Observational Study

Role of relaxin in diastasis of the pubic symphysis peripartum

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Abstract

BACKGROUND
Separation of the pubic symphysis can occur during the peripartum period. Relaxin (RLX) is a hormone primarily secreted by the corpus luteum that can mediate hemodynamic changes during pregnancy as well as loosen the pelvic ligaments. However, it is unknown whether RLX is associated with peripartum pubic symphysis separation and if the association is affected by other factors.

AIM
To study the association between RLX and peripartum pubic symphysis separation and evaluate other factors that might affect this association.

METHODS
We performed a cross-sectional study of pregnant women between April 2019 and January 2020. Baseline demographic characteristics, including gestational age, weight, neonatal weight, delivery mode and duration of the first and second stages of labor, were recorded. The clinical symptoms were used as a screening index during pregnancy, and the patients with pubic symphysis and inguinal pain were examined by color Doppler ultrasonography to determine whether there was pubic symphysis separation. Serum RLX concentrations were evaluated 1 d after delivery using an enzyme-linked immunosorbent assay, and pubic symphysis separation was diagnosed based on postpartum X-ray examination.
We used an independent-sample t test to analyze the association between serum RLX levels and peripartum pubic symphysis separation. Multivariate regression analysis was used to evaluate whether the association between RLX and peripartum pubic symphysis separation was confounded by other factors, and the association between RLX and the severity of pubic symphysis separation was also assessed. We used Pearson correlation analysis to determine the factors related to RLX levels as well as the correlation between the degree of pubic symphysis separation and activities of daily living (ADL) and pain.

**RESULTS**

A total of 54 women were enrolled in the study, with 15 exhibiting (observational group) and 39 not exhibiting (control group) peripartum pubic symphysis separation. There were no statistically significant differences in terms of maternal age, gestational age, pre-pregnancy weight, weight gain during pregnancy, delivery modes, or duration of the first or second stages of labor between the 2 groups. We did, however, note a statistically significant difference in serum RLX concentrations and neonatal weight between the observational and control groups (122.3 ± 0.7 µg/mL vs 170.4 ± 42.3 µg/mL, P < 0.05; 3676.000 ± 521.725 g vs 3379.487 ± 402.420 g, P < 0.05, respectively). Multivariate regression analyses showed that serum RLX level (odds ratio (OR): 1.022) and neonatal weight (OR: 1.002) were associated with pubic symphysis separation peripartum. The degree of separation of the pubic symphysis was negatively correlated with ADL and positively correlated with pain. There was no statistically significant association between serum RLX levels and the severity of pubic symphysis separation after adjusting for confounding factors.

**CONCLUSION**

Serum RLX levels and neonatal weight were associated with the occurrence, but not the severity, of peripartum pubic symphysis separation.

**Key Words:** Pregnancy; Pubic symphysis separation; Relaxin; Neonatal weight; Cross-sectional study; Activities of daily living

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**Core Tip:** Peripartum separation of the pubic symphysis is not a frequent pregnancy complication, but it can cause chronic pelvic pain and difficult ambulation. Furthermore, it limits activities of daily living (ADL). We performed a cross-sectional study and identified an association between postpartum serum relaxin (RLX) levels and neonatal weight with peripartum separation of the pubic symphysis. The degree of separation of the pubic symphysis was positively correlated with the degree of pain and was negatively correlated with ADL. Serum RLX levels and neonatal weight may be used to identify women at a high risk of pubic symphysis separation peripartum.

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**INTRODUCTION**

Separation of the pubic symphysis refers to dislocation of the pubic fibrocartilages on both sides of the pelvis due to pregnancy or external forces. Soft-tissue injuries, such as the widening of the pubic symphysis or dislocation of the pubic symphysis, with local pain and difficulty in lifting lower limbs, often occur in pregnant and postpartum women. A pubic symphysis gap wider than 10 mm combined with clinical symptoms typically engenders a diagnosis of perinatal pubic symphysis diastasis (PSD). Since the first case published by Reis et al in 1932, the incidence reported in China and
We performed a cross-sectional study and included pregnant women who delivered at

MATERIALS AND METHODS

Study design and participant selection

We performed a cross-sectional study and included pregnant women who delivered at
our hospital between April 2019 and January 2020. Our inclusion criteria were pregnant women who agreed to a blood test for RLX levels and agreed to a postpartum pelvic X-ray to evaluate PSD. Clinical symptoms were used as the screening index during pregnancy. Patients with pubic symphysis and inguinal pain were examined by color Doppler ultrasonography to determine whether there was pubic symphysis separation, and by pelvic X-ray examination after delivery to assess the degree of separation. None of the patients had a history of separation of the pubic symphysis, and patients with severe liver, renal, or cardiac diseases or other underlying conditions were excluded.

Study protocol
We recorded general information regarding the puerpera, including maternal age, pre-pregnancy weight, weight gain, duration of the first and second stages of labor, and neonatal weight. We documented the distance of PSD by pelvic X-ray. Patients with pubic symphysis separation during pregnancy were initially screened by clinical manifestations such as pain at the pubic symphysis, and color Doppler ultrasonography was then performed to determine whether there was pubic symphysis separation.

RLX levels in blood samples collected 1 d after delivery were determined for each study participant. The concentration of serum RLX was determined by an ELISA method as follows: (1) 4 mL of each patient’s blood was taken from the antecubital vein and placed in a test tube without anticoagulant. The serum was separated by centrifugation at 1000 r/min for 15 min at 4°C, and the separated serum was immediately stored at -80°C for testing; and (2) The level of serum RLX was then measured with an ELISA kit using plate wells coated with human RLX antibody (Redd Biological Preparation Co., United States).

Fifteen parturients had PSD and 39 parturients did not have PSD. Of the 15 parturients with diastasis, 8 showed pubic symphysis separation as confirmed by color Doppler ultrasonography, 5 underwent cesarean sections, 3 had spontaneous deliveries, and 7 exhibited pubic symphysis separation after delivery. Of these 15 patients, 13 showed pubic symphysis separation with a gap > 1 cm, and 2 patients had a superior and inferior pubic symphysis dislocation > 1 cm, with a separation distance < 1 cm, including 5 patients who received three-dimensional (3D) adjustment of the pelvis under suspension. Of the parturients without symphysis pubis separation, 19 underwent cesarean section and 20 delivered spontaneously.

We collected postpartum blood samples from 5 patients to detect the levels of RLX relative to the voluntary condition of the patients (Figure 1). After 6 wk of fixation, the clinical symptoms in 4 patients disappeared and the pelvic band was removed. In one patient with a 4.185-cm separation, the clinical symptoms disappeared, and the pelvic band was removed after 8 wk of fixation. Figure 2 shows the X-ray film of the pelvis before separation and reduction of the pubic symphysis in a postpartum woman who had a 4.185-cm gap. Figure 3 shows a pelvic X-ray after reduction of the pubic symphysis and removal of the pelvic band after 2 wk.

Statistical analysis
We used SPSS (version 20.0; IBM, United States) for statistical analysis. Continuous data are presented as mean ± SD and categorical data are presented as percentages. An independent sample t test and Chi-squared test were used to compare the 2 groups. Differences were considered statistically significant at P < 0.05. Unconditional multivariate logistic regression analysis was used to analyze the potential multiple factors related to pubic symphysis separation. We used multiple linear regression analysis to explore the associations between serum RLX levels as well as other factors with the degrees of pubic symphysis separation. Pearson correlation analysis was used to study the factors related to RLX levels, and to assess any correlations between the degree of separation of the pubic symphysis, activities of daily living (ADL) and pain.

RESULTS
A total of 54 peripartum women were enrolled in our study; 15 had pubic symphysis separation (observational group), and 39 did not have separation (control group). Of the 15 women with separation, 5 underwent cesarean section, 3 delivered spontaneously, and 7 exhibited pubic symphysis separation after delivery. Of these 15 patients, 13 exhibited pubic symphysis separation with a gap > 1 cm, and 2 patients had a superior and inferior pubic symphysis dislocation of > 1 cm, with a separation...
Figure 1  Changes in relaxin levels in 5 patients with pubic symphysis separation.

Figure 2  Pre-reduction X-ray image of a patient with a nearly 5-cm separation of the pubic symphysis.

distance of < 1 cm. Five patients also received 3D adjustment of the suspended pelvis. With regard to the controls without symphysis pubis separation, 19 cases underwent cesarean sections and 20 cases delivered spontaneously. Comparisons between the observational group and the control group are listed in Tables 1 and 2. Except for serum RLX levels and neonatal weight, there were no statistically significant differences in the variables measured between these 2 groups.

**Multivariate regression analysis of parturients with pubic symphysis separation**

For our unconditional, multivariate logistic regression analysis (using the forward-step method), the following were entered into the equation: RLX level, neonatal weight, gestational age, maternal age, age at delivery, weight gain during pregnancy, duration of the first stage of labor, and duration of the second stage of labor. With separation = 1 and no separation = 0, the final variables left in the equation were infant weight and RLX level. The odds ratio (OR) values were 1.002 and 1.022, respectively, suggesting that infant weight and RLX levels were independent risk factors for pubic symphysis separation (Table 3).

**Multivariate analysis of patients with separation of the pubic symphysis during pregnancy and postpartum**

There were no significant differences in RLX levels, diastatic gap, neonatal weight, gestational age, age at delivery, pre-pregnancy weight, weight gain during pregnancy,
or duration of the first or second stage of labor with pubic symphysis separation during the pregnancy or postpartum periods (Table 4).

Multivariate analysis of the degree of separation of the pubic symphysis
Taking the degree of separation as the dependent variable, multivariate linear regression analysis was performed. The following independent variables were entered into the equation: Gestational age, age at delivery, pre-pregnancy weight, neonatal weight, durations of the first and second stages of labor, and weight gain during pregnancy. We observed no statistical significance following this analysis, even after variable transformation due to the non-normal distribution of most of the independent variables. Thus, there was no obvious correlation between the degree of separation and the factors tested (Table 5).

Correlation analysis between RLX levels and other factors: We analyzed the correlations between the levels of RLX and other factors in this study, and found no correlations for gestational age, age at delivery, pre-pregnancy weight, neonatal weight, weight gain during pregnancy, or delivery duration (Table 6).

Analysis of the correlations between the degree of separation and Barthel index and visual analog scale score: Analysis of the correlations between the degree of separation and ADL (Barthel index) and pain (visual analog scale) is shown in Table 7.
### Table 4 Comparison of multiple factors between pregnant and postpartum parturients in the observational group

| Factor                                 | Pregnancy diastasis | Postpartum diastasis | t     | P value |
|----------------------------------------|---------------------|----------------------|-------|---------|
| Relaxin content (µg/mL)                | 162.049 ± 43.178    | 177.774 ± 42.994     | -0.705| 0.493   |
| Diastatic gap (cm)                     | 1.285 ± 0.458       | 2.168 ± 1.151        | -1.896| 0.08    |
| Weight of baby (g)                     | 3807.143 ± 440.519  | 3561.250 ± 588.058   | 0.905 | 0.382   |
| Gestational age (wk)                   | 39.754 ± 0.837      | 39.858 ± 0.896       | -0.229| 0.822   |
| Age at delivery (yr)                   | 30 ± 3.559          | 29.375 ± 5.041       | 0.273 | 0.789   |
| Pre-pregnancy weight                   | 78.500 ± 8.646      | 72.813 ± 7.445       | 1.370 | 0.194   |
| Weight gain during pregnancy           | 18.5 ± 2.345        | 18.75 ± 3.105        | -0.165| 0.872   |
| First stage of labor (min)             | 282.50 ± 173.241    | 378.13 ± 129.723     | -0.890| 0.400   |
| Second stage of labor (min)            | 83.50 ± 94.045      | 47.50 ± 28.909       | 1.063 | 0.319   |

### Table 5 Multivariate linear regression of the degree of diastasis

| Variables              | Unstandardized coefficient | Standardization coefficient | t     | P value | Tolerance | Variance inflation factor |
|------------------------|----------------------------|-----------------------------|-------|---------|-----------|--------------------------|
| B                      | Standard error             | Beta                        |       |         |           |                          |
| Variables              | -8.200                     | 29.024                      | -0.283| 0.825   |           |                          |
| Gestational age (wk)   | 0.653                      | 0.695                       | 0.477 | 0.520   | 0.361     | 2.772                    |
| Age at delivery (yr)   | -0.137                     | 0.111                       | -0.562| 0.433   | 0.451     | 2.215                    |
| Pre-pregnancy weight   | -0.077                     | 0.103                       | -0.601| 0.593   | 0.143     | 7.008                    |
| Baby weight (kg)       | 0.000                      | 0.002                       | -0.136| 0.893   | 0.146     | 6.859                    |
| First stage of labor (min) | -0.001                 | 0.006                       | -0.150| 0.874   | 0.167     | 6.002                    |
| Second stage of labor (min) | 0.000                   | 0.010                       | 0.008 | 0.987   | 0.560     | 1.786                    |
| Relaxin content (µg/mL)| 0.013                      | 0.014                       | 0.494 | 0.524   | 0.327     | 3.056                    |
| Weight gain during pregnancy | 0.366                 | 0.175                       | -0.938| 0.283   | 0.465     | 2.151                    |

### Table 6 Analysis of the correlation between the levels of relaxin and other factors

| Factor                                | Pearson’s correlation coefficient | R² | P value |
|---------------------------------------|----------------------------------|----|---------|
| Gestational age (wk)                  | 0.145                            | 0.024         | 0.034   |
| Age at delivery (yr)                  | 0.118                            | 0.012         | 0.022   |
| Pre-pregnancy weight (kg)             | -0.081                           | 0.560         | 0.931   |
| Weight gain during pregnancy (kg)     | 0.012                            | 0.986         | 0.808   |
| Neonatal weight (g)                   |                                  |               |         |
| Delivery duration                     |                                  |               |         |

### Table 7 Analysis of the correlation between the degree of separation and Barthel index and visual analog scale score

| Factor                              | Pearson’s correlation coefficient | R² | P value |
|-------------------------------------|----------------------------------|----|---------|
| Degree of separation                |                                  |    |         |
| Barthel index                       | 0.828                            | 0.960         |         |
| Visual analog scale                 | 0.000                            | 0.000         |         |
DISCUSSION

Natural anti-fibrotic substances are present in the body to maintain overall homeostasis; RLX is one of these substances. RLX can inhibit fibroblast proliferation and differentiation by inhibiting pro-fibrotic factors, such as transforming growth factor-β1 (TGF-β1) and angiotensin II, and stimulate matrix degradation induced by metalloproteinases. RLX also reduces the degree of scar formation\[18\]. Unemori et al\[19\] and Mookerjee et al\[20\] found that RLX inhibited the differentiation of renal fibroblasts and collagen deposition by inhibiting phosphorylation of Smad2, thus interfering with TGF-β1\[21,22\]. An increase in RLX levels also causes ligament and tendon injury. Therefore, the higher levels of RLX in pregnant women might exert a stronger anti-fibrotic effect, which would lead to ligament relaxation and damage. The level of RLX is highest in the first 3 mo of pregnancy and in the perinatal period\[23\], which leads to the relaxation of pelvic ligaments, especially in the latter period. Compression by fetal weight and other forces during labor can then quickly lead to separation of the pubic symphysis.

For the current study, we enrolled 15 parturients with pubic symphysis separation in the observational group and 39 parturients without separation in the control group. An independent-sample t test and unconditional multivariate logistic regression analysis showed that RLX levels and fetal weight were associated with separation of the pubic symphysis. The increased levels of RLX apparently caused relaxation of the peri-pelvic ligaments, with the peri-pubic symphysis ligament only damaged when the fetus was older. We concluded from this that the high level of RLX was the principal cause of the damage we observed, with reports of RLX levels dropping approximately 4 wk after delivery. We therefore cannot ignore the role(s) of RLX in the relaxation of ligaments during pregnancy and delivery as well as in the healing process, to overcome the late separation of the pubic symphysis. Only when the levels of RLX in the puerperal body return to normal can the typical healing process begin. Although RLX levels and newborn weight were associated with pubic symphysis separation, the OR values from the regression analysis were lower. Future studies that entail a larger sample size and longer follow-up period need to be performed in order to confirm our study results.

A diastasis greater than 14 mm usually indicates attendant damage to the sacroiliac joint\[24\]; this is consistent with our observation that when separation of the pubic symphysis exceeded 14 mm, there was a displacement of the ilium relative to the sacrum. The treatment methods reported in the literature\[8,13,15\], including bed rest, stents, pelvic belt support, and walking aids, were not adjusted according to the separations observed in patients. The pubic symphysis and the sacroiliac joint allow the sacrum and hip bone to form a complete bone ring, and dislocation of the pubic symphysis must be accompanied by movement of the sacroiliac joint. If we do not correct this in a timely fashion, the dislocated symphysis will heal in the wrong position after 8 wk of fibrous regeneration. The ilium is connected downward toward the lower limbs through the hip joint, and the change in the position of the ilium on both sides causes unequal length of the lower limbs on either side. In order to adjust for this, the body must be compensated through the spine; however, scoliosis will occur when the compensation time is overly long. Patients with separation of the pubic symphysis without systematic treatment at our outpatient clinic exhibited scoliosis 6 mo after delivery (the specific timing of the scoliosis was uncertain). When the...
diastatic-gap distance or position of the pubic symphysis is abnormal, changes in the abdominal muscles attached to the ilium and pubic symphysis (such as the rectus inferior), thigh adductors (such as the adductor magnus and adductor longus, along with pectoral lymph nodes, gluteus maximus, and gluteus medius), lumbar muscles (such as the psoas major and iliohypogastric), and back muscles (such as the erector spinae and latisissimus dorsi) can also cause chronic pain in patients with separation of the pubic symphysis. In some patients, we found that the pain was relieved or even disappeared completely after 8 wk; however, new pain symptoms appeared 3 mo later.

There is currently no unified standard for the diagnosis and treatment of perinatal pubic symphysis separation in China or elsewhere. In our study, we found that although the incidence of pubic symphysis separation was not high, the pain and the limitations on ADL greatly affected an individual’s quality of life. To improve the overall health of women, more attention must therefore be given to the possible separation of the pubic symphysis during the perinatal period.

Limitations of our study included a small sample size at a single study center. We also did not study the dynamic changes in serum RLX levels during the peripartum period or uncover a reason for the increase in RLX. Future studies should address these issues.

CONCLUSION

In conclusion, we demonstrated that serum RLX levels and neonatal weight were associated with peripartum separation of the pubic symphysis. Serum RLX levels, as well as neonatal weight, might therefore be used to identify peripartum women with a high risk for pubic symphysis separation. Pregnant women with low serum RLX levels also might consider prophylactic measures and screens for peripartum pubic symphysis separation. Serum RLX levels and neonatal weight were associated with the occurrence, but not the severity, of peripartum pubic symphysis separation.

ARTICLE HIGHLIGHTS

Research background
Although the incidence of postpartum pubic symphysis separation is not high, the pain and mobility disorders caused by it seriously affect the quality of life of women. However, current research has not elucidated the etiology and treatment of this disease. The purpose of this study was to determine whether increased relaxin (RLX) levels were a risk factor for pubic symphysis separation, and whether other factors were involved.

Research motivation
To study the association between RLX and peripartum pubic symphysis separation, and to evaluate other factors that might affect this association. In the future, we hope to predict the risk of pubic symphysis diastasis by determining RLX levels and controlling the possible factors involved, in order to reduce the incidence of postpartum pubic symphysis separation.

Research objectives
We studied the relationships between RLX levels/other factors and the occurrence of pubic symphysis separation, and determined that maternal RLX levels and neonatal weight were risk factors for symphysis pubis separation. This information can be used to guide clinical judgment on the risk of pubic symphysis separation, and thereby reduce its incidence.

Research methods
We performed a cross-sectional study on pregnant women between April 2019 and January 2020. Baseline demographic characteristics, including gestational age, weight, neonatal weight, delivery mode and duration of the first and second stages of labor, were recorded, as well as the pubic symphysis separation, maternal capability for daily life activities, and pain scores. Several statistical methods were used to analyze the data. Previous studies did not include as many factors as we have shown herein,
and investigators did not conduct comparative studies.

Research results
In the present study, it was found that RLX levels and neonatal weight were risk factors for peripartum separation of the pubic symphysis. We wished to determine the possible pathogenic factors leading to symphyseal pubis separation; however, the sample size of our study was not large, and further research is needed.

Research conclusions
Serum RLX levels and neonatal weight were associated with the occurrence, but not the severity, of peripartum pubic symphysis separation.

Research perspectives
In our future studies, we will expand the sample size to further explore the role of RLX levels in peripartum pubic symphysis separation. We will also continue to observe the significant changes in RLX levels in peripartum pubic symphysis separation and subsequent healing.

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