

## Risk Factors and Pain Characteristics Assessment in Women with Urologic Disease related Chronic Pelvic Pain

Oana MĂGUREAN<sup>1</sup>, Mihai LUCAN<sup>2,\*</sup>, and Gheorghita IACOB<sup>2</sup>

<sup>1</sup> "Alfred Rusescu" Institute for Mother and Child Care, Bd. Lacul Tei, no. 120, sector 2, Bucharest, Romania.

<sup>2</sup> Clinical Institute of Urology and Renal Transplantation, Str. Clinicilor, no. 4-6, 400006 Cluj-Napoca, Romania.

E-mails: magurean.oana@gmail.com, mihai.lucan@renaltransplant.ro, gheorghita.iacob@gmail.com

\* Author to whom correspondence should be addressed; Tel.: +40264591827

Received: 20 January 2012 / Accepted: 29 February 2012 / Published online: 10 March 2012

### Abstract

*Purpose:* The aim of our study was to evaluate factors predisposing or related to chronic pelvic pain in women, and whether those factors allows classification using generalized cluster analysis, consistent with the presence of chronic pelvic pain. *Material and method:* A survey was done on 2469 women referred to Clinical Institute of Urology and Renal Transplantation, Cluj-Napoca, Romania, between January 2006 - December 2010. Patients were stratify in regard with presence of chronic pelvic pain (GrA) and assessed in regard with demographic and habitual risk factors, medical and reproductive history, lifestyle, and pain characteristics. Identified factors were used for classification using generalized cluster analysis by k-mean technique. The results were assessed in terms of correlation with the presence of chronic pelvic pain. *Results:* On univariate analysis, marital status and higher education were protective while complications at delivery and physical work were risk factors for chronic pelvic pain. Age at presentation and age at menarche were lower in GrA, while caffeine and alcohol consumption, number of cigarettes smoked per day, pain intensity, coexistence of pain related to periods, deep intercourse, bladder filling, and voiding have been increased in GrA. Classification of patients correlates with the presence of chronic pelvic pain ( $p < 0.001$ ). *Conclusions:* Age, marital status, level of education, type of activity, complications at delivery, caffeine and alcohol consumption are risk factors related to chronic pelvic pain in women referred for urologic conditions. Pain intensity is related to chronic pelvic pain, regardless of type and localization. Classification of patients using k-mean technique cluster analysis correlates significantly statistic with chronic pelvic pain.

**Keywords:** Generalized cluster analysis; Chronic pelvic pain.

### Introduction

Chronic pelvic pain has a significant impact on patients' quality of life with increased social and economic costs [1]. Most studies are referring to gynecological related chronic pelvic pain, emphasizing the significance of general, gynecological, and obstetric factors such as: length of education, employment, marriage, lifetime drug/alcohol abuse, age at menarche, parity, abortion, length of menstrual cycle, duration of menstrual cycle, endometriosis, pelvic inflammatory disease, previous cesarean sections, physical or sexual abuse during childhood or adult, psychosomatic symptoms [2]. In a significant proportion of patients, a definite diagnosis cannot be done rising the

question of neuropsychological mechanisms affecting nociceptive or non-nociceptive perception level [3]. Thus, patient history and clinical examination may become more significant than several diagnostic investigations.

Chronic pelvic pain may be associated with many other disorders than those of the reproductive organs. Recent studies showed that gynecologic related pelvic pain comprise only 20.2% from the medical assistance of a primary care practice, the other 68.5% being urinary or gastrointestinal related [4, 5].

Frequently, inefficiency of chronic pelvic pain treatment has been related to inability to prove an underlying pathology [4, 5] or to a particular alteration in pain perception [6]. Identifying the pain etiology should remain a goal since it will increase the chance to treat.

There is a lack of data regarding chronic pelvic pain in women having urologic diseases.

## Purpose

The aim of our study was to evaluate factors predisposing or related to chronic pelvic pain in women, and whether those factors allows classification using generalized cluster analysis, consistent with the presence of chronic pelvic pain, regardless of pain duration.

## Material and Method

### *Patients Selection*

A supervised prospective survey was conducted among 3498 consecutive patients. In the study were included all female patients with age over 18 years, referred to Clinical Institute of Urology and Renal Transplantation, Cluj-Napoca, Romania, for urologic or gynecologic conditions: urinary stone disease, bladder tumor, recurrent urinary infection, interstitial cystitis, uterine leiomyoma, endometriosis, adnexal tumors, genital prolapse, abdominal adhesion syndrome, between January 2006 and December 2010. Approval for the study was obtained from the Ethics Committee of the institution and all patients provided written informed consent. The patients were stratified in two groups: GrA: patients with chronic pelvic pain and GrB: patients without chronic pelvic pain.

### *Methods*

**Questionnaire.** A questionnaire was designed to allow assessment of known demographic and habitual risk factors, medical and reproductive history, lifestyle, and pain characteristics related to chronic pelvic pain, including: age, height, body weight, marital status, education, type of work, previously surgical treatment, obstetrical history (number of pregnancies, number of full 9 months pregnancies, complications during pregnancy, labor, delivery or post partum), menstrual history (age at menarche, menstrual periods, days between periods, duration of menses, pain before or within menses, regular periods), health habits (exercises per week, caffeine intake, cigarettes, duration of smoking in years, alcohol intake, vegetarian diet, protein diet), history of abuse (physical abuse, sexual abuse as child or adult), urinary symptoms (loss of urine, difficulties passing urine, number of voiding during day and night, urgency after voiding), pain intensity, pain location, and pain type. The pain intensity was assessed using a visual analog scale with 10 degrees: 0 - no pain, 10 - the worst pain imaginable. Chronic pelvic pain was defined as any pain located under the umbilicus level, debilitating or requiring medical assistance, lasting over 6 months [7].

**Statistics.** Women with chronic pelvic pain were assessed in terms of risk factors and pain characteristics to identify relevant factors for chronic pelvic pain using the risk ratio assessment with 95% confidence interval and p value, and Mann Whitney U test.

Identified factors were used for patient classification using generalized cluster analysis in order to assess similarities between patients and the concordance with the presence of chronic pelvic pain. It was used the k-mean technique with maximization of the Euclidian distance.

The relationship between the two clusters and chronic pelvic pain was assessed by Chi-square test. The statistical assessment was carried out using STATISTICA 8. Statistical significance was considered for  $p < 0.05$ .

**Results**

Of the 3498 patients, 2469 were willing to participate (response rate 70.58%, CI: 69.04%-72.08%). Chronic pelvic pain was recorded in 704 patients (28.51%, CI: 27.65%-30.35%).

Risk ratio assessment for marital status, history of abuse, level of education, type of activity, complication at delivery, abundance of menses, regularity of periods, and vegetarian diet is presented in Table 1.

**Table 1.** Risk factors associated with the presence of chronic pelvic pain.

	Chronic pelvic pain				RR	CI (95%) limits		P
	GrA		GrB			Lower	Higher	
	Freq.	%	Freq.	%				
Marital status - Single	238	33.81 (30.34-37.45)	682	38.68 (36.37-40.96)	0.86	0.75	0.98	0.03
History of abuse	169	24.01 (20.93-27.37)	470	26.63 (24.59-28.77)	0.90	0.78	1.05	0.19
Higher education	283	40.20 (36.57-43.94)	806	45.65 (43.33-48.02)	0.85	0.75	0.97	0.01
Physical work	345	49.01 (45.26-52.76)	750	42.49 (40.18-44.84)	1.21	1.06	1.37	0.00
Complications at delivery	126	17.90 (15.18-20.98)	259	14.67 (13.07-16.43)	1.18	1.01	1.39	0.05
Heavy menses	220	31.25 (27.87-34.84)	523	29.63 (27.52-31.83)	1.06	0.92	1.21	0.44
Normal menses	315	44.74 (41.04-48.51)	779	44.14 (41.81-46.49)	1.02	0.90	1.15	0.79
Reduced menses	169	24.01 (20.93-27.37)	463	26.23 (24.21-28.36)	0.92	0.79	1.06	0.26
Irregular menstrual cycle	329	46.73 (43.00-50.50)	771	43.68 (41.36-46.04)	1.10	0.96	1.24	0.18
Vegetarian diet	270	38.35 (34.76-42.07)	678	38.41 (36.14-40.73)	0.99	0.88	1.14	1.00

Freq. = frequency, RR = relative risk, CI = confidence interval, p = probability

Assessment of the continuous variables: age, number of pregnancies, age at menarche, interval between, duration of menstrual flow, exercise per week, caffeine intake, smoking, alcohol, pain intensity, pain related to menses, pain at deep intercourse, painful urgency, dysuria, pain while sitting, pain intensity in regard with location: parasacrat, lumbar, hypo-gastric or perineal, or pain characteristics: throbbing, stabbing, cramping, aching, or hot-burning are presented in Table 2.

The generalized cluster analysis was done using selected variables: marital status, level of education, type of activity, complication at delivery, age, age at menarche, caffeine and alcohol consumption, cigarettes per day, pain intensity, pain preceding menses, pain during menses, pain at deep intercourse, painful urgency, and dysuria.

The patients were classified in two groups by k-mean technique with maximizing the Euclidian distance, for a training error of 1.127671. Centroids for K-mean clustering are presented in Table 3 and the graph of means for continuous variables are presenting in Figure 1.

Results of the generalized cluster analysis are presented in Table 5 for categorical variables and in Table 6 for continuous variables.

Membership to cluster 1 is statistically significant correlated with the presence of the chronic pelvic pain (GrA), respectively membership to cluster 2 is correlated with the absence of the chronic pelvic pain (GrA) (Table 6).

**Table 2.** Mann-Whitney U test results. Number of valid cases

	GrA (n=704)		GrB (1765)		U	p-level
	Mean	95%CI	Mean	95%CI		
Age	34.62	33.76-35.47	40.62	40.00-41.24	460620.0	0.0000
Number of pregnancies	1.12	1.06-1.19	1.20	1.16-1.24	593167.0	0.0652
Age at menarche	11.84	11.75-11.93	12.09	12.03-12.15	551617.0	0.0000
Interval between menses	22.14	21.95-22.33	22.02	21.89-22.14	604888.0	0.3023
Duration of menstrual flow	3.50	3.42-3.58	3.48	3.43-3.53	614757.0	0.6735
Exercise (times / week)	1.47	1.42-1.53	1.51	1.47-1.54	608620.0	0.3475
Caffeine (cups/day)	5.40	5.18-5.62	4.87	4.72-5.01	557826.5	0.0000
Cigarettes (number/day)	13.95	13.10-14.80	11.89	11.42-12.36	562644.0	0.0001
Alcohol (ml pure/week)	243.54	231.83-255.25	152.47	146.74-158.19	432099.0	0.0000
Pain intensity	6.51	6.35-6.66	3.10	3.01-3.18	151076.0	0.0000
Pain precedes menses	1.03	0.84-1.22	0.06	0.03-0.08	536144.0	0.0000
Pain during menses	0.81	0.64-0.98	0.09	0.06-0.12	562527.5	0.0000
Pain at deep intercourse	1.03	0.84-1.22	0.10	0.07-0.13	538898.5	0.0000
Painful urgency	3.64	3.37-3.92	1.21	1.12-1.29	415820.5	0.0000
Dysuria	5.24	5.01-5.48	2.89	2.80-2.98	336432.5	0.0000
Pain while sitting	0.55	0.42-0.67	0.39	0.33-0.46	615149.0	0.5011
Parasacrat pain	0.08	0.02-0.14	0.01	0.00-0.02	615980.0	0.0081
Lumbar pain	1.37	1.17-1.58	0.64	0.57-0.71	609120.5	0.2677
Hypo-gastric pain	2.65	2.40-2.91	1.12	1.03-1.20	578325.0	0.0012
Inguinal pain	0.63	0.49-0.78	0.46	0.40-0.52	598753.5	0.0145
Perineal pain	0.11	0.05-0.18	0.02	0.01-0.04	614031.5	0.0089
Throbbing pain	1.91	1.67-2.14	0.60	0.53-0.67	549309.0	0.0000
Stabbing pain	0.93	0.75-1.11	0.84	0.76-0.92	554650.0	0.0000
Cramping pain	0.79	0.62-0.96	0.82	0.74-0.89	547044.5	0.0000
Aching pain	0.82	0.65-0.99	0.26	0.21-0.30	588492.5	0.0000
Hot-burning pain	1.85	1.61-2.08	0.48	0.42-0.54	537014.0	0.0000

CI = confidence interval for p=95%, U = statistic for Mann Whitney test, p = p value for U.

**Table 3.** Centroids for K-mean clustering

	Cluster	
	1	2
Marital status - Single	No	No
Higher education	No	Yes
Physical work	Yes	No
Complications at delivery	No	No
Age	36.33	41.47
Age at menarche	12.09	11.98
Caffeine (cups/day)	5.30	4.74
Cigarettes (number/day)	12.50	12.45
Alcohol (ml pure/week)	188.10	168.86
Pain intensity	4.30	3.84
Pain precedes menses	0.38	0.29
Pain during menses	0.32	0.27
Pain at deep intercourse	0.38	0.35
Painful urgency	2.37	1.43
Dysuria	3.77	3.35
Number of cases	1231	1238
Percentage(%)	49.86	50.14

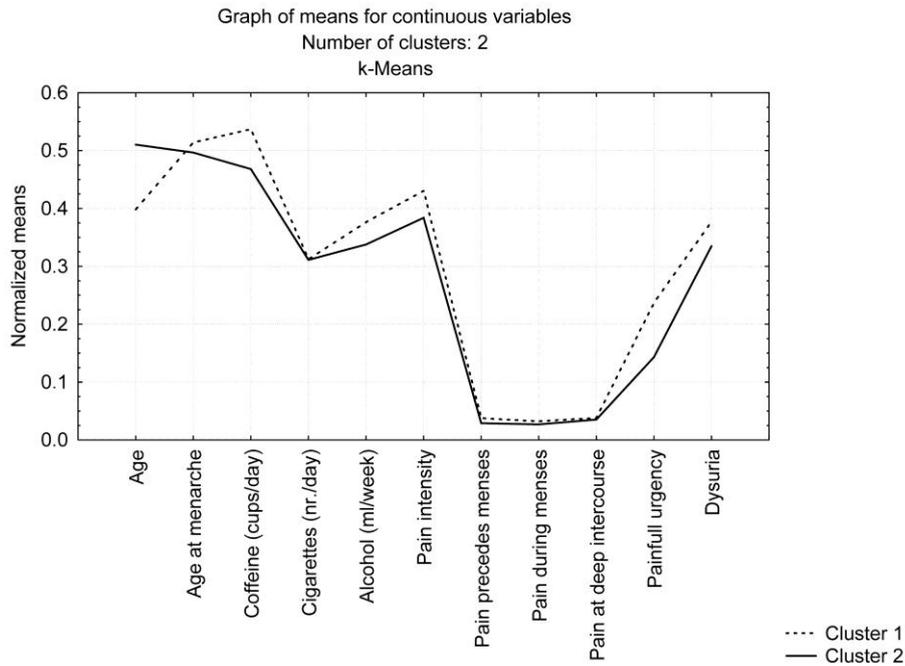


Figure 1. Graph of means for continuous variables

Table 4. Generalized cluster analysis k-means results for categorical variables with chi-square results.

		Cluster 1		Cluster 2		Chi-square	p value
		Freq.	%	Freq.	%		
Marital status - Single	Yes	407	33.06	513	41.44	18.521	0.000017
	No	824	66.94	725	58.56		
Higher education	Yes	19	1.54	1070	86.43	1804.129	0.000000
	No	1212	98.46	168	13.57		
Physical work	Yes	1077	87.49	18	1.45	1851.221	0.000000
	No	154	12.51	1220	98.55		
Complications at delivery	Yes	213	17.30	172	13.89	5.452	0.019546
	No	1018	82.70	1066	86.11		

Table 5. Generalized cluster analysis k-means results for continuous variables with analysis of variance

	Cluster 1		Cluster 2		U	p-level
	Mean	CI	Mean	CI		
Age	36.33	35.63-37.02	41.48	40.74-42.21	588670.5	0.000000
Age at menarche	12.06	11.99-12.13	11.99	11.91-12.06	740732.5	0.230072
Caffeine (cups/day)	5.30	5.12-5.47	4.74	4.58-4.91	685234.0	0.000015
Cigarettes (number/day)	12.50	11.89-13.12	12.45	11.89-13.01	748938.5	0.461213
Alcohol (ml pure/week)	188.06	180.16-195.96	168.86	161.17-176.55	708456.0	0.002507
Pain intensity	4.30	4.17-4.44	3.84	3.71-3.97	681860.0	0.000006
Pain precedes menses	0.38	0.29-0.47	0.29	0.21-0.37	755784.5	0.726102
Pain during menses	0.32	0.24-0.41	0.27	0.20-0.34	757806.5	0.813316
Pain at deep intercourse	0.38	0.29-0.47	0.35	0.27-0.44	759666.0	0.895649
Painful urgency	2.37	2.21-2.54	1.43	1.30-1.57	616793.0	0.000000
Dysuria	3.77	3.63-3.92	3.35	3.22-3.48	698658.5	0.000349

CI = confidence interval for p=95%, U = statistic for Mann Whitney test, p = p value for U.

**Table 6.** Two way summary table: observed versus classified by generalized cluster analysis

Chronic pelvic pain		Cluster 1	Cluster 2	Total
Yes: GrA		411	293	704
	Column %	33.39	23.67	
	Row %	58.38	41.62	
	Total %	16.65	11.87	
No: GrB		820	945	1765
	Column %	66.61	76.33	
	Row %	46.46	53.54	
	Total %	33.21	38.27	
Total		1231	1238	2469
Total%		49.86	50.14	100.00

Chi-square (Yates) = 28.1366, degree of freedom=1,  $p=0.000001$

## Discussion

Chronic pelvic pain in women referred to our urological department comprises 28.1%, double than the estimated in the general population [1].

On univariate analysis marital status single was protective for chronic pelvic pain ( $RR=0.8599$ ,  $p=0.0268$ ) as it was higher education ( $RR=0.8518$ ,  $p=0.0136$ ), while complications at delivery ( $RR=1.1800$ ,  $p=0.0493$ ) and physical work ( $RR=1.2059$ ,  $p=0.0035$ ) were risk factors. Other factors: history of abuse, abundance of menses, regularity of period, and vegetarian diet lack statistic significance.

Age was significantly statistic lower in the chronic pelvic pain group (Gr.A.) as it was the age at menarche, while caffeine and alcohol consumption is higher as is cigarettes smoked per day. Caffeine and alcohol consumption is related to changing of the nociceptive threshold or the activity of brain area responsible for producing the pain sensation. The other factors: number of pregnancies, interval between menses, duration of menstrual flow, and exercises lack any statistic significance.

A clear cut characteristic of patients with chronic pelvic pain is it's intensity which is statistic significant increased independent of location: parasacrat, inguinal, or perineal, and independent of pain characteristics: throbbing, stabbing, cramping, aching, or hot-burning.

Coexistence of pain related to periods (pain preceding or during menses), pain at deep intercourse, bladder filling pain and voiding pain have also, increased intensity in the presence of chronic pelvic pain.

Since pain intensity is a prerequisite for diagnosis of chronic pelvic pain [7], it is not surprisingly that it is significantly increased in this patient category. Yet, pain intensity is not enough since it may be intense in the absence of chronic pelvic pain.

Classification of patients in two groups, in regard with marital status, level of education, type of activity, complications at delivery, age, age at first menses, caffeine and alcohol consumption, smoking, pain intensity, pain preceding or during menses, pain at deep intercourse, pain related to bladder filing and dysuria, using cluster analysis was done with an increased training error of 1.127671.

Assessment of the results indicate that level of education is statistic significant correlated with the cluster 2 while physical work is statistic significant more frequent in cluster 1. Even significant statistic, marital status and complications at delivery seems less related to belonging to one of the two groups.

Regarding the continuous variables, age was lower in the cluster 1, while caffeine and alcohol consumption were increased. Pain intensity was also increased as it was associated pain related to bladder filing and dysuria.

When compared with the presence of the chronic pelvic pain, cluster 1 is statistic significant (chi-square corrected (Yates) 28.1366, degree of freedom=1,  $p=0.000001$ ) correlated with the presence of chronic pelvic pain (GrA).

Most epidemiological data related to women having chronic pelvic pain, deal with the gynecological diseases. There are scarce data regarding the chronic pelvic pain in women referred to urologic departments.

Our data indicate a high proportion of women referred for urologic diseases having chronic pelvic pain. In this study, all patients have a cause related to their pain. Gynecological related risk factors have statistic significance on univariate analysis as general risk factors such as age, education, type of activity and caffeine and alcohol consumption.

Classifying in regard with such significant factors lead to two clusters which are statistical significant correlated with the presence of chronic pelvic pain, yet with less clinical relevance. Moreover, after classification, some factors lack significant differences between clusters: age at menarche, the amount of smoking, pain related to menses or intercourse.

While, caffeine and alcohol consumption may be related to nociceptive alterations and decrease in pain threshold, the other factors may be related to the contribution of different types of pathology involved.

This study is limited due to the heterogeneity of the pathology involved and the complexity of factors involved in producing and maintaining the chronic pelvic pain. On the other hand, we were searched for chronic pelvic pain in association with a clearly identifiable pathology. Exploring the nociceptive pathway and perception may also, contribute to understanding and treatment of the pain component.

Further assessment of relations within specific urologic pathology is currently carried out.

Chronic pelvic pain definition continues to raise controversies especially when underlying etiology could not be demonstrated especially when the diagnostic falls within the practice of different medical specialties.

Definition of the chronic pelvic pain requires a pain length longer than 6 months; it should be clinically significant and unrelated to physiological conditions. Pain should produce functional disability, interfere with normal activities or require medical treatment [7, 8]. In our study, pain intensity was significantly higher in patients with chronic pelvic pain.

Limiting definition of chronic pelvic pain in the absence of a obvious pathology [9] is conflicting at least with the case of endometriosis. On the other hand, presence of a pelvic pathology may not be the cause of a chronic pelvic pain or the pain intensity may not be correlated with the amplitude of the underlying pathology.

Chronic pelvic pain was traditional considered related to gynecological pathology [2]. However, gynecologic causes counts for only 20.2% of the cases while urinary and gastrointestinal causes represent 68.5%. Moreover, 25-50% of women have been given more than one diagnostic [4, 5]. Thus, thoroughly medical history, clinical, laboratory and imagistic assessment should identify all organs and systems involved and provide the best chance for an etiologic treatment.

Sometimes, health care providers question the existence of such pathology in the absence of a demonstrable cause. However, it is important to recognize the existence of such a pain syndrome where pain is the main symptom [10].

## **Conclusions**

Age, marital status, level of education, type of activity, complications at delivery, caffeine and alcohol consumption are risk factors related to chronic pelvic pain in women referred for urologic conditions. Pain intensity is related to chronic pelvic pain, regardless of type and localization. Classification of patients using k-mean technique cluster analysis correlates significantly statistic with chronic pelvic pain.

## **Ethical Issues**

The study did not interfere with diagnostic and treatment of the patients.

### Conflict of Interest

The authors declare that they have no conflict of interest.

### Authors' Contributions

All authors have equally contributed to the study. All authors read and approved the final manuscript.

### References

1. Mathias SD, Kuppermann M, Liberman RF, Lipschutz RC, Steege JF. Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. *Obstet Gynecol* 1996;87(3):321-7.
2. Latthe P, Mignini L, Gray R, Hills R, Khan K., Factors predisposing women to chronic pelvic pain: systematic review. *BMJ*. 2006 Apr 1;332(7544):749-55. Epub 2006 Feb 16.
3. Vercellini P, Somigliana E, Viganò P, Abbiati A, Barbara G, Fedele L., Chronic pelvic pain in women: etiology, pathogenesis and diagnostic approach. *Gynecol Endocrinol*. 2009 Mar;25(3):149-58
4. Zondervan KT, Yudkin PL, Vessey MP, Dawes MG, Barlow DH, Kennedy SH. Patterns of diagnosis and referral in women consulting for chronic pelvic pain in UK primary care. *Br J Obstet Gynaecol* 1999;106(11):1156-61.
5. Zondervan KT, Yudkin PL, Vessey MP, Dawes MG, Barlow DH, Kennedy SH., Prevalence and incidence of chronic pelvic pain in primary care: evidence from a national general practice database. *Br J Obstet Gynaecol* 1999;106(11):1149-55.
6. Fenton BW. Limbic associated pelvic pain: a hypothesis to explain the diagnostic relationships and features of patients with chronic pelvic pain. *Med Hypotheses* 2007;69(2):282-6.
7. Howard FM., The role of laparoscopy in chronic pelvic pain: promise and pitfalls. *Obstet Gynecol Surv* 1993;48(6):357-87.
8. Paul Martyn. Update On: Chronic Pelvic Pain. *Can J Diagn* 2004;21(1):57-60.
9. Warren JW, Morozov V, Howard FM. Could chronic pelvic pain be a functional somatic syndrome? *Am J Obstet Gynecol* 2011;205(3):199.e1-5.
10. Giamberardino MA. Recent and forgotten aspects of visceral pain. *Eur J Pain* 1999;3(2):77-92.