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Bacterial abundance and antimicrobial resistance patterns of uropathogens among pregnant women with asymptomatic bacteriuria: Association with glycemic status

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ABSTRACT

Objectives: Antimicrobial resistance (AMR), a growing global menace, poses a significant threat to maternal and fetal health. Gestational diabetes mellitus (GDM) causes double trouble in pregnancy, increasing the risk of a variety of infectious morbidities while also raising the possible association with AMR. Asymptomatic bacteriuria (ASB) is a common problem in pregnancy, but little research has been done to date explicitly examining the relationship between GDM and ASB and yielded conflicting results. Even fewer studies have specifically examined the relationship between GDM and AMR in women with ASB. Retrieving the most recent information on the disease burden, the range of causative pathogens, their patterns of AMR, and associated risk factors in pregnant women is crucial to stop the exponential rise in AMR in pregnancy and improve maternal and neonatal outcomes of infectious morbidities. Hence, this study was planned to investigate the association between glycemic status and the contemporary bacterial profile, antimicrobial resistance(AMR), and associated variables among pregnant women with ASB

Study design: This prospective, hospital-based, cross-sectional study was conducted among 320 pregnant women; divided into two groups, GDM and non-GDM. Data regarding sociodemographic and clinical characteristics were collected using a structured questionnaire. Clean-catch midstream urine samples were investigated for the presence of significant bacterial uropathogens and their AMR pattern was determined using recommended culture methods.

Results: We found ASB in 46.25% of study participants with significantly higher occurrence in the GDM group. Dominant isolates were Escherichia coli followed by Klebsiella pneumoniae. AMR was noted in 51.35% and multidrug resistance(MDR) in 23.65% of isolates. Overall AMR, MDR and higher degrees of AMR were higher among uropathogens isolated from the GDM group as compared to the non GDM group, although the difference was not statistically significant.

Conclusion: The high occurrence of ASB in pregnancy along with substantially high AMR in this study suggests the need for effective infection control and stewardship programmes. By defining the association of ASB and AMR with hyperglycemia, our study calls for the exploitation of this potential association in halting the pandemic of AMR and in improving the management of infectious morbidities, thus in-turn alleviating their undesired maternal and infant outcomes.

1. Introduction

Asymptomatic bacteriuria (ASB), constitutes one of the most common bacterial infections that complicates pregnancy [1]. The global prevalence of ASB in pregnancy ranges from 2% to 10% [2] but prevalence of up to 86.6% has been reported from low and middle-income

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Table 1
Sociodemographic and clinical characteristics of the study population.

Variable	Category	Non GDM n	GDM n	Significance of difference
Mean age ± SD		24.65± 3.55	26.21± 4.02	F = 2.887 P = 0.090
Mean Prepregnancy BMI ± SD		23.48± 3.86	25.71± 4.70	F = 3.926 P = 0.048
Mean gestational weight gain ± SD		9.65± 2.34	11.46± 3.42	F = 16.247 P < 0.001
Residence	Urban	138	115	$\chi^2 = 0.308$
	Rural	34	33	P = 0.579
Occupation	Housewife	163	141	$\chi^2 = 0.042$
	Working	9	7	P = 0.837
Literacy	Illiterate	20	9	$\chi^2 = 2.970$
	Literate	152	139	P = 0.085
Socio-economic status	Upper	7	4	$\chi^2 = 0.454$
	Middle	60	53	P = 0.797
	Lower	105	91	
Life style	Sedentary	97	96	$\chi^2 = 2.384$
	Active	75	52	P = 0.123
Parity	Primigravida	82	66	*$\chi^2 = 5.143$*
	Multigravida	87	72	*P = 0.076*
	Grand multigravida	3	10	
Gestational age at recruitment	24–31 weeks	96	80	$\chi^2 = 0.100$
	32–38 weeks	76	68	P = 0.752

P-value indicate level of significance. F is value of ANOVA test and χ2 is value of Chi square test.
Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); GDM, gestational diabetes mellitus; SD, standard deviation.

Table 2
Antimicrobial susceptibility profile of uropathogens isolated from asymptomatic pregnant women with and without GDM.

Bacterial Total Pathogens isolates		Antimicrobial Susceptible		Antimicrobial Resistant	
		Non GDM n (%)	GDM n (%)	Non GDM n (%)	GDM n (%)
Gram Positive bacteria					
Staphylococcus aureus	2	0 (0)	1 (50)	0 (0)	1(50)
Enterococcus faecalis	6	3(50)	2 (33.3)	1(16.67)	0(0)
Gram Negative bacteria					
Acinetobacter baumanni	15	3(20)	6 (40)	2 (13.33)	4 (26.67)
Enterobacter aerogenes	2	0 (0)	2 (100)	0 (0)	0 (0)
Enterobacter cloacae	10	5 (50)	3 (30)	0 (0)	2 (20)
Escherichia coli	86	16 (18.60)	19 (22.10)	22 (25.58)	29 (33.72)
Klebsiella pneumoniae	25	7 (28)	5 (20)	3 (12)	10 (40)
Proteus vulgaris	1	0 (0)	0 (0)	0 (0)	1(100)
Pseudomonas aeruginosa	1	0 (0)	0 (0)	0 (0)	1(100)
Total	148	34 (47.22)	38 (52.78)	28 (36.84)	48 (63.16)

Abbreviations: GDM, gestational diabetes mellitus

countries [LMIC] [3]. Because of its high prevalence and associated adverse consequences on maternal and foetal outcomes, ASB warrants special consideration throughout pregnancy.

Diabetes mellitus (DM) and gestational diabetes mellitus (GDM), whose prevalence is rapidly increasing worldwide, have been found to be an important risk factor for urogenital infections and deteriorating outcomes of infectious disorders [4,5]. Hyperglycemia and infection pose double trouble in pregnancy as both independently cause not only short-term fetomaternal complications but can also lead to foetal programming and adverse long-term fetomaternal consequences [4,6]. Few studies have been done to date, to explore the association of ASB with hyperglycemia in pregnancy and have reported conflicting results [7–11].

Accurate identification of the causative uropathogen and prescription of proper antimicrobials is critical for the successful management of ASB in pregnancy and in avoiding its untoward effects on the mother and the fetus. However, the issue of selecting appropriate antimicrobial treatment is more challenging in pregnancy. Besides being cost-effective, well-tolerated and safe for the mother and fetus, the chosen antimicrobial needs to have minimal rates of resistance. Recent studies are showing increased resistance of uropathogens to the majority of antibiotics in pregnancy [12,13]. Various factors contributing to this rising AMR, include lack of infection prevention, indiscriminate antimicrobial use and several other unknown factors, that are not yet adequately studied. Hyperglycemia constitutes one such factor, whose link to AMR has not yet been conclusively established and opinions from earlier studies are divided [14–16]. The emerging association of hyperglycemia with AMR can pose a further threat in pregnancy. Besides limiting the armamentarium of healthcare providers in fighting infectious diseases, it can further contribute to vertical transmission of resistant bacteria from mother to child, in turn further increasing the prevalence of AMR.

The problem needs special attention in LMIC countries like India, where infectious diseases still continue to be the leading cause of maternal and neonatal morbidity and mortality. With the already increased prevalence of both GDM and ASB, increasing AMR and its suspected association with hyperglycemia pose a further concern.

Few studies have been conducted worldwide on this subject and to the best of our knowledge, none from India. Hence, this prospective study was designed to determine the prevalence of ASB, causative bacterial uropathogens, their AMR profile and associated factors among pregnant women with and without hyperglycemia, attending a tertiary care hospital in Northern India.

2. Materials and Methods

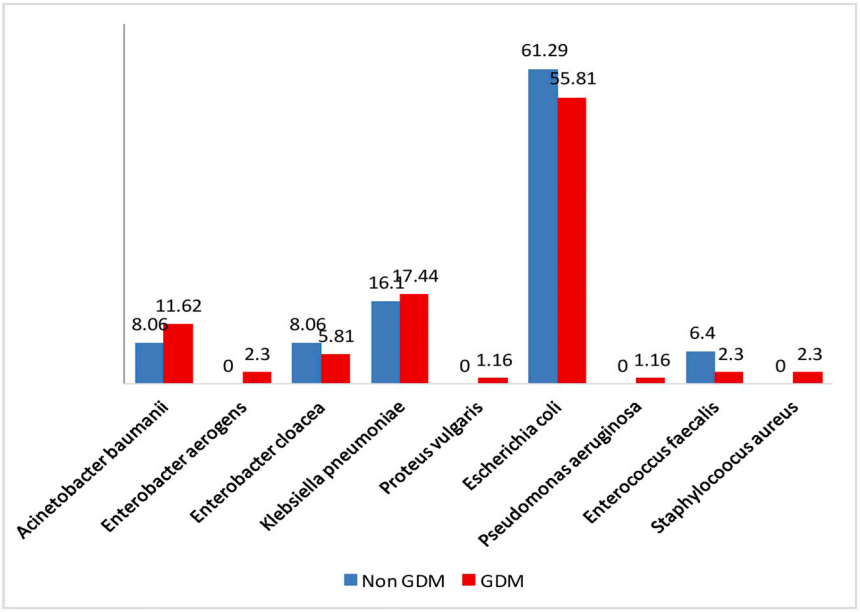
2.1. Study design, setting and population

This prospective, cross-sectional study consecutively enrolled pregnant women, attending the antenatal outpatient department of a tertiary medical hospital, in Northern India; from November 2020 to December 2022. The study was approved by the Institutional Ethics Committee. All patients provided written informed consent.

Between 24 and 28 weeks of pregnancy, all participants underwent a 75-g 2-hour oral glucose tolerance test (OGTT) and GDM was diagnosed according to International Association of Diabetes and Pregnancy Study Group recommendations [17]. All participants were asked to submit a urine sample for culture and sensitivity.

Women with the following characteristics were excluded: (1) symptoms of UTI at the time of enrolment (urgency, dysuria, haematuria, lower abdominal or loin pain with or without fever), (2) Use of antimicrobials within last two weeks of enrolment, (3) Patients with overt diabetes or any other aliment of renal or endocrine origin, (4) Patients with recurrent UTIs or on prophylactic antimicrobial treatment, (5) Patients who declined to participate in the study.

After applying exclusion criteria final sample consisted of 320 pregnant women. Based on their glycemic status, the study population was divided into two groups: (1) the GDM group, including 148 women with varying degrees of hyperglycemia, and (2) the non-GDM group,



Abbreviations: GDM, gestational diabetes mellitus

Fig. 1. : Distribution of bacterial pathogens isolated from urine culture of asymptomatic pregnant women with and without Gestational Diabetes Mellitus.

including 172 women with normoglycemia.

2.2. Specimen collection and transportation

Each study participant was given a sterile, screw-capped and wide-mouth container and was instructed on how to collect 6–12 ml of fresh, clean-catch, midstream urine sample. The container was then labelled with a unique sample number, date and time of collection and immediately transported to our microbiology laboratory for analysis. Samples that were not processed within 2 h were kept refrigerated at 4°C until they were analysed.

2.3. Bacterial Isolation, identification and antimicrobial susceptibility testing

The collected urine samples were directly plated on Cystine Lactose Electrolyte Deficient agar media using a calibrated inoculating wire loop (0.001ml). The culture plates were incubated overnight at 37 °C. After 24–48 h colonies were counted and bacterial growth of $\geq 10^5$ CFU/ml of urine was considered significant. Using the standard microbiological technique, all positive cultures with significant bacteriuria were identified at the species level by their colony properties, Gram-staining characteristics, and biochemical profiles.

The isolated microbes were subjected to antimicrobial susceptibility testing by Kirby- Bauer disk diffusion technique using Muller-Hinton agar medium (Hi Media Laboratories Pvt, Ltd). The zone of growth inhibition was evaluated and classified as susceptible (S), intermediate (I), or resistant (R) using the Clinical and Laboratory Standards Institute guidelines, after 18–24 h of incubation at 37°C [18].

2.4. Data processing, quality control, processing, quality control, and analysis

Sociodemographic and clinical characteristics and associated factors information were collected in a structured pre-validated questionnaire by a trained investigator. A trained laboratory scientist performed all culture and biochemical tests using standard operating procedures. Corresponding reference strains from the American Type Culture Collection (ATCC), were used as quality control parameters for culture and antimicrobial susceptibility testing.

Data were verified, coded and first entered into an Excel spreadsheet and then imported to SPSS version 23 software (SPSS Inc., Chicago, IL, USA) for analysis. Continuous data were expressed as means ± standard deviations. Categorical data were expressed as frequencies and analysed using the Chi-square test. Logistic regression analysis was performed to evaluate and describe the strength of associations between dependent and independent variables. P-value of <0.05 was considered statistically significant.

3. Results

3.1. Socio-demographic and clinical characteristics

The mean age of the patients was 25.37± 3.84 years (19–36 years) and the mean BMI was 24.52±4.41. Besides pre-pregnancy BMI, which was higher in the GDM group, no statistically significant difference was noted regarding other sociodemographic and clinical characteristics among the two groups(Table 1).

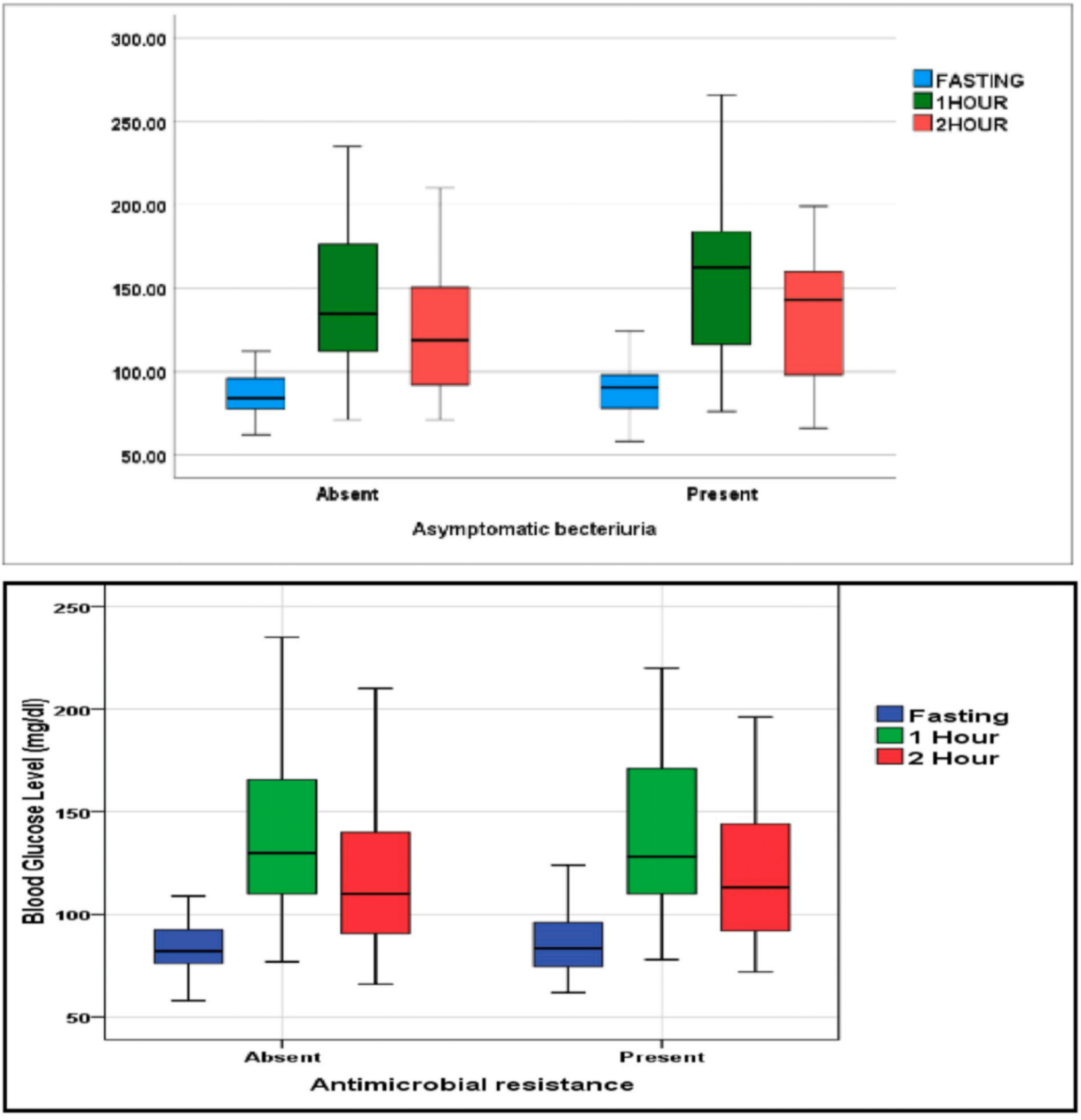


Fig. 2. : Association of mean fasting, 1-hour and 2-hour blood glucose levels with (a) asymptomatic bacteriuria and (b) antimicrobial resistance.

Table 3
Multidrug resistance pattern of uropathogens isolated from asymptomatic pregnant women with and without GDM.

	Non GDM						GDM					
	Drug Resistance						Drug Resistance					
Bacterial pathogens	**R1 n (%)**	**R2 n (%)**	**R3 n (%)**	**R4 n (%)**	**R5 n (%)**	**R6 n (%)**	**R1 n (%)**	**R2 n (%)**	**R3 n (%)**	**R4 n (%)**	**R5 n (%)**	**R6 n (%)**
Gram positive Bacteria												
Staphylococcus aureus	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)
Enterococcus faecalis	0 (0)	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	0 (0)	0 (0)	1 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (12.5)	0 (0)	0 (0)	0 (0)
Gram negative Bacteria												
Enterobacter cloacae	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	1 (10)
Enterobacter aerogenes	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Klebsiella pneumoniae	1 (4)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)	5 (20)	2 (8)	0 (0)	0 (0)	1 (4)	2 (8)
Escherichia coli	15 (17.4)	1 (1.2)	2 (2.3)	2 (2.3)	0 (0)	2 (2.3)	15 (17.4)	0 (0)	1 (1.2)	2 (2.3)	3 (3.5)	8 (9.3)
Proteus vulgaris	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Acinetobacter baumannii	0 (0)	0 (0)	1 (6.7)	0 (0)	1 (6.7)	0 (0)	1 (6.7)	0 (0)	0 (0)	1 (6.7)	2 (13.3)	0 (0)
Pseudomonas aeruginosa	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
Total	16 (11.4)	1 (0.7)	4 (2.9)	3 (2.1)	1 (0.7)	2 (1.4)	21 (15.0)	3 (2.1)	2 (1.4)	4 (2.9)	6 (4.3)	11 (7.9)

Abbreviations: GDM, gestational diabetes mellitus; R1, Resistance to one drug; R2, Resistance to two drugs; R3, Resistance to three drugs; R4, Resistance to four drugs; R5, Resistance to five drugs; R6, Resistance to six or more drugs

3.2. Asymptomatic bacteriuria and association with glycemic status

In the present study, ASB was detected in 46.25%(148/320). 9 different uropathogen species were isolated from the urinary samples. The majority were Gram-negative [94.6% (140/148)] and only 5.4%(8/148) were Gram-positive bacteria. Overall, the most common isolate was Escherichia coli [58.1%(86/148)], followed by Klebsiella pneumoniae [16.9%(86/148)]. .

We found a significantly higher prevalence of ASB among the GDM group [58.11%(86 /148)] as compared to the non-GDM group [36.04% (62/172)] ($P<0.001$). Gram-negative bacteria were more prevalent, 95.34%(82/86) and 93.54%(58/62); than gram-positive bacteria, 4.65%(04/86) and 6.4%(04/62) respectively, among both groups (Fig. 1). While no significant difference was noted for Escherichia coli and Klebsiella pneumoniae among the two groups, the percentage of isolates for uropathogens like Acinetobacter baumanii, Enterobacter aerogenes, Proteus vulgaris, Pseudomonas aeruginosa and Staphylococcus aureus was higher in GDM group (Fig. 1).

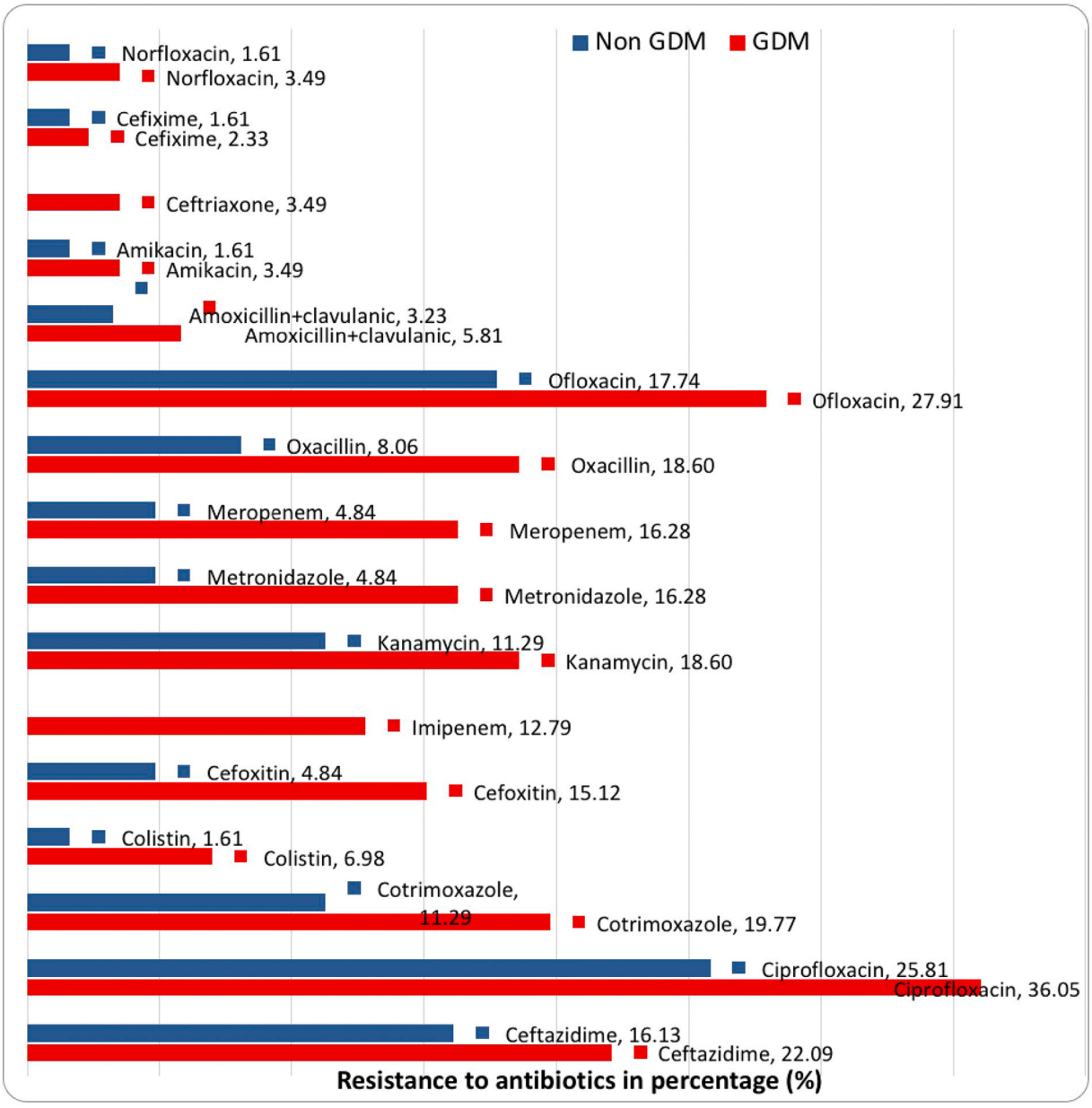
Moreover, we also found mean 1-hour and 2-hour blood glucose levels on OGTT of women with ASB (152.34±38.49, 133.52±34.70) to be significantly higher than of those without ASB (141.54±39.82, 122.581±35.12) [$t(318) = 2.456$; $P=0.015$, $t(318) = 5.795$; $P=0.006$] (Fig. 2a). However, similar trend was not seen with fasting blood glucose levels.

3.3. Antimicrobial resistance and association with glycemic status

51.35%(76/148) of isolated uropathogens showed resistance to one or more antimicrobials and multidrug resistance was noted in 23.65% (35/148)(Table 3). Maximum resistance was noted for antimicrobials like ofloxacin (74.76%), amoxicillin-clavulanic acid (70%) and amikacin (57.1%). Some degree of resistance was even noted for antimicrobials like meropenem (11.10%), colistin (5.74%) and imipenem (7.91%), however, no resistance was found for nitrofurantoin, vancomycin and fosfomycin (Table S1). Overall both AMR and MDR were higher among uropathogens isolated from the GDM group [63.16%(48/76) and 68.57%(24/35)] as compared to non GDM group [36.84%(28/76) and 31.43%(11/35)]; although the difference was not statistically significant [$P=0.244$ and $P=0.146$]. Additionally, a higher degree of AMR was noted more among strains isolated from women with GDM. Thirteen bacterial isolates (eleven among the GDM group and two among non GDM group) showed resistance to six or more antibiotic classes (Table 3). Furthermore, we found that for the majority of antimicrobials, higher resistance was noted among hyperglycemic women and for some antibiotics like ceftriaxone and imipenem, resistance was only noted among the GDM group (Fig. 3). While evaluating mean blood glucose values on OGTT with AMR, we failed to find any significant difference between the two groups (Fig. 2b).

3.4. Factors associated with ASB and AMR

Hyperglycemia and rural residence were found to have a significant



Abbreviations: GDM, gestational diabetes mellitus

Fig. 3. : Comparison of resistance to antimicrobials in asymptomatic bacteriuria among pregnant women with and without Gestational Diabetes Mellitus.

Table 4
Bivariate and multivariate regression analysis of factors associated with ASB among pregnant women (n = 320).

Variables	Categories	COR (95%Cl)	p value	AOR (95%Cl)	p value
Age	< 20 years	1 *		1 *	
	20–25 years	1.451 (0.682–3.085)	0.334	1.202 (0.525–2.754)	0.663
	26–30 years	1.557 (0.704–3.444)	0.274	1.173 (0.482–2.851)	0.725
	> 30 years	1.934 (0.717–5.217)	0.193	1.601 (0.491–5.217)	0.435
Residency	Urban	1 *		1 *	
	Rural	1.840 (1.066–3.175)	0.028	1.764 (0.992–3.137)	0.053
Occupation	Housewife	1 *			
	Working	0.899 (0.326–2.476)	0.837	0.761 (0.224–2.412)	0.642
Literacy	Illiterate	1 *		1 *	
	Literate	0.449 (0.200–1.005)	0.051	0.522 (0.207–1.320)	0.170
SES	Upper class	1 *		1 *	
	Middle class	0.626 (0.289–1.358)	0.236	0.714 (0.291–1.758)	0.464
	Lower class	1.146 (0.571–2.298)	0.701	0.956 (0.418–2.163)	0.902
Life Style	Sedentary	1 *		1 *	
	Active	1.717 (1.093–2.698)	0.019	1.327 (0.770–2.287)	0.309
Parity	Primigravida	1 *		1 *	
	Multigravida	1.303 (0.826–2.054)	0.255	1.318 (0.782–2.221)	0.320
	Grandmultigravida	1.487 (0.572–3.869)	0.416	0.912 (0.289–2.864)	0.872
Gestational age	24–31 weeks	1 *		1 *	
	32–38 weeks		0.752	1.591 (0.994–2.545)	0.053
BMI	Underweight	1 *		1 *	
	Normal	1.121 (0.241–5.213)	0.884	1.375 (0.234–8.072)	0.725
	Overweight	0.933 (0.194–4.499)	0.931	1.257 (0.200–7.915)	0.807
	Pre obese	1.514 (0.318–7.208)	0.603	1.915 (0.298–12.297)	0.494
	Obese	1.030 (0.203–5.234)	0.971	1.386 (0.193–9.928)	0.745
Glycemic status	Normoglycemic	1 *		1 *	
	Hyperglycemic	2.461 (1.567–3.864)	< 0.001	3.187 (1.926–5.271)	< 0.001

COR: crude odds ratio; AOR: adjusted odds ratio; 1*: reference category; 95% CI: 95% confidence interval; BMI: body mass index; SES: socioeconomic status; $p < 0.05$ is statistically significant

association with ASB among pregnant women (Table 4). The receiver operating characteristic (ROC) curve for the factors associated with the ASB showed the area under the curve (AUC) was 72.4% (95% CI: 66.9–77.9), indicating good performance for the discriminating ability of the model (Fig. 4). On analyzing factors associated with AMR, we didn't find a significant association with any of the studied variables (Table 5). The ROC curve for the factors associated with the AMR showed AUC was 70.8% (95% CI: 62.4–79.2), indicating good performance for the discriminating ability of the model (Fig. 5).

While assessing the correlation of sociodemographic and clinical characteristics of the population with the pathogens isolated, we found no significant association. The common isolates i.e. Escherichia coli and Klebsiella pneumoniae, as well as the general classifications of gram-positive and gram-negative organisms, failed to demonstrate any significant association(Tables S2, S3).

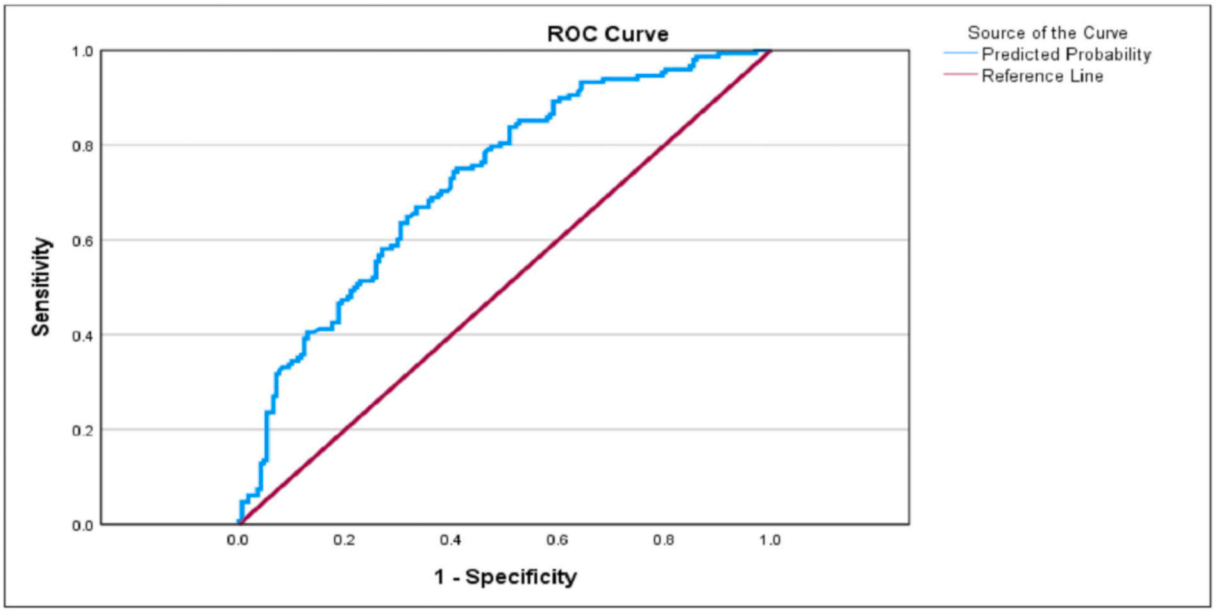
4. Discussion

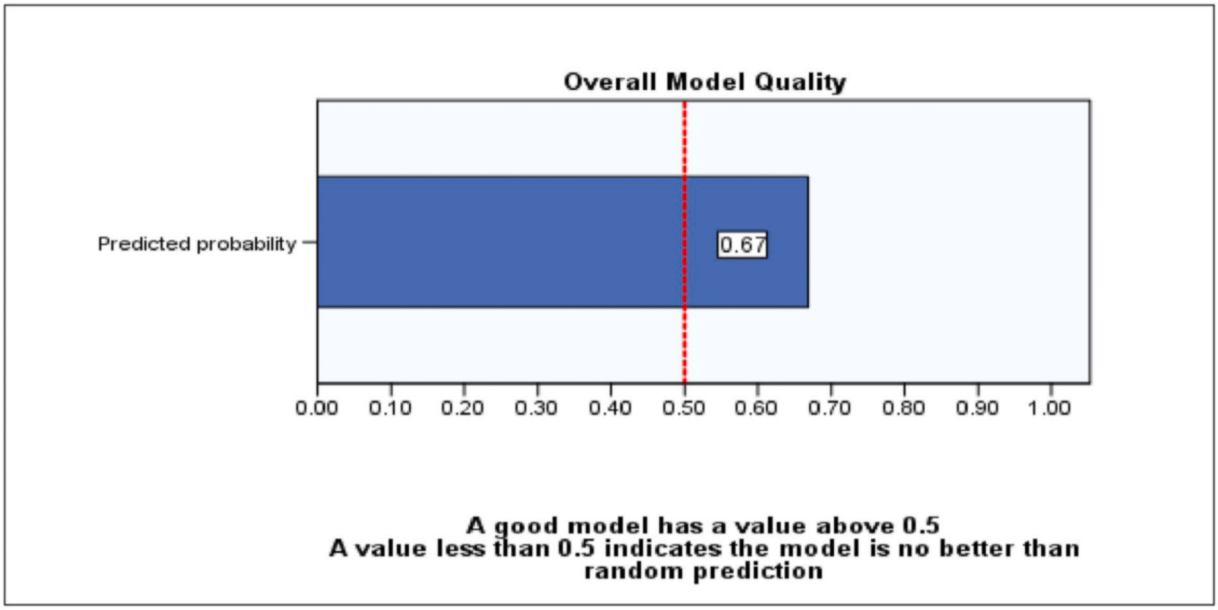
To halt the escalating rise in AMR in pregnancy and improve maternal and neonatal outcomes of infectious morbidities, it is essential to retrieve the most recent data from different geographic locations, on the burden of the disease, the range of causative pathogens, their patterns of AMR, and associated risk factors in pregnant women in general and those with high-risk factors like GDM in particular. This will ultimately contribute to improving the present and long-term health of both the women and their offspring.

In this study, the prevalence of ASB was 46.25% which is in accordance with a few prior studies [19,20] but is much higher than the global prevalence and the prevalence reported from other LMIC countries like Ethiopia [21] and Nigeria [22]. This high prevalence of ASB is disturbing given the harm it can do if untreated or treated improperly, and is indicative of the menace ASB causes in the studied region. We found that gram-negative bacteria were more prevalent, with Escherichia coli and Klebsiella pneumoniae being the predominant isolate, in both groups. Similar to us several other investigations evaluating ASB have found a higher proportion of Gram-negative uropathogens, in both normoglycemic and hyperglycemic pregnant women [5,7–11]. However, few have found a predominance of Gram-positive bacteria including Staphylococcus, also [3]. This preponderance of Escherichia coli and Klebsiella pneumoniae in our study is a cause of concern considering the recent reports which suggest them to be among the most common resistant pathogens [12,13].

Additionally, we found a higher prevalence of ASB in women with GDM. The majority of prior research has reported a higher prevalence of ASB in diabetics [5] but to date, sufficient robust studies have not explored ASB in pregnant women with GDM. Scant available literature has revealed conflicting results. Analogous to our findings few have shown a higher prevalence of ASB and UTI in pregnant women with GDM [6–8], while the rest others found no significant difference [9–11]. Besides hyperglycemia, no significant association was demonstrated with any other factors except for rural residence. Epidemiological studies in the past have shown varied associations of ASB with different variables [21,23], but still a lot of controversy exists in the literature and more research is needed to ascertain; which factors are associated with ASB and the strength of their association.

This study also reported worrying rates of AMR and MDR. Quite a high proportion of uropathogens were even resistant to more than three antibiotic classes. Studies done in the past have reported varied patterns





Abbreviations: ROC, Receiver Operating Characteristics.

Fig. 4. : ROC Curve for the factors associated with asymptomatic bacteriuria.

Table 5
Bivariate and multivariate regression analysis of factors associated with AMR among uropathogens isolated from pregnant women with ASB (n = 148).

Variables	Categories	COR (95%Cl)	p value	AOR (95%Cl)	p value
Age	< 20 years	1 *		1 *	
	20–25 years	1.750 (0.427–7.171)	0.437	1.738 (0.305–9.920)	0.534
	26–30 years	2.733 (0.922–8.107)	0.070	3.370 (0.855–13.287)	0.083
	> 30 years	2.356 (0.637–6.281)	0.235	1.991 (0.524–7.557)	0.312
Residency	Urban	1 *		1 *	
	Rural	1.162 (0.526–2.566)	0.710	1.255 (0.476–3.308)	0.647
Occupation	Housewife	1 *		1 *	
	Working	0.695(0.113–4.287)	0.695	0.491 (0.064–3.780)	0.495
Literacy	Illiterate	1 *		1 *	
	Literate	1.576(0.491–5.065)	0.445	1.637 (0.414–6.473)	0.482
SES	Upper class	1 *		1 *	
	Middle class	0.260 (0.026–2.597)	0.251	0.292 (0.024–3.484)	0.330
	Lower class	0.650 (0.331–1.278)	0.212	0.572 (0.260–1.259)	0.165
Life Style	Sedentary	1 *		1 *	
	Active	1.374 (0.705–2.675)	0.350	1.548 (0.716–3.346)	0.266
Parity	Primi	1 *		1 *	
	Multigravida	1.333 (0.251–7.075)	0.735	1.331(0.123–14.391)	0.814
	Grandmultigravida	0.846 (0.16–4.477)	0.844	1.02 0 (0.099–10.457)	0.987
Gestational age	24–31 weeks	1 *		1 *	
	32–38 weeks	0.536(0.278–1.036)	0.064	0.567 (0.279–1.153)	0.117
BMI	Normal	1 *		1 *	
	Overweight	0.465(0.171–1.264)	0.133	0.342 (0.096–1.222)	0.099
	Pre obese	0.296 (0.093–0.940)	0.039	0.318 (0.079–1.274)	0.106
	Obese	0.818 (0.279–2.401)	0.714	0.791 (0.208–3.006)	0.731
Glycemic status	Normoglycemic	1 *		1 *	
	Hyperglycemic	0.652 (0.338–1.257)	0.202	0.765 (0.356–1.645)	0.493

COR: crude odds ratio; AOR: adjusted odds ratio1*: reference category; 95% CI: 95% confidence interval; BMI: body mass index; SES: socioeconomic status; $p < 0.05$ is statistically significant

of AMR in uropathogens [12,13,20–22]. Such variations can be explained by the fact that disparities exist in different geographic locations, environmental conditions and study settings. While ascertaining AMR for specific antibiotics, we observed that all isolated uropathogens, were susceptible to nitrofurantoin, vancomycin and fosfomycin, indicating the potential for their prescription for the management of ASB in the study area. On the contrary, a high degree of resistance was noted for drugs like ofloxacin, amoxicillin-clavulanic acid and amikacin. Almost similar patterns of resistance have been observed in studies carried out across India and its neighbouring countries [20,23]. Resistance to commonly prescribed antimicrobials is another area of concern considering these are frequently prescribed empirically and resistance to them, questions treatment effectiveness. Furthermore, it results in the need for prescribing higher-generation antimicrobials which are more expensive and not easily available in LMIC countries.

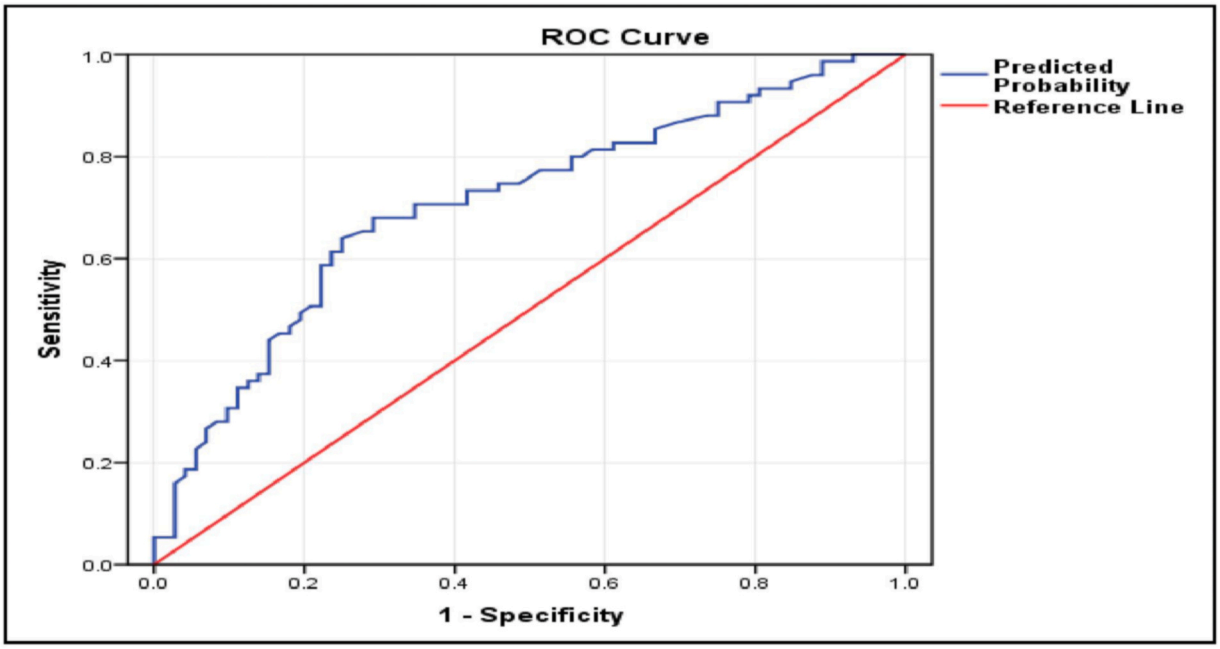
When the association of AMR was sought with glycemic status, we noted higher AMR and MDR in strains isolated from the GDM group although the difference was not statistically significant. However, large multicentric studies are required to further prove or disprove this association.

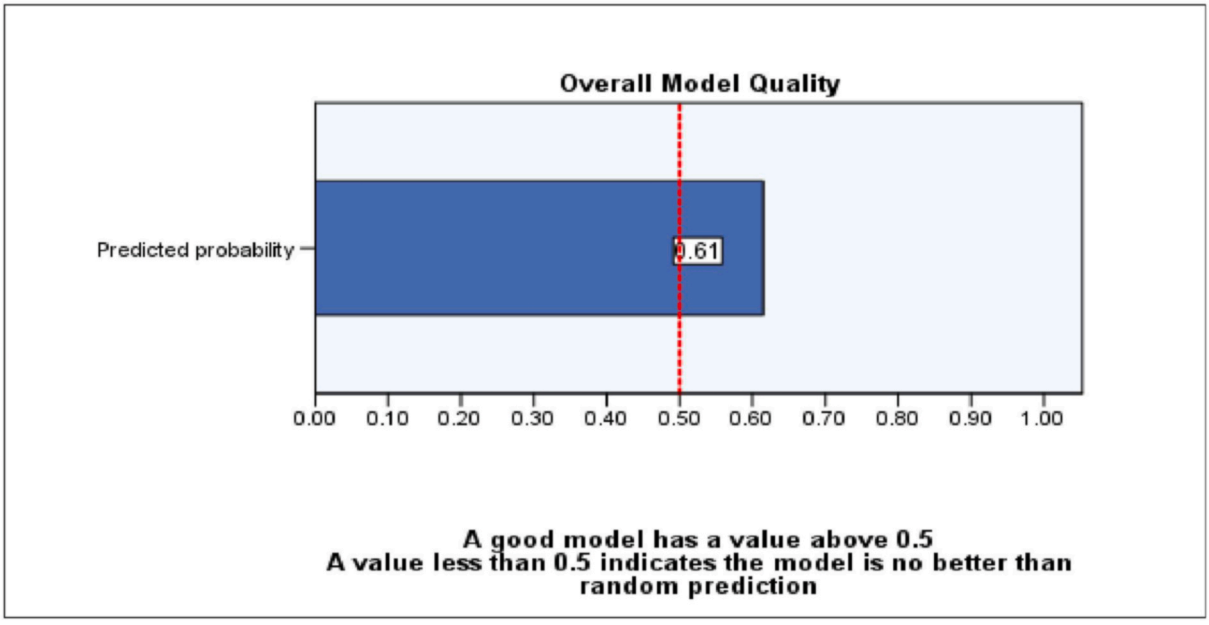
Our study also attempted to test for the association of sociodemographic factors with the prevalence of AMR bacterial isolates but failed to find any significant association. These results are comparable to studies from Ethiopia and Zambia [24,25], which also didn't find a statistically significant correlation between sociodemographic and clinical features except for phenotypic and genotypic traits. We also speculate that our inability to find any significant association may have been due to a small sample size, different population characteristics, and the non-inclusion of several other clinical variables such as previous UTI or catheterisation from our analysis. These findings additionally point towards the necessity of undertaking future large-scale studies, which consider the evaluation of varied sociodemographic and clinical features of the population including genotypic and phenotypic traits.

There are some limitations to this study that need to be mentioned. We were unable to test all of the drugs due to the limited availability of some of the susceptibility drug discs. Additionally, it would have been more valuable if bacterial isolates were identified using the 16sRNA technique and other indicators of glycemia such as HbA1c, and inflammatory mediators were also included, which could not be done due to financial constraints. Due to the cross-sectional nature of the study, the cause-and-effect relationship between ASB, AMR and hyperglycemia could not be ascertained. Furthermore, owing to the comparatively small sample size and study being conducted at a single hospital, its findings might not be representative of the general population as a whole. However, despite these limitations, we believe the findings of the study are indispensable, as the present study is one of its kind to investigate the association between glycemic status and the contemporary bacterial profile, AMR pattern, and associated variables among pregnant women with ASB, in LMIC like India.

5. Conclusion

The substantially high prevalence of ASB and AMR in pregnant women in this study is an alert for both prenatal healthcare providers and policymakers. It warrants the need for effective infection control and stewardship programmes as well as routine epidemiological surveillance of AMR in different geographical locations and among different populations.





Abbreviations: ROC, Receiver Operating Characteristics.

Fig. 5. : ROC Curve for the factors associated with antimicrobial resistance.

By deciphering the association of AMR with glycemic alterations in pregnancy, our study serves as the foundation for the exploitation of this potential association in halting the pandemic of AMR and in preserving antimicrobial effectiveness for future generations, thereby contributing towards the advancement of public health.

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CRediT authorship contribution statement

All named authors meet the ICMJE criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published. Individual contributions of each author are as follows: **Dr Dalia Rafat**, contributed to the study design, study planning, data acquisition, data analysis and drafting manuscript. **Dr Anubha Agrawal,** contributed to study planning, data acquisition, data analysis and drafting manuscript. **Dr Shamsi Khalid,** contributed to data acquisition, data analysis and drafting manuscript. **Dr Asad U Khan,** contributed to the study planning, data acquisition and drafting manuscript. **Dr Tabassum Nawab,** contributed to the study design, data analysis and drafting manuscript. **Dr Asfia Sultan,** contributed to study planning, data acquisition and drafting a manuscript of this article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.eurox.2023.100263.

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