TITLE: Prevalence and Risk Factors for Infections in a Pregnant Adolescent Population

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ABSTRACT

Study Objective

Our objective was to identify risk factors associated with maternal infections and placental inflammation in pregnant adolescents attending an urban adolescent maternity clinic.

Design

This cross-sectional, descriptive study used survey and medical chart data collected at entry and prospectively across gestation. The prevalence of maternal infections and placental inflammation was determined and potential risk factors were identified.

Setting

Rochester Adolescent Maternal Program (RAMP) in Rochester, NY

Participants

Racially and ethnically diverse pregnant adolescents ($n=158 \leq 18$ y at entry) were recruited.

Main Outcome Measures

Main outcome measures were diagnosis of an infection or inflammatory condition in relation to demographic, anthropometric, dietary, socioeconomic, and health data.

Results

The three most prevalent infections diagnosed in this study population were recto-vaginal colonization of group B Streptococcus (GBS) (38%), bacterial vaginosis (BV) (40%) and candida (42%). African-American teens (AOR=4.6; 95% CI: 1.74-13.02) and those with higher pre-pregnancy BMI (ppBMI; AOR=1.2; 95% CI: 1.04-1.31) were more likely to test positive for BV across gestation. Older maternal age decreased the likelihood of positive tests for trichomoniasis (OR=0.51; 95% CI: 0.26-0.92) and gonorrhea (OR=0.38; 95% CI: 0.16-0.82).

Higher mean dietary vitamin D intake (mcg/d) was associated with a lower likelihood of testing positive for recto-vaginal GBS (OR=0.87; 95% CI: 0.77-0.98).

Conclusions

Addressing modifiable risk factors associated with dietary intake and pre-pregnancy weight may help reduce health disparities among pregnant minority adolescents. Additionally, targeted sexual health education may greatly benefit younger female adolescents.

Keywords: pregnancy; sexually transmitted infections; adolescents; minority health

INTRODUCTION

The U.S. teen pregnancy rate remains the highest among developed countries (57 pregnancies per 1,000 females ages 15-19 years)¹ with Hispanic and African-American teens comprising the majority of this population.² Unplanned pregnancies pose significant challenges to reproductive health as they have been linked to risky sexual behaviors³ and adverse infant health outcomes.⁴ Compared to young adult women (aged 20-24 years), pregnant teens are more likely to be unmarried, have inadequate prenatal care, and not achieve recommended pregnancy weight gains. In addition, neonates born to teens are at greater risk for low Apgar scores, prematurity, and increased risk of neonatal mortality.⁵

During pregnancy, sexually-transmitted, urogenital, and placental infections are of major concern. U.S. teens and young adults (15-24 years old) compromise 50% of new sexually-transmitted infection (STI) cases each year.⁶ Maternal infections during pregnancy and their transmission to the neonate during labor and delivery have been linked to adverse health outcomes, including premature birth,⁷ low birth weight (LBW) (<2500 g),⁸ and newborn lung and eye infections.⁹ Therefore, the Centers for Disease Control and Prevention (CDC) recommends screening all pregnant females for chlamydia, hepatitis B, human immunodeficiency virus (HIV), and syphilis over the course of pregnancy and those deemed high-risk should also be screened for gonorrhea and hepatitis C.¹⁰ In addition, screening for recto-vaginal group B streptococcal colonization (GBS) is recommended for all pregnant women between 35-37 weeks of gestation.¹⁰ In contrast, some infections such as bacterial vaginosis (BV) are not routinely screened for during pregnancy despite a growing body of research linking BV to undesirable birth outcomes.¹¹

Most of the research exploring infection risk factors has focused on adult populations and risk factors vary depending on the infection in question. Previously identified risk factors for BV include low socioeconomic status, race, smoking, higher body mass index (BMI), having a past pregnancy, and increased number of sexual partners.^{12, 13} Urinary tract infections are common during pregnancy, and the American College of Obstetrics and Gynecology (ACOG) recommends screening all pregnant women for asymptomatic bacteriuria during the first prenatal visit and third trimester.¹⁴ Prior studies have reported several risk factors for urinary tract infections (UTIs) occurring over pregnancy, including pre-eclampsia, hypertension, low socioeconomic status, and anemia.¹⁵ Younger age^{16,17} and the consumption of fruit juices and milk products containing probiotics has also been associated with a reduced risk of recurrent UTIs in non-pregnant adult women.¹⁸

Much less is known about risk factors in other age groups and little is known about these relationships in pregnant adolescents, a population which is at increased risk for STIs and adverse neonatal outcomes. The primary objective of this study was to describe the prevalence of, and identify potential risk factors (health behaviors, demographic, socioeconomic, anthropometric, and dietary) for common infections across gestation in a racially and ethnically diverse group of pregnant adolescents (≤ 18 years of age).

MATERIALS AND METHODS

Study Population

A group of 158 pregnant adolescents (≤ 18 years old) were recruited from the Rochester Adolescent Maternal Program (RAMP) in Rochester, New York from 2006-2009 for a study designed to examine maternal and fetal bone health. Adolescents were recruited in proportion to

the racial and ethnic composition of the patient population (65% African American, 35% Caucasian, and 25% Hispanic) (**Table 1**). All eligible adolescents were approached by the study coordinator, and the majority agreed to volunteer to participate in this research study. Participants were eligible for the study if they were between 12 and 30 weeks gestation at entry, carrying a single fetus, and at least 13 years of age. Additional eligibility and exclusion criteria have been previously described.¹⁹ Adolescents were longitudinally followed from study entry until delivery and medical chart data were abstracted from entry into prenatal care until delivery. Informed written consent was obtained from all participants after fully explaining the study and study procedures in accordance with the institutional guidelines. The study was approved by the Institutional Review Boards at Cornell University and the University of Rochester.

Data Collection

At study entry, key health and demographic data were obtained by the study health project coordinator as previously described.¹⁹⁻²⁰ Socioeconomic status indicators assessed included health insurance, participation in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), or welfare/public assistance programs. Self-reported risk taking behaviors (before and during pregnancy) were queried, including use of alcohol and cigarettes categorized as never used, prior use, or current use. Self-reported use of marijuana as well as “other drugs” (cocaine, stimulants, sedatives, and narcotics) were described as ever used versus never used before or during pregnancy. Birth control use (yes/no) prior to conception was ascertained. Pre-pregnancy body mass index (ppBMI) was calculated and categorized as underweight ($<18.5 \text{ kg/m}^2$), normal weight ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($\geq 25.0 \text{ kg/m}^2$), or obese ($\geq 30.0 \text{ kg/m}^2$) using self-reported height and weight following the World Health Organization guidelines.²¹

Adolescents attended up to three prenatal study visits, at which time maternal anthropometrics and all survey instruments were completed. The mean micronutrient and macronutrient intakes were obtained using a 24-hour dietary recall and the estimated average requirement (EAR) and acceptable macronutrient distribution range (AMDR) were used to classify adequate vs. inadequate nutrient intake as previously described.²⁰ A prenatal supplement survey was used to assess frequency of supplement as daily vs. not daily for analysis purposes.

Data on 18 pre-defined infections and inflammatory conditions were abstracted from the participant's prenatal medical records (STIs, UTIs, vaginal infections, placental inflammatory conditions, and other viral and bacterial infections) by our study health project coordinator. The prevalence of each condition was calculated and presented in **Table 2**. For each condition reported, the date of clinician diagnosis or date of laboratory results for the condition and prescribed treatments were recorded. Classifications used for conditions monitored were determined by obstetrics and gynecology clinicians and co-authors at the University of Rochester Medical Center (URMC).

Statistical Analysis

Potential determinants of infections and inflammatory conditions including: demographic factors (race, ethnicity, maternal age at time of infection diagnosis, age at menarche, gynecological age at conception), socioeconomic status (SES) (WIC participation, use of public assistance, and health insurance participation), anthropometric factors (ppBMI), dietary factors (micronutrient and macronutrient intake), and health behaviors (self-reported use of prenatal supplements and substance abuse behaviors) were assessed using chi-square test of independence for categorical variables and bivariate logistic regression for continuous variables. Fisher's exact

test was used when data in cross tabulations were sparse or unbalanced ($n < 5$). Outcomes of infection (positive/negative) and inflammation (presence/absence) were analyzed as categorical variables while potential risk factors were analyzed as either categorical or continuous variables. Multiple logistic regression was used to simultaneously assess the association of multiple risk factors on infection outcomes. Results were considered statistically significant at $P < 0.05$. All analyses were performed using JMP 11.0 (SAS Institute).

RESULTS

In this study population, 73% (114/157) of teens were enrolled in WIC, 18% (22/121) used public assistance programs, and 91% (143/158) had some form of health insurance. Most of the teens 68% (108/158) reported that they had obtained at least a 10th grade or higher level of education. From among the indicators of socioeconomic status available, none were significantly associated with the outcomes of interest.

Of the infections and inflammatory conditions presented in **Table 2**, 30.4% (48/158) of teens had at least one diagnosed STI, 25.3% (40/158) had one, 3.8% (6/158) had two, and 1.3% (2/158) had three STIs across gestation. For the 64% (101/158) of teens found to have at least one vaginal infection, 45.6% (72/158) had one and 18.4% (29/158) had two recorded diagnoses across gestation. For teens that had their placentas sent to pathology at delivery due to medically indicated concerns, 60% (27/45) had pathologic evidence of placental inflammation. The odds of having a vaginal infection were 2.4 times higher in those with a STI (OR=2.4; 95% CI: 1.1-5.4) compared to teens who were not diagnosed with a STI during pregnancy.

Significant associations between study outcomes and maternal race, age at conception, and maternal age were noted. The unadjusted odds of having bacterial vaginosis were 4 times higher

in African Americans compared to Caucasians (OR=4.0; 95% CI: 1.59-10.37). The odds of testing positive for at least one of the following STIs: chlamydia, gonorrhea, and trichomoniasis were 3.7 times higher for African-American teens. For every 1 year increase in age at conception, the odds of having tested positive for trichomoniasis decreased by 0.51 (OR=0.51; 95% CI: 0.26-0.95) and the odds of testing positive for gonorrhea decreased by 0.35 (OR=0.35; 95% CI: 0.16-0.80). Because maternal age and age at conception are highly correlated ($P<0.0001$), similar associations were found between maternal age and testing positive for trichomoniasis and gonorrhea (**Table 3**).

Prior and current history of substance use was reported as follows: 32% (51/158) prior and 0.6% (1/158) current use of alcohol, 13% (21/158) prior and 11% (17/158) current use of cigarettes. In addition, 30% (48/158) and 3.2% (5/158) of teens reported use of marijuana or other drugs, respectively, sometime throughout their life. No significant associations were evident between drug and alcohol use and any of the outcomes monitored.

In this study population, approximately 50% of teens reported taking their standard prenatal supplements daily across gestation.²⁰ No significant relationship was observed between infection outcomes as a function of supplement use.

As previously published, the majority (70-90%) of these teens did not meet the EAR for several essential micronutrients.²⁰ No associations were found between macronutrient intake or water soluble nutrients and infection outcomes. However, low intake of two fat soluble vitamins (A and D) was associated with increased risk for placental chorioamnionitis and recto-vaginal GBS, respectively (**Table 3**).

Table 1 displays the distribution of ppBMI in the adolescents based on WHO classifications. Compared to underweight and normal weight teens, overweight and obese teens

had a 3.3 times greater odds of testing positive for BV (OR=3.3; 95% CI: 1.28-9.31). Because of this association, additional risk factors for BV were also adjusted for ppBMI and findings remained statistically significant. These adjusted odds ratios are presented in **Table 4**.

DISCUSSION

In this group of 158 pregnant adolescents, candida, bacterial vaginosis, recto-vaginal GBS, and cystitis were the four most commonly diagnosed infections. Because not all of these infections are routinely screened as part of standard obstetrical care and many are asymptomatic, our prevalence data likely underestimate the true prevalence of these infections in this pregnant adolescent population.

Limited data exist on STI prevalence in adolescent pregnant populations. Using the 2003-2004 NHANES data, we found that the estimated prevalence of STIs in our study population was higher than the weighted prevalence reported among sexually-experienced females in the U.S. aged 14-19 years for gonorrhea (3% vs. 2.5%), chlamydia (13% vs. 7.1%), and trichomoniasis (7.0% vs. 3.6%), but lower for genital herpes (1% vs. 3.4%) and human papillomavirus (HPV) (7.6% vs. 29.5%).²² The lower prevalence of HPV in these pregnant teens compared to the 2003-2004 national data is possibly a result of HPV vaccine administration in the U.S. since mid-2006 and changes in screening guidelines. In contrast, risk of BV in our study population was 25% higher than NHANES data (2001-2004) in which a 29.2% prevalence of BV was evident in women 14-49 years old.¹²

The prevalence of sexually transmitted infections such as chlamydia and gonorrhea is known to be higher among teens and young women.²³ Our findings have identified younger maternal age as a risk factor for infection with gonorrhea and trichomoniasis. These findings

differ from national data that found older women (20-24 years) have a higher prevalence than adolescent females 15-19 years old,²⁴ and from NHANES 2003-2004 data that reported a significantly higher STI prevalence among 18-19 year old females when compared to 14-15 year old adolescent females.²² Both of the national comparative data were not focused on pregnant adolescent populations. It is possible that disparities in STI prevalence exist between non-pregnant and pregnant adolescent populations and that the latter group may exhibit higher risk sexual behaviors especially at a younger age.

Finally 26% of teens in our study had a UTI (25% cystitis and 1% had pyelonephritis). Women, especially those who are pregnant are at an increased risk for UTIs.²⁵ Although asymptomatic bacteriuria (ASB) in non-pregnant women is relatively benign, ASB along with elevated progesterone levels during pregnancy can increase the risk of pyelonephritis.^{26, 27} While ASB is thought to be present in 2-10% of all pregnant women,²⁸ prevalence data on acute cystitis is limited. Current estimates for symptomatic UTIs are limited but 1-3% of pregnant females are believed to have acute cystitis and 0.5-2% have acute pyelonephritis.²⁹

No associations were found between the socioeconomic risk factors assessed and the infection outcomes. Previous research has found that fewer years of education and having Medicaid insurance are associated with higher prevalence of BV among non-pregnant women.³⁰ We found no association between health insurance status and outcomes, which may be due to limited variability in the types of insurance used as 69% of teens with insurance used some form of Medicaid and only 10% reported no insurance. No data on family income was obtained which might have provided additional information on socioeconomic status.

In this study, African-American race was significantly correlated with increased risk of BV. A similar association between African-American race and BV was reported in a study of

298 non-pregnant women receiving care at a county health department site.³⁰ Using data from NHANES III, young adult African Americans have been shown to have a higher prevalence of chlamydia, gonorrhea, and trichomoniasis compared to whites.³¹ We were unable to find an association between race and individual STIs but when these three STIs were combined into one category, the odds of testing positive for at least one of the three STIs was 3.7 times higher in African American teens.

Higher maternal ppBMI has been linked to increased risk of several adverse birth outcomes.³² In this teen cohort, higher ppBMI was associated with increased risk BV. In non-pregnant women and men, obesity has been linked to a variety of infections: UTIs,³³ periodontitis,³⁴ and influenza A (H1N1).³⁵ Although the exact biological mechanisms underlying the observed associations between obesity and infection risk remain unclear, immune system dysregulation has been hypothesized.³⁶

In these adolescents 38% had recto-vaginal colonization of GBS a higher prevalence than the 25% reported among U.S. pregnant women.³⁷ We observed an association between low maternal dietary vitamin D intake and increased odds of testing positive for recto-vaginal GBS which may be due to the known effects of vitamin D on innate and adaptive immunity³⁸ and the lower vitamin D status found among minority pregnant women³⁹ and adolescents.⁴⁰

Poor maternal intake of the vitamin A was associated with an increased risk of chorioamnionitis, an inflammation of the placenta due to bacterial infection. Vitamin A is a micronutrient widely believed to have anti-inflammatory effects,⁴¹ and our findings with chorioamnionitis suggest that vitamin A may also be important in mediating pregnancy-specific inflammatory conditions.

Our retrospective, cross-sectional study had several limitations. We used self-reported dietary intake data which is subject to both under- and over-reporting and that may be more challenging to recall in an adolescent population. With this study design, we are unable to infer a causal relationship for any of the significant associations noted. Furthermore, it is difficult to describe the prevalence of these infections as being unique to pregnancy as some infections may have been contracted prior to pregnancy. Moreover, in teens diagnosed with multiple infections across gestation, it is not always known if the second diagnosis of the infection is a new incident infection or simply represents failure to effectively treat the prior infection as not all teens are re-tested post-treatment.

To our knowledge, this is the first study to explore risk factors for a wide range of diagnosed infections in a pregnant adolescent population receiving age-appropriate care from a prenatal adolescent clinic. This group of racially and ethnically diverse pregnant adolescents exhibited a higher prevalence of several sexually transmitted and vaginal infections compared to data from non-pregnant teen and adult populations. Several risk factors for infections and inflammatory conditions across pregnancy were identified including: African-American race, higher pre-pregnancy BMI, younger age at diagnosis, and low intake of fat-soluble vitamins A and D. Further research is needed to understand the biological mechanisms which may be underlying the observed associations. These data may be useful for clinicians and sexual health educators who seek to reduce the infection burden among pregnant adolescents. In addition, these results support the need for promoting modifiable dietary and weight gain recommendations for improved maternal health.

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Table 1: Subject Characteristics of the 158 Pregnant Adolescents^a

Characteristics	Value
Age at enrollment (years)	17.1 ± 1.1 (158)
Race, %	
African American	63.3 (100/158)
Caucasian	35.4 (56/158)
Native American	1.3 (2/158)
Ethnicity, %	
Hispanic	24.7 (39/158)
Non-Hispanic	75.3 (119/158)
GA at entry into prenatal care (wks)	10.5 ± 4.7 (137)
GA at delivery (wks)	39.2 ± 3.0 (152)
Pre-pregnancy BMI (ppBMI) (kg/m ²)	24.7 ± 5.4 (156)
Underweight (<18.5), %	6.4 (10/156)
Normal (18.5-24.9), %	57 (89/156)
Overweight (≥ 25.0), %	19 (30/156)
Obese (≥ 30.0), %	17 (27/156)
WIC enrollment, %	72.6 (114/157)
Prior birth control use, %	16.5 (26/158)

^aValues are presented as the mean ± SD or % (n); GA, Gestational age; WIC, Special Supplemental Nutrition Program for Women, Infants, and Children.

Table 2: Prevalence of Maternal Infection and Inflammatory Conditions Across Pregnancy in 158 Pregnant Adolescents

<u>Sexually Transmitted Infections (STIs):</u>		<u>Vaginal Infections:</u>	
Gonorrhea	3%	Candida	42%
Chlamydia	13%	Bacterial Vaginosis	40%
Syphilis	0.6%	<u>Placental Inflammation (n=45)^a:</u>	
Genital Warts	4%	Chorioamnionitis	14%
Genital Herpes	1%	Chronic Vilitis	0.6%
Trichomoniasis	7%	Deciduitis	9%
Human Papillomavirus	7.6%	Acute Funisitis	11%
		<u>Other Infections:</u>	
<u>Urinary Tract Infections (UTIs):</u>		Hepatitis B	0%
Pyelonephritis	1%	Hepatitis C	0.6%
Cystitis	25%	<u>Other (Carrier State):</u>	
		Group B Strep	38%

^aValues presented are only from a sub-sample of adolescents (N=45) whose placentas were sent to pathology for medically indicated purposes.

Table 3: Individual Risk Factors Associated with Maternal Infections and Inflammatory Conditions in 158 Pregnant Adolescents

Risk Factors	Odds Ratio (OR) (95% Confidence Interval)
Gonorrhea	
Maternal age (years)	0.38 (0.16-0.82)
Trichomoniasis	
Maternal age (years)	0.51 (0.26-0.92)
Chorioamnionitis	
Vitamin A <530 RAE ^a	3.71 (1.10-13.7)
Recto-vaginal Group B Strep	
Vitamin D intake (mcg/d)	0.87 (0.77-0.98)

^aRAE, retinoic acid equivalent. Logistic regression statistical analyses were performed.

Table 4: Maternal Risk Factors Associated with Selected Infections Across Gestation in 158 Pregnant Adolescents

Risk Factors	Adjusted Odds Ratio (AOR) (95% Confidence Interval)
Bacterial Vaginosis	
Maternal Race (African American)	4.61 (1.74-13.02)
Maternal ppBMI (kg/m ²) ^a	1.16 (1.04-1.30)

^appBMI, pre-pregnancy body mass index. Odds ratios were obtained using multiple logistic regression.