Eur Spine J
DOI 10.1007/s00586-012-2162-x

REVIEW ARTICLE

Pregnancy-related pelvic girdle pain and its relationship with relaxin levels during pregnancy: a systematic review

Daniela Aldabe · Daniel Cury Ribeiro · Stephan Milosavljevic · Melanie Dawn Bussey

Received: 13 September 2011 / Revised: 11 January 2012 / Accepted: 18 January 2012

Abstract
Purpose The present systematic review assessed the level of evidence for the association between relaxin levels and pregnancy-related pelvic girdle pain (PPGP) during pregnancy.
Methods PRISMA guidelines were followed to conduct this systematic review. Electronic search was carried out using six different databases. Observational cohorts, cross-sectional or case–control studies focused on the association between relaxin levels and PPGP during pregnancy were included. Studies selection was conducted by two reviewers who screened firstly for titles, then for abstracts and finally for full articles. Risk of bias was assessed using the Newcastle–Ottawa scale and the quality of evidence by the guidelines proposed by the Cochrane back review group.
Results 731 references were identified. Six articles met the inclusion criteria and were considered for this systematic review. The main reason for the studies exclusion was PPGP related to gynaecological reasons. Five studies were case–control and one study was a prospective cohort. Four studies were ranked as high while two were ranked as low quality. Among the high quality studies, three found no association between PPGP and relaxin levels.
Conclusions Based on these findings, the level of evidence for the association between PPGP and relaxin levels was found to be low. PPGP assessment and controlling for risk factors were found to increase bias leaving uncertainty in interpretation of these findings and a need for further research.

Keywords Pregnancy-related pelvic girdle pain · Relaxin · Low back pain · Pregnancy · Systematic review

Introduction

Pregnancy-related pelvic girdle pain (PPGP) is a common musculoskeletal disorder affecting approximately 20% of all pregnant women [1]. Women who experience this disorder frequently present with reduced capacity for functional activities [2], and are three times more likely to have post-partum depressive symptoms [3]. Although the aetiology of PPGP remains unknown, several studies suggest it is linked to increased pelvic mobility leading to pelvic joint instability and pain [4–6].

Validated biomechanical models of the pelvis support the concept of the sacroiliac joint (SIJ) being stabilized by active and passive structures surrounding the pelvis [7, 8]. For instance, it has been shown that pelvic ligaments, such as the long dorsal, the iliolumbar and the sacrotuberous play key roles in pelvic stabilization such as, preventing excessive nutation and contranutation [9, 10]. Additionally, active structures such as gluteus maximus, erector spinae, the biceps femoris and the thoracolumbar fascia attach to these ligaments and to the sacroiliac joint (SIJ) and contribute to stabilization [10–12]. The sacrospinous and sacrotuberous ligaments also improve pelvic stability by providing proprioceptive information regarding pelvic position [13].

D. Aldabe (✉) · M. Dawn Bussey
School of Physical Education, University of Otago,
56 Union Street, Dunedin 9016, New Zealand
e-mail: daldabe@gmail.com

D. C. Ribeiro · S. Milosavljevic
Centre for Physiotherapy Research, School of Physiotherapy,
University of Otago, 325 Great King Street, Dunedin 9016,
New Zealand

D. C. Ribeiro
Otago Polytechnic, Otago Institute of Sport and Adventure,
41 Harbour Terrace, Private Bag, Dunedin 1910, New Zealand

Published online: 04 February 2012

Consequently, some studies advocate the use of a pelvic belt during pregnancy to structurally stabilise the pelvic girdle, relative to the SIJ, as a useful intervention for reducing PPGP symptoms [14, 15]. However, the effectiveness of such intervention is still in debate [16].

Relaxation of the pelvic ligaments is a physical change required during pregnancy and delivery. Such change begins at the tenth to twelfth week of pregnancy [17] and is considered to be a consequence of hormonal changes that occur about the same time [18]. Relaxin, a peptide hormone of the insulin-like growth factor family, has been associated with collagen remodelling in mammalians, including guinea pig, mouse, and human [19–21]. Secreted by the corpus luteum and placenta from early pregnancy, this hormone level increases to a considerable level during the first trimester, remaining steady at this level until late pregnancy and then becoming serologically undetectable in the first few days post-partum [22]. It is believed that relaxin increases pelvic laxity, and predisposes separation of the pubic symphysis, by altering the structure of collagen [23]. However, experimental studies have not shown a direct relationship between high levels of relaxin and increased pelvic mobility or peripheral joint mobility in pregnant women [5, 24].

Debate exists within the literature regarding the potential role of the hormone relaxin in the manifestation of PPGP. While some studies argue relaxin loosens the pelvic ligaments and increases instability [17, 23, 25, 26] others do not accept that such relationship has been proven [1, 27]. These conflicting arguments have created a need for a systematic review to determine the level of evidence for pregnant women with higher levels of relaxin being more likely to develop PPGP. To our knowledge, no previous systematic review has addressed this question.

Methodology

The review was conducted following the guidelines described by the PRISMA Statement [28]. For more details regarding to the methods of this systematic review, a protocol developed prior to the research was constructed and is available from the corresponding author upon request.

Eligibility criteria

Inclusion criteria were

1. Observational studies such as cohort, cross-sectional and case–control;
2. Studies focusing on the causal relationship between PPGP and relaxin levels during pregnancy;
3. Study population: pregnant women in any stage of pregnancy with no age limits.

No language restriction was imposed.

Exclusion criteria were

1. Randomised and literature review studies, as well as, thesis and dissertations;
2. Studies unrelated to PPGP or where PPGP has not been defined as a musculoskeletal disorder.

Information sources

The electronic search was carried out using the following databases: Medline (1966 to July 2011), Amed (1985 to July 2011), EMBASE (1988 to July 2011), Proquest (July 2011), Web of Science (July 2011) and Scopus (July 2011).

Search

A literature search was carried out to identify all available published articles on the relation and/or association between PPGP and relaxin levels. The identification of terms used in the search and the search strategy were developed in consultation with a health sciences librarian at the University of Otago. The search terms were based on keywords from previous publications as well as database-specific search terms [subject terms, subject headings (SH) and MeSh]. A string search was created adding 'OR' and 'AND' to combine the keywords and the subjects areas. The keywords used related to relaxin and PPGP were 'relaxin' or 'hormone' or 'reproductive hormone' and 'pelvic girdle pain' or 'low back pain' or 'pelvic pain' or 'peripartum pelvic pain' or 'posterior pelvic pain' or 'pelvic insufficiency'. Additionally, one author (DA) scanned the reference lists of retrieved articles.

Study selection

All studies identified through the electronic search were stored in Endnote® software (v.14 Thomson Reuters). Duplicate results were identified and removed by the principal investigator (DA). During screening by DA and DCR all titles were identified through electronic search as well as additional records identified through other sources. At the second stage of selection of studies, summary and full-text articles were screened, by the same two assessors (DA and DCR), against the predetermined inclusion and exclusion criteria. Titles, abstracts and manuscript were not blinded for journal titles, authors and institutions, since blinding has previously been shown not to affect the study selection and data extraction [29]. If multiple reporting from the same study was found, only one study

was included with all others referenced. Disagreement between the reviewers during the screening process was determined by consensus. If consensus could not be reached a third reviewer (MB) provided the majority opinion.

Data collection process

Data extraction from selected studies followed guidelines proposed by the Cochrane Back Review Group [30]. This was firstly performed by the principal investigator (DA) and subsequently confirmed by DCR. The following data were extracted: study design, year of the study, sample size population, gestational period of the population, levels of relaxin, type of assay used for measuring relaxin levels, PPGP assessment description, statistical analysis, main findings and conclusion.

Risk of bias in individual studies

The risk of bias in individual studies was independently assessed by two authors (DA and DRC) using the Newcastle–Ottawa scale (NOS) for observational studies [31]. This instrument was developed for the assessment of case–control and cohort studies. It has three main categories: selection of the participants, comparability of the groups and ascertainment of either the exposure (for case–control) or outcome of interest (for cohort studies). A maximum score of nine points was given for the study that fulfilled all quality criteria. For the purpose of this review, studies with five or more points were considered as high quality [32, 33].

The following criteria were used when assessing for risk of bias in individual studies (Tables 2, 3). For both item 1 (selection for case–control studies) and 6 (outcome for cohort studies), studies were awarded when pelvic pain location and at least one specific test for PPGP were described. The PPGP-specific tests considered as valid were posterior pelvic pain provocation, active straight leg raise, modified Trendelenburg, Patrick's Faber and Menell's tests. All these tests were accepted as having either high sensitivity or specificity for sacroiliac or symphysis joint pain [1].

Group comparability (both case control and cohort studies) for history of low back pain (LBP), history of PPGP during or after pregnancy, body mass index (BMI), parity, smoking and stress levels were considered for personal factors and psychosocial factors. These factors have been described as strong risk factors for developing PPGP [34–38]. Studies controlling for one or more than one of the above listed factors were awarded with one or two points, respectively.

For item 6 (exposure for case control studies) and item 3 (selection for cohort studies) recognition was given to studies that quantified relaxin levels using enzyme-linked immunosorbent assay (ELISA) and presented its coefficients of variation and serum samples were blindly analysed. Studies measuring relaxin concentrations using ELISA, without the above information described, or porcine radioimmunoassay were not awarded any point. This quality assessment restriction was due to the high variability shown in studies using ELISA [39] and the considerable differences observed between porcine and human relaxin levels during pregnancy [40].

Inter-rater reliability for assessment of risk of bias agreement between reviewers was measured by means of Kappa analysis. For this, the Statistical Package for the Social Science (Version 16 SPSS Inc. IL, USA) was utilized.

Quality of evidence assessment

The quality of evidence for the relationship between PPGP and relaxin levels was conducted by following the 2009 guidelines for systematic reviews proposed by the Cochrane Back review group [30]. Five levels of evidence were considered:

- High quality of evidence: a minimum of 75% of the studies have same findings, direct and precise data and no risk of bias was identified.
- Moderate quality of evidence: 1 of the domains is not met.
- Low quality of evidence: 2 domains are not met.
- Very low quality of evidence: 3 domains are not met.

Results

Study selection

In total, 731 references were extracted from all searched databases. Among them, 189 were from ProQuest, 187 from Web of Science, 109 from Embase, 166 from Scopus, 77 from Medline and 3 from Amed. Removal of duplicates resulted in 246 references. Following consensus, review of titles and abstracts 239 references were excluded as they did not meet the inclusion or exclusion criteria. The overall research strategy and screening can be seen in Fig. 1. Two studies, written by Kristiansson et al. [41, 42], used the same group population, and consequently, only one study was included in this review [41]. Therefore, a total of six articles were included for this review.

Study characteristics

Table 1 shows the main characteristics of each study. Briefly, five were case–control studies and one was a prospective

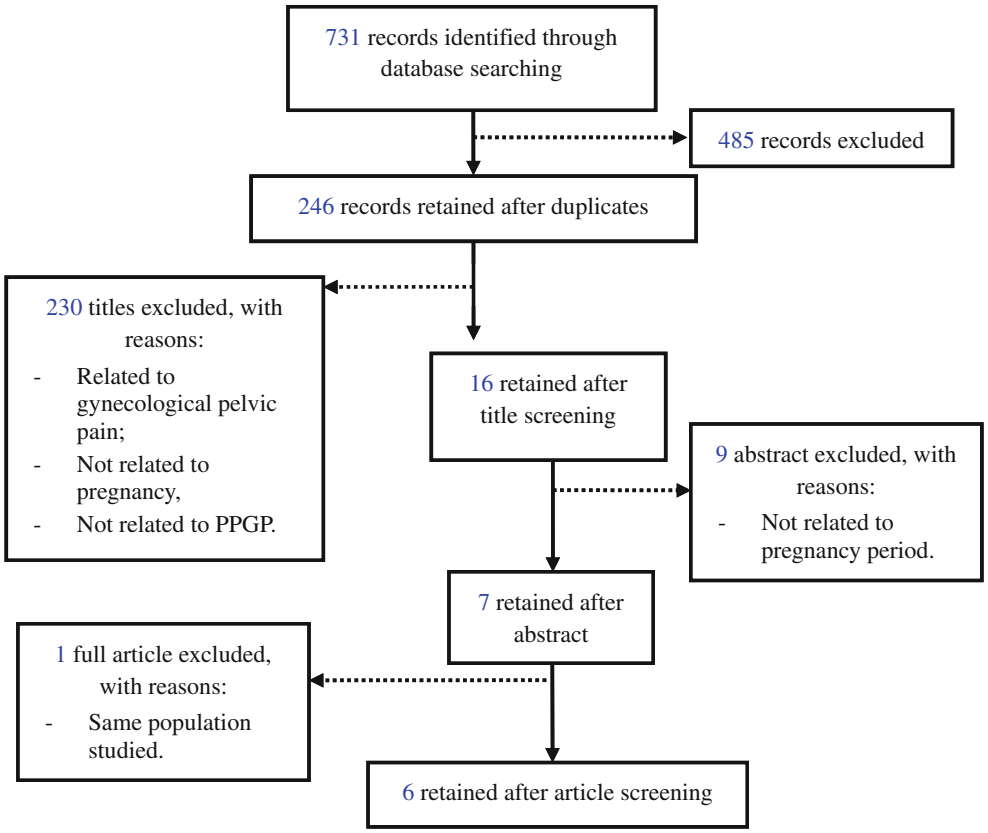

Fig. 1 Selection process

cohort study. The oldest study dated 1986 and the most recent, 2000 [39]. Clinical tests more often used were modified Trendelenburg test [39, 43, 44], ASLR [39, 41], sacrotuberous ligament palpation [41, 44] and symphysis palpation [39, 44]. ELISA was used for measuring relaxin levels in all studies, apart from [43], who used homologous porcine radioimmunoassay. Intra and interassay coefficient of variation were described in all studies, except for Albert et al. [45]. The pregnancy period analysed among studies varied considerably. The pregnancy period can be seen in Table 1.

Risk of bias within studies

Prior to reviewer consensus inter-rater reliability for chosen manuscripts was found to be fair (Cohen's kappa: 0.38). The quality scores of the studies are shown in Tables 2 and 3. Four studies received five or more points [39, 41, 44, 45] and two studies less than five [43, 46]. Thus, four out of six studies were considered as high quality studies.

Results of individual studies

The results from individual studies can be seen in Table 4. A positive association between relaxin levels and PPGP was found in two out of six studies [41, 43]. However, four studies could not demonstrate any association between PPGP and relaxin levels [39, 41, 44–46].

MacLennan et al. [43] were the first to publish such association. For this study, participants were divided in two different groups (control and PPGP group) and they were assessed over two pregnancy periods: 6–26th and 27–42nd weeks. According to this study, subjects with PPGP presented significantly higher relaxin levels ($p = 0.02$, $p < 0.00005$). Mean and standard deviations values were only graphically described and no data tables were presented. Kristiansson et al. [41] also found a positive relationship between relaxin levels and PPGP in a prospective study which followed pregnant women from early pregnancy until the 36th week. The authors found that women who presented with pain at the symphysis and trochanteric region presented significantly higher relaxin levels ($p = 0.04$ and 0.02 respectively).

Conversely Petersen et al. [46] did not find any association between relaxin levels and PPGP (p value not described). In this study, the PPGP group were subcategorised according to level of pain: slight, moderate and severe. Pelvic girdle pain level was found not to be associated with levels of relaxin. Similarly, Hansen et al. [44] could not demonstrate any association between relaxin

Table 1 Study characteristics

	Study	Design	Year	PPGP assessment	Relaxin assessment (intra and inter assay CV)	Pregnancy period
1	MacLennan et al.	Case–control	1986	Modified Trendelenburg test	Homologous porcine radioimmunoassay (11 and 9.5%)	6–42nd week
2	Petersen et al.	Case–control	1994	Presence or not of PPGP	ELISA (17 and 23%)	30th week
3	Kristiansson et al.	Prospective Cohort	1996	Pain drawing ASLR P4 STL palpation Symphysis palpation Hip motion assessment	ELISA (5 and 12%)	12–36th week and another one in between
4	Hansen et al.	Case–control	1996	Symphysis palpation Modified Trendelenburg test Iliopsoas muscle Palpation SIJ palpation STL palpation Patrick test	ELISA (2.7 and 4.5%)	30–38 weeks
5	Albert et al.	Case–control	1997	Pain location 16 physical tests—not described	ELISA (CV not presented)	32–33 weeks
6	Björklund et al.	Case–control	2000	Palpation of lumbar spine, SIJ and symphyseal joint ASLR Modified Trendelenburg	ELISA (10% and 12/13/16%)	12 and 36th week

Table 2 Risk of bias for case–control studies based on Newcastle–Ottawa Quality assessment scale

Study	Selection				Comparability	Exposure			Total#
	1	2	3	4	5	6	7	8	
MacLennan et al.	B	B	C	B	C	C	A*	B	1
Petersen et al.	B	B	C	B	C	A*	A*	A*	3
Hansen et al.	A*	A*	A*	A*	A*	A*	A*	A*	8
Albert et al.	A*	A*	A*	A*	C	C	A*	A*	6
Björklund et al.	A*	A*	A*	A*	A*B*	A*	A*	A*	9

Selection: *1* is the case definition adequate? *2* Representativeness of the cases, *3* selection of controls, *4* definition of controls; comparability: *5* comparability of cases and controls on the basis of the design or analysis; exposure: *6* ascertainment of exposure, *7* same method of ascertainment for cases and controls, *8* non-response rate

[#] Total score is calculated by the sum of asterisks (*)

Table 3 Risk of bias for cohort studies based on Newcastle–Ottawa Quality assessment scale

Study	Selection				Comparability	Outcome			Total#
	1	2	3	4	5	6	7	8	
Kristiansson et al.	A*	A*	A*	A*	A*B*	A*	A*	B*	9

Selection: *1* Representativeness of the exposed cohort, 2 selection of the non-exposed cohort, *3* ascertainment of exposure, *4* demonstration that outcome of interest was not present at start of study; comparability: *5* comparability of cohorts on the basis of the design or analysis; outcome: *6* assessment of outcome, *7* Was follow-up long enough for outcomes to occur, *8* adequacy of follow-up of cohorts

[#] Total score is calculated by the sum of asterisks (*)

Table 4 Relaxin levels and study groups

Author	Control group (*n*) or baseline	Relaxin levels mean/median (SD/range)	PPGP group (*n*) or follow-up	Relaxin levels mean/median (SD/range)	*P* value	Main findings
MacLennan et al.	6–26th weeks (85)	Not clearly stated	6–26th weeks (127)	Not clearly stated	0.02	Relaxin levels are higher in PPGP group
	27–42nd weeks (93)		27–42nd weeks (158)		<0.00005	
Petersen et al.	No pain (16)	343 (16)	Slight pain (59)	332 (20)	NS	No difference in relaxin levels between groups
			Moderate pain (8)	342 (16)		
			Severe pain (1)	381		
Kristiansson et al.	No pain (200)	Not clearly stated	Pain at symphysis	Not clearly stated	0.04	Positive correlation between mean relaxin levels and symphyseal pain
			Pain at trochanteric region		0.02	
Hansen et al.	<24th week (9)	1,087 (170–1,250)	<24th week	736 (278–1,251)	0.99	No difference in relaxin levels between groups
	24th week–delivery (12)	551 (20–1,251)	Chronic pain (8)	676 (568–781)	0.99	
			Ex positive (3)			
			24th week–delivery	556 (278–1,251)	0.99	
			Chronic pain (20)	605 (154–1,163)	0.99	
			Ex positive (18)			
Albert et al.	Matched controls (455)	556 (403)	Pelvic girdle syndrome (125)	552 (286)	NS	No difference in relaxin levels between groups
		498 (244)	Symphysiolysis (44)	589 (348)		
		532 (283)	One-sided SIJ pain (118)	592 (323)		
		516 (256)	Double-sided SIJ pain (168)	579 (305)		
Björklund et al.	12th week (35)	1,233 (590)	12th week (11)	1025 (256)	NS	No difference in relaxin levels between groups
	36th week (36)	733 (323)	36th week (11)	725 (397)		
			36th week referral group (19)	633 (358)		

concentrations and PPGP ($p = 0.99$). Three groups were retrospectively defined: control, chronic pain (patients who presented with PPGP symptoms during pregnancy and 2 months after delivery) and ex-positive groups (patients who presented with PPGP only during pregnancy). Although they also measured relaxin levels after pregnancy, this systematic review is only comparing information relative to pre-partum period. Additionally, we maintained the same group categories (control, chronic and ex positive), as it was not possible to group their results.

Albert et al. [45] also found similar results. In their study, PPGP group was subcategorized into four groups: pelvic girdle syndrome, symphysiolysis, one-sided SIJ pain and double-sided SIJ pain. PPGP group did not differentiate from controls in terms of relaxin levels *p* value not described). Likewise, Björklund et al. [39] did not found association between PPGP and relaxin levels ($p = 0.927$). In this research the authors conducted a cross-sectional and cohort study. Three groups were investigated: controls and cases, from the cohort, and referral, from the cross-sectional study. The latter group consisted of pregnant women who were diagnosed with PPGP at the 36th week of pregnancy. Pregnant women in the 12th week of pregnancy were followed until the 36th week in the cohort study and case and control groups.

Discussion

The aim of this systematic review was to determine the level of evidence for a high level of relaxin during pregnancy being associated with PPGP. Four out of six studies (66%) did not find an association between levels of relaxin and PPGP. As the level of quality (risk of bias) of these studies varied widely from 3 to 9 out of a total possible score of 9 the average quality of evidence for relaxin not being related to PPGP was considered low. According to the 2009 Guidelines for Systematic Reviews, high quality evidence can be considered when at least 75% of the studies have consistent findings with none having a risk of bias [30].

Apart from one study [46], the overall level of quality score of the studies reporting no associations between related relaxin levels and PPGP were considered high. One of the main strengths of these studies was the physical assessment conducted for the PPGP diagnosis. PPGP assessment was clearly shown in Björklund et al. [39], Hansen et al. [44] and Albert et al. [45] studies and they comprised at least one physical test. In the latter study, intertester reliability was conducted in all the tests [47]. Several studies have suggested that pelvic girdle pain should be diagnosed by eliminating low back or gynaecological symptoms [1, 48, 49]. Thus, specific pain provocation and functional tests, as well as, pain location should be demonstrated [50].

One study conducted by Petersen et al. [46] that did not demonstrate association between PPGP and relaxin levels, presented the highest risk of bias when assessing PPGP. In this study, pregnant women were included in the PPGP group if they presented with pain in the pelvic area causing restriction in their daily activities. Moreover, a disability scale categorised these women with slight, moderate and severe disabling pelvic pain. However, neither the pain location assessment criterion, nor the reliability or validity for the disability index [51], was demonstrated. Valid, reliable, sensitive and specific physical tests and a clear demonstration about pain location are necessary when assessing PPGP [52]. Studies which do not clearly perform and/or describe these aspects can lead to misleading conclusions.

Björklund et al. [39] and Hansen et al. [44] also controlled PPGP risk factors. Hansen et al. [44] controlled for parity and Björklund et al. [39] for history of LBP, BMI and parity. As risk factors for the development of PPGP are numerous, they should be controlled when cause and effect associations are investigated. Prior histories of LBP or PPGP and strenuous work have been described as the strongest risk factors for newly developed PPGP [53]. More recent studies also report that parity, BMI and smoking can represent risk factors [36–38, 54]. Further bias was identified in the Petersen et al. [46] and Albert et al. [45] manuscripts relative to the control of personal and psychosocial factors among cases and controls. Neither of these studies demonstrated control of the history of LBP or PPGP, parity, smoking, BMI or stress.

All studies which do not find a positive association between relaxin and PPGP, measured relaxin concentrations by means of ELISA and all, apart from one [45], described specific information with regard to its variability. ELISA interassay and interassay coefficients of variation among studies that did not relate relaxin to PPGP varied from 2.7 to 23%, meaning low variability between samples and assays. Interestingly, the only study which used a radioimmunoassay with an antibody to porcine assay found a positive association between relaxin levels and PPGP [43]. Given that porcine relaxin has approximately 50% homology in amino acid sequence, this might be the cause of such result [55].

Conclusion

Three of four high quality studies could not find a positive association between relaxin and PPGP. However, the manner of assessing PPGP and controlling for risk factors introduces bias leaving uncertainty in interpretation and a need for further research. Such future research should standardise assessment procedures for PPGP and, at a minimum, uniformly control for stress and a history of LBP and PPGP in study design.

Acknowledgments Support was provided by the University of Otago (PhD Scholarship). The authors would like to thank Judy Fischer (Faculty Librarian) in assisting with the electronic search strategy for this study.

Conflict of interest None.

References

1. Vleeming A et al (2008) European guidelines for the diagnosis and treatment of pelvic girdle pain. Eur Spine J 17(6):794
2. Rost CC et al (2004) Pelvic pain during pregnancy: a descriptive study of signs and symptoms of 870 patients in primary care. Spine (Phila Pa 1976) 29(22):2567–2572
3. Gutke A, Josefsson A, Oberg B (2007) Pelvic girdle pain and lumbar pain in relation to postpartum depressive symptoms. Spine Phila Pa (1976) 32(13):1430–1436
4. Mens JM et al (1999) The active straight leg raising test and mobility of the pelvic joints. Eur Spine J 8(6):468–473
5. Mens JMA, Pool-Goudzwaard A, Stam HJ (2009) Mobility of the pelvic joints in pregnancy-related lumbopelvic pain: a systematic review. Obstet Gynecol Surv 64(3):200–208
6. Ritchie JR (2003) Orthopedic considerations during pregnancy. Clin Obstet Gynecol 46(2):456–466
7. Snijders CJ, Vleeming A, Stoeckart R (1993) Transfer of lumbosacral load to iliac bones and legs: Part 1: biomechanics of self-bracing of the sacroiliac joints and its significance for treatment and exercise. Clin Biomech 8(6):285–294
8. Snijders C, Vleeming A, Stoeckart R (1993) Transfer of lumbosacral load to iliac bones and legs: part 2: loading of the sacroiliac joints when lifting in a stooped posture. Clin Biomech 8(6): 295–301
9. Pool-Goudzwaard A et al (2001) The sacroiliac part of the iliolumbar ligament. J Anat 199(04):457–463
10. Vleeming A, Stoeckart R, Snijders C (1989) The sacrotuberous ligament: a conceptual approach to its dynamic role in stabilizing the sacroiliac joint. Clin Biomech 4(4):201–203
11. Vleeming A et al (1996) The function of the long dorsal sacroiliac ligament: its implication for understanding low back pain. Spine (Phila Pa 1976) 21(5):556–562
12. Pool-Goudzwaard A et al (2003) The iliolumbar ligament: its influence on stability of the sacroiliac joint. Clin Biomech 18(2): 99–105

13. Varga E, Dudas B, Tile M (2008) Putative proprioceptive function of the pelvic ligaments: biomechanical and histological studies. Injury 39(8):858–864
14. Nilsson-Wikmar L et al (2005) Effect of three different physical therapy treatments on pain and activity in pregnant women with pelvic girdle pain: a randomized clinical trial with 3, 6, and 12 months follow-up postpartum. Spine (Phila Pa 1976) 30(8):850–856
15. Mens JM et al (2006) The mechanical effect of a pelvic belt in patients with pregnancy-related pelvic pain. Clin Biomech (Bristol, Avon) 21(2):122–127
16. Ho SS et al (2009) Effectiveness of maternity support belts in reducing low back pain during pregnancy: a review. J Clin Nurs 18(11):1523–1532
17. Heckman JD, Sassard R (1994) Musculoskeletal considerations in pregnancy. J Bone Jt Surg Ser A 76(11):1720–1731
18. Petersen LK et al (1995) Variations in serum relaxin (hRLX-2) concentrations during human pregnancy. Acta Obstet Gynecol Scand 74(4):251–256
19. Hisaw FL (1926) Experimental relaxation of the pubic ligament of the guinea pig. Proc Soc Exp Biol Med 23(23):661–663
20. Samuel CS et al (1996) The effect of relaxin on collagen metabolism in the nonpregnant rat pubic symphysis: the influence of estrogen and progesterone in regulating relaxin activity. Endocrinology 137(9):3884–3890
21. Unemori EN, Amento EP (1990) Relaxin modulates synthesis and secretion of procollagenase and collagen by human dermal fibroblasts. J Biol Chem 265(18):10681–10685
22. Bell R et al (1987) Relaxin in human pregnancy serum measured with an homologous radioimmunoassay. Obstet Gynecol 69(4):585
23. Owens K, Pearson A, Mason G (2002) Pubic symphysis separation. Fetal Matern Med Rev 13(2):141
24. Schauberger CW et al (1996) Peripheral joint laxity increases in pregnancy but does not correlate with serum relaxin levels. Am J Obstet Gynecol 174(2):667–671
25. Borg-Stein J, Dugan SA (2007) Musculoskeletal disorders of pregnancy, delivery and postpartum. Phys Med Rehabil Clin N Am 18(3):459–476, ix
26. MacLennan AH, MacLennan SC (1997) Symptom-giving pelvic girdle relaxation of pregnancy, postnatal pelvic joint syndrome and developmental dysplasia of the hip. The Norwegian Association for Women with Pelvic Girdle Relaxation (Landforeningen for Kvinner Med Bekkenlosningsplager). Acta Obstet Gynecol Scand 76(8):760–764
27. van Dongen PWJ et al (1999) Hypermobility and peripartum pelvic pain syndrome in pregnant South African women. Eur J Obstet Gynecol Reprod Biol 84(1):77–82
28. Moher D et al (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 151(4): 264–269, W64
29. Berlin JA (1997) Does blinding of readers affect the results of meta-analyses? University of Pennsylvania Meta-analysis Blinding Study Group. Lancet 350(9072):185–186
30. Furlan AD et al (2009) 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine (Phila Pa 1976) 34(18):1929–1941
31. Wells G et al (2011) The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital Research Insitute. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm. Accessed 15 Jul 2011
32. Wai EK et al (2010) Causal assessment of occupational bending or twisting and low back pain: results of a systematic review. Spine J 10(1):76–88
33. Roffey DM et al (2010) Causal assessment of awkward occupational postures and low back pain: results of a systematic review. Spine J 10(1):89–99
34. Wu WH et al (2004) Pregnancy-related pelvic girdle pain (PPP), I: terminology, clinical presentation, and prevalence. Eur Spine J 13(7):575
35. Albert HB et al (2006) Risk factors in developing pregnancy-related pelvic girdle pain. Acta Obstet Gynecol Scand 85(5): 539–544
36. Biering K et al (2010) Smoking and pregnancy-related pelvic pain. BJOG 117(8):1019–1026
37. Robinson HS et al (2010) Pelvic girdle pain—associations between risk factors in early pregnancy and disability or pain intensity in late pregnancy: a prospective cohort study. BMC Musculoskelet Disord 11:91
38. Bjelland EK et al (2010) Pelvic girdle pain in pregnancy: the impact of parity. Am J Obstet Gynecol 203(2):146 e1–e6
39. Björklund K et al (2000) Symphyseal distention in relation to serum relaxin levels and pelvic pain in pregnancy. Acta Obstet Gynecol Scand 79(4):269–275
40. Knobil E, Neill JD (2006) The physiology of reproduction, vol 1, 3rd edn. Elsevier, Amsterdam
41. Kristiansson P, Svardsudd K, vonSchoultz B (1996) Serum relaxin, symphyseal pain, and back pain during pregnancy. Am J Obstet Gynecol 175(5):1342–1347
42. Kristiansson P, Svärdsudd K, von Schoultz B (1999) Reproductive hormones and aminoterminal propeptide of type III procollagen in serum as early markers of pelvic pain during late pregnancy. Am J Obstet Gynecol 180(1):128–134
43. MacLennan AH et al (1986) Serum relaxin and pelvic pain of pregnancy. Lancet 2(8501):243–245
44. Hansen A et al (1996) Relaxin is not related to symptom-giving pelvic girdle relaxation in pregnant women. Acta Obstet Gynecol Scand 75(3):245–249
45. Albert H et al (1997) Circulating levels of relaxin are normal in pregnant women with pelvic pain. Eur J Obstet Gynecol Reprod Biol 74(1):19–22
46. Petersen LK, Hvidman L, Uldbjerg N (1994) Normal serum relaxin in women with disabling pelvic pain during pregnancy. Gynecol Obstet Invest 38(1):21–23
47. Albert H, Godskesen M, Westergaard J (2000) Evaluation of clinical tests used in classification procedures in pregnancy-related pelvic joint pain. Eur Spine J 9(2):161–166
48. Gutke A, Kjellby-Wendt G, Oberg B (2010) The inter-rater reliability of a standardised classification system for pregnancy-related lumbopelvic pain. Man Ther 15(1):13–18
49. Mens JM et al (2001) Reliability and validity of the active straight leg raise test in posterior pelvic pain since pregnancy. Spine (Phila Pa 1976) 26(10):1167–1171
50. Robinson HS et al (2010) Pelvic girdle pain, clinical tests and disability in late pregnancy. Man Ther 15(3):280–285
51. Artal R, Toole MO, White S (2003) Guidelines of the American College of Obstetricians and Gynecologists for exercise during pregnancy and the postpartum period/commentary. Br J Sports Med 37(1):6
52. Vermani E, Mittal R, Weeks A (2010) Pelvic girdle pain and low back pain in pregnancy: a review. Pain Pract 10(1):60–71
53. Bastiaanssen JM et al (2005) A historical perspective on pregnancy-related low back and/or pelvic girdle pain. Eur J Obstet Gynecol Reprod Biol 120(1):3–14
54. Biering K et al (2011) Pregnancy-related pelvic pain is more frequent in women with increased body mass index. Acta Obstet Gynecol Scand 90(10):1132–1139
55. Sherwood OD (2004) Relaxin's physiological roles and other diverse actions. Endocr Rev 25(2):205–234