

2-23-2011

# A Pilot Study Of The Prevalence Of Leg Pain Among Women With Endometriosis

Stacey A. Missmer  
*Harvard University*

Geoffrey M. Bove  
*University of New England, gbove@une.edu*

Follow this and additional works at: [http://dune.une.edu/biomed\\_facpubs](http://dune.une.edu/biomed_facpubs)



Part of the [Medical Sciences Commons](#)

---

## Recommended Citation

Missmer, Stacey A. and Bove, Geoffrey M., "A Pilot Study Of The Prevalence Of Leg Pain Among Women With Endometriosis" (2011). *Biomedical Sciences Faculty Publications*. 8.  
[http://dune.une.edu/biomed\\_facpubs/8](http://dune.une.edu/biomed_facpubs/8)

This Article is brought to you for free and open access by the Biomedical Sciences Faculty Works at DUNE: DigitalUNE. It has been accepted for inclusion in Biomedical Sciences Faculty Publications by an authorized administrator of DUNE: DigitalUNE. For more information, please contact [bkenyon@une.edu](mailto:bkenyon@une.edu).



Published in final edited form as:

*J Bodyw Mov Ther.* 2011 July ; 15(3): 304–308. doi:10.1016/j.jbmt.2011.02.001.

## A Pilot Study of the Prevalence of Leg Pain Among Women with Endometriosis

Stacey A. Missmer, ScD<sup>a,b,c</sup> and Geoffrey M. Bove, DC, PhD<sup>d</sup>

<sup>a</sup>Department of Obstetrics, Gynecology, and Reproductive Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

<sup>b</sup>Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

<sup>c</sup>Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts

<sup>d</sup>University of New England College of Osteopathic Medicine, Biddeford, Maine

### Abstract

Radiating leg pain is a common symptom presenting in manual therapy practices. Although this symptom has been reported as a complication of endometriosis, its prevalence and characteristics have not been studied. We surveyed members of a national endometriosis support group with endometriosis using a self-administered, mailed questionnaire. The main outcome measures were the prevalence and characteristics of leg pain. Of 94 respondents, leg pain was reported by 48 women (51%), and was bilateral in 59% of these symptomatic women. The likelihood of experiencing leg pain was related to weight gain since age 18, age, and height. The most common treatments tried included exercise, over-the-counter medications, and massage therapy, all with variable results. These data support leg pain as a prevalent complication of endometriosis, and that the disease may affect multiple peripheral nerves. Manual therapists should remain aware to this possible etiology for radiating pain.

### Keywords

endometriosis; epidemiology; leg pain; sciatic nerve

## INTRODUCTION

Endometriosis is the third leading cause of gynecologic hospitalization in the United States (Eskenazi & Warner, 1997). Despite the high health care costs and morbidity associated with endometriosis, the etiology of endometriosis has not been fully delineated. The pathophysiology likely includes hormonal, anatomic, genetic, and immune factors. Risk may be associated with factors that increase the volume, frequency, and duration of retrograde

© 2011 Elsevier Ltd. All rights reserved.

**Corresponding Author:** Geoffrey M. Bove, DC, PhD, Associate Professor, University of New England College of Osteopathic Medicine, 11 Hills Beach Rd., Biddeford, ME 04005, Lab: 207 602 2921, Fax: 207 602 5931, gbove@une.edu.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

An abstract version of part of this manuscript was presented as a poster at the Society for Neuroscience annual meeting.

menstruation and promote implantation and growth of endometrial plaque (Oral & Arici, 1997).

Women with endometriosis have been hypothesized to have a greater risk of chronic, cyclic leg pain that is independent of any referred dysmenorrheal pain. However, the prevalence of leg pain from all causes among women with endometriosis is unknown. A search of the literature revealed numerous case studies of sciatica due to endometriosis, and outcomes of surgical interventions that confirmed the origin of pain as from endometrioma on the lumbosacral plexus or intrapelvic sciatic nerve (Binkovitz et al, 1991; Bjornsson, 1976; Denton & Sherrill, 1955; Descamps et al, 1995; Dhote et al, 1996; Papapietro et al, 2002; Takata & Takahashi, 1994; Torkelson et al, 1988; Vaisberg, 1964; Yekeler et al, 2004; Zager et al, 1998). Leg pain was incidentally reported by >40% of the 4000 respondents to a survey by the Endometriosis Association (Sinai et al, 2008), but specifics of the pain (location, timing, duration) were not assessed. These data suggest that endometriosis involving peripheral nerves is a common cause of leg pain in women. While the direct involvement of peripheral nerves has been referred to as “unusual” (Binkovitz et al, 1991) and “rare” (Dhote et al, 1996) (Torkelson et al, 1988; Yekeler et al, 2004), under-recognition of leg pain among women with endometriosis has been cited (Zager et al, 1998). This may be in part because the symptoms are similar to those often attributed to pathologies of the spinal structures, such as lumbar intervertebral discs and paraspinal muscles and joints. Manual therapists are likely to encounter patients with leg pain due to endometriosis, and need to recognize this etiological possibility.

Because there had not been a formal determination of the prevalence and details of leg pain existing with endometriosis, we performed a survey designed to elucidate details about leg pain that may coexist or be caused by endometriosis.

## MATERIALS AND METHODS

This research was approved by the Institutional Review Board of the Beth Israel Deaconess Medical Center.

### Study population and data collection

The Endometriosis Association is a national support group in the United States that is focused on progress in treatment and research of endometriosis. A total of 306 members with the disease who resided in the geographic vicinity of Boston, Massachusetts were mailed a 4-page questionnaire to be completed and returned in a postage paid envelope. The time allowed from initial mailing to receipt of the final questionnaire was 3 months. No repeat mailings or other methods to increase response rate were employed. Because endometriosis is sufficiently validated by self reporting when a woman reports laparoscopic confirmation (Missmer et al, 2004), the first question asked was whether endometriosis had been confirmed laparoscopically. Women who did not report laparoscopic confirmation were not asked to complete the questionnaire and were not included in the results. The questionnaire then asked details of demographic and anthropometric characteristics, reproductive history, and pain symptoms. Those who reported suffering from leg pain were asked to provide details of their pain including clinical help sought and treatments attempted. In addition, they completed pain drawings.

Analysis of the pain diagrams was performed with acknowledgment of the limitations regarding the determination of the involved nerve(s), which is difficult even during clinical evaluation, particularly when deep pain is involved. As previously performed (Bove et al, 2005), we subdivided the leg into 4 regions: proximal anterior (hip to knee), distal anterior

(knee to foot), proximal posterior, and distal posterior. Respondent marks within these boundaries were counted as noting presence of pain in this region of the leg.

### Statistical analysis

Using SAS Statistical Software Version 8.2 (SAS Institute Inc., Cary, NC), we compared the distribution of demographic, anthropometric, dietary intake, and reproductive history characteristics between women with laparoscopically confirmed endometriosis who did and did not report experiencing leg pain. Unconditional logistic regression was used to calculate the crude and multivariable odds ratios (OR) and 95% confidence intervals (CI) that are presented as estimates of the relative risk (Rothman & Greenland, 1998). In the final models, we included all variables that were observed to be significantly associated with leg pain as potential confounders. We conducted tests for trend in ordinal categorical exposures by creating an ordinal variable in which the median value or midpoint of each category was assigned to all participants in that group and then calculated a Wald statistic (Lemeshow & Hosmer, 1989). Statistical significance was placed at the 0.10 level.

## RESULTS

Of the 306 mailed questionnaires, 19 were returned due to inaccurate address information. Of those who received the pilot mailing, a total of 94 women (33%) returned a completed questionnaire indicating laparoscopically confirmed endometriosis. These women ranged in age from 16 – 58 with a median age of 42. The women were primarily Caucasian (98%) and premenopausal (74%). Five women were pregnant or breast feeding at the time of questionnaire completion. The median time since diagnosis of endometriosis was 10 years (range = 1 – 33 years).

A total of 48 women (51%) reported leg pain. While neither current weight nor weight at age 18 were significantly associated with risk of leg pain, we observed a borderline significant 2% increase in risk for each pound gained since age 18 (p-value, test for linear trend = 0.06; Table 1). In addition, as age increased, the risk of having leg pain increased (p-value, test for linear trend = 0.09). We also observed a linear association with height (p-value, test for linear trend = 0.08). No other participant characteristics were associated with the likelihood of leg pain.

Forty-five of the 48 women with leg pain depicted their pain on profile diagrams (Fig. 1). Pain severity encompassed the entire range, from mild to severe, and was more often reported in more than 1 region (1.8 regions  $\pm$  1 SD). Most women (60%) reported proximal anterior leg pain. The distal anterior region was involved in 31% of women. The proximal and distal posterior regions were involved in 40%, and 47% of women, respectively.

Women reported bilateral, unilateral left-, and unilateral right- sided leg pain (59%, 24%, and 17%, respectively; Table 2). Pain was most likely to be experienced during menstruation and just prior to the start of menses. This observation is consistent with the catamenial nature of the disease, where the symptoms result from immune mediated inflammation due to the presence of sloughed endometrial cells. Only 10% claimed that there was no relationship with their menses (i.e., they answered no to all queries). The majority of women (68%) who provided details about efforts to diminish their leg pain symptoms reported mentioning their leg pain to a clinician, and one-third of these women were referred to specialists. Nearly half of the patients were not offered any treatment option for this symptom. However, the majority of women attempted various treatments, and more than 2/3 reported some benefit.

## DISCUSSION

In this cross-sectional pilot study among women with endometriosis, we observed that the prevalence of self-reported leg pain was 51%. The prevalence of leg pain among a comparable group of women is not known, but the few studies available estimate the point and lifetime prevalence of sciatic pain from all etiologies to be 2–5% and 2.5 – 21%, respectively (Hofmann et al, 2002; Riihimaki et al, 1994; Videman et al, 2005; Younes et al, 2006). These data support that endometriosis is a prominent cause of radiating leg pain.

It is acknowledged that the population observed in this pilot study may not be generalizable. Members of the Endometriosis Association are a self-selected group of women who have chosen to join a support group and pay annual dues, and their diagnosis, medical details, and experience of endometriosis are strictly self-reported. While these support group member women may represent those with more endometriosis-related sequelae (Sinaii et al, 2008), these data were limited to respondents who reported laparoscopic confirmation of endometriosis, and therefore are more reliable than self-reports alone (Missmer et al, 2004).

Given the many causes of leg pain, it is unknown what proportion of our subjects had leg pain due to endometriosis directly affecting one or more peripheral nerve, and what proportion had pain due to co-existing pathologies. It was also not possible to identify cases of referred pain. While we plan to perform examinations of such women in the future, such differential diagnosis is often not possible. However, even if the true proportion of women who suffer from leg pain directly related to an endometriotic lesion affecting a peripheral nerve is much lower than 51%, and given that endometriosis among women of reproductive age is estimated to be as great as 10% (Eskenazi & Warner, 1997), leg pain with endometriosis represents a significant public health concern. Further studies including control groups and physical examinations are warranted based on these initial observations.

The variability of the pain distributions supports the hypothesis that leg pain associated with endometriosis can affect many different and even multiple nerves in the same woman. Most nerves to the lower limbs pass through the abdominal and pelvic cavities, only separated from the intraperitoneal space by the peritoneum. Inflammatory endometrioma that are attached to the peritoneum in close proximity to a nerve are likely to inflame the nerve and the axons it contains, and indeed show a predilection for nerves (Anaf et al, 2004; Anaf et al, 2000). Such a neuritis could cause local or radiating pain; this is supported by data from rat models (Bove & Light, 1997; Bove et al, 2003; Bove et al, 2009; Sauer et al, 1999). It is also possible that nerve inflammation due to endometriosis leads to abdominal and pelvic pain as well as leg pain, by affecting the nerves supplying the viscera. Finally, afferent activity in these nerves could be sufficient to form what has been called the “peripheral generator” (Gracely et al, 1992; Hedo et al, 1999). In this concept, the nociceptive afferent signals from a pathology induce and then maintain a form of spinal cord or higher center sensitization, which then can lead to the perception of pain in areas that are neurologically remote from the location of the pathology, i.e. are innervated by different nerves. Thus, the pain or other sensations could be perceived in a much wider distribution than would seem appropriate to the pathology.

While the sample size for this pilot study is relatively small, these data yield the first quantification of the leg pain experience of women with endometriosis. We hypothesize that this symptom, though prevalent, may elude clinical detection, and indeed may be masked by referred dysmenorrheal pain. It is possible that women do not make the connection between their abdominal / pelvic pain and their leg pain, or are not forthcoming in discussing this with their physician (Zager et al, 1998). Moreover, because non-pelvic pain associated with

endometriosis is not well described in the literature, it is also possible that physicians and other therapists do not customarily ask details about such symptoms.

The etiology of radiating leg pain is often obscure. When a patient presents with radiating leg pain, most clinicians look for pathologies of the musculoskeletal system, such as altered spinal mechanics or focal muscle hypertonicities (“trigger points”), which can lead to similar symptoms. The initial findings reported here support the concept that endometriosis that directly involves nerves should also be considered in women with endometriosis. While there may not be pathognomonic symptoms aside from the radiating pain distribution, neurological and orthopedic examinations should prove consistent with peripheral nerve involvement. Our goal is that the results of this pilot study will lead to improved diagnostic awareness of this prevalent consequence of endometriosis.

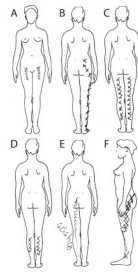
## Acknowledgments

Financial support was provided by a grant to Dr. Bove from the National Institute for Child Health and Human Development.

## References

- Anaf V, El NI, Simon P, Van de SJ, Fayt I, Simonart T, Noel JC. Preferential infiltration of large bowel endometriosis along the nerves of the colon. *Hum.Reprod.* 2004; 19:996–1002. [PubMed: 15016784]
- Anaf V, Simon P, El NI, Fayt I, Buxant F, Simonart T, Peny MO, Noel JC. Relationship between endometriotic foci and nerves in rectovaginal endometriotic nodules. *Hum.Reprod.* 2000; 15:1744–1750. [PubMed: 10920097]
- Binkovitz LA, King BF, Ehman RL. Sciatic endometriosis: MR appearance. *J Comput.Assist.Tomogr.* 1991; 15:508–510. [PubMed: 2026822]
- Bjornsson OG. Cyclic sciatica of endometriosis. Case report. *Acta Chir Scand.* 1976; 142:415–416.
- Bove GM, Light AR. The nervi nervorum: missing link for neuropathic pain? *Pain Forum.* 1997; 6:181–190.
- Bove GM, Ransil BJ, Lin HC, Leem JG. Inflammation induces ectopic mechanical sensitivity in axons of nociceptors innervating deep tissues. *Journal of Neurophysiology.* 2003; 90:1949–1955. [PubMed: 12724363]
- Bove GM, Weissner W, Barbe MF. Long lasting recruitment of immune cells and altered epi-perineurial thickness in focal nerve inflammation induced by complete Freund's adjuvant. *J.Neuroimmunol.* 2009
- Bove GM, Zaheen A, Bajwa ZH. Subjective nature of lower limb radicular pain. *J Manipulative Physiol Ther.* 2005; 28:12–14. [PubMed: 15726030]
- Denton RO, Sherrill JD. Sciatic syndrome due to endometriosis of sciatic nerve. *South.Med.J.* 1955; 48:1027–1031. [PubMed: 13267573]
- Descamps P, Cottier JP, Barre I, Rosset P, Laffont J, Lansac J Body. Endometriosis of the sciatic nerve: case report demonstrating the value of MR imaging. *Eur J Obstet Gynecol Reprod Biol.* 1995; 58:199–202. [PubMed: 7774750]
- Dhote R, Tudoret L, Bachmeyer C, Legmann P, Christoforov B. Cyclic sciatica. A manifestation of compression of the sciatic nerve by endometriosis. A case report. *Spine.* 1996; 21:2277–2279.
- Eskenazi B, Warner ML. Epidemiology of endometriosis. *Obstet Gynecol Clin North Am.* 1997; 24:235–258. [PubMed: 9163765]
- Gracely RH, Lynch SA, Bennett GJ. Painful neuropathy: altered central processing maintained dynamically by peripheral input. *Pain.* 1992; 51:175–194. [PubMed: 1484715]
- Hedo G, Laird JMA, LopezGarcia JA. Time-course of spinal sensitization following carrageenan-induced inflammation in the young rat: A comparative electrophysiological and behavioural study in vitro and in vivo. *Neuroscience.* 1999; 92:309–318. [PubMed: 10392852]

- Hofmann F, Stossel U, Michaelis M, Nubling M, Siegel A. Low back pain and lumbagosciatica in nurses and a reference group of clerks: results of a comparative prevalence study in Germany. *International Archives of Occupational & Environmental Health*. 2002; 75:484–490. [PubMed: 12172895]
- Lemeshow, S.; Hosmer, DW. *Applied logistic regression*. New York, NY: Wiley; 1989.
- Missmer SA, Hankinson SE, Spiegelman D, Barbieri RL, Marshall LM, Hunter DJ. Incidence of laparoscopically confirmed endometriosis by demographic, anthropometric, and lifestyle factors. *Am.J Epidemiol*. 2004; 160:784–796. [PubMed: 15466501]
- Oral E, Arici A. Pathogenesis of endometriosis. *Obstet Gynecol Clin North Am*. 1997; 24:219–233. [PubMed: 9163764]
- Papapietro N, Gulino G, Zobel BBB, Di Martino A, Denaro V. Cyclic sciatica related to an extrapelvic endometriosis of the sciatic nerve - New concepts in surgical therapy. *J Spinal Disord Tech*. 2002; 15:436–439. [PubMed: 12394671]
- Riihimaki H, Viikari-Juntura E, Moneta G, Kuha J, Videman T, Tola S. Incidence of sciatic pain among men in machine operating, dynamic physical work, and sedentary work. A threeyear follow-up. *Spine*. 1994; 19:138–142. [PubMed: 8153819]
- Rothman, KJ.; Greenland, S. *Modern Epidemiology*. Philadelphia, PA: Lippincott-Raven; 1998.
- Sauer SK, Bove GM, Averbek B, Reeh PW. Rat peripheral nerve components release calcitonin gene-related peptide and prostaglandin E-2 in response to noxious stimuli: Evidence that nervi nervorum are nociceptors. *Neuroscience*. 1999; 92:319–325. [PubMed: 10392853]
- Sinaii N, Plumb K, Cotton L, Lambert A, Kennedy S, Zondervan K, Stratton P. Differences in characteristics among 1,000 women with endometriosis based on extent of disease. *Fertil.Steril*. 2008; 89:538–545. [PubMed: 17498711]
- Takata K, Takahashi K. Cyclic sciatica. A case report. *Spine*. 1994; 19:89–90. [PubMed: 8153814]
- Torkelson SJ, Lee RA, Hildahl DB. Endometriosis of the sciatic nerve: a report of two cases and a review of the literature. *Obstet Gynecol*. 1988; 71:473–477. [PubMed: 3279360]
- Vaisberg M. Cyclic sciatica due to endometriosis. *N.Y State J Med*. 1964; 64:1983–1987. [PubMed: 14180886]
- Videman T, Ojajarvi A, Riihimaki H, Troup JD. Low back pain among nurses: a follow-up beginning at entry to the nursing school. *Spine*. 2005; 30:2334–2341. [PubMed: 16227898]
- Yekeler E, Kumbasar B, Tunaci A, Barman A, Bengisu E, Yavuz E, Tunaci M. Cyclic sciatica caused by infiltrative endometriosis: MRI findings. *Skeletal Radiol*. 2004; 33:165–168. [PubMed: 14740181]
- Younes M, Bejia I, Aguir Z, Letaief M, Hassen-Zrour S, Touzi M, Bergaoui N. Prevalence and risk factors of disk-related sciatica in an urban population in Tunisia. *Joint Bone Spine*. 2006; 73:538–542. [PubMed: 16725362]
- Zager EL, Pfeifer SM, Brown MJ, Torosian MH, Hackney DB. Catamenial mononeuropathy and radiculopathy: a treatable neuropathic disorder. *J Neurosurg*. 1998; 88:827–830. [PubMed: 9576249]



**Figure 1.**

Parts of pain drawings from 6 different respondents to the survey. “xx” marks were used for pain, and dots for numbness or other sensory aberrations. The distributions are consistent with involvement of (A) the femoral nerve; (B) the gluteal and lateral femoral cutaneous nerves; (C–E) the lumbosacral plexus, sciatic, and/or posterior femoral cutaneous nerve; (F) lateral femoral cutaneous nerve (Maigne, 1979). There was no distinction assessed between deep versus cutaneous symptoms. It should be noted that nerve distributions vary considerably between individuals.



**Table 1**

Characteristics associated with leg pain among responding women with laparoscopically confirmed endometriosis, compared to responding women without leg pain [n = 48 of 94 (51%)].

Participant characteristic	UV OR (95% CI)	P-value *
Time since diagnosis of endometriosis (years)	0.96 (0.91–1.02)	0.15
Current age (years)	0.96 (0.93–1.01)	0.09
Current height (inches)	0.87 (0.74–1.02)	0.08
Current weight (pounds)	1.01 (0.99–1.02)	0.39
Weight at age 18 (pounds)	0.99 (0.97–1.01)	0.49
Weight change since age 18 (pounds)	1.02 (1.00–1.04)	0.06
Current body mass index (kg/m <sup>2</sup> )	1.07 (0.98–1.16)	0.13
Currently overweight (BMI ≥25 kg/m <sup>2</sup> )	2.07 (0.90–4.77)	
Body mass index at age 18 (kg/m <sup>2</sup> )	1.02 (0.89–1.18)	0.73
Age at menarche	1.20 (0.85–1.69)	0.30
Ever used oral contraceptives	1.80 (0.40–8.07)	
Parous	1.00 (0.44–2.29)	
Currently pregnant or lactating	0.58 (0.09–3.63)	
Hysterectomy	1.02 (0.34–3.12)	
Postmenopausal	0.60 (0.23–1.56)	

UV OR = univariate odds ratio, CI = confidence interval

\* Two-sided Wald statistic p-value, test for linear trend.

**Table 2**

Pain and coping characteristics of women who reported experiencing leg pain [n = 48 of 94 (51%)].

	N (%) or median (range)	
<b>Pain location and severity</b>		
Pain in both legs	27 (59%)	
Pain in left leg only	8 (17%)	
Pain in right leg only	11 (24%)	
VAS score for all legs	5.0 (1 – 10)	
<b>Menstrual cycle timing of leg pain</b>		
During menstruation (early follicular phase)	22 (73%)	
Immediately after menstruation (late follicular phase)	10 (34%)	
During ovulation (early luteal phase)	12 (41%)	
Prior to next cycle start (late luteal phase)	19 (66%)	
All of the time	7 (24%)	
Not menstrual cycle-linked (i.e. no for each time)	3 (10%)	
<b>Medical intervention</b>		
Ever mentioned leg pain to a health professional	30 (68%)	
Received referral to an		
Orthopedist	3 (10%)	
Chiropractor	2 (7%)	
Neurologist	5 (16%)	
Attempted treatments		
Clinician did not suggest treatment	12 (46%)	
	Treatments Tried	Reported Pain Improvement
Exercise	33 (80%)	23 (70%)
Prescription drugs	15 (35%)	11 (79%)
Over-the-counter drugs	26 (60%)	16 (62%)
Herbs	8 (20%)	4 (50%)
Heat or cold therapy	20 (48%)	18 (90%)
Massage therapy	25 (61%)	19 (79%)
Acupuncture	12 (31%)	8 (67%)