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Self-medication of urinary tract infections in Ecuadorian pregnant women: An analysis of its associated factors and complications from cross-sectional data

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Abstract:
Background*: Urinary tract infection is one of the most common infections during pregnancy and its importance lies in the complications that have been reported in the pregnant woman and in the newborn. It is estimated that 40% of women have had a UTI at some time in their lives, and approximately 2-7% of pregnant women present UTI at some time during pregnancy, being more frequent in multiparous women, in low socioeconomic environments and according to age (the older the woman is, the greater her predisposition to this type of infection).2 Asymptomatic bacteriuria (AB) occurs in 17-20% of pregnancies. Self-medication is a worldwide public health problem. In our country, the medical community experiences this problem in all areas of care due to self-medication. In studies carried out by the Ministry of Health, 50% of the Ecuadorian population in urban areas self-medicate and 63% in rural areas. The main objective of the present work is to warn about the importance of the increase in microbial resistance through various mechanisms, one of the best known being the production of extended-spectrum beta-lactamases. In spite of the wide coverage of existing antibiotics to treat urinary tract infection, infection does not disappear in certain cases due to bacterial resistance caused by inadequate self-medication.*
Materials and Methods: *A nationally representative sample of women over 12 years of age from the 2018 National Health and Nutrition Survey was used. Those women who manifested any episode of urinary tract infection, at some point during their pregnancy, were taken into account. In addition, heteroscedasticity and multicollinearity tests were used to rule out possible statistical modeling problems and a binary logistic linear regression model where Odds Ratio (OR) with their 95% confidence intervals (95% CI) were estimated for each of the independent variables. In addition, we used specificity tests to check the fit between our dependent and independent variables.*
Results*: Our results show that income, age, ethnicity, schooling level, and area of residence are important factors that may explain the reason for self-medication in pregnant women. Specifically, we found that pregnant women with low income (OR=1.47), indigenous ethnicity (OR=1.69) and low level of schooling (OR=2.46) predict self-medication. On the other hand, having had a urinary tract infection during pregnancy and having self-medicated produced complications such as heavy bleeding (OR=1.47), isepsis (OR=1.65), strong contractions (OR=1.65), nausea and vomiting (OR=1.65). These results remained relatively unchanged when we used different control variables in the linear regressions.*
Conclusion: *Urinary tract infections (asymptomatic bacteriuria, cystitis and acute pyelonephritis) are the most frequent complications during pregnancy. Therefore, it can be concluded that antibiotics are being used indiscriminately and improperly by pregnant women, without measuring the potential risks of the practice of self-medication. The findings of this research allow us to affirm that there is an urgent need to begin to modify people's behavior regarding the use of antibiotics. Training campaigns should be carried out to make people aware of the importance of not resorting to this practice when their health is undermined, and it should be indicated that they should go to the health services so that a physician can indicate the type and time during which they should take the medication.*
Key Word*: Self-medication, Pregnancy, Bacterial Resistance.*

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I. Introduction

Urinary tract infection in pregnancy is a common cause of perinatal complication and the third leading cause of neonatal sepsis.[1]. In pregnancy, it includes the following clinical entities: Asymptomatic Bacteriuria (AB), Cystitis and Acute Pyelonephritis (AP).[2]. Lower urinary tract infection, specifically AB

affects 2 to 7% of all pregnancies and is detected in the first trimester of gestation in 75% of cases. It is an entity that becomes important since 30-50% of untreated AB will evolve to pyelonephritis in pregnancy, additionally it is related to preterm delivery in 50% of cases, low birth weight in 66% of cases and some studies have reported an increase in the incidence of preeclampsia. Cystitis has not been shown to be related to adverse perinatal outcomes. Similarly, the presence of urinary tract infection has been reported to increase the risk of sepsis and neonatal pneumonia.[3].

Urinary tract infections (UTI) are one of the most common infectious complications of pregnancy. In Ecuador, in 2014, genitourinary conditions in pregnancy were reported with 8.08% of the rate per 10,000 inhabitants and ranked eighth in relation to the 10 leading causes of morbidity and mortality.[4]. It is estimated that 30 to 50% of pregnant women with asymptomatic bacteriuria will subsequently develop clinical manifestations of symptomatic infection, such as fever, dysuria, frequency and urgency; many of them will progress to urinary tract infection.[5]Many of them will progress to pyelonephritis, which in turn may be associated with acute renal failure, sepsis and septic shock.[6]. Pyelonephritis occurs with a frequency of 2 to 4% among pregnant women and is usually accompanied by fever, costovertebral pain and pyuria.[7]. The microorganisms involved are mainly enterobacteria, among which are: Escherichia coli , Klebsiella sp, Proteus mirabilis and Enterobacter sp. In addition, there are some Gram-positive cocci that are frequent etiological agents, such as Staphylococcus saprophyticus and Enterococcus faecalis.[8]. Escherichia coli is present in approximately 80 to 90% of urinary tract infections.[9].

Antibiotic resistance, a serious global health problem, has caused many diseases to stop responding to commonly used antibiotics. To this end, in 2015, the World Health Organization approved a global action plan aimed at protecting these medicines for future generations through five strategic objectives: improving awareness and knowledge of antimicrobial resistance; strengthening surveillance and research; reducing the incidence of infections; optimizing the use of antimicrobials; and ensuring sustainable investments in the fight against antimicrobial resistance.[6]. In some series, bacterial resistance of Escherichia coli to antibiotics such as ampicillin is between 28-39%, to trimethoprim-sulfamethoxazole 31%, to cephalosporins between 9 to 19% and to cefuroxime at 1%.[10]. Therefore, the use of ampicillin for the initial treatment of urinary tract infection has been questioned due to its high rates of bacterial resistance in the different populations studied.[11].

Bacterial resistance of Escherichia coli to antibiotics is related to the consumption of antibiotics, favors the creation, adaptation and dissemination of antimicrobial resistance mechanisms whose increasing prevalence makes it essential to rationally guide the empirical treatment of urinary tract infection in the out-of-hospital setting, which is a common and recommended practice.[12]. The resistance of pathogens to antimicrobial agents is a problem of extreme importance for the selection of the ideal first-line antibiotic, showing variations and requiring constant updating, microbiological surveillance of the antibiotic sensitivity of the main uropathogens that affect our environment. The fear of self-medication, mainly in pregnant women, is the complications that it entails, mainly due to antimicrobial resistance. As we have already mentioned, the main complications in pregnancy range from asymptomatic bacteriuria with deleterious effects on maternal and fetal comorbidity such as pyelonephritis, low birth weight and high mortality.[13]. Maternal sepsis due to UTI has gained prominence in developed countries despite the introduction of antibiotic therapy, and the systematic use of infection control measures in health care. However, maternal sepsis due to UTI unfortunately still results in high maternal comorbidity, including death.[14].

Taking into account the high number of patients who come to our offices with urinary symptoms and most of them with recurrences in spite of the antibiotic treatment applied, we proposed to carry out a study to update the prevalence of community urinary tract infection in our environment and the susceptibility to the antimicrobials used in empirical treatment. However, little is known locally about antibiotic susceptibility in pregnant patients with urinary tract infection. The aim of the present work is to determine the antibiotic resistance profile for the germs most frequently implicated in urinary tract infection during pregnancy.

II. Material And Methods

Study Design and Population: A cross-sectional study was conducted with data obtained from the 2018 National Health and Nutrition Survey of Ecuador (ENSANUT), whose data were obtained and presented by the National Institute of Statistics and Census (INEC). After cleaning the database, a total of 20182 Ecuadorian women, of childbearing age older than 10 years old up to 49 years old, were obtained.

Inclusion and Exclusion Criteria: Data from women between the ages of 10 and 49 years of childbearing age were included. Women who did not self-medicate for urinary tract infections were excluded.

Source of Information: The ENSANUT 2018 is a survey included in the National Statistical Program that employs probability sampling applied every 5 years and whose target population is all household members in the 24 provinces of Ecuador. The ENSANUT 2018 includes the form HOGAR where all the characteristics of the Ecuadorian population are evidenced to make representative estimates at the national level, urban-rural, by

geographic domain for the 24 provinces of the country. In addition, the anthropometric measurements of women who self-medicated when they suffered urinary tract infection can also be found.

Study Variables. Our dependent variable is the question of whether a woman self-medicated during pregnancy when she had a urinary tract infection (coded 1 and 0 otherwise). In addition, we used other variables as possible predictors of self-medication such as wages, region of origin, age, ethnicity, marital status, educational level, employment status, urban density, economic development of the province, area of residence.

Statistical Analysis. The ENSANUT 2018 survey database was analyzed with the statistical package Stata v15 (Stata Corporation, College Station, Texas, USA). A value of $p<0.05$ was considered to determine statistical significance between variables. Discrete choice linear models were used to determine the overall correlation between the variables of interest. The association was evaluated using prevalence ratios with their respective 95% confidence intervals with an analysis for each of the variables included in the study, with the independent variable of interest being the sociodemographic conditions of each participant. Specifically, the following equation was used to evaluate the predictors of urinary tract self-medication during pregnancy:

$$Urinary\ tract\ self-medication_i = \beta_0 + \beta_1 X_i + \sum_{j=2}^{12} \beta_j Z_i + \varepsilon_i \quad (1).$$

Where $Urinary\ tract\ self-medication_i$ represents whether a woman self-medicated when she had a urinary tract infection, X_i represents a set of sociodemographic variables, and Z_i represents a set of territorial control variables. Finally, ε_i represents the stochastic error term.

III. Results

First, we performed exploratory statistics on the different questions regarding urinary tract self-medication in pregnant women. Table 1 shows that the percentage of women who reported having had a urinary tract infection was 72.32%. This means that a large number of women have suffered from this disease. In addition, 37.88% of women reported that they self-medicate (if we add the three categories that refer to self-medication), while 52.23% of pregnant women reported that they did visit a health center. This fact is worrisome, since more than one third of pregnant women do not use a health center or a specialized physician to treat this type of relatively serious ailment.

Table 1. Percentage of women reporting urinary tract infection and self-medication in pregnant women.

Variable and response	Percent
Urinary tract infection during pregnancy	
Yes	72.32%
No	27.68%
To whom did you go first when complications (urinary tract infection) occurred during pregnancy?	
Health facility or health personnel	52.23%
Pharmacy or apothecary	16.56%
Stayed at home/home remedies	13.21%
Traditional personnel (midwife, yachac, shaman, curandero)	8.11%
Other, which one?	9.43%

Table 2 below shows the descriptive statistics of the sociodemographic variables used for the linear regression model. Here we observe that the average labor income of the women is $422 USD, 42.7% of the women are from the highland region, the average age is 28.34 years and 81.03% of the women are mestizo. In addition, 40.7% of the women are single and 38.1% are married. We also note that 43.4% of the women have a high school education and 64.57% of the women are employed. Regarding territorial characteristics, we observe that on average there are 151 inhabitants per square kilometer, the provincial gross value added (economic development) is on average $1297.65 USD and 59.33% of the women live in the urban area.

Table 2. Descriptive statistics of the variables used in this study.

Variable	Mean-Percent	Min	Max	95% CI		
Labor income						
Income in dollars	422.12	0	30	403.27	-	415.45
Region of origin						
Sierra	38.5%	0	1	38	-	39

Costa	42.7%	0	1	41.21	-	43.09
Amazon	16.3%	0	1	15.98	-	17.01
Galapagos	2%	0	1	1.96	-	2.51
Age						
Age in years	28.34	14	41	24.12	-	32.54
Ethnicity						
Indigenous	7.1%	0	1	6.6	-	7.28
Afro-Ecuadorian	5.3%	0	1	4.90	-	5.98
Mongrel	81.03%	0	1	80.22	-	81.86
White	1.4%	0	1	1.2	-	1.9
Montubio or Others	4.6%	0	1	4	-	5.1
Marital status						
Married	38.1%	0	1	38	-	39
Single	40.7%	0	1	41.21	-	43.09
Widow	18.3%	0	1	15.98	-	19.01
Divorced	2%	0	1	1.96	-	2.51
Educational level						
None	0.7%	0	1	0.3	-	1.1
Basic Education	27.3%	0	1	27.1	-	28.3
Middle/High School Education	43.4%	0	1	43.41	-	44.12
Higher Education	27.1%	0	1	26.87	-	27.98
Employment status						
Employee	64.57%	0	1	17.97	-	19.12
Unemployed	35.43%	0	1	80.05	-	82,66
Urban density						
Inhabitants per square kilometer	151.01	1152.5	321	146.32	-	160.33
Economic development of the province						
Provincial GVA per capita	1297.65	540.5	321	836.43	-	1456.67
Area						
Urbana	59.33%	0.54	0	55.51	-	61.51
Rural	44.49%	0.36	0	41.49	-	46.49

Next, we performed a formal test to rule out the presence of multicollinearity among our independent variables. In **Table 3** we present a multicollinearity analysis. We use the Variance Inflator Factor (VIF) to perform this test. Previous literature indicates that a VIF greater than 5 can demonstrate that there is multicollinearity in our data. As we can see, no variable presents a VIF greater than 5, therefore we discard multicollinearity problems in our independent variables. This analysis is important since multicollinearity problems cause instability of the parameters of a regression, incorrect signs and higher standard errors, which translates into statistical insignificance of the parameters.

Table 3. Multicollinearity test of the estimated model

Variable	VIF	SQRT VIF	Tolerance	R-Squared
Labor income	1.88	1.75	0.8872	0.0227
Region of origin	1.25	1.22	0.2221	0.1188
Age	1.88	1.75	0.8872	0.0227
Ethnicity	1.77	1.22	0.2212	0.1122
Marital status	1.22	1.85	0.7210	0.2780
Educational level	1.12	1.27	0.8127	0.0252
Employment status	1.22	1.74	0.8827	0.2252
Urban density	1.57	1.85	0.7210	0.2780

Economic development of the province	1.44	1.75	0.8752	0.0252
Area	1.72	1.11	0.8875	0.2087
Mean VIF	1.82			

Next, to further explore the pattern found in **Table 1,** we performed a linear regression analysis to observe and analyze the influence of various sociodemographic factors on the likelihood of self-medicating a urinary tract infection. For this we used a logit model as shown in **Table 4.** In the table, the dependent variable is the dichotomous variable that takes the value of 1 if a woman reported self-medicating a urinary tract infection during pregnancy. Here we observe that, there are negative odd ratios of some variables. For example, income has a negative influence on the probability of self-medicating during pregnancy. This occurs because women with higher income are more likely to attend or pay for a doctor. Specifically, an increase in income decreases 2 times the probability of self-medicating during pregnancy (OR= 2.078, CI= 2.035; 2.086). Other variables with positive odd ratios are age, married, widowed and divorced marital status. We also observed that a higher educational level decreases the probability of self-medicating during pregnancy. This is because more educated women are aware of the risks of self-medication during pregnancy. On the other hand, being unemployed increases the probability of self-medicating, while living in a denser urban area with a higher level of economic development decreases the probability of self-medicating.

Table 4. Logistic regression analysis between Pap smear performance and socioeconomic factors

	OR	P-value	95% CI
Var. dep.: if urinary tract infection = 1, 0 otherwise			
Labor income			
Income in dollars	-2.078*	0.035	-2.035--2.086
Region of origin			
Sierra	Ref.		
Costa	-1.083*	0.030	-1.010--1.369
Amazon	1.511	0.149	1.002-1.824
Galapagos	2.402	0.152	2.322-2.575
Age			
Age in years	0.822*	0.035	0.521-1.128
Ethnicity			
Indigenous	Ref.		
Afro-Ecuadorian	1.035	0.932	1.003-1.056
Mongrel	0.933**	0.006	0.626-2.086
White	0.903	0.864	0.276-1.071
Montubio or Others	0.818	0.620	0.692-0.991
Marital status			
Married	Ref.		
Widow	0.693	0.799	0.593-1.770
Divorced	0.976	0.981	0.083-2.034
Educational level			
None	Ref.		
Basic Education	2.262	0.125	2.221-2.860
Middle/High School Education	2.337	0.109	2.191-2.889
Higher Education	-2.783*	0.060	-2.042- -2.889
Employment status			
Employee	Ref.		
Unemployed	1.099	0.634	1.0093-1.482
Urban density			
Inhabitants per square kilometer	-1.654**	0.023	-1.570--7.242
Economic development of the province			
Provincial GVA per capita	-1.092**		-1.017--2.097
Area			
Urbana	Ref.		
Rural	1.456	0.123	1.570 - 1.242
Constant	5.790***	0.007	5.472-5.940
Observations	20182		
AIC	1848.35		
BIC	2011.41		
Chi^2	152.4		
Chi^2 *p-value*	0.000		
Log-likehood	-898.174		

Notes: Asterisks mean: *p <0.10,**p < 0.05, ***p < 0.01.

Then, the confusion matrix of the model is shown. In **Table 5** we can see that the model we estimated is correctly specified. In the model we use as the dependent variable denoting whether a woman self-medicated during pregnancy for a urinary tract infection, which is 75.12% specified by the independent variables. That is,

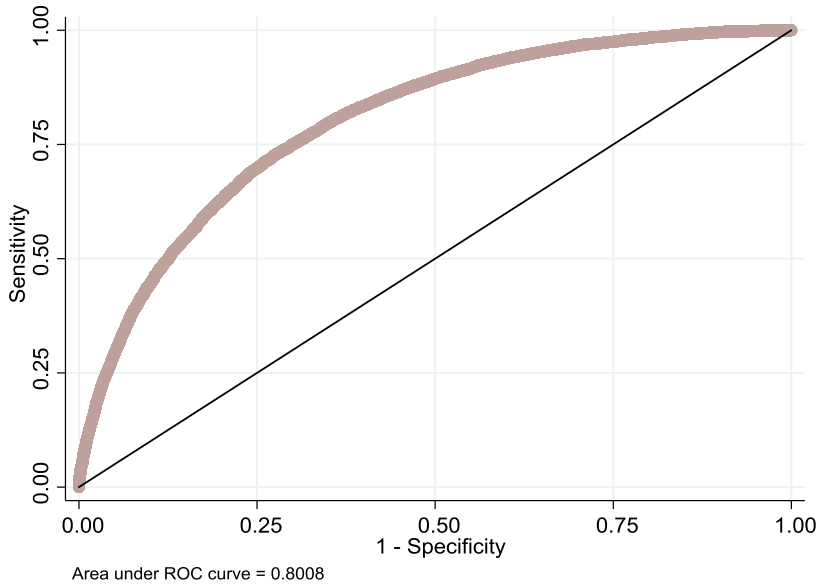
the independent variables predict that a woman will self-medicate during pregnancy in 75.12% of the cases. It is worth mentioning that this percentage is relatively high, being an acceptable level higher than 60%.

Table 5. Confusion matrix of the estimated models

Model of hormonal contraceptive methods			
	True		
Classified	D	~D	Total
	3281	1423	1689
	2451	2231	6987
Total	4288	2966	5785
Correctly classified			75.12%

Finally, to determine the fit and explanation of the independent variables, the ROC curve was applied with the probabilities estimated by applying logistic regression. The ROC curve in **Figure 3** coincides with the probability of correctly distinguishing a case of a woman who self-medicated during pregnancy from another who did not, through the significant predictor variables, with the worst case scenario being when the area is equal to 0.50. In our case, the significant variables, such as family income, the woman's schooling, being employed and urban density, represented an area under the curve of 0.80880 (95% CI: 0.752-0.854), considering that they adequately predict (positively or negatively) the cases of women who did self-medicate during pregnancy ($p < 0.001$).

Figure 3. ROC curve of the estimated model.



IV. Discussion

Urinary tract infection is one of the most frequent medical complications in pregnancy; the physiological changes associated with pregnancy predispose to the development of complications that can significantly affect the mother and fetus. Despite the development of new antibiotics, urinary tract infection continues to be associated with high maternal and fetal morbidity and mortality.[15]. In the treatment of urinary tract infection during pregnancy, ampicillin has been used as the antibiotic of first choice since the 1970s.[16]This drug is dispensed freely and without prescription, which is why currently, it has been shown that ampicillin is not useful due to the high rates of resistance in our environment, in addition, its absorption decreases by 50% during pregnancy.[17]. Based on the above, our results showed that 37.88% of the women reported that they self-medicate (if we add the three categories that refer to self-medication), while 52.23% of pregnant women reported that they did go to a health center. This fact is worrisome, since more than one third of pregnant women do not use a health center or a specialized physician to treat this type of relatively serious ailment.

Another important factor is that income has a negative influence on the probability of self-medicating during pregnancy. This occurs because women with higher income are more likely to attend or pay for a doctor.

Specifically, an increase in income decreases 2 times the probability of self-medicating during pregnancy (OR= 2.078, CI= 2.035; 2.086). Other variables with positive odd ratios are age, married, widowed and divorced marital status. We also observed that a higher educational level decreases the probability of self-medicating during pregnancy. This is because more educated women are aware of the risks of self-medication during pregnancy. On the other hand, being unemployed increases the probability of self-medicating, while living in a denser urban area with a higher level of economic development decreases the probability of self-medicating, results that coincide with the research of Bello et al., 2011, in which he refers that the risk factors previously described for self-medication in pregnant women were: unemployed women, underemployed women, and women in the third trimester of pregnancy. Likewise, a high level of education and being married were protective factors for self-medication.[18].

Another important result was that a higher level of education decreases the probability of self-medication during pregnancy. This fact occurs because more educated women are aware of the risks of self-medication during pregnancy, results that coincide with the work of Mikou S, Buire AC and Trenque T, 2008, in which he mentions that many pregnant women do not have adequate knowledge of the possible adverse effects that they or their baby could suffer; moreover, previous studies show that the information provided by health personnel on the possible teratogenic risk of over-the-counter drugs is insufficient.19. Regarding self-medication, we can observe that the independent variables predict that a woman will self-medicate during pregnancy in 75.12% of the cases. It is worth mentioning that this percentage is relatively high, being an acceptable level higher than 60%. Taking into account the recommendation not to use an antibiotic empirically when its resistance to a germ exceeds 20%, we do not recommend the use of ampicillin as the antibiotic of first choice in urinary tract infection in pregnant patients. The mechanisms of resistance acquired by different bacteria have caused the response to treatment to be different; from which derives the importance of following up the management of these infections and controlling the indiscriminate use of antibiotics, the pathogenic flora and the resistance index.

V. Conclusión

The choice of an antibiotic for the treatment of urinary tract infection during pregnancy requires knowledge of the most frequent germs and their bacterial resistance profile. Ampicillin should be eliminated as an initial therapeutic option given the high resistance rate of the most frequent pathogens. In our population, knowledge of the resistance profile of the germs most frequently involved in urinary tract infection during pregnancy allows us to choose the best available treatment and guarantee a high rate of therapeutic success. To prevent the negative effects of self-medication, we should educate patients and the population in general, provide information and counseling on the proper use of medications and ensure that before prescribing a medication, without being authorized to do so, the possibility of early pregnancy and the damage that could be caused should be considered, leaving this act of double responsibility to the physician. Preventive programs based on direct work with patients, educational talks and sessions where personal experiences are presented may constitute an alternative solution. Self-medication is a public health problem, much more so if it is related to any stage of pregnancy; inevitably, it is necessary to carry out intervention studies aimed at reducing the rates of self-medication in the general population and, especially, in pregnancy. The tool to achieve this will be prevention, but it will have to be prevention with education, since self-medication during pregnancy constitutes an act of double irresponsibility, since it can have consequences for the mother and the product.

Antimicrobial resistance is increasing worldwide to dangerous levels. New resistance mechanisms are appearing and spreading around the globe day by day, jeopardizing our ability to treat infectious diseases. The general population should: take antibiotics only when prescribed by a certified professional; not demand antibiotics that are not necessary; prevent infections by washing hands, preparing food hygienically, avoiding intimate contact with sick people, ensuring safe sex and keeping vaccinations up to date. Health policy planners in different countries should: Implement national antibiotic resistance action plans; improve surveillance for antibiotic-resistant infections strengthen policies, programs and implementation of infection prevention and control measures; regulate and encourage appropriate use of quality-assured medicines; report on the impact of antibiotic resistance; invest in research and development of new antibiotics, vaccines, diagnostics and other tools. Healthcare professionals can*:* Prevent infections by ensuring clean hands, instruments and environment; prescribe and dispense antibiotics only when necessary and use *Clinical Practice Guidelines* created by experts; report resistant infections to epidemiological surveillance teams and educate patients on this topic.

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