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**Original Research Article**

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## **Factors that influence antimicrobial agents prescribing in pregnancy: An exploratory study**

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### **Abstract**

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**Purpose:** This study is aimed at determining the demographic factors of pregnant women that are associated with antimicrobial prescription and profile frequently diagnosed infectious diseases among antenatal clinic attendees.

**Methods:** Medical case files of 1300 pregnant women attending the antenatal care clinic of a women and children's health care facility in Benin City was systematically selected for a period of one year for review. Data extracted from the last medical encounter include age, gestational age, weight, diagnosis and the name of the antimicrobial agent prescribed. Frequencies and percentages were calculated and association of antimicrobial prescription with demographic variables was investigated with the aid of chi-square test. P-values <0.05 were interpreted as significant

**Results:** Majority of the medical case files did not contain some of the women's socio-demographic data which were of interest in this study. The woman's age ( $p=0.0003$ ), body weight ( $p=0.002$ ) and number of

children ( $p=0.028$ ) statistically influenced prescription of antimicrobial agents during pregnancy. Women who had more live children were more likely to receive prescription of antimicrobial agent during pregnancy. The results indicate that upper respiratory tract infection (URTI) was the most frequent infectious medical condition (33.3%) across the categories of age groups, trimesters, body weights and number of children. This was followed by malaria, urinary tract infection (UTI) and candida. Amoxicillin (42.6%) and nystatin were commonly used in the treatment of URTI and candida respectively.

**Conclusion:** There appears to be an association between prescriptions for antimicrobial agents and demographic factors of pregnant women. The most prevalent infectious medical condition is URTI which is mostly managed with amoxicillin.

**Keywords:** Antibiotics, Benin City, infection, pregnant women, prescription

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**Indexing:** Index Copernicus, African Index Medicus

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### **Introduction**

Pregnancy is a special physiological condition where drug therapy presents a special concern about risk to baby and mother, and decision to prescribe medications may be influenced by some pregnancy-specific factors. Pregnant women may be more susceptible to several infectious diseases and physicians may be hesitant in prescribing some antimicrobial agents to pregnant women. This is because many antimicrobial agents are capable of crossing the placenta thereby raising concerns of adverse effects on both pregnant woman and foetus.<sup>1,2</sup> Avoidance of drug use during pregnancy may not be practical and in fact, may be harmful because some

women do have medical conditions that require drug treatment.

Antimicrobial agents are among the most widely, and often injudiciously, used therapeutic agents worldwide.<sup>3-6</sup> Information on the use of medications during pregnancy is limited.<sup>7</sup> It is known that physiology of pregnancy affects the pharmacokinetics of administered medications. Socioeconomic factors have been shown to have some impact on antibiotic prescription in young children,<sup>8</sup> but how this affects pregnant women in the women and children hospital located in Benin City have not been investigated. Understanding how social and demographic factors of pregnant women influence antimicrobial prescriptions

may possibly guide preventive strategies that could help to avoid unnecessary use of antibiotics.<sup>9</sup> Therefore, the objective of this study is to determine the demographic factors that are associated with antibiotic prescriptions in pregnant women and to identify the most common infectious illness and the antimicrobial agent that is most frequently prescribed.

## Methods

### Setting

This study was conducted in a government owned women and children's hospital located in Benin City, the capital of Edo State, Nigeria.

### Data collection

This was a retrospective study. The hospital numbers of pregnant women visiting the study site for antenatal care within the last one year was obtained after permission and study protocol approval has been given by the hospital administration. Every tenth hospital number on a list was then selected for inclusion, and the corresponding medical case-notes were then reviewed for the study. The data extracted from the last medical encounter as recorded in the case notes were weight and age of the pregnant women; gestational age and the number of live births that the women have had in the past. Also collected was the diagnosis, prescription (or non-prescription) of an antimicrobial agent and the name of the drug that was prescribed.

### Data analysis

The collected data was entered into Microsoft excel and checked several times for accuracy. Frequencies and percentages were computed for all variables of interest only with non-missing data since our study is exploratory. With the aid of GraphPad Instat 3.0 that reports exact p-values; Chi-square test was used to investigate if any association exists between demographic factors and the prescription of an antimicrobial agent. Values of  $p < 0.05$  were interpreted as significant.

## Results

Out of the 1300 medical case notes of pregnant women that were screened only 160 (14.0%) of them received an antimicrobial agent prescription. One hundred and forty-one (10.9%) of the cases had a diagnosis for an infection. Since the number of prescriptions issued were more than the recorded cases of infections, the results seem to imply that some patients (19) may have received an antimicrobial agent prescription without an indicated

diagnosis. About 33% (47) of the infectious medical conditions were upper respiratory tract infections (URTI) with malaria being the second most frequent (28; 19.9%). Amoxicillin (60; 42.6%) was the most prescribed antimicrobial agent. All the pregnant women who had candida infection were given nystatin tablets (23) sometimes in combination with clotrimoxazole or tioconazole.

### Demographic factors influencing the use of antibiotics during pregnancy

Pregnant women between the ages of 26 and 35 years old were significantly ( $P=0.0003$ ) prescribed antimicrobial agents. A significant number of pregnant women at their first trimester received antimicrobial agents than their counterparts who were at second and third trimesters. Similarly, women who had body weights greater than 100Kg and those with more children were more likely to be prescribed antimicrobial agents ( $P < 0.05$ ). It thus appears that a significant association exists between age, body weight, gestational age and number of children previously given birth to by pregnant women and the probability that they will be prescribed an antimicrobial agent (Table 1).

Most of the medical case files of those women who received antimicrobials as indicated in Table 1 did not contain any medical diagnosis for which the women were treated. Thus, the number of cases of infections indicated in table 2 below was lower than the number of women that received prescriptions for antimicrobial agents under each category. Upper respiratory tract infection (42; 36.8%) was the most common infection among the three age groups, and amongst all the variables. The other prevalent infections were urinary tract infections and malaria.

There were missing data about the diagnoses in some medical case files even when antimicrobial agents were prescribed. In the treatment of candida; all the pregnant women received nystatin (23) making it the most frequently prescribed sometimes with tioconazole or clotrimazole cream. Monotherapies of amoxicillin, amoxicillin / clavulanate, erythromycin and ampicillin / cloxacillin were medications prescribed in the treatment of upper respiratory tract infection (URTI) with amoxicillin being the most frequently prescribed 75.4% (35/47) of the time. Fifty percent of the cases of urinary tract infections (UTI) were also managed with amoxicillin. Similar medications were used in the management of lower abdominal pain. However, 7 pregnant women were prescribed erythromycin for the management of either URTI or UTI (Table 3).

**Table 1:** Relationship between the characteristics of pregnant women and the frequency of antimicrobial prescription

Variable	No. of women who received antimicrobial agents (%)	No. of women who did not receive antimicrobial agents (%)	P value	X <sup>2</sup>
<b>Age (yr)</b>				
≤ 25	37 (42.5)	50 (57.5)	0.0003	15.948
26 – 35	69 (78.4)	19 (21.6)		
≥ 36	14 (56)	11 (44)		
<b>Gestational age</b>				
1 <sup>st</sup> trimester	11 (23.9)	35 (76.1)	0.002	12.322
2 <sup>nd</sup> trimester	57 (16.9)	337 (83.1)		
3 <sup>rd</sup> trimester	72 (9.7)	671 (90)		
<b>Body weight (kg)</b>				
40 – 60	45 (12)	330 (88)	0.023	9.556
61 – 80	75 (11.6)	572 (88.4)		
81 – 100	30 (12.3)	214 (87.7)		
>100	10 (29.4)	24 (70.6)		
<b>No. of children</b>				
0	13 (20.6)	50 (79.4)	0.028	10.884
1	22 (28.6)	55 (71.4)		
2	9 (20.5)	35 (79.5)		
3	9 (47.4)	10 (52.6)		
≥4	11 (47.8)	12 (52.2)		

**Table 2:** Rates of infections across demographic variables

Variable	n	Infectious cases (n, %)	Candida	URTI	UTI	Malaria	Others
<b>Age (yrs)</b>							
≤25	87	37(42.5)	8	16	4	2	7
26-35	88	64(72.7)	7	19	13	18	7
≥36	25	13(52.0)	0	7	1	5	0
Total			15	42	18	25	14
<b>Gestational age</b>							
1st trimester	46	8(17.4)	0	2	3	2	0
2nd trimester	394	51(12.9)	12	13	11	7	8
3rd trimester	743	40(5.4)	7	15	8	6	4
Total			19	30	22	15	13
<b>Body weight (Kg)</b>							
40–60	375	40(10.7)	6	13	7	7	7
61–80	647	64(9.9)	7	22	9	14	12
≥101	244	29(11.9)	3	10	4	4	8
81–100	34	8(23.5)	0	2	0	3	3
Total			16	47	20	28	30
<b>No. of children</b>							
0	63	13(20.6)	2	6	3	2	0
1	77	18(23.4)	3	7	5	0	3
2	44	6(13.6)	0	2	1	3	0
3	19	11(57.9)	1	4	1	4	1
4	23	5(21.7)	2	3	0	0	0
Total			8	22	10	9	4

URTI: upper respiratory tract infection; UTI: urinary tract infection; Others=LAP: lower abdominal pain, amoebiasis, diarrhea, pyelonephritis etc. Total number of encounters in different patient categories do not tally due to missing data from case notes

## Discussion

Only 14% of the cases reviewed in this study received a prescription for an antimicrobial agent. Considering the high prevalence of infectious diseases in developing countries this appears to be low when compared to the 20-49% reported for developed nations.<sup>9</sup> This was not due to standardized practice because our investigation did not reveal any

antibiotics prescribing protocol that guide the use of antimicrobial agents in the study site. Several factors could therefore, be responsible for the observed low prescription rate; either the prescribers are extremely cautious in ensuring the safety of the fetus or, as we observed earlier, not all cases of prescribed medications were recorded in the medical case files. Hence a high probability exists that in the presence of complete data a higher value may be observed.

**Table 3:** Antimicrobial medications prescribed for the treatment of common infections amongst pregnant women

Medical condition	No. of cases	Amoxicillin	Amoxicillin/ Clavauamic acid	Nystatin	Tioconazole	Metronidazole	Erythromycin	Clotrima-zole	Ampicillin/ Cloxacillin
Candida	23			23	11			11	
URTI	47	35	3				5		4
UTI	20	10	4		1	1	2		2
LAP	10	8				1			1
Cellulitis	4					2			2
Amoebiasis	10	3				10			
Diarrhoea	5	4							1

URTI: upper respiratory tract infection; UTI: urinary tract infection; LAP: lower abdominal pain.

Our result shows that upper respiratory tract infection is the most common infectious medical encounter during pregnancy which is in agreement with results of other studies.<sup>10</sup> Women who had more live children were more likely to receive prescription of antimicrobial agent during pregnancy, signifying that these women had more cases of infections than other women who had less number of children. This result is in agreement with previously reported findings among pregnant Sydney women which indicated that nulliparous women had lower rate of self-reported infection than women who had other children. As children are known to be very susceptible to infection<sup>10</sup>, it could be that women involved in our study contract infections from their infected children.

It was observed that penicillins were the most frequently prescribed antimicrobial agents used in the treatment of infections recorded in this study. It could be due to the fact that the medications are relatively safe in pregnancy and as such, the physicians were comfortable in prescribing them. The use of erythromycin base is considered safe for use in pregnancy and is listed as an FDA category B drug in the United States.<sup>11</sup> However, the use of erythromycin estolate is relatively contraindicated in pregnancy<sup>12</sup> because of possible reversible hepatotoxicity. It was observed that for the management of urinary tract infections, prescriptions of penicillin monotherapy were given to the pregnant women. Although, the clinical outcomes of treatment was not assessed in this study there is the possibility that this medication may not effectively treat the infections. The use of antibiotics is associated with antimicrobial resistance, which is a major challenge in the treatment of infections worldwide.<sup>13</sup> Evidence shows that urinary pathogens isolated from patients attending a diagnostic laboratory in the Southern part of Nigeria were resistant to ampicillin.<sup>14</sup> In a separate study carried out in Ibadan, Adeyemo *et al.* (1994) found a 100% resistance to ampicillin by *E. coli* isolates.<sup>15</sup> Thus, the use of the right antimicrobial agent in the treatment of infections during pregnancy at the study site is advocated. This will minimize unnecessary exposure of the unborn baby to non-efficacious

medications; prevent prolonged treatment and therapeutic failure; and also, prevent progression of the infection to its complications.

Since health talks are given to women during antenatal clinic visits, identification of high risk pregnant women who are susceptible to infections hence more likely to receive an antimicrobial prescription can help to properly target health education interventions.<sup>9</sup>

In all cases reviewed the weight of pregnant women were consistently recorded. This is possibly done to ensure the proper monitoring of the development of the fetus. All other variables such as age (including gestational age) and number of previous live births had incomplete information documentation in the case files. Also prescriptions for antimicrobial agents were written without a properly documented diagnosis. Despite this limitation, the sample of cases reviewed in this exploratory study appears to have been able to detect differences between those women who received a prescription for an antimicrobial agent and those who did not.

## Conclusion

The factors associated with antimicrobial agents' prescriptions in pregnant women are weight, age, trimester and number of previous live births. The most prevalent infectious medical condition requiring an antimicrobial agent was URTI. Amoxicillin was the most commonly prescribed antibiotics. Our findings show that there is need to improve antibiotics selection in this facility. In addition, we advocate proper documentation of patients' data in casenotes which does not only facilitate better patient care but is vital for research and legal issues.

## Declarations

### Conflict of Interest

No conflict of interest associated with this work.

**Contribution of Authors**

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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