

Sexual and physical abuse and gynecologic disorders

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STUDY QUESTION: Is sexual and/or physical abuse history associated with incident endometriosis diagnosis or other gynecologic disorders among premenopausal women undergoing diagnostic and/or therapeutic laparoscopy or laparotomy regardless of clinical indication?

SUMMARY ANSWER: No association was observed between either a history of sexual or physical abuse and risk of endometriosis, ovarian cysts or fibroids; however, a history of physical abuse was associated with a higher likelihood of adhesions after taking into account important confounding and mediating factors.

WHAT IS KNOWN ALREADY: Sexual and physical abuse may alter neuroendocrine-immune processes leading to a higher risk for endometriosis and other noninfectious gynecologic disorders, but few studies have assessed abuse history prior to diagnosis.

STUDY DESIGN, SIZE, DURATION: The study population for these analyses includes the ENDO Study (2007–2009) operative cohort: 473 women, ages 18–44 years, who underwent a diagnostic and/or therapeutic laparoscopy or laparotomy at 1 of the 14 surgical centers located in Salt Lake City, UT, USA or San Francisco, CA, USA. Women with a history of surgically confirmed endometriosis were excluded.

PARTICIPANTS/MATERIALS, SETTING AND METHODS: Prior to surgery, women completed standardized abuse questionnaires. Relative risk (RR) of incident endometriosis, uterine fibroids, adhesions or ovarian cysts by abuse history were estimated, adjusting for age, race/ethnicity, education, marital status, smoking, gravidity and recruitment site. We assessed whether a history of chronic pelvic pain, depression, or STIs explained any relationships via mediation analyses.

MAIN RESULTS AND ROLE OF CHANCE: 43 and 39% of women reported experiencing sexual and physical abuse. No association was observed between either a history of sexual or physical abuse, versus no history, and risk of endometriosis (aRR: 1.00 [95% confidence interval (CI): 0.80–1.25]); aRR: 0.83 [95% CI: 0.65–1.06]), ovarian cysts (aRR: 0.67 [95% CI: 0.39–1.15]); aRR: 0.60 [95% CI: 0.34–1.09]) or fibroids (aRR: 1.25 [95% CI: 0.85–1.83]); aRR: 1.36 [95% CI: 0.92–2.01]). Conversely, a history of physical abuse, versus no history, was associated with higher risk of adhesions (aRR: 2.39 [95% CI: 1.18–4.85]). We found no indication that the effect of abuse on women's adhesion risk could be explained by a history of chronic pelvic pain, depression or STIs.

LIMITATIONS, REASONS FOR CAUTION: Limitations to our study include inquiries on childhood physical but not sexual abuse. Additionally, we did not inquire about childhood or adulthood emotional support systems, found to buffer the negative impact of stress on gynecologic health.

WIDER IMPLICATIONS OF THE FINDINGS: Abuse may be associated with some but not all gynecologic disorders with neuroendocrine-inflammatory origin. High prevalence of abuse reporting supports the need for care providers to screen for abuse and initiate appropriate follow-up.

STUDY FUNDING/COMPETING INTERESTS: Supported by the Intramural Research Program, Eunice Kennedy Shriver National Institute of Child Health and Human Development (contracts NOI-DK-6-3428, NOI-DK-6-3427, and I0001406-02). The authors have no potential competing interests.

Key words: physical abuse / sexual abuse / epidemiology / endometriosis / pelvic adhesions

Introduction

About one in every three women worldwide has experienced rape, physical violence and/or stalking by an intimate partner (Black *et al.*, 2010; World Health Organization, 2016). Women who are physically and/or sexually abused experience negative health outcomes stemming from abuse including depression, post-traumatic stress disorder, substance abuse and suicidal tendencies (Campbell, 2002; Bonomi *et al.*, 2007; Kiely *et al.*, 2010) along with chronic pain, gastrointestinal disorders and cardiac symptoms such as hypertension and chest pain (Campbell, 2002). While sexual and physical abuse are linked with several gynecologic disorders including recurrent vaginal and urinary tract infections as well as sexually transmitted infections (STIs) (Campbell, 2002; Bonomi *et al.*, 2007; Black *et al.*, 2010; Kiely *et al.*, 2010; American College of Obstetricians and Gynecologists, 2012) little is known regarding the effects that abuse has on other common gynecologic disorders (Campbell, 2002; Wise *et al.*, 2013).

Enduring abuse has been hypothesized to suppress the immune system as a result of chronic psychological stress (Campbell, 2002), thereby increasing a woman's risk for endometriosis and uterine fibroids (Tariverdian *et al.*, 2009; Boynton-Jarrett *et al.*, 2011; Wise *et al.*, 2013). Specifically, high percentages of neutrophils as well as low relative numbers of monocytes, activated lymphocytes and natural killer cells have been implicated in the development and/or the progression of endometriosis (Tariverdian *et al.*, 2009), while various growth factors, cytokines and matrix metalloproteinases are thought to lead to increased uterine fibroid growth (Wise *et al.*, 2013). Additionally, stress-induced alterations in reproductive hormones have been posited to increase risk for gynecologic disorders (Campbell, 2002).

Severely victimized women are estimated to seek medical care twice as often compared with nonvictims (Koss *et al.*, 1991). This increased medical care usage has large societal and economic effects with the roughly one-quarter of a million hospital visits resulting from female abuse consuming more than 8.3 billion dollars annually in direct medical and mental healthcare services in the USA (Centers for Disease Control and Prevention, 2003). When women present with gynecologic symptoms associated with sexual and physical abuse such as chronic pelvic pain, diagnostic laparoscopy is often performed as an initial investigation to determine pathologic causes such as endometriosis or other gynecologic conditions; however, the previous research shows that up to 40% of women reporting chronic pelvic pain are found to have no visible pathology (Howard, 1993).

While important epidemiologic work has been done investigating physical and sexual abuse across the lifespan and risk for uterine fibroids (Boynton-Jarrett *et al.*, 2011; Wise *et al.*, 2013) no formal investigation of the relationship between abuse reporting captured prior to diagnosis and risk for other noninfectious gynecologic disorders has been undertaken. The primary objective of this study was to assess if sexual and/or physical abuse history is associated with incident endometriosis diagnosis or other gynecologic disorders (including uterine fibroids, adhesions or ovarian

cysts) among premenopausal women undergoing diagnostic and/or therapeutic laparoscopy or laparotomy regardless of clinical indication. Additionally, we wished to assess whether known factors associated with an abuse history, including chronic pelvic pain, depression and STIs, may mediate any association between abuse history and gynecologic pathology.

Materials and Methods

Study population

This study sample comprised 495 women who participated in the ENDO (Endometriosis, Natural History, Diagnosis and Outcomes) Study (Buck Louis *et al.*, 2011). Specifically, participating women had to be currently menstruating, between the ages of 18 and 44 years, and scheduled to undergo a diagnostic and/or therapeutic laparoscopy or laparotomy regardless of clinical indication at 1 of the 14 surgical centers located in Salt Lake City, UT, USA or San Francisco, CA, USA between 2007 and 2009. Surgical indications for laparoscopy/laparotomy included pelvic pain ($n = 206$, 42%), pelvic mass ($n = 74$, 15%), irregular menses ($n = 60$, 12%), fibroids ($n = 49$, 10%), tubal ligation ($n = 48$, 10%) and infertility ($n = 35$, 7%) (Buck Louis *et al.*, 2011). Women with a medical history of surgically confirmed endometriosis (prevalent disease) or who could not communicate in English or Spanish were excluded. Other exclusion criteria included currently pregnant or breastfeeding ≥ 6 months, injectable hormonal usage within the past 2 years, and a cancer diagnosis other than nonmelanoma skin cancer.

Ethical approval

Full human subjects' approval was obtained by all participating research institutions; all women provided informed consent before any data collection.

Data collection

Prior to surgery, all women completed a computer-assisted personal interview (CAPI) capturing demographic and lifestyle factors, reproductive and physical/sexual abuse history along with an intensive pelvic pain assessment (Schliep *et al.*, 2015). Following the in-person CAPIs, anthropometric assessments were conducted by trained female nurses or research assistants according to standardized procedures (Buck Louis *et al.*, 2011).

Sexual and physical abuse assessment

Woman completed questions on (i) adult sexual abuse and (ii) childhood and adult physical abuse (Leserman *et al.*, 1995). Regarding adult (age ≥ 14 years) sexual abuse, women reported (yes/no) whether, against their will, they had experienced anyone 'expose the sex organs of their body,' 'threaten to have sex with you,' 'touch the sex organs of your body,' 'made you touch the sex organs of their body' or 'forced you to have sex'. Additionally, women reported whether as a child (age < 14 years) or adult (age ≥ 14 years) they had never, seldom, occasionally or often experienced an older person/another adult 'hit, kick or beat you' and/or 'seriously threaten your life'.

Outcome assessment

Surgeons completed a standardized operative report immediately after surgery to capture gynecologic post-operative diagnosis including normal pelvis, endometriosis, uterine fibroids, pelvic adhesions, benign ovarian

cysts, neoplasms and congenital müllerian cysts. For women with endometriosis, surgeons indicated disease severity using the revised American Society for Reproductive Medicine's (rASRM) staging criteria (American Society for Reproductive Medicine, 1997). Stage of disease (I–IV: minimal, mild, moderate and severe) was automatically calculated via the rASRM weighted point score.

Covariate assessment

Body mass index (BMI) was calculated from height (measured using a portable stadiometer) and body weight (measured using calibrated electronic scales) as a part of the standardized anthropometric assessment. Physical activity was assessed via the International Physical Activity Questionnaire (IPAQ) and categorized into low, moderate and high categories as per standard protocol (Craig et al., 2003; International Physical Activity Questionnaire, 2005). Women reported whether they experienced pain lasting >6 months that was either cyclic (i.e. painful menstrual cramps not relieved by over-the-counter medications) or chronic (i.e. pain located in or near the bladder or vaginal canal not associated with menses) (Schliep et al., 2015). Women also reported whether they had previously undergone pelvic surgery, tubal sterilization, endometrial biopsy or D&C, and if so, age of the surgery. Depression was assessed via the Beck Depression Inventory-Fast Screen (BDI-FS). For purposes of this study, depression was defined as scoring at or above the cut-point for depressive symptoms that are associated with a highly probable diagnosis of major depressive disorder (depressed [≥ 4 BDI-FS score] versus not depressed [< 4 BDI-FS score]) (Beck et al., 2000).

Statistical analysis

The number (percentage) of women answering yes to having each and any type of adult sexual or child/adult physical abuse was calculated. We assessed statistical significance for differences in any sexual and physical abuse reporting (yes/no) and participant characteristics (demographic, lifestyle, reproductive history and primary indication for surgery) using either Student's *t*-test (per the Satterthwaite method for unequal variances) for continuous variables and χ^2 or Fisher's exact tests for categorical variables.

Multivariable relative risk (RR) estimation by the Poisson regression with robust error variance was used to determine the RR of being diagnosed with a gynecologic disorder including incident endometriosis, uterine fibroids, adhesions and ovarian cysts (yes versus no for each) by sexual and physical abuse type adjusting for the *a priori* determined confounders of age (continuous), marital status (married/living as married, other), education (high school or less, college or more), race/ethnicity (Hispanic, Non-Hispanic White, Non-Hispanic Black, Asian/Pacific Islander/Native American and other/multiracial), current smoker (yes/no), gravidity (gravid/nulligravid) and study site (California or Utah). Additional covariates were considered including household income (below poverty line, within 180% of poverty, above poverty), BMI (continuous), physical activity (low, moderate, high), prior abdominal or pelvic surgeries, chronic pelvic pain, depression and STIs. Based on an *a priori* hypothesis that chronic pain, depression and STIs may not only be confounders but may mediate the relationship between abuse and gynecologic disorders, a counterfactual approach to mediation analysis was applied to estimate the RR for the natural direct effect (NDE) and natural indirect effect (NIE) of physical and sexual abuse on adhesions mediated through these factors (Valeri and VanderWeele, 2013). All analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC, USA) and Stata Version 12.1 (StataCorp LP, College Station, TX, USA).

Results

Twenty-two women of enrolled cohort of 495 had surgeries canceled, while 2 women did not complete the sexual and physical abuse question

leaving 471 women included in the analyses. Sexual and physical abuse were commonly reported among women in the ENDO Study with 202 (43%) women reporting some type of sexual abuse and 185 (39%) reporting some type of physical abuse (Fig. 1). Among the women who reported experiencing some type of sexual abuse, 56 (27%) reported experiencing all 5 types of sexual abuse, 37 (18%) with 4 types, 28 (14%) with 3 types, 26 (13%) with 2 types and 55 (27%) with 1 type (Fig. 2).

Women who reported any sexual abuse ($n = 202$; 43%) compared with no sexual abuse ($n = 269$; 57%) were less likely to be married (70.3 versus 80.2%, $P = 0.01$) and college educated (75.6 versus 83.6%, $P = 0.03$) and more likely to be below the poverty line (16.0 versus 8.3%, $P = 0.01$), a current smoker (18.3 versus 10.0%, $P = 0.01$), experiencing chronic pelvic pain (48.0 versus 31.2%, $P = 0.001$), depressed (24.8 versus 15.3%, $P = 0.01$), ever sexually active (90.6 versus 83.3%, $P = 0.02$), gravid (74.3 versus 61.7%, $P = 0.004$), parous (63.4 versus 52.6%, $P = 0.02$) and having been diagnosed with pelvic inflammatory disease (4.5 versus 0.4%, $P = 0.003$), genital herpes (7.4 versus 2.3%, $P = 0.01$) or chlamydia (10.4 versus 2.6%, $P < 0.001$) (Table I). Women who reported any physical abuse ($n = 185$; 39%) compared with no physical abuse ($n = 286$, 61%) were less likely to be non-Hispanic white (66.5 versus 80.8%, $P = 0.01$), married (70.1 versus 80.0%, $P = 0.02$), and college educated (74.6 versus 83.9%, $P = 0.01$) and more likely to be below the poverty line (16.0 versus 8.3%, $P = 0.01$), a current smoker (20.5 versus 9.1%, $P < 0.001$), have a higher BMI (29.2 ± 9.0 versus 27.1 ± 7.1 , $P = 0.01$), depressed (24.9 versus 15.8%, $P = 0.01$), ever sexually active (91.4 versus 83.2%, $P = 0.01$), gravid (77.3 versus 60.5%, $P < 0.001$), parous (65.4 versus 51.9%, $P = 0.004$), and having been diagnosed with pelvic inflammatory disease (4.3 versus 0.7%, $P = 0.01$), genital herpes (8.7 versus 1.8%, $P < 0.001$), trichomoniasis (6.0 versus 2.5%, $P = 0.03$), chlamydia (13.0 versus 1.4%, $P < 0.001$) and human papilloma virus (11.9 versus 5.9%, $P = 0.01$). Neither sexual nor physical abuse showed any clear associations with primary indication for surgery.

Overall, there were no significant differences between women with versus without a history of sexual or physical abuse and having a post-operative diagnosis of any gynecologic pathology versus a normal pelvis, with the exception of a borderline higher RR for gynecologic pathology among women reporting having been sexually threatened as adults or having had their lives threatened as a child compared with no report (Fig. 3).

When looking at specific gynecologic conditions, we found that women with versus without any history of sexual or physical abuse had a null or trend towards reduced risk of endometriosis and ovarian cysts, after adjusting for age, marital status, education, race/ethnicity, smoking, gravidity and study site (Table II). Conversely, women with any history of sexual or physical abuse were more likely to have fibroids and more notably adhesions compared with women without any abuse history. Specifically, women who had experienced any type of child or adult physical abuse had a 2.39 higher RR (95% confidence interval (CI): 1.18–4.85) of having a primary post-operative diagnosis of adhesions compared with women with no history of physical abuse after adjustment for confounding factors. Further adjustment for household income, BMI, physical activity, chronic pelvic pain, depression and STIs did not appreciably alter our findings, nor did adjustment for prior pelvic or abdominal surgery.

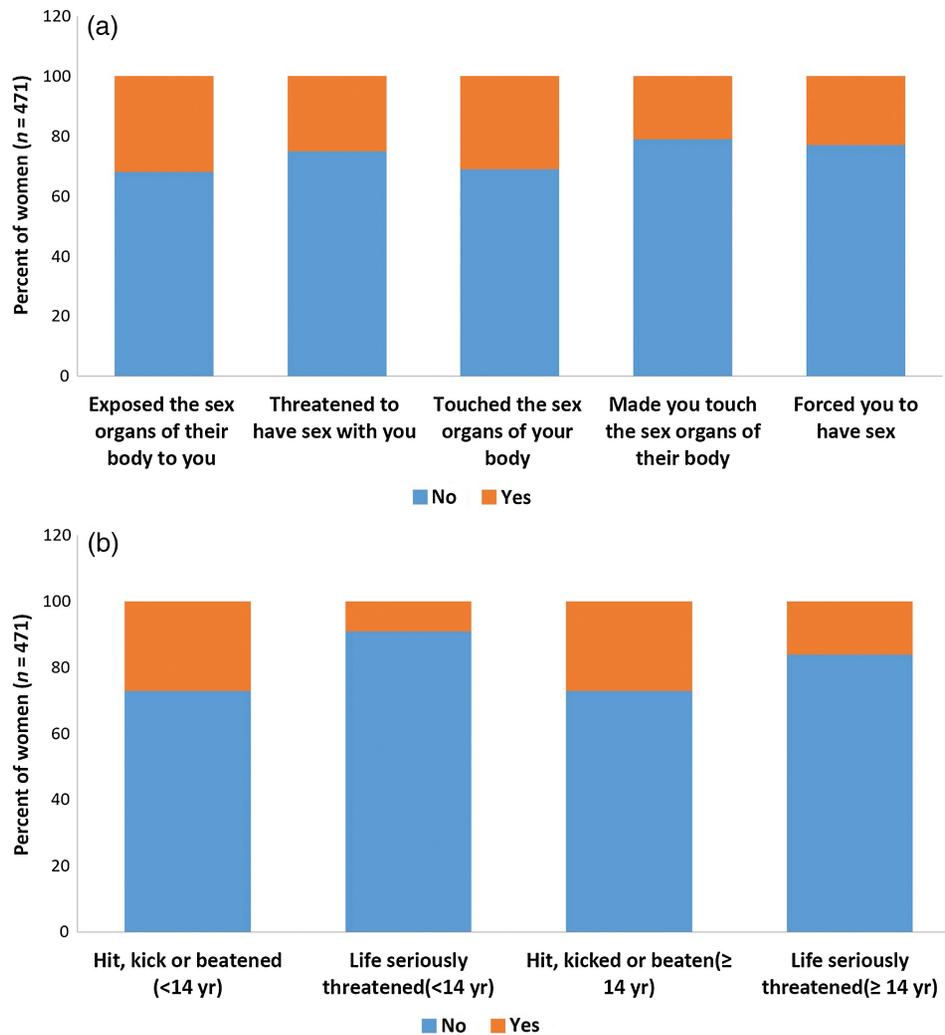


Figure 1 Prevalence of sexual (a) and physical abuse (b) reporting in the ENDO Study.

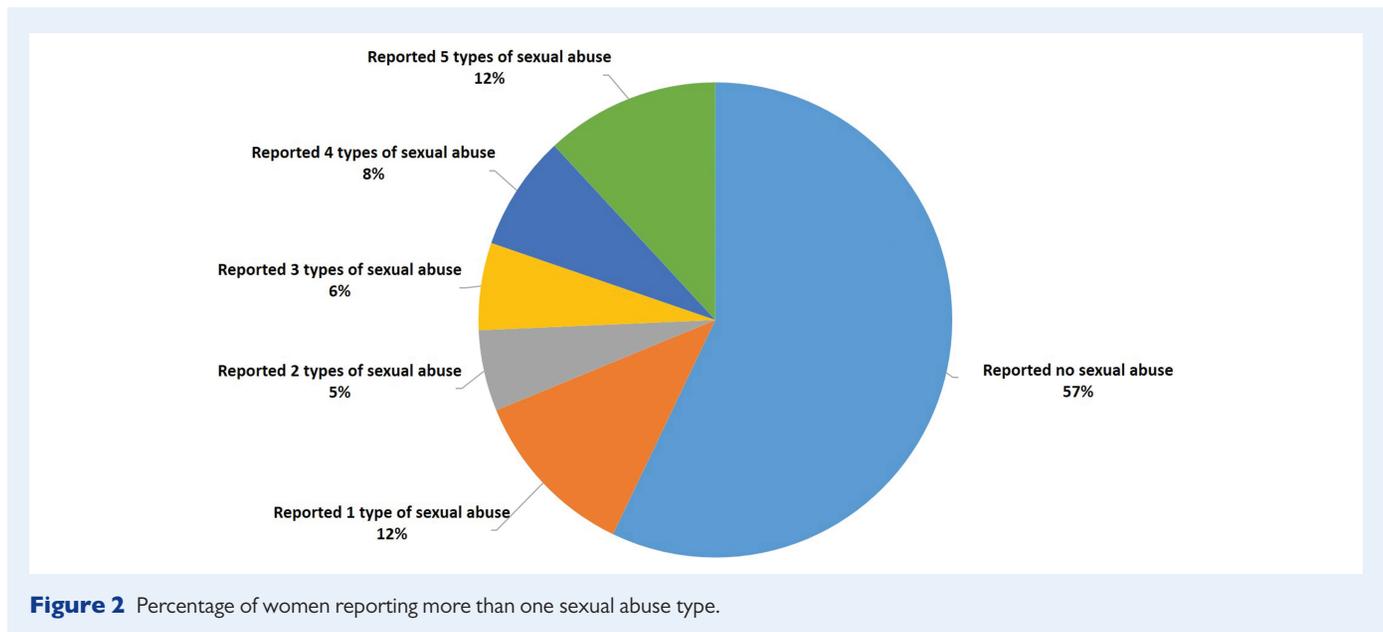
Regarding our mediation analyses, there were no indications that the effect of abuse on risk of adhesions could be explained by a history of chronic pelvic pain or depression (RR_{NIE} : 1.02 [95% CI: 0.96–1.09]; RR_{NIE} : 0.91 [95% CI: 0.82–1.00], respectively) after controlling for confounding factors (Table III). In other words, the risk of adhesions among physically abused women was elevated by only 2% as a result of their chronic pain and reduced by 9% as a result of their depression. The NDE indicates that even if physically abused and not physically abused women had equal levels of chronic pain and depression, abused women would still have a 121 and 172% higher risk of adhesions compared with women who had not been abused (RR_{NDE} : 2.21 [95% CI: 1.07–4.60]), (RR_{NDE} : 2.72 [95% CI: 1.26–5.70], respectively). While there was a somewhat stronger, albeit nonsignificant, indication that the effect of abuse on STIs could be partially explained by a history of STIs (RR_{NIE} : 1.35 [95% CI: 0.95–1.94]), the NDE indicated that even if abused and not abused women had equal levels of STIs, women who had suffered from abuse would still have a 74% higher risk of adhesions compared with women who had not suffered from abuse (RR_{NDE} :

1.74 [95% CI: 0.67–4.42]) leading to a significant total effect (TE) (RR_{TE} : 2.36 [95% CI: 1.14–4.90]).

Discussion

In this novel epidemiologic study where abuse history was obtained prior to diagnostic and/or therapeutic laparoscopy/laparotomy, we observed that women who experienced child and adult physical abuse had a higher risk of being diagnosed with adhesions but no notable significant associations were found between sexual and physical abuse history and endometriosis, fibroids or ovarian cysts. These findings were upheld in mediation analyses that considered women's history of chronic pelvic pain, depression or STIs. Of note is the high prevalence of self-reported abuse among women undergoing laparoscopy/laparotomy for various clinical indications, supporting the need for appropriate screening by women's healthcare providers.

Our findings showing a null association between women's abuse history and surgically diagnosed incident endometriosis or ovarian



cysts is corroborated by two prior studies. Among 25 women undergoing laparoscopy for chronic pelvic pain and 30 asymptomatic women undergoing laparoscopy for tubal fulguration or infertility investigation, researchers found no significant differences between women with versus without visually diagnosed endometriosis with regard to sexual assault/abuse among either the cases or controls (Harrop-Griffiths *et al.*, 1988). Similarly, in a more recent study among 98 patients, women with chronic pelvic pain and without endometriosis reported the highest frequency of sexual and physical abuse compared with women with chronic pelvic pain and with endometriosis or nonpain controls (Thomas *et al.*, 2006). In contrast to the above findings and our results, two studies have reported a positive association between women's abuse history and self-reported endometriosis. One cross-sectional study among 1348 female migraine sufferers with self-identified history of endometriosis reported a nonadjusted significant correlation between experiencing physical and sexual abuse and endometriosis (Tietjen *et al.*, 2010). Additionally, preliminary data from the Nurses' Health Study (1989–2005) reported a significant positive association between women's childhood physical and sexual abuse and self-reported endometriosis diagnosis (Wieser *et al.*, 2012). Given that previous research has reported that endometriosis can lead to reduced sex life quality (Ferrero *et al.*, 2005) and relationship dissolution (Fagervold *et al.*, 2009; De Graaff *et al.*, 2013), which could trigger abuse by an intimate partner, additional longitudinal research that captures women's abuse experiences prior to endometriosis diagnosis using gold-standard methods of assessment and that appropriately accounts for known confounding factors is needed before causal conclusions can be made.

While we failed to observe any significant association between women's abuse history and diagnosis of endometriosis, we did observe a significant higher risk for adhesions, a finding supported by previous research (Heim *et al.*, 1999). In a small study of 10 patients with chronic pelvic pain and 14 pain-free, infertile control patients (all of whom underwent diagnostic laparoscopy), high prevalence rates of sexual and physical abuse for patients with versus without adhesions were found (50.0 versus 21.4% for sexual abuse and 40.0 versus

21.4% for physical abuse) (Heim *et al.*, 1999). While abdominal or pelvic surgery is the most common cause of pelvic adhesions (ten Broek *et al.*, 2013), additional support of sexual or physical abuse leading to adhesions can be found in case reports (Kumar *et al.*, 2006).

While overall we found no statistically significant association between uterine fibroids and sexual or physical abuse, the pattern of a higher fibroid risk most notably among women reporting childhood physical abuse (adjusted RR: 1.22, 95% CI: 1.01–1.48) is consistent with prior research (Boynton-Jarrett *et al.*, 2011; Wise *et al.*, 2013). In the Nurses' Health Study, 68 505 predominately white (97%) women, aged 25–42 years at enrollment, who completed a retrospective questionnaire on childhood violence exposure were assessed for incident diagnoses of ultrasound- or hysterectomy-confirmed uterine fibroids (Boynton-Jarrett *et al.*, 2011). Compared with women reporting no abuse, abused women had a higher uterine fibroid risk of 1.08 (95% CI: 1.03–1.13), 1.17 (1.10–1.24), 1.23 (1.14–1.33), 1.24 (1.10–1.39) and 1.36 (1.18–1.54) for increasing cumulative abuse exposures after multivariable adjustment (Boynton-Jarrett *et al.*, 2011). In the Black Women's Health Study, 9910 premenopausal women were followed from 2005 to 2011 for self-reported uterine fibroid diagnoses with baseline assessment of physical and sexual abuse within each life stage (Wise *et al.*, 2013). Relative to never being abused, RRs were 1.16 (95% CI: 1.02–1.33) for childhood physical abuse, 1.34 (95% CI: 1.09–1.66) for childhood sexual abuse, and 1.17 (95% CI: 0.99–1.39) for both childhood physical and sexual abuse. These findings merit further study.

Teasing apart the effects of women's sexual and physical abuse experiences on their gynecologic health is difficult given that most gynecologic disorders lack a specific diagnostic biomarker and many are interrelated. For example, endometriosis is thought to be due in part to retrograde menstruation of hormone-sensitive endometrial cells and tissues, which elicit an inflammatory response that in turn is accompanied by adhesions and fibrosis (Giudice, 2010). Many of these gynecologic conditions with inflammatory etiology have been linked to hormonal dysregulation, which have also been tied to stressful life events (Miller *et al.*, 2009). The rationale behind the significantly higher risk of adhesions,

Table 1 Participant characteristics by report of sexual and physical abuse history.

Operative cohort	Sexual abuse Yes n = 202 (43%)	Sexual abuse No n = 269 (57%)	P	Physical abuse Yes n = 185 (39%)	Physical abuse No n = 286 (61%)	P
Demographics						
Age (mean ± SD)	33.6 ± 6.7	32.4 ± 7.2	0.07	33.7 ± 6.6	32.5 ± 7.2	0.06
Race/ethnicity (n [%])			0.46			0.01
Hispanic	32 (15.8)	31 (11.5)		34 (18.4)	29 (10.1)	
Non-Hispanic white	147 (72.8)	207 (77.0)		123 (66.5)	231 (80.8)	
Non-Hispanic black	5 (2.5)	3 (1.1)		4 (2.2)	4 (1.4)	
Asian/Pacific Islander/Native American	10 (5.0)	18 (6.7)		13 (7.0)	15 (5.2)	
Other/multiracial	8 (4.0)	10 (3.7)		11 (5.9)	7 (2.4)	
Married (n [%])	142 (70.3)	214 (80.2)	0.01	129 (70.1)	227 (80.0)	0.02
Education (n [%])			0.03			0.01
≤High school	49 (24.4)	44 (16.4)		47 (25.4)	46 (16.1)	
>College	152 (75.6)	225 (83.6)		138 (74.6)	239 (83.9)	
Household income (n [%])			0.01			0.01
Below poverty line	32 (16.0)	22 (8.3)		23 (12.7)	31 (10.9)	
Within 180% of poverty	28 (14.0)	25 (9.4)		31 (17.1)	22 (7.7)	
Above poverty	140 (70.0)	219 (82.3)		127 (70.2)	232 (81.4)	
Current smoker	37 (18.3)	27 (10.0)	0.01	38 (20.5)	26 (9.1)	<0.001
Study site			0.45			0.66
Utah	179 (88.6)	232 (86.3)		163 (88.1)	248 (86.7)	
California	23 (11.4)	37 (13.8)		22 (11.9)	38 (13.3)	
Health						
BMI (mean [SD])	28.6 ± 8.6	27.5 ± 7.4	0.14	29.2 ± 9.0	27.1 ± 7.1	0.01
Physical activity (n [%])			0.92			0.50
Low	29 (17.1)	46 (18.7)		33 (20.8)	42 (16.3)	
Moderate	62 (36.5)	88 (35.8)		54 (34.0)	96 (37.4)	
High	79 (46.5)	112 (45.5)		72 (45.3)	119 (46.3)	
Depression (n [%])	50 (24.8)	41 (15.3)	0.01	46 (24.9)	45 (15.8)	0.01
Sexual and reproductive history						
Ever sexually active	183 (90.6)	224 (83.3)	0.02	169 (91.4)	238 (83.2)	0.01
Gravid	150 (74.3)	166 (61.7)	0.004	143 (77.3)	173 (60.5)	<0.001
Parous	128 (63.4)	141 (52.6)	0.02	121 (65.4)	148 (51.9)	0.004
Pelvic pain (n [%])	97 (48.0)	84 (31.2)	<0.001	77 (41.6)	104 (36.7)	0.25
Cyclic pain (n [%])	85 (42.1)	99 (36.8)	0.25	75 (40.5)	109 (38.1)	0.60
Gynecologic infections ^a						
Pelvic inflammatory disease	9 (4.5)	1 (0.4)	0.003	8 (4.3)	2 (0.7)	0.01
Condylomas	2 (1.0)	0 (0)	0.18	2 (1.1)	0 (0)	0.08
Genital herpes	15 (7.4)	6 (2.3)	0.01	16 (8.7)	5 (1.8)	<0.001
Gonorrhea	2 (1.0)	0 (0)	0.18	1 (0.5)	1 (0.4)	0.48
Trichomoniasis	11 (5.5)	7 (2.6)	0.15	11 (6.0)	7 (2.5)	0.03
Chlamydia	21 (10.4)	7 (2.6)	<0.001	24 (13.0)	4 (1.4)	<0.001
Human papilloma virus	21 (10.4)	18 (6.7)	0.18	22 (11.9)	17 (5.9)	0.02
Primary indication for surgery						
Pelvic pain	86 (42.8)	119 (44.2)	0.75	78 (42.4)	128 (44.4)	0.66
Pelvic mass	34 (16.9)	40 (14.9)	0.55	25 (13.6)	49 (17.0)	0.32
Menstrual irregularity	27 (13.4)	33 (12.3)	0.71	23 (12.5)	37 (12.9)	0.91

Continued

Table I Continued

Operative cohort	Sexual abuse Yes n = 202 (43%)	Sexual abuse No n = 269 (57%)	P	Physical abuse Yes n = 185 (39%)	Physical abuse No n = 286 (61%)	P
Fibroids	22 (11.0)	26 (9.7)	0.65	20 (10.9)	29 (10.1)	0.78
Tubal ligation	18 (9.0)	30 (11.2)	0.44	25 (13.6)	23 (8.0)	0.05
Infertility	14 (7.0)	21 (7.8)	0.73	13 (7.1)	22 (7.6)	0.82

^aWomen could have more than one reported STI. No participant reported ever having a syphilis diagnosis.

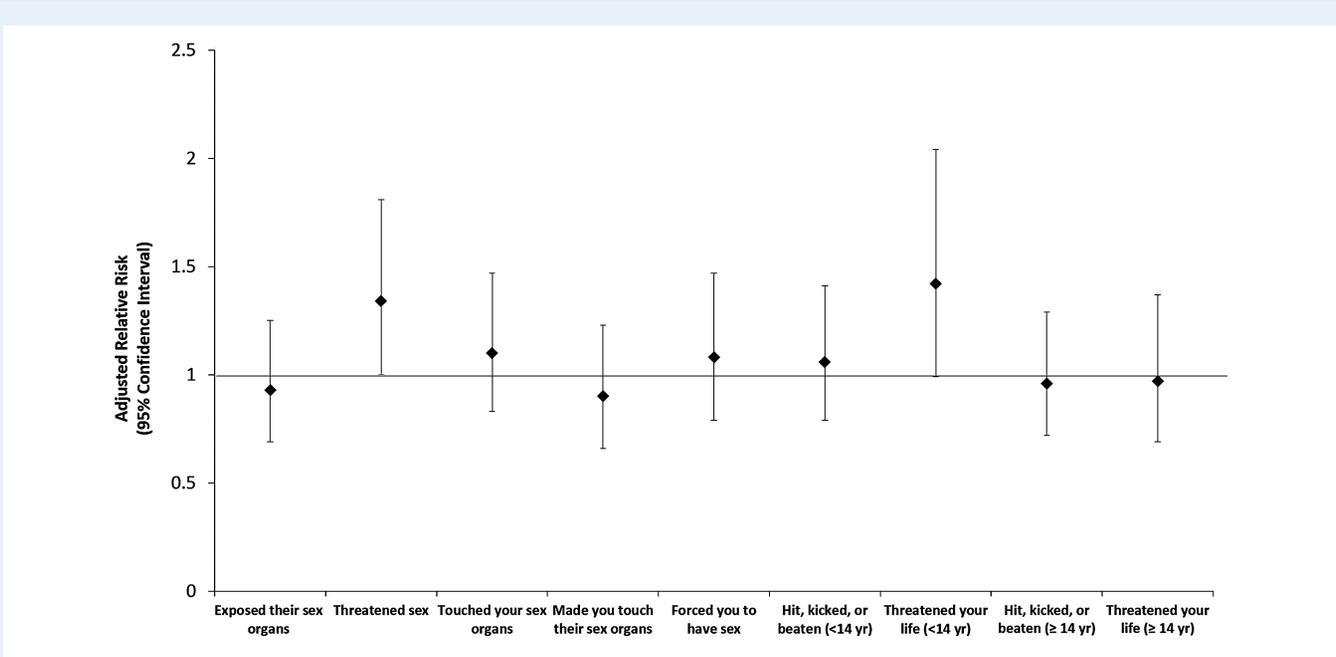


Figure 3 Adjusted RR of having a post-operative diagnosis of gynecologic pathology versus normal pelvis by abuse history. Post-operative gynecologic pathology included endometriosis, uterine fibroids, pelvic adhesions, benign ovarian cysts, neoplasms and congenital müllerian cysts. Adjusted for age, marital status (yes/no), education (college or above/high school or less), race/ethnicity, current smoker (yes/no), gravidity (yes/no) and study site.

but not endometriosis or ovarian cysts, in our study deserves further investigation. While we hypothesized that the relationship between abuse experiences and gynecologic pathology could potentially be explained by several mediating factors, including chronic pelvic pain, depression or STIs, our mediation analysis showed that neither pelvic pain nor depression had a mediating effect. While it is well documented that chlamydia and pelvic inflammatory disease may result in adhesion formation (Pellati et al., 2008), we found that the effect of abuse on risk of adhesions was only partially mediated by STIs. Consequently, STI prevention or timely diagnosis and treatment may reduce but not completely eliminate an abused woman’s risk for adhesions.

Strengths of our study include prospective assessment of incident endometriosis and other gynecologic pathology using gold-standard methods of surgically visualized diagnosis. Previous research found substantial interrater agreement between experienced surgeons reviewing operative digital images from the ENDO Study (Schliep et al., 2012). To reduce recall bias, we evaluated sexual and physical abuse, along with multiple known confounding factors, prior to a woman knowing

her disease status via CAPIs. Giving women the ability to report on sensitive subjects such as abuse history via a CAPI accompanied by a trained research nurse may have provided a more conducive setting for honest reporting.

Limitations to our study include inquiries on childhood physical but not sexual abuse. Additionally, we did not inquire about childhood or adulthood emotional support systems, found to buffer the negative impact of stress on gynecologic health (Boynton-Jarrett et al., 2011; Wise et al., 2013). While our study was predominately comprised of Caucasian women, 15.8% of women enrolled in the ENDO study were Hispanic, close to the US national average of 16.9% (United States Census Bureau, 2012). Furthermore, with 43 and 27% of women reporting some type of sexual and physical abuse, respectively, prevalence of abuse was relatively high despite limited racial and geographic diversity. Finally, it should be noted that our study relied on observational data in which many comparisons were performed, 5% of which could be statistically significant purely by chance. However, this study was based on a strong biologic hypothesis driven by prior evidence showing a link

Table II Adjusted RR (95% CI) of endometriosis, fibroids, adhesions and ovarian cysts among women enrolled in the ENDO study by report of sexual and physical abuse history (n = 471).^a

	Endometriosis (n = 190; 40%) versus no endometriosis (n = 281; 60%)	Fibroids (n = 74; 16%) versus no fibroids (n = 397; 84%)	Adhesions (n = 33; 7%) versus no adhesions (n = 438; 93%)	Ovarian cysts (n = 52; 11%) versus no ovarian cysts (n = 419; 89%)
Relative risk (95% CI)				
Sexual abuse	1.00 (0.80–1.25)	1.25 (0.85–1.83)	1.72 (0.86–3.43)	0.67 (0.39–1.15)
Exposed their sex organs	0.91 (0.71–1.17)	1.37 (0.94–2.00)	1.56 (0.79–3.06)	0.72 (0.39–1.30)
Threatened sex	0.79 (0.59–1.07)	1.21 (0.76–1.93)	1.87 (0.88–3.99)	0.59 (0.29–1.19)
Touched your sex organs	0.89 (0.68–1.15)	1.12 (0.76–1.65)	1.69 (0.83–3.44)	0.85 (0.49–1.49)
Made you touch their sex organs	0.90 (0.66–1.23)	1.20 (0.72–2.01)	1.66 (0.75–3.68)	0.37 (0.15–0.91)
Forced you to have sex	0.99 (0.74–1.32)	1.02 (0.66–1.58)	1.68 (0.79–3.56)	0.59 (0.30–1.19)
Physical abuse	0.83 (0.65–1.06)	1.36 (0.92–2.01)	2.39 (1.18–4.85)	0.60 (0.34–1.09)
Hit, kicked or beaten (< 14 years)	0.88 (0.77–1.01)	1.22 (1.01–1.48)	1.32 (1.00–1.73)	0.77 (0.53–1.10)
Threatened your life (< 14 years)	0.75 (0.55–1.01)	1.27 (0.91–1.76)	0.90 (0.47–1.71)	0.46 (0.19–1.12)
Hit, kicked or beaten (≥ 14 years)	0.85 (0.73–0.99)	1.14 (0.91–1.43)	1.23 (0.92–1.66)	0.99 (0.72–1.34)
Threatened your life (≥ 14 years)	0.85 (0.69–1.04)	1.17 (0.87–1.56)	1.07 (0.65–1.75)	0.89 (0.61–1.31)

^aAdjusted for age, marital status (yes/no), education (college or above/high school or less), race/ethnicity, current smoker (yes/no), gravidity (yes/no) and study site.

Table III Estimates of the natural direct, natural indirect and total effect of the association between physical abuse and adhesions mediated through chronic pelvic pain, depression or STIs.^a

Natural direct effect RR_{NDE} (95% CI)	Natural indirect effect RR_{NIE} (95% CI)	Total effect RR_{TE} (95% CI)
Chronic pelvic pain		
2.21 (1.07–4.60)	1.02 (0.96–1.09)	2.26 (1.09–4.68)
Depression		
2.72 (1.29–5.70)	0.91 (0.82–1.00)	2.47 (1.17–5.20)
STIs		
1.74 (0.67–4.42)	1.35 (0.95–1.94)	2.36 (1.14–4.90)

^aAdjusted for age, marital status (yes/no), education (college or above/high school or less), race/ethnicity, current smoker (yes/no), gravidity (yes/no) and study site.

between endometriosis and gynecologic pathology. This formed the basis for our study design and analysis.

Considering our and previous research findings, women with past sexual and/or physical abuse may be a higher risk for pelvic adhesions and possibly fibroids, but not endometriosis and/or ovarian cysts; although additional life course approaches for understanding gynecologic disorders relative to prior abuse are needed before definitive conclusions can be made. As surgical treatment of pelvic adhesions may have limited efficacy for pain symptoms and potentially may lead to further adhesion formation, women with a history of sexual or physical abuse as well as pelvic pain may benefit from psychological evaluation and support prior to surgical intervention. The high prevalence of women in the ENDO Study reporting having been sexually and/or physically abused, mirroring statistics reported in nationally representative surveys (Black *et al.*, 2010), underscores the need for women's healthcare practitioners

to screen women for abuse history so that appropriate clinical follow-up can be provided (American Society for Reproductive Medicine, 2012).

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Authors' roles

K.C.S., S.L.M., Z.C. and G.M.B.L. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. C.M.P. and G.M.B.L. supervised the study. K.C.S., S.L.M., E.B.J., C.M.P., J.B.S., Z.C. and G.M.B.L. were involved in the study concept and design. C.M.P., Z.C. and G.M.B.L. were responsible for acquisition of data. K.C.S., S.L.M., Z.C., G.M.B.L. and M.E.W. did the analysis and interpretation of data. K.C.S., S.L.M., E.B.J., C.M.P., H.T.S., J.B.S., Z.C., U.B., M.E.W. and G.M.B.L. drafted the manuscript and critically revised the manuscript for important intellectual content.

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Conflict of interest

None declared.

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