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Recurrent PID, Subsequent STI, and Reproductive Health Outcomes: Findings from the PID Evaluation and Clinical Health (PEACH) Study

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Abstract

PEACH trial data was used to evaluate the relationship between subsequent STI and recurrent PID on infertility and chronic pelvic pain (CPP). Recurrent PID was associated with an almost two-fold increased in infertility and more than four-fold increase in CPP. Subsequent STI was associated with CPP, but not infertility.

The Centers for Disease Control and Prevention (CDC) estimates that 800,000 women are affected by pelvic inflammatory disease (PID) each year in the United States.[1] PID has the potential to result in significant reproductive health morbidity including tubal infertility, ectopic pregnancy, and chronic pelvic pain (CPP).[2-4] Prior studies have demonstrated that women who have recurrent PID are at greater risk for reproductive morbidity than those women who are able to avoid subsequent disease.[2] Our knowledge of the longitudinal outcomes for affected women who experience recurrent PID is primarily derived from seminal data published by Weström and colleagues using a Scandinavian cohort of inpatients diagnosed with PID between 1960 and 1984.[2] Since that time, there have been shifts in the biological organisms associated with PID diagnoses and in behaviors.[5-9] Prior studies have reported predominance of infection with *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT), but newer work demonstrates that a third of PID cases are caused by these organisms.[9] Also, in contrast to historical management of PID which was uniformly to hospitalize, management PID now relies on outpatient therapy and shorter hospital stays when utilized.[10-12] Thus, an re-analysis of the impact of recurrent PID and subsequent sexually transmitted infections (STI) is warranted. In this study, we examine longitudinal secondary data from the PID Clinical Health and Evaluation (PEACH) study.

The PEACH) study is a multicenter randomized clinical trial designed to evaluate treatment strategies for PID. The methods for the PEACH study have been well reported in the

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literature,[13-15] but will be briefly reviewed here. Women aged 14-38 diagnosed with mild to moderate PID were recruited to participate in the trial between 1996-1999. In order to be included in the trial, participants had to have 1) pelvic discomfort for less than 30 days, 2) pelvic organ discomfort on bimanual examination, and 3) leukorrhea, mucopurulent cervicitis, and/ or known positivity for GC or CT via laboratory testing. Exclusion criteria included: 1) being identified as "at risk" for acute morbidity in the outpatient setting (e.g. pregnancy, inability to tolerate an outpatient regimen, tubo-ovarian abscess, potential surgical abdomen); pelvic pain ≥30 days; allergy to study drugs; antibiotic treatment within 7 days of recruitment; gynecologic surgical procedure (including abortion) or delivery of an infant within the last 30 days; prior hysterectomy or salpingectomy; and homelessness.

One thousand five hundred fifteen women were approached about participation and after the exclusion of women who were ineligible or refused, 831 women were randomized to the inpatient and outpatient treatment arms. Inpatient antibiotic therapy consisted of 48 hours of intravenous cefoxitin (2g every 6 hours) and oral doxycycline (100 mg twice daily) while on an inpatient unit with oral doxycycline dosing to complete 14 days at discharge. Outpatient antibiotic therapy consisted of a single dose of cefoxitin 2g intramuscularly and probenecid 1g orally, followed by 14 days of oral doxycycline 100mg twice daily. All patients were advised to rest, notify partners for treatment, and to abstain from sexual intercourse during treatment. At baseline, all participants completed a short interview (demographics, reproductive health history, sexual behavior) and had a gynecologic examination with specimen collection for *GC* (culture) and *CT* (polymerase chain reaction (Roche laboratories)), gram stain for bacterial vaginosis, and an endometrial biopsy for histological determination of endometritis. Participants were clinically re-evaluated a t 5- and 30-days. Each participant was then contacted quarterly for a telephone interview for 84-months during which interim diagnoses of subsequent STI and/or PID, pelvic pain, and infertility were assessed. This analysis was approved by the Johns Hopkins Institutional Review Board.

Measures

The primary outcomes of interest for this analysis were infertility and CPP at 84 months. Each of the primary outcome variables were measured as (yes, no) and dichotomously coded (1, 0). Infertility was defined when a sexually active woman with at least 12 months of follow-up did not conceive despite rare or no use of contraceptive method. Women were considered to have CPP if pelvic pain was reported during at least 2 consecutive follow-ups (i.e. minimum duration of 6 months). As previously reported,[14] recurrent PID was similar by self-report and medical record review. Other variables of interest given the potential relationship to longitudinal outcomes included age, race, parity, prior GC infection, prior CT infection, pregnancy outcomes, and self-reported infertility from the baseline interview. Summary statistics were generated for each of the descriptive variables and the primary outcome variables using SAS (SAS, version 9.2, Cary, NC). Within the age group strata, we first conducted analyses (not shown) to examine whether there were differences by intervention status - inpatient versus outpatient therapy - from the parent study.[13,14] In all bivariate analyses, chi-square and t-tests were used to evaluate differences for proportions and continuous variables, respectively. Multivariate logistic regression models were used to

evaluate the relationship between recurrent PID and/or recurrent STI and self-reported CPP and infertility. Models were adjusted for age, race, parity, prior PID, prior CT, and prior GC. In order to provide contrast to self-reported infertility findings, models predicting pregnancy and live birth were also performed and were adjusted for self-reported infertility at baseline. Finally, subgroup analyses were conducted for adolescents (≤19 years of age) to determine the potential impact of adolescence on the observed general outcomes in women.

At baseline, participants were primarily African American (75%), low income (77.5%) young women with regular access to healthcare (65%). (Table 1) All had clinical PID. At 84-months of follow-up, 21.3% had recurrent PID, 19.0% were categorized as infertile, and 42.7% reported CPP. Fifty-seven percent of women became pregnant and 42.0% had a live birth. There were no differences in pregnancies and live births based on recurrent PID. However, women who had recurrent PID were 1.8 times more likely to report infertility (AOR=1.8, 95% CI: 1.2; 2.8) and 4.2 times more likely to report CPP (AOR=4.2, 95% CI: 2.8; 6.2) than women without a recurrent episode of PID; adjusting for age, race, parity, prior PID, GC, and CT. Women with subsequent lower genital tract infections (STI) were 2.3 more likely to have CPP that those without STI (AOR=2.3, 95% CI: 1.2; 3.2), but not more likely to have infertility.

In the adolescent (≤19 years) sub-analysis, 71% of adolescents had a pregnancy, 51% had a live birth, 18 % were characterized as infertile, and 39% had CPP. There were no statistically significant differences in pregnancy (AOR: 1.1; 95% CI: 0.5:2.2), live birth (AOR: 0.9; 95% CI: 0.4; 1.7), adjusting for race, parity, prior PID, prior PID, GC, and CT, and self-reported infertility at baseline based on recurrent PID status. Adolescents with PID were also not significantly more likely to be categorized as having infertility (AOR: 1.9; 95% CI: 0.8; 4.4), however were 5.0 times more likely to describe CPP (AOR: 5.0; 95% CI: 2.3-10.6), controlling for race, parity, and prior PID, GC, and CT. (Table 2)

Women with recurrent episodes of PID are significantly more likely to report problems with infertility and CPP at 84 months. Our findings substantiate the established relationship between recurrent PID and adverse sequelae despite recent observations in the microbiology of PID and highlight CPP as a major longitudinal outcome for affected women. This work also draws attention to the notion that it is not just recurrent PID, but also recurrent lower genital tract infection (STI) that contributes to sequelae. It also supports to the concept of tertiary prevention, particularly since women affected by upper genital tract infection represent a smaller, but important and well- defined target group for intervention. Adolescents are also an important sub-target given the adverse risks to those so early in their reproductive trajectory. The strength of the study findings derive from use of the PEACH study sample which provides the most comprehensive longitudinal data available to date with urban American women affected by mild-moderate PID. It also provides excellent treatment efficacy data under the best possible conditions.

Our findings, however, must also be considered in light of several general limitations. Although the PEACH trial was designed to be generalizable to patients with clinically suspected PID diagnosed in urban settings, the sample may not be generalizeable to other dissimilar populations in the United States or those who would not participate in a trial. For

example, prior research among young women with PID suggests less than 25% of participants are using any form of contraception at the time of diagnosis,[17] whereas more than 70% of women in the PEACH trial reported contraceptive use.[18] Although the trial relied on clinical PID criteria for recruitment resulting in some patients without true PID, the design mimics current clinical practice. Finally, longitudinal outcome assessment relied on self-reported data from interviews conducted over the 84-month follow-up. While this poses a risk for reporting biases, medical record reviews substantiate recurrent PID diagnoses indicating the relative accuracy of self-reported medical histories by participants.

Young women with a history of PID are a clearly defined target group for public health intervention. Acute PID should prompt linkage of affected patients to tailored risk-reduction services to prevent the longitudinal sequelae associated with PID.

References

1. Sutton MY, Sternberg M, Zaidi A, St.Louis ME, Markowitz LE. Trends in pelvic inflammatory disease hospital charges and ambulatory visits, United States, 1985-2001. Sex Transm Dis. 2005; 32(12):778–84. [PubMed: 16314776]
2. Weström L, Joesoef R, Reynolds G, Hagdu A, Thompson SE. Pelvic inflammatory disease and fertility. A cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. Sex Transm Dis. 1992; 19:185–192. [PubMed: 1411832]
3. Weström L. Effect of pelvic inflammatory disease on fertility. Venereology. 1995; 8:219–222. [PubMed: 12291198]
4. Weström LV. Chlamydia and its effect on reproduction. J Br Fer Soc. 1996; 1:23–30. [PubMed: 12346973]
5. Sweet RL. Pelvic inflammatory disease: Etiology, diagnosis, and treatment. Sex Transm Dis. 1981; 8:308–315. [PubMed: 7330755]
6. Sweet RL. Colonization of the endometrium and fallopian tubes with ureaplasma urealyticum. Pediatr Infect Dis. 1986; 5:S244–6. [PubMed: 3540895]
7. Kamwendo F, Forslin L, Bodin L, Danielsson D. Decreasing incidences of gonorrhea- and Chlamydia-associated acute pelvic inflammatory disease. A 25-year study from an urban area of central Sweden. Sex Transm Dis. 1996; 23:384–391. [PubMed: 8885069]
8. Haggerty CL, Totten PA, Astete SG, Ness RB. Mycoplasma genitalium among women with nongonococcal, nonchlamydial pelvic inflammatory disease. Infect Dis Obstet Gynecol. 2006; 2006:30184. [PubMed: 17485798]
9. Short VL, Totten PA, Ness RB, Astete SG, Kelsey SF, Haggerty CL. Clinical presentation of Mycoplasma genitalium infection versus Neisseria gonorrhoeae infection among women with pelvic inflammatory disease. Clin Infect Dis. 2009; 48:41–47. [PubMed: 19025498]
10. Pelvic inflammatory disease: Guidelines for prevention and management. MMWR Recomm Rep. 1991; 40:1–25.
11. centers for disease control and prevention. Sexually transmitted diseases treatment guidelines 2002. MMWR Recomm Rep. 2002; 51:1–78.
12. Centers for Disease Control and Prevention. Workowski KA, Berman SM. Sexually transmitted diseases treatment guidelines, 2006. MMWR Recomm Rep. 2006; 55:1–94. [PubMed: 16888612]
13. Ness RB, Trautmann G, Richter HE, et al. Effectiveness of treatment strategies of some women with pelvic inflammatory disease: A randomized trial. Obstet Gynecol. 2005; 106:573–580. [PubMed: 16135590]
14. Ness RB, Soper DE, Holley RL, et al. Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: Results from the pelvic inflammatory disease evaluation and clinical health (PEACH) randomized trial. Am J Obstet Gynecol. 2002; 186:929–937. [PubMed: 12015517]

15. Ness RB, Soper DE, Peipert J, et al. Design of the PID evaluation and clinical health (PEACH) study. Control Clin Trials. 1998; 19:499–514. [PubMed: 9741869]

16. Westrom L. Effect of pelvic inflammatory disease on fertility. Venereology. 1995; 8:219–222. [PubMed: 12291198]

17. Trent M, Chung SE, Burke M, Walker A, Ellen JM. Results of a randomized controlled trial of a brief behavioral intervention for pelvic inflammatory disease in adolescents. J Pediatr Adolesc Gynecol. 2009

18. Trent M, Haggerty CM, Jennings JJ, Lee S, Bass DC, Ness R. Adverse adolescent reproductive health outcomes after pelvic inflammatory disease. Arch Ped Adol Med. Jan; 2011 165(1):49–54. PMID: 21199980.

Table 1

Selected Baseline Demographics

Baseline Measure	% (N)
Race/Ethnicity	74.5% (621)
Black	16.0% (133)
White	6.1% (51)
Hispanic	3.1% (26)
Native American/Alaskan Native	
Insurance Status	43.8% (364)
Uninsured	13.8% (115)
Private	33.5% (278)
Public	
Ever Pregnant	75.2% (625)
Prior history of PID	37.4% (311)
New Sexual Partner	9.3% (78)
Any Contraceptive use past 4 weeks	61.0% (508)

Table 2

Logistic Regression Models: Recurrent PID, Subsequent STI, & Reproductive Health Outcomes: All Participants and Adolescent girls ≤ 19 years

All Participants				
	Recurrent PID (N =168)	**No Recurrent PID (N = 621)**	**OR (95% CI)**	**Adjusted OR (95% CI)***
Pregnancy**	95 (56.5)	356 (57.3)	1.0 (0.7 – 1.4)	1.0 (0.6 – 1.4)
Live Birth*	61 (36.3)	270 (43.5)	0.7 (0.5 – 1.1)	0.7 (0.5 – 1.0)
Infertility	44 (26.2)	104 (16.7)	1.8 (1.2 – 2.6)	1.8 (1.2 – 2.8)
Chronic pelvic pain	115 (68.5)	213 (35.3)	4.0 (2.8 – 5.7)	4.2 (2.8 – 6.2)
	Subsequent STI (N = 195)	**No Subsequent STI (N = 596)**	**OR (95% CI)**	**Adjusted OR (95% CI)***
Pregnancy**	124 (63.6)	330 (55.4)	1.4 (1.0 – 2.0)	1.0 (0.7 – 1.5)
Live Birth*	91 (46.7)	239 (40.1)	1.3 (.09 – 1.8)	1.0 (0.7 – 1.4)
Infertility	41 (21.0)	104 (17.4)	1.3 (0.8 – 1.9)	1.4 (0.9 – 2.2)
Chronic pelvic pain	105 (53.8)	218 (37.7)	1.9 (1.4 – 2.7)	2.3 (1.6 – 3.2)
Adolescent Girls ≤ 19 years				
	Recurrent PID (N = 50)	**No Recurrent PID (N =149)**	**OR (95% CI)**	**Adjusted OR (95% CI)***
Pregnancy**	34 (68.0)	108 (72.5)	0.8 (0.4 – 1.6)	1.1 (0.5 – 2.2)
Live Birth	22 (44.0)	80 (53.7)	0.7 (0.4 – 1.3)	0.9 (0.4 – 1.7)
Infertility	13 (26.0)	23 (15.4)	1.9 (0.9 – 4.2)	1.9 (0.8 – 4.4)
Chronic pelvic pain	34 (68.0)	44 (30.1)	4.9 (2.5 – 9.8)	5.0 (2.3 – 10.6)
	Recurrent STI (N = 69)	**No Recurrent STI (N = 132)**	**OR (95% CI)**	**Adjusted OR (95% CI)***
Pregnancy**	47 (68.1)	97 (73.5)	0.8 (0.4 – 1.5)	0.9 (0.5 – 1.8)
Live Birth	32 (46.4)	71 (53.8)	0.7 (0.4 – 1.3)	0.9 (0.5 – 1.6)
Infertility	17 (24.6)	18 (13.6)	2.1 (1.0 – 4.3)	1.9 (0.9 – 4.2)
Chronic pelvic pain	36 (52.2)	42 (32.6)	2.3 (1.2 – 4.1)	2.3 (1.2 – 4.5)

* *Adjusted for age, race, parity, prior PID, prior GC and prior CT. Models predicting pregnancy and live birth are additionally adjusted for self-reported infertility at baseline.*

** Models predicting pregnancy and live birth were also performed and were adjusted for self-reported infertility at baseline