Redefining Pregnancy-Induced Rhinitis

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Summary

Background: Pregnancy-induced rhinitis (PIR) is a form of chronic non-allergic rhinitis not present before pregnancy that manifests itself during pregnancy with complete resolution of symptoms after delivery.

Objective: The objective of this ambidirectional longitudinal cohort study is to evaluate the prevalence of PIR and to investigate the appearance and character of its symptoms, and its impact on the quality of life.

Methodology: Six hundred eighty-one (681) women were recruited in the study. They completed questionnaires about nasal symptoms a day after delivery and each woman with nasal symptoms was interviewed 30 days later and data on symptom duration and quality were recorded.

Results: The prevalence of PIR was 31.86% (N=217), 47.14% (N=321) women had no nasal symptoms and 21% (N=143) of participants had prior sinonasal disease. The clinical presentation of pregnancy rhinitis included nasal obstruction as the most common symptom, followed by rhinorrhea, postnasal secretion, nose itching, sneezing, and hyposmia. The median duration of PIR was 4 months with their complete resolution of symptoms between 2th and 16th day after delivery in the majority of respondents. PIR was diagnosed significantly more often if the women carried a female child. PIR affected their quality of life during pregnancy in 53,9% women (N=117), with an average VAS score of 8. It seems that pregnancy may affect the course of previously present sinonasal disease (allergic rhinitis, chronic rhinosinusitis, nonallergic rhinitis, or non-infectious rhinitis prior to the pregnancy).

Conclusions: PIR is a common clinical entity with a wide range of symptoms with a direct impact on the quality of life in pregnancy. We propose a new definition of pregnancy-induced rhinitis.

Introduction

Pregnancy-induced rhinitis (PIR) is defined clinically as nasal congestion not present prior to pregnancy, typically manifesting itself in the second or third trimester, lasting 6 or more weeks with no known allergic cause, and resolving completely within 2 weeks after delivery. (1) It is classified as a hormone induced rhinitis in a separate group of non-allergic rhinitis patients alongside rhinitis caused by hormonal imbalances during menstrual cycles, puberty, menopause and specific endocrine disorders such as hypothyroidism and acromegaly. (2)

Although the potential connection between nasal symptoms and pregnancy was noted by Hippocrates, epidemiological data and knowledge of clinical features and pathogenesis are scarce. Reflecting on the prevalence of PIR, there is huge variability, from less than 10% to almost 50%. (3) There are studies showing association between PIR and snoring and OSAS during pregnancy and preeclampsia, gestational hypertension, intrauterine growth restriction and lower APGAR scores in neonates. (4)

The nasal mucosa of pregnant women contains several receptors for sex hormones which make it susceptible to hormonal activity causing mucosal congestion. (5) The mechanisms of sex hormone action on the nasal mucosa in provoking nasal physiological changes are still unclear. There are no recent studies focusing on this important issue, although a significant number of pregnant women have PIR and report disturbed quality of life due to its symptoms.

This ambidirectional non-randomized longitudinal cohort study was aimed at evaluating the associations between nasal physiological changes and the duration and severity of PIR symptoms and attempted to illustrate the distinction between true pregnancy-induced-rhinitis and rhinitis during pregnancy which could be any other rhinitis present prior to pregnancy, with allergic rinitis being the most common.

Materials and Methods

Data were compiled using an anonymous questionnaire consisting of 28 questions. The questionnaires were filled out by women in their immediate postnatal period at the Department of Gynecology and Obstetrics, University Hospital Center Sestre milosrdnice, Zagreb, Croatia. All women included in the study gave informed consent. It was approved by the University Hospital Center Bioethical Board adhering to the Helsinki Declaration Revision of 1989. Our study is an ambidirectional (with a retrospective and prospective arm) non-randomized longitudinal cohort study, since it had a retrospective gathering of data during pregnancy, and a month of prospective follow-up to determine symptom duration in the postpartal period. The questionnaires were completed in assitance of an otorhinolaryngology resident to accurately record the data of 681 women, in the time period from March 2017 until March 2020.

Patients were eligible if diagnosed with pregnancy-induced rhinitis, completed informed consent forms, and provided complete data in the first and follow-up interview. Exclusion criteria were incomplete data or follow-up or failure to obtain informed consent.

Pregnancy-induced rhinitis was diagnosed if the respondent had a minimum 6 weeks of unexplained nasal congestion and/or rhinorrhea and/or postnasal secretion and/or hyposmia and/or nose itching and/or sneezing and/or headache whith no previous sinonasal disease such as allergic rihnitis, non-allergic rhinitis, and chronic rhinosinusitis during pregnancy.

The survey was conducted at two points in time. All respondents were interviewed in the first day of puerperium. Each woman with identified nasal symptoms was interviewed again. At this second time point, one month after delivery, women were asked whether and when the symptoms had disappeared.

Demographic information regarding women's age, gravidity, weight before pregnancy, and weight gain in pregnancy, smoking habits, newborn baby gender and APGAR score were collected. One part of the questionnaire focused on presence or absence of symptoms of pregnancy rhinitis (nasal congestion, rhinorrhea, postnasal secretion, hyposmia, nose itching, sneezing, headache) and another part focused on the time of the first onset of symptoms during pregnancy, duration of symptoms in pregnancy and their presence in immediate postpartum. Women were also asked to specify the month of gestation when the symptoms were most intense and symptom intensity.

The third part of the questionnaire focused on quality of life: did the symptoms affect sleep during pregnancy or the quality of life during pregnancy in general. The effect was recorded by a visual analog scale from 0 to 10.

Statistical analysis

Data were compiled into a Microsoft Excel file. All statistical tests were performed using IBM SPSS Statistics (Version 25.0), descriptive statistics was used for data analysis shown as percentage of total (%) and observed frequencies (N). For comparing categorical variables, the $\chi 2$ test was performed to determine differences.

P value < 0.05 was considered significant and odds ratio (OR) with 95% confidence intervals (CI) was calculated for all significant differences. Data were tested for normality and homogeneity of variance with Sharpio-Wilk and Kolmogorov-Smirnov test. Pearson correlation was calculated to see weather there is correlation between weight gain and duration of symptoms. Mann Whintey U test was performed for difference between duration of symptoms between women who carried different gender of a newborn, for difference in weight gain and presence or absence of each symptom and also for difference between women age and presence or absence of pregnancy rhinitis.

Results

During the study period, 681 women completed the questionnaires. The prevalence of pregnancy rhinitis was 31.86% (N=217). A total of 47.14% (N=321) postpartal women had no nasal symptoms and 21% (N=143) of participants had prior sinonasal disease and were analyzed separately, as presented in Table 1.

The demographic data of 538 (79%) respondents with no prior sinonasal disease (age, gravidity, weight before pregnancy, weight gain during pregnancy) are shown in Table 2.

Connections between presence and duration of symptoms between newborn gender, women's age, APGAR score, gravidity, weight before pregnancy, weight gain in pregnancy, and smoking habits were analyzed. Women's age and newborn gender correlated with pregnancy rhinitis symptoms (p=0.034). There was no significant correlation between weight gain and duration of symptoms regarding APGAR score, gravidity, weight before pregnancy, weight gain in pregnancy, and smoking habits (p=0.218).

Mann -Whitney U test suggests statistically significant difference in age between women with PIR (Median=33 n=217) and women without PIR (Median=32 n=321) U=31079, z= -2.125 p=0.034, r=0.09, which would be classified as a weak correlation.

Out of 538 women, 233 (43,3%) gave birth to female newborns and 305 (56,7%) to male newborns. Of 217 women who developed symptoms of PIR, 110 (50.7%) gave birth to a male child and 107 (49.3%) to a female child. Out of 321 women who did not develop symptoms of PIR, 195 (60.7%) gave birth to a male newborn, and 126 (39.3%) gave birth to a female newborn. There was a statistically significant association between the newborn gender and presence of symptoms ($\chi 2$ (1) = 5.33, p=0.021, OR: 1.51 (95%CI 1.06-2.13)). Women carrying a female child were 1.51 times more likely to develop symptoms of PIR, as shown in Figure 1.

The onset of symptoms during pregnancy doesn't follow a normal distribution. Data were tested for normality and homogeneity of variance and both p-values using the Sharpio-Wilk and Kolmogorov-Smirnov test ($p<0.001$), as seen on Figure 2.

The duration of symptoms was variable. The median of continuous symptom duration was 4 months (16 weeks) with a maximum duration of 32 weeks, shown in Figure 3.

Out of 217 women with PIR, 53.5% (N=116) also had symptoms in the postnatal period and 46.5% (N=101) had no symptoms after delivery. In 116 women who had postpartal symptoms, the minimum duration of symptoms was 2 days and the median was 7 days after delivery. In 38 (32.76%) women, symptoms disappeared between 2nd and 5th postnatal day, in 51 (43,97%) women, symptoms dissapeared from 5th to 10th day postpartum and for 15 (12,93%) women the termination of symptoms was between the 10th and 15th postnatal day. After resolution, the symptoms did not reappear later in the first postnatal month. The duration of symptoms after delivery is demonstrated in Figure 4.

Most of the participants (N=88) reported constant intensity of symptoms during the pregnancy. Sixty-five (65) participants reported symptoms to be most bothersome in the 9th month of pregnancy and 22 participants declared that the symptoms were most intense during the 5th month of pregnancy.

The symptoms weren't present throughout the entire pregnancy, as shown in Figure 5. Out of 217 subjects, 92.2% had symptoms in the third trimester, 70.5% in the second trimester, and 23% in the first trimester. There is a statistically higher likelihood (0.21, 95% CI: 0.1437 - 0.2903) of symptoms occurring in the third trimester compared to the second trimester ($z=5.8$; $p<0.0001$).

The most common symptom was nasal congestion, present in 98,2% (N=213) of women with pregnancy rhinitis. Women evaluated the intensity of nasal congestion on Likert point scale

from 0 to 5 (mean value 3.27, SD 1.13), shown in Figure 6. A majority (39,2%) of women have chosen 3, for 25,8% it was 4, 15,2% women chose 5, while 12,9% women said it was 2, and lastly 5,1% marked it with 1. Four women had no nasal congestion. Other symptoms of pregnancy rhinitis were rhinorrhea, nose itching, hyposmia, headache, postnasal secretion, and sneezing with a share in the respondents, as shown in Figure 7.

Analyzing the symptoms that occurred in our respondents, almost all of them (96.3%) had more than one symptom, most (69.6%) had more than 2 symptoms and some (38,2%) more than 3. The most common symptom was nasal congestion, predominantly in association with other symptoms. The most common combination of two symptoms was nasal congestion and rhinorrhea and the combination of three symptoms most commonly included nasal congestion, rhinorrhea and postnasal secretion.

One hundred thirty-four (61,8%) women stated that symptoms caused problems with sleeping, and 117 (53,9%) stated that symptoms of pregnancy rhinitis affected their quality of life during pregnancy. The most common Visual Analog Scale (VAS) scale rating of the impact on the quality of life was 8 (mean 5.65, SD 2.45), shown in Figure 8.

In addition, 143 (21%) women have been diagnosed with one or more sinonasal diseases and were treated before pregnancy. Allergic rhinitis was found in 108 women and 44 women had preexisting chronic rhinosinusitis or non-allergic rhinitis. Some of them were diagnosed with both or all three sinonasal disease before pregnancy. Pregnancy affected the course of usual sinonasal symptoms of women. Of these, 27 (18.9%) women had no sinonasal symptoms during pregnancy, 42 (29.4%) had usual symptoms during pregnancy, and 21 (14.7%) claimed a lower intensity of symptoms despite not using any therapy. A worsening of symptoms was found in 53 (37.1%) women from that group, as seen in Figure 9.

Discussion

Pregnancy-induced rhinitis is a non-allergic rhinitis present during pregnancy that resolves spontaneously within 2 weeks after delivery. According to Non-allergic rhinitis: Position paper of the European Academy of Allergy and Clinical Immunology, PIR is classiffied as a hormonal rhinitis, caused by hormonal imbalances during menstrual cycles, puberty, pregnancy, menopause, and specific endocrine disorders such as hypothyroidism and acromegaly. (1,2)

A consensus on the definition of pregnancy-induced rhinitis did not exist until proposed by Ellegård and Karlsson, due to unclear distinction between pregnancy-induced rhinitis and rhinitis during pregnancy, data on its frequency, clinical course and impact on quality of life. (1)

During pregnancy, there is a sustained release of hormones. (6) These hormones interact with receptors in the nasal mucosa and may have indirect effects. (7-10). Serum progesterone and estrogen concentrations rise gradually as the pregnancy progresses, and if there is a distinct effect on the nasal mucosa, the consequent congestion should increase towards the time of delivery. (6) There is evidence of hormonal activity through histamine receptors by increasing the expression of H1 receptors in nasal epithelium and microvascular endothelial cells. (11) Cytokines also may play a role in mucosal changes in the nasal mucosa during pregnancy. (7,8,12)

Nonetheless, there are conflicting opinions about whether elevated hormone concentrations can influence nasal congestion. Regardless of pregnancy, there are studies which show that female patients have different interaction between mast cell activation and neurogenic inflammation. In our previous research, female patients with allergies tended to have higher substance P (SP) concentrations both before and after nonspecific nasal provocation tests. We found that differences between post-allergen and post–hypertonic saline provocation was highly significant in female patients, as opposed to male patients. (13)

Differential diagnoses are numerous as there are different types of rhinitis with very similar symptoms. The crucial distinciton is the time of symptom onset. However, different types of rhinitis can coexist. One condition could be present before pregnancy and coexist with PIR, causing commorbidity of two etiologically different nasal mucosal inflamatory processes. Hence, PIR may be a basis for the development of other rhinitis medicamentosa and chronic rhinosinusitis. (14)

Allergic rhinitis should be considered first, as it is the most comon type of rhinitis. In allergic rhinitis, symptoms such as rhinorrhoea, nasal itching and sneezing usually take precedence over nasal obstruction, which is the leading symptom in PIR. Another problem could be newly occurring allergic rhinitis during pregnancy. (15) In our study, 21% of subjects had sinonasal disease prior to pregnancy, mostly allergic rhinitis. It seems that pregnancy can affect the course of usual sinonasal symptoms and in over 50% of patients, symptoms were aggravated. Rhinitis medicamentosa usually exists before pregnancy, is present during pregnancy and does not

resolve after delivery. It can also be caused by attempting to relieve nasal obstruction during pregnancy caused by PIR. (14,16) One of the first studies using the term pregnancy rhinitis was focused on chronic rhinosinusitis during pregnancy. (17)

Nasal obstruction coupled with inevitable weight gain in pregnancy predisposes women for the development of obstructive sleep apnea (OSA). (1,4) Snoring and OSAS could lead to lower Apgar scores, but we did not find any difference in APGAR scores in newborns depending on presence of PIR. (12)

The prevalence of PIR varies in literature. The criteria often differ, as a universal definition is still lacking. One study monitored the presence and severity of nasal obstruction symptoms in 79 pregnant women in the 8^{th} and 9^{th} month of pregnancy. One third of the subjects had significant symptoms of nasal congestion during pregnancy. (18,19) Another study lists 21% of 160 women having nasal obstruction associated with pregnancy. (20) One of the biggest studies on 1546 pregnant women examined the presence of nasal congestion during gynecological visits at 12, 20, 30 and 36 weeks of gestation. Results showed that 11% of patients had nasal congestion at each of the four visits, 35% at none, and 42% had obstruction at week 36. Unfortunately, there was no discrimination of obstruction caused by other etiologes such se infection and allergy. (21) A similar study with 54 subjects excluded pregant women with allergy or rhinosinusitis and reported nasal obstruction in an increasing number of subjects in the final gestational weeks; present in 16% during week 12 and in 30% during week 36. (22)

The first study with a clear distinction between PIR and other types of rhinitis recruited 838 pregnant women, with a reported incidence of PIR of 22%. It focused on nasal obstruction and congestion. (23) Another study with 109 recruited primigravida diagnosed with PIR and/or rhinitis of other etiology during pregnancy found 22% of women had allergic rhinitis, 13% had rhinitis of some other etiology and only 9% had PIR. (24) Results analyzing subjective and objective parameters (NOSE scores and acoustic rhinometry) in 85 women with PIR and 26 pregnant women as a control group showed that the volume of the nasal cavity decreased with the progression of pregnancy, but NOSE scores did not correlate with objective findings. (25)

In our study, 538 (79%) subjects did not have rhinitis prior to pregnancy. Within this group, 31.86% was diagnosed with PIR. Previously published results report prevalence ranging from 9 to 42% and our data are close to Ellegård data. There is no typical time of symptom onset. Symptoms may first occur in the second or third trimester and our study shows they may be identified from the second month of pregnancy onward. (9)

Ellegård postulates that there is no association between PIR and parity and gender of the newborn. (26) We found a statistically significant ($p < 0.05$). Correlation between female newborns and presence of PIR. There are reports of predominance of cytokines and angiogenesis factors indicative of Th2 lymphocyte response in women carrying female children relative to the more dominant Th1 cellular immune response in those carrying a male child. (27) We can speculate that pregnant women who cary a female child are more likely to have mast cell degranulation and histamine release due to a Th2 response, which then binds to the highly expressed histamine receptors in the nasal epithelium, possibly contributing to the onset of pregnancy rhinitis symtoms.

Smoking was not found to be a risk factor for the development of pregnancy rhinitis in our study, contrary to data from two other studies where the incidence of pregnancy rhinitis was significantly higher in women with a smoking habit (risk ratio 1.7, 95% CI 1.1-2.5). (26)

Although nasal obstruction is the dominant symptom of PIR, it is not the only symptom. Focusing on only one symptom may overshadow other symptoms. We noted that all other symptoms of rhinitis are present to some extent and impair the quality of life. Other symptoms include rhinorrhea, post-nasal secretion, hyposmia, itchy nose, serial sneezing and headache. Almost all of the women (96.3%) had more than one symptom, most (69.6%) had more than two symptoms and some (38,2%) had three or more symptoms.

In our study, the median duration of PIR was 4 months with a range of 1,5 to 7 months. When we compare data from two other studies, PIR may appear anywhere from the 3rd to 7th month of gestation. (5,12)

Resolution of symptoms after delivery did not depend on the time of initial appearance of symptoms, corresponding to the Ellegård study data. (12) Within one week after delivery, 76% of women were symptom-free. The remaining 24% reported recovery within 4 weeks.

One study examined the quality of life in pregnant women with allergic and non-allergic rhinitis using the SNOT-22 test. It found a statistically significant difference in quality of life between pregnant women in the second and third trimester. (28) Our study used a VAS scale from 0 to 10, and the majority of respondents rated disorders caused by symptoms of pregnant rhinitis with an 8. This clearly shows that greater awareness and engagement of the physician in dealing with this bothersome clinical entity is required.

The limitations of this study include the potential for recall bias with reporting past symptoms, but all of the women were interviewed at the same time, and the methodology of recording their symptoms was uniform throughout the study. All of the women were interviewed during their postpartal stay in the hospital, at a time when they could still vividly recall the details of their pregnancy and related symptoms.

Conclusion

A significant number of pregnant women have PIR and it affects their quality of life. The results of this study suggest that it may be more prevalent with rising age and in women carrying female newborns, with a higher likelihood of symptoms occurring in the third trimester with symptom resolution in the first postpartal week. Pregnancy may also aggravate previously diagnosed sinonasal disease in a significant portion of patients. We recommend a new definition of PIR which takes in account a wide range of clinical aspects. It is based on definitions of Ellegard and Karlsson and a position paper of the European Academy of Allergy and Clinical Immunology on Non-Allergic Rhinits. The suggested definition is: PIR is a non-allergic, non-infectious symptomatic inflammation of the nasal mucosa caused by a hormonal imbalance during pregnancy, lasting 6 or more weeks and resolving spontaneously within 4 weeks post-delivery, caracterized with the presence of at least one nasal symptom (nasal obstruction, but also rhinorrheoea, nose itching, sneezing and/or hyposmia).

Authorship contribution

Tomislav Baudoin, Andro Košec, Nikolina Bacan, Boris Jelavić, Krunoslav Kuna and Tena Šimunjak and all contributed to protocol/project development, data collection or management, data analysis, manuscript writing/editinghD: protocol/project development, data collection or management, data analysis, manuscript writing/editing.

Conflict of interest

No conflict of interest exists.

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Tables and Figures

Table 1. Share of individual respondents in the sample.

	Number (N)	**%**
Pregnancy rhinitis	217	31.86
Allergic rhinitis or NINAR or Chronic rhinosinuitis before pregnancy	143	21
No sinonasal symptoms before or during pregnancy	321	47.14
TOTAL	681	100

The demographic data of 538 (79%) respondents with no prior sinonasal disease (age, gravidity, weight before pregnancy, weight gain during pregnancy) are shown in Table 2.

Table 2. Demographic data of all postpartum women depending on presence of PIR

	Parameters	**Age**	**Gravidity**	**Weight before pregnancy**	**Weight gain**
No prior sinonasal disease, diagnosed with pregnancy induced rhinitis	**N**	217			
	Mean(±SD)	32.56(±4.89)	1.63(±0,92)	66,94(±13.07)	14.48(±4.6)
	Min	17	1	42	4
	Max	47	11	126	34
No prior sinonasal disease, were not diagnosed with	**N**	321			
	Mean(±SD)	31.51(±5.36)	1.68(±0.99)	65.61(±12.63)	13.5(±4.54)
	Min				
	Max				

pregnancy induced rhinitis					
Allergic rhinitis or NINAR or Chronic rhinosinuitis before pregnancy	**N**	143			
	Mean(±SD)	32,39(±4,63)	1,71(±0,87)	66,01(±13,3)	13,81(±4,47)
	Min	18	1	46	4
	Max	43	5	120	30

Figure Legends

Figure 1. Distribution of women of those with and without pregnancy-induced rhinitis divided by the gender of their newborns

Figure 2. The onset of first symptoms by months of gestation

Figure 3. Extent of symptoms during pregnancy measured in weeks

Figure 4. Extent of symptoms in postpartum period.

Figure 5. Presence/absence of pregnancy rhinitis symptoms in 1st 2nd and 3rd trimester

Figure 6. Intensity of nasal congestion score from 0 (no congestion) to 5 (very high)

Figure 7. Symptoms of PIR.Frequency (N) and percentage (%) of their occurrence from the total of 217 postnatal women who developed pregnancy rhinitis.

Figure 8. Impact of pregnancy rhinitis on quality of life measured on the *Visual Analog Scale* (VAS)

Figure 9. Changes in the intensity and behavior of symptoms in a group of women who were diagnosed with allergic rhinitis, nonallergic rhinitis or chronic rhinosinuitis prior to pregnancy