptomatic women in the first half of pregnancy. This policy has reduced the incidence of SPTD in several interventional and observational studies [21–23]. A Cochrane review in 2015 analyzed one trial in which there was a significant reduction in SPTD in the group actively screened and appropriately treated for LGTI before 20 weeks [24].

On the other hand, there is great variation in the prevalence of BV among asymptomatic pregnant women depending on many factors, including the ethnic/geographic background. This polymicrobial condition of the vagina is incompletely understood, link to preterm labor is elusive in asymptomatic women probably because host immune response plays a key role in determining pregnancy outcome. Understandably, the evidence is not consistently supportive of the above-mentioned active screen + treat policy [25–27]. International organizations viz US Preventive Services Task Force in 2008, European (IUSTI/WHO) guideline on the management of vaginal discharge in 2011, have recommended against routine screening of asymptomatic low-risk pregnant women for LGTI including BV.

However, screening policies should be formulated based on the local prevalence of the problem and the possible link to adverse outcome. Indian literature, including ours, reveals a high prevalence of LGTI in the mid-trimester among asymptomatic women, which is strongly associated with

SPTD. Hence, we propose that active screening of LGTI should be advocated in our setup, in the mid-trimester. Further, randomized trials are warranted to know if appropriate treatment of LGTI in the mid-trimester significantly reduces SPTD. Cost–benefit analysis of such an approach is urgently needed in the background of high health-care costs incurred due to SPTB in the low-resource settings.

Coming to other individual screening parameters, none except short cervix seemed to predict SPTD. Urine tests and serum inflammatory markers were not predictive of SPTD. Overall screen positivity was too high (144, 63%) to apply to the general obstetric population. Although screen positivity was associated with SPTL, there seems to be no added benefit of using multimodality screening. Instead, gram staining of the high vaginal swab in the mid-trimester seems to be the single best screening test due to the high yield as well as the strong prediction of SPTD among the screen-positive women. At the same time, multimodal screening seems to be beneficial in identifying women at risk of preterm delivery. Screen-negative women are unlikely to deliver before 34 weeks.

Limitations: A proportion of symptomatic women were treated for LGTI based on clinical appearance of vaginal discharge during speculum examination, not based on any bedside or microbiological testing (26 before 22 weeks, and 23 after 22 weeks). This being our institutional protocol would have had an impact on the incidence of SPTD. Also, completely asymptomatic but screen-positive women were not treated, as we do not follow an "active screen and treat" policy. Such an interventional study must be performed in the local population, to help formulate local guidelines on prevention of SPTD.

Conclusion

In this multimodality screening approach on the unselected obstetric population at mid-trimester, vaginal swab and gram staining showed a high prevalence of full and partial BV. The presence of BV, specifically partial BV, showed a strong link with SPTD.

Compliance with Ethical Standards

Conflict of interest Vidyashree Ganesh Poojari, Samantha Dawson, Akhila Vasudeva, Nivedita Hegde, Geetha Kaipa, Vandana Eshwara, Chaitanya Tellapragada, and Pratap Kumar declare that they have no conflict of interest.

Ethical Statement Kasturba Medical College and Kasturba Hospital, Manipal—Institutional ethics committee clearance obtained (IEC Number–403/2015)

Informed Consent An informed consent was obtained from all patients for being included in the study.

References

1. Georgiou HM, Di Quinzio MKW, Permezel M, Brennecke SP. Predicting preterm labour: current status and future prospects. Dis Markers. 2015. https://doi.org/10.1155/2015/435014.
2. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, Adler A, Vera Garcia C, Rohde S, Say L, Lawn JE. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379:2162–72.
3. Lamont RF. Antibiotics to prevent preterm birth. In: Keelan JA, Newnham JP, editors. Advances in the prevention and treatment of inflammation-associated preterm birth, Frontiers Media SA; 2016. p. 79–87.
4. Nwankwo TO, Aniebue UU, Umeh UA. Syndromic diagnosis in evaluation of women with symptoms of vaginitis. Curr Infect Dis Rep. 2017. https://doi.org/10.1007/s11908-017-0558-9.
5. Kim M-A, Lee YS, Seo K, Kallapur SG. Assessment of predictive markers for placental inflammatory response in preterm births. PLoS ONE. 2014;9(10):e107880.
6. Mengistie Z, Woldeamanuel Y, Asrat D, Adera A. Prevalence of bacterial vaginosis among pregnant women attending antenatal care in Tikur Anbessa University Hospital, Addis Ababa, Ethiopia. BMC Res Notes. 2014;20(7):822. https://doi.org/10.1186/1756-0500-7-822.
7. Mohammadzadeh F, Dolatian M, Jorjani M, Majd HA. Diagnostic value of Amsel's clinical criteria for diagnosis of bacterial vaginosis. Glob J Health Sci. 2015;7(3):8–14.
8. Mengistie Z, Woldeamanuel Y, Asrat D, Yigeremu M. Comparison of clinical and gram stain diagnosis methods of bacterial vaginosis among pregnant women in Ethiopia. J Clin Diagn Res. 2013;7(12):2701–3.
9. Witkin SS. Limitations of treating pregnant women based solely on vaginal pH. British J Obstet Gynecol. 2018;125(12):1610. https://doi.org/10.1111/1471-0528.15281.
10. Hoffman MK, Bellad MB, Charantimath US, et al. A comparison of colorimetric assessment of vaginal ph with Nugent score for the detection of bacterial vaginosis. Infect Dis Obstet Gynecol. 2017. https://doi.org/10.1155/2017/1040984.
11. Zemouri C, Wi TE, Kiarie J, Seuc A, Mogasale V, Latif A, Broutet N. The performance of the vaginal discharge syndromic management in treating vaginal and cervical infection: a systematic review and meta-analysis. PLoS ONE. 2016;11(10):e0163365.
12. Lima TM, Teles LR, de Oliveira A, Campos FC, Barbosa RD, Pinheiro AK, et al. Vaginal discharge in pregnant women: comparison between syndromic approach and examination of clinical nurs- ing practice. Rev Esc Enferm USP. 2013;47(6):1265–71. https://doi.org/10.1590/S0080-623420130000600002.
13. Gupta A, Garg P, Nigam S. Bacterial vaginosis in pregnancy (<28 weeks) and its effect on pregnancy outcome: a study from a western up city. Indian J Clin Pract. 2013;23(11):740–4.
14. Tellapragada C, Vandana KE, Bhat PV, Rao C, Kamath A, Nayak S, Shashidhar V, Acharya S, Mukhopadhyay C. Lower genital tract infections during pregnancy and adverse pregnancy outcomes: a hospital-based observational cohort study. BMC Infect Dis. 2014;14(Suppl 3):E35.
15. Tellapragada C, Eshwara VK, Bhat P, Kamath A, Aletty S, Mukhopadhyay C. Screening of vulvovaginal infections during pregnancy in resource constrained settings: implications on preterm

delivery. J Infect Public Health. 2017;10(4):431–7. https://doi.org/10.1016/j.jiph.2016.06.003.
16. Abdelaziz ZA, Ibrahim ME, Bilal NE, Hamid ME. Vaginal infections among pregnant women at Omdurman Maternity Hospital in Khartoum. Sudan. J Infect Dev Ctries. 2014;8(4):490–7. https://doi.org/10.3855/jidc.3197.
17. Krauss-Silva L, Almada-Horta A, Alves MB, Camacho KG, Moreira ME, Braga A. Basic vaginal pH, bacterial vaginosis and aerobic vaginitis: prevalence in early pregnancy and risk of spontaneous preterm delivery, a prospective study in a low socioeconomic and multiethnic South American population. BMC Pregnancy Childbirth. 2014;14:107. https://doi.org/10.1186/1471-2393-14-107.
18. Christine CA, Eva KP, Elizabeth C, Ruth AQ, Julie P, Kimberly O. Prevalence and risk factors for infections in a pregnant adolescent population. J Pediatr Adolesc Gynecol. 2017;30(1):71–5.
19. Farr A, Kiss H, Holzer I, Husslein P, Hagmann M, Petricevic L. Effect of asymptomatic vaginal colonization with Candida albicans on pregnancy outcome. Acta Obstet Gynecol Scand. 2015;94(9):989–96. https://doi.org/10.1111/aogs.12697.
20. Bretelle F, Rozenberg P, Pascal A, Favre R, Bohec C, Loundou A, et al. High Atopobium vaginae and Gardnerella vaginalis vaginal loads are associated with preterm birth. Clin Infect Dis. 2015;60(6):860–7. https://doi.org/10.1093/cid/ciu966.
21. Farr A, Kiss H, Hagmann M, Marschalek J, Husslein P, Petricevic L. Routine use of an antenatal infection screen-and-treat program to prevent preterm birth: long-term experience at a tertiary referral center. Birth. 2015;42(2):173–80. https://doi.org/10.1111/birt.12154.
22. Roberts CL, Algert CS, Rickard KL, Morris JM. Treatment of vaginal candidiasis for the prevention of preterm birth: a systematic review and meta-analysis. Syst Rev. 2015;4:31. https://doi.org/10.1186/s13643-015-0018-2.
23. Folger AT. Maternal Chlamydia trachomatis infections and preterm birth: the impact of early detection and eradication during pregnancy. Matern Child Health J. 2014;18(8):1795–802. https://doi.org/10.1007/s10995-013-1423-6.
24. Sangkomkamhang US, Lumbiganon P, Prasertcharoensuk W, Laopaiboon M. Antenatal lower genital tract infection screening and treatment programs for preventing preterm delivery. Cochrane Database Syst Rev. 2015;1(2):CD006178. https://doi.org/10.1002/14651858.cd006178.pub3.
25. Brabant G. Bacterial vaginosis and spontaneous preterm birth. J Gynecol Obstet Biol Reprod (Paris). 2016;45(10):1247–60. https://doi.org/10.1016/j.jgyn.2016.09.014.
26. Haahr T, Ersboll AS, Karlsen MA, Svare J, Sneider K, Hee L, Weile LK, et al. Treatment of bacterial vaginosis in pregnancy in order to reduce the risk of spontaneous preterm delivery—a clinical recommendation. Acta Obstet Gynecol Scand. 2016;95(8):850–60. https://doi.org/10.1111/aogs.12933.
27. Laura MJ. Bacterial Vaginosis and Preterm Birth. J Midwifery womens health. 2011;15(6):575–83. https://doi.org/10.1111/j.1542-2011.2011.00086.x.

About the Author

Dr. Vidyashree Ganesh Poojari (MS, DNB, ICOG fellowship in Gynecological Endoscopy) is presently working as Associate Professor in the Department of Obstetrics and Gynecology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India. Her area of interests are high-risk pregnancy and minimal invasive pelvic surgeries. She is a member of Institutional Research Committee. She is presently Joint Secretary of Manipal OBG Society.

Affiliations

Vidyashree Ganesh Poojari[1] · Samantha Dawson[1] · Akhila Vasudeva[1] · Nivedita Hegde[1] · Geetha Kaipa[2] · Vandana Eshwara[2] · Chaitanya Tellapragada[3] · Pratap Kumar[1]

✉ Akhila Vasudeva
akhilavasudeva@gmail.com

[1] Department of Obstetrics and Gynecology, Kasturba Medical College, Manipal Academy of Higher Education (MAHE), Manipal, Karnataka, India

[2] Department of Microbiology, Kasturba Medical College, Manipal Academy of Higher Education (MAHE), Manipal, Karnataka, India

[3] Department of Laboratory Medicine, Karolinska Institutet, Solna, Sweden