

Article type : Main research article

Pregnancy, puerperium and perinatal constipation – an observational hybrid survey on pregnant and postpartum women and their age-matched non-pregnant controls

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Running title: Constipation in pregnancy and puerperium

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/1471-0528.16559](https://doi.org/10.1111/1471-0528.16559)

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Abstract

Objective To evaluate the prevalence of constipation during pregnancy and early puerperium.

Design Observational survey.

Setting Secondary and tertiary hospital in Finland.

Population Pregnant (N=474) and postpartum (N=403) women and a control group of 200 non-pregnant women who did not give birth within a past year.

Methods Women reported bowel function and other gastrointestinal symptoms with a structured questionnaire using 11-point numerical rating scale (0=no symptom, 10=most severe symptom) and binominal yes/no questions during the second and third trimesters and few days and one month after childbirth.

Main outcome measure Prevalence of constipation based on the Rome IV criteria.

Results The data consist of five cohorts of women: second trimester (N=264), third trimester (N=210), after vaginal delivery (N=200) or caesarean section (N=203), and a control group (N=200). The prevalence of constipation was 40% in pregnant women and 52% ($p<0.001$) in postpartum women, which was a higher prevalence than that in the control group, where 21% had constipation ($p<0.001$). A few days after delivery, the prevalence of constipation was lower after vaginal delivery (47%) than caesarean section (57%, $p<0.039$). One month postpartum, the prevalence of constipation was low: 9% after vaginal delivery ($p=0.002$ compared to the control group) and 15% after caesarean section. Other gastrointestinal symptoms were common, pregnant women had the highest prevalence (34%) of nausea/vomiting.

Conclusion The prevalence of constipation was 2-3-fold higher in pregnant women and a few days after delivery than in non-pregnant women. During puerperium, bowel function returned to or below that reported in non-pregnant women.

Funding The present study had no external funding.

Keywords: Pregnancy, Constipation, Postpartum, Puerperium, Bowel Function

Tweetable abstract: Constipation is common in pregnancy and after delivery, but bowel function returns early in puerperium.

Introduction

Functional constipation is a common gastrointestinal (GI) disorder, with a prevalence of 16% in the adult population and up to 33% in adults over 60 years of age ^{1,2}. Risk factors for constipation are, among others, age, female sex and a low-fibre diet. In Finland, the prevalence of self-reported constipation is higher in fertile-age women, 19-49-year-old, 25-30%, than in men of same age, 17-23 % ³.

Constipation during pregnancy and after delivery is, first, an unpleasant symptom that may have a negative effect on the quality of life ⁴. Second, constipation can cause pelvic floor dysfunction ⁵, which may manifest as faecal or urinary incontinence, overactive bladder or pelvic organ prolapse ⁶. Excessive straining can damage the pudendal nerve and thereby impair the function of the pelvic floor musculature ⁷. Severe constipation can cause haemorrhoids or rectal prolapse and contribute to pelvic organ prolapse ⁵. On the other hand, labour injuries to the pelvic floor muscles and anal sphincters may result in postpartum constipation ⁸.

Constipation is the second most common GI symptom during and after pregnancy. Earlier studies indicate that nearly 40% of pregnant women suffer from constipation ^{9,10}. Constipation is common after childbirth, and in Bradley's study ¹¹, the prevalence at three months after delivery was 24%.

Gastrointestinal function during pregnancy and in postpartum should receive attention because severe constipation may have a substantial impact on the pregnancy experience and may affect the mother's physical and social health status and impair the relationship between mother and newborn ¹². In Finland, the fertility rate of 1.41 is historically low, and the number of children born in 2018 decreased by 20% compared to the number in 2010 ¹³. We hypothesised that evidence-based updated counselling on pregnancy-GI symptoms and their management could improve the pregnancy experience and decrease the prospect that these symptoms present an obstacle in planning the next pregnancy.

To update the knowledge, we designed the present study on the prevalence of constipation during pregnancy and postpartum. We surveyed the prevalence of constipation and other GI symptoms in women during the second and third trimesters and in postpartum and compared these figures to an age-matched, non-pregnant control group. The primary outcome measure was the prevalence of constipation during pregnancy and postpartum based on the Rome IV criteria ¹⁴. Our study hypothesis was that the prevalence of constipation is higher in pregnancy and early puerperium

than that in a control population. Null hypothesis was that the prevalence of constipation is similar across the study groups.

Methods

This study was an observational, hybrid survey, cross-sectional for pregnant and non-pregnant women and longitudinal for postpartum women, of five cohorts of women in Kuopio University Hospital (KUH), Kuopio, Finland, and in Satakunta Central Hospital (SCH), Pori, Finland, between August 2012 and October 2014. The study design was approved by the Research Ethics Committee of the Hospital District of Northern Savo, Kuopio, Finland (53/2012), and it had institutional approval. Patients were not involved in the development of the research.

The study consisted of five cohorts: women in the second trimester (gestation weeks 19-25), the third trimester (gestation weeks 35-42), women who gave birth vaginally, including vaginal-operative deliveries, women who gave birth by caesarean section, either elective or while in labour, and a control group of fertile-age women who were not pregnant or had not given a birth during the previous 12 months. The groups of pregnant women were recruited during their normal pregnancy follow-up visits in the two hospitals. Women in the second trimester, enrolment August-October 2012, were enrolled when they attended a routine prenatal structural ultrasonography screening in the maternity clinics of the two hospitals and women in the third trimester, enrolment August- October 2012, during a routine prenatal obstetrician visit at gestational weeks 35-42. As the women came on these visits in the maternity clinics, they were given written information of the study and the questionnaires to be filled during the visit and to return them in the return box in a closed envelope. The women in the postpartum groups were recruited from the maternity wards of the two hospitals, enrolment December 2013-October 2014, before discharge by HK, MKo, CS and SS. The control group consisted of 18- to 40-year-old women who were staff of KUH and SCH and who voluntarily and anonymously answered the questionnaire. Written information of the study and the questionnaires were shared for two weeks period on the break rooms in different facilities and administration centre. Female employees willing to participate were asked to return filled questionnaires in the return boxes in a closed envelop. Exclusion criteria included an inability to understand the questionnaire written in Finnish. Filling in the anonymous questionnaire after the presentation written information was considered consent to participate. Participants in the postpartum groups provided written consent after the presentation of oral and written information.

In this study, 1078 women gave their informed consent, including 264 in the second trimester, 210 in the third trimester, 200 after vaginal delivery and 203 after caesarean section. In the control group, there were 200 women (Figure 1, flowchart).

Questionnaires

Demographic variables were collected as follows; woman's age, height, weight, gestational weeks, parity and deliveries, and mode of vaginal delivery (spontaneous or operative) and urgency of caesarean section. For the vaginal delivery group we search the patients records for use of episiotomy and perineal and/or vaginal tears. New-born demographics were collected as follows; weight, height and Apgar-scores at one and five minutes.

For GI function, we asked whether participants had a history of constipation during previous pregnancies. Women were questioned about bowel function and other GI symptoms during this pregnancy/after delivery with a structured questionnaire. Symptoms were rated using an 11-point NRS (0=no symptom, 10=most severe symptom) and answering binominal yes/no questions.

Constipation was assessed by three methods: the Rome IV criteria, self-report, and the Bowel Function Index (BFI). The Rome IV criteria define functional constipation as the presence of at least two out of six symptoms: straining, lumpy or hard stools, a sensation of incomplete evacuation, a sensation of anorectal obstruction/blockage, manual manoeuvres to facilitate defecation and fewer than three spontaneous bowel movements per week. Symptoms must be present at 25% of the defecations and last at least three months. Loose stools should be present only rarely without the use of laxatives, and irritable bowel syndrome criteria should not be met¹⁴. Self-reported constipation was a personal judgement of constipation on an 11-point NRS (0=no constipation, 10=most severe constipation). The BFI was calculated as a mean of three variables, the ease of defecation, the feeling of incomplete bowel evacuation and personal judgement of constipation, on an 11-point NRS. The cut-off value for constipation on the BFI was set at 3/10 or higher¹⁵.

Women who gave birth answered the questionnaire twice: first before discharge from the maternal ward a few days after delivery at the hospital and then by telephone interview (CS, MKo, HK) one month after delivery. The other three groups answered the questionnaire only once.

The core outcome set was the prevalence of constipation based on the Rome IV criteria.

Secondary outcome measures were the prevalence of self-reported constipation, constipation on the BFI, other GI symptoms, need for and efficacy of preventive measurements and treatments for constipation, and risk factors for gestational constipation.

Statistical analysis

The distribution of continuous data was checked with the Shapiro–Wilk test, and the equality of variances was tested with Levene's test. The Kruskal-Wallis and Mann-Whitney U tests were used when continuous data were not normally distributed. Categorical data were analysed using the χ^2 -test. We used the Pearson correlation coefficient and the Spearman correlation coefficient to test correlations between variables. For multiple comparisons, the Bonferroni correction was applied. Data are presented as the number of cases (%) and the mean (standard deviation, SD), and when data were not normally distributed, the median (minimum, maximum) are presented. For the primary outcome measure, we calculated the 95% confidence intervals (95% CIs). A two-sided P-value of <0.05 was considered statistically significant.

Results

Subject characteristics

The characteristics of the 1078 participants are presented in Table 1. There were 676 (63%) women in KUH and 402 (37%) in SCH. Among all groups studied, the women in the second trimester were the youngest (mean age 29 years), and the women who gave birth by caesarean section were the oldest, with a mean age of 31 years ($p=0.001$). The response rate at the one-month follow-up call was 181 of 200 (91%) women with vaginal delivery and 176 of 203 (87%) women with caesarean section.

Prevalence of constipation

The median stool frequency was 7/week, but the between-subject variation was large, 1-21 stools/week.

Based on the Rome IV criteria, 40% (95% CI: 36-45%) of pregnant women and 52% (95% CI: 47-57%, $p<0.001$) of postpartum women had constipation, which was a higher prevalence than in the

control group, where 21% (95% CI: 15-26%, $p < 0.001$) had constipation. In the control group, 93 women had given birth before, and the prevalence of constipation was 26%, compared to 16% in women who had no deliveries. The data are presented in Figure 2.

During the second and third trimester, the prevalence of constipation was similar; in the second trimester, 44% (95% CI: 38-50%), and in the third trimester, 36% (95% CI: 29-42%, $p = 0.084$) of women had constipation.

Constipation was most common in early postpartum; a few days after vaginal delivery, 47% (95% CI: 40-54%), and a few days after caesarean section, 57% (95% CI: 50-64%, $p = 0.039$) of women had constipation. One month after childbirth, the prevalence of constipation was low; 9% (95% CI: 5-13%, $p = 0.002$ compared to the control group) after vaginal delivery and 15% (95% CI: 10-21%; $p = 0.204$ compared to the control group) after caesarean section.

The Bowel Function Index provided a similar prevalence of constipation compared to the Rome IV criteria in the control group during pregnancy and one month after delivery but a slightly higher prevalence at a few days after delivery. On the BFI, the prevalence of constipation in the control group was 19%, in the second trimester 39%, in the third trimester 33%, a few days after vaginal delivery 55%, and a few days after caesarean section 75%. One month after vaginal delivery, the prevalence of constipation based on the BFI was 12%, and after caesarean section it was 19%.

The prevalence of constipation based on self-report was higher than that based on the Rome IV criteria in each group. In the second trimester, 61%; in the third trimester, 55%; a few days after vaginal delivery, 77%; and a few days after caesarean section, 88% of women self-reported constipation. One month after vaginal delivery 29%, and after caesarean section 32% of women self-reported constipation, which was similar to the prevalence reported in the control group, where 37% of women reported constipation. The data are presented in Table S1.

Constipation during the six months before current pregnancy had a weak positive correlation with constipation during pregnancy: second trimester ($r = 0.228$) and third trimester ($r = 0.260$).

Constipation during the previous pregnancy was also weakly positively correlated with constipation in current pregnancy: second-trimester ($r = 0.284$) and third trimester ($r = 0.285$). In the control group, 93 (47%) women had delivered before, and 49 (53%) women had had constipation

during the previous pregnancy. In the control group, constipation during pregnancy had a positive correlation with current constipation ($r=0.267$).

Prevalence of other symptoms

Most women had other GI symptoms during pregnancy and a few days after vaginal delivery. Different symptoms were also common in the control group. The prevalence was lowest one month after childbirth. The three most common GI symptoms in pregnant women were thirst (67%), flatulence (64%) and a sense of pressure (57%), and a few days after delivery, the most common GI symptoms were thirst (82%), flatulence (81%) and stomach ache (68%). In the control group, the most common symptoms were feeling bloated (65%), flatulence (65%) and thirst (52%). Pregnant women had considerably more nausea and/or vomiting (34%) than women a few days after delivery (15%) and women in the control group (13%), and the prevalence was lowest one month after delivery (3.4%) ($p<0.001$). One month postpartum, women had fewer GI symptoms than a few days after delivery ($p<0.001$) and fewer than women in the control group ($p<0.001$). Data on GI symptoms and other symptoms are presented in Table 2.

Discussion

Main findings

Novel findings of our study were, first, that we have reported the prevalence of constipation a few days after delivery, and the prevalence was high both after caesarean section (57%) and after vaginal delivery (47%) based on Roma IV criteria. Second, during puerperium, bowel function returned relatively early; at four weeks postpartum, the prevalence of constipation was 12%, which was substantially lower than that reported in the age-matched, non-pregnant and non-lactating population (21%) and lower than that reported earlier in puerperium^{11,16,17}. Third, the prevalence of constipation was similar in the second (44%) and third trimesters (36%).

Strengths and Limitations

One of the strengths of the present study was that we had an age-matched control group of women. This study design provided concurrent data on bowel function in women during pregnancy and

puerperium and in fertile, non-pregnant, non-lactating women. Another strength was the evaluation of constipation with three different tools. The agreement between the Rome IV criteria and the BFI was high. The prevalence of constipation based on self-report had a moderate agreement with that based on the Rome IV criteria, and in the control group, it was consistent with that of another study cohort during the same years in Finland³. Consistently, the prevalence of nausea and vomiting in pregnancy¹⁸ and GI and other symptoms one month postpartum were also similar to those reported recently¹⁹. It seems that we were able to minimise selection bias as the subject characteristics were similar in the five study groups. Thus, we believe our data are sound. One of the main limitations was that we did not use a longitudinal study design, except in postpartum women. On the other hand, the cross-sectional design allowed participants to answer anonymously questions that are sensitive for some people. Moreover, the study groups were relatively large, with 200 women or more in each group. The response rate to the second questionnaire in postpartum women was also high (89%); thus, our data were less likely to have participation bias than those studies with substantially lower response rates. A potential bias was the selection of hospital staff as the control group. Hospital staff are assumed to have a different vigilance of health compared to the general population. To minimise selection bias, the questionnaires in the control group were shared to all occupational groups working in the hospitals facilities. Moreover, the prevalence of constipation in the control group was consistent with a recent nationwide survey in Finland³.

Interpretation

Consistent with earlier reports, our data indicate that the prevalence of constipation is 2- to 3-fold higher in women during pregnancy than in non-pregnant women^{2,3,11}. The main reasons for this are the effects of placental sex hormones on GI transit time and GI motility, mechanical changes with advancing gestation, changes in water absorption, dietary factors, and reduced physical activity during pregnancy²⁰. Similar to other reports, in fertile-age women, the prevalence of constipation based on self-report was 2-fold higher than that based on the Rome criteria¹⁶. The prevalence of self-reported constipation of 37% in non-pregnant women in the present study is consistent with another recent nationwide survey in Finland, supporting that our data are sound³.

In the present study, 40% of pregnant women had constipation based on the Rome criteria ¹⁴. The prevalence of constipation during the second trimester was similar (44%) to that reported in the Derbyshire study ²¹, which reported a prevalence of 39%, but was substantially higher than that reported in the Bradley study (26%) ¹¹. In contrast to previous studies ^{11,21}, in our study, the prevalence of constipation was not lower in the third trimester. The prevalence of constipation in the third trimester (36%) was higher than that of earlier studies, reporting a prevalence of 16-21% ^{11,21}. We assume that these contradictory results can be based on different study designs. Our study design was cross-sectional, whereas that of the Derbyshire ²¹ and Bradley¹¹ studies were longitudinal. The response rate in those two studies in the third trimester were relatively low (66-68%), which could have caused participation bias.

Few data have been published on constipation early after childbirth. In the present study, the prevalence was highest in early postpartum, a few days after delivery, as 52% of women had constipation based on the Rome criteria and 82% had constipation based on self-reports. In the Cookling study, ¹⁷ constipation was reported as a minor problem by 45% and as a major problem by 4% of 229 Australian women one week postpartum. Before vaginal delivery midwives often encourage women to empty the bowel with enemas during the first stage of labour to facilitate foetal head to descend in the pelvis. Then, bowel after delivery might be empty since during vaginal delivery women do not have the appetite. Also, constipation in the puerperium may be a result of anal sphincter injury induced by childbirth as have stated in a study where using endoanal ultrasonography researchers found clinically occult anal sphincter defects in up to one-third of vaginal deliveries ²². Pelvic floor muscle injuries and pudendal nerve tears as well as reduced exercise and dehydration may then be behind defecation problems.

In the present study, bowel function recovered relatively early in puerperium. At four weeks postpartum, 12% had constipation. In earlier studies, the prevalence of constipation at 4-12 weeks postpartum was 17-29% ^{11,17,21}. In a study by Ponce et al. ¹⁶, at six weeks postpartum, the prevalence of constipation based on self-report was 42%, similar to our study, but based on the Rome criteria, it was 25%, which is 2-fold higher than that in the present study.

The Rome criteria are considered the gold standard to evaluate constipation, although they are not validated for pregnancy ¹⁴. The BFI is designed to evaluate opioid-induced constipation, and self-reported constipation is women's personal judgement of constipation. We found that the Rome criteria and the BFI provided similar prevalence in all groups except the early postpartum cohort.

A few days after delivery, the BFI gave a higher prevalence of constipation (65%) than the Rome criteria (52%). The prevalence of constipation based on self-report was substantially higher in all groups than that based on the Rome criteria. These three measures are distinctly different tools for bowel function evaluation. The BFI is calculated as a mean of three variables, personal judgement of constipation, the ease of defecation and the feeling of incomplete bowel evacuation, on an 11-point NRS¹⁵. As the BFI includes characteristics of the two other methods, it is worth evaluating its performance further in this population.

In the present study, a history of constipation during the six months before current pregnancy and in previous pregnancies was associated with a risk of constipation. Other studies have shown similar data indicating a history of constipation as a risk factor for constipation in pregnant women^{11,23}. Constipation is not only a symptom but a risk factor for other GI complications. In a recent study, where anal symptoms and risk factors were evaluated up to three months postpartum two thirds (61%) of women had constipation during pregnancy and postpartum. In that study two thirds (68%) of women developed anal symptoms and constipation was major risk factor for anal problems, of which haemorrhoidal complications and anal fissure were the most common²⁴. In pregnant women, counselling should be provided, with appropriate advice on how to prevent and treat constipation.

Conclusion

The prevalence of constipation was 2- to 3-fold higher in women during pregnancy than in non-pregnant women. The prevalence was highest during the first days after delivery, but at four weeks postpartum, bowel function was similar or superior to that in non-pregnant women. A history of constipation was a risk factor for constipation during pregnancy.

Acknowledgements The authors wish to thank the women who participated in the study.

Disclosure of Interests Authors have no conflicts of interest. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to Authorship Conception & planning: SH, HK, CS, SS, MKo; Data collection: MKu, SH, HK, CS, SS, KV, MKo; Formal analysis: MKu, SH, CS, HK, KV; Writing original draft: MKu, HK; Review & editing: MKu, SH, LA, HK, CS, SS, KV, MKo; Supervision: HK, MKo; Resources: SH, SS, MKo

Details of Ethics Approval The study design was approved by the Research Ethics Committee of the Hospital District of Northern Savo, Kuopio, Finland (53/2012; June 29, 2012), and institutional approval was obtained from both hospitals.

Funding The present study had no external funding.

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Legends to figures

Figure 1. Flowchart of the study. KUH = Kuopio University Hospital, SCH = Satakunta Central Hospital. Second Trimester = gestation weeks 19-25, Third trimester = gestation weeks 30-42.

Figure 2. Prevalence of constipation using the Rome IV criteria. Data are presented as the number of cases.

Table 1. Subject characteristics. Data are presented as number of cases or mean (SD) and [minimum-maximum].

Variable	Second trimester N = 264	Third trimester N = 210	Vaginal delivery N = 200	Caesarean section N = 203	Control group N = 201
Hospital (KUH/SCH)	165/99	106/104	133/67	121/82	151/50
Age (years)	29 (4.6); [17-42]	30 (5.8); [14-52]	29 (5.5); [16-45]	31 (5.5); [16-45]	30 (5.5); [19-40]
Height (cm)	166 (0.6); [152-183]	165 (0.6); [149-184]	166 (0.6); [150-183]	163 (0.6); [145-179]	166(0.6); [149-182]
Weight (kg)	75 (16); [47-133]	84 (17); [50-145]	83 (16); [53-147]	89 (18); [57-150]	66 (13); [42-109]
Gestational weight gain (kg)	NA	NA	14 (6); [-2-30]	14 (8); [-2-57]	NA
BMI (kg/m ²)	27 (5.6); [18-51]	31 (5.8); [21-51]	30 (5.1); [21-29]	33 (6.7); [22-58]	24 (4.3); [17-40]
• BMI <25	• 110 (42%)	• 30 (14%)	• 25 (13%)	• 9 (4%)	• 138 (69%)
• BMI 25-29.9	• 79 (30%)	• 67 (32%)	• 52 (25%)	• 45 (22%)	• 41 (20%)
• BMI ≥30	• 60 (23%)	• 103 (49%)	• 71 (36%)	• 97 (48%)	• 20 (10%)
• Missing	• 15 (6%)	• 10 (5%)	• 52 (26%)	• 52 (26%)	• 2 (1%)
Gestational weeks	21 (1.0); [19-25]	37 (2.0); [37-42]	39 (1.5); [26-42]	38 (3.0); [26-42]	NA
Parity:	1.2 (1.6); [0-11]	1.4 (1.6); [0-11]	0.6 (0.7); [0-3]	0.8 (1.1); [0-8]	0.9 (1.2); [0-6]
• 0	113 (43%)	70 (34%)	95 (48%)	92 (45%)	107 (54%)
• ≥1	148 (57%)	138 (66%)	105 (53%)	111 (55%)	93(47%)
History of constipation: yes/no	58 (22%)/205 (78%)	41 (20%)/166 (80%)	NA	NA	NA
Constipation in previous pregnancy: yes/no	73 (49%)/75 (51%)	61 (44%)/77 (56%)	NA	NA	49 (53%)/44 (47%)
Foetal weight (kg)	NA	NA	3.6 (0.5); [2.3-5.3]	3.2 (0.9); [0.6-4.7]	NA

Apgar-score (0-10) <ul style="list-style-type: none"> • 1 min • 5 min 	NA	NA	<ul style="list-style-type: none"> • 8.8 (0.8); [5-10] • 9.0 (0.5); [6-10] 	<ul style="list-style-type: none"> • 8.2 (1.7); [2-10] • 8.6 (1.0); [5-10] 	NA
Mode of vaginal delivery <ul style="list-style-type: none"> • Vacuum • Episiotomy • Perineal/Vaginal tear • Induced labour 	NA	NA	<ul style="list-style-type: none"> • 11 (6 %) • 28 (14 %) • 35 (18 %) • 37 (19 %) 	NA	NA
Urgency of caesarean section <ul style="list-style-type: none"> • Elective • Urgent • Emergency • Missing 	NA	NA	NA	<ul style="list-style-type: none"> • 73 (36 %) • 112 (55 %) • 13 (6 %) • 5 (2 %) 	NA

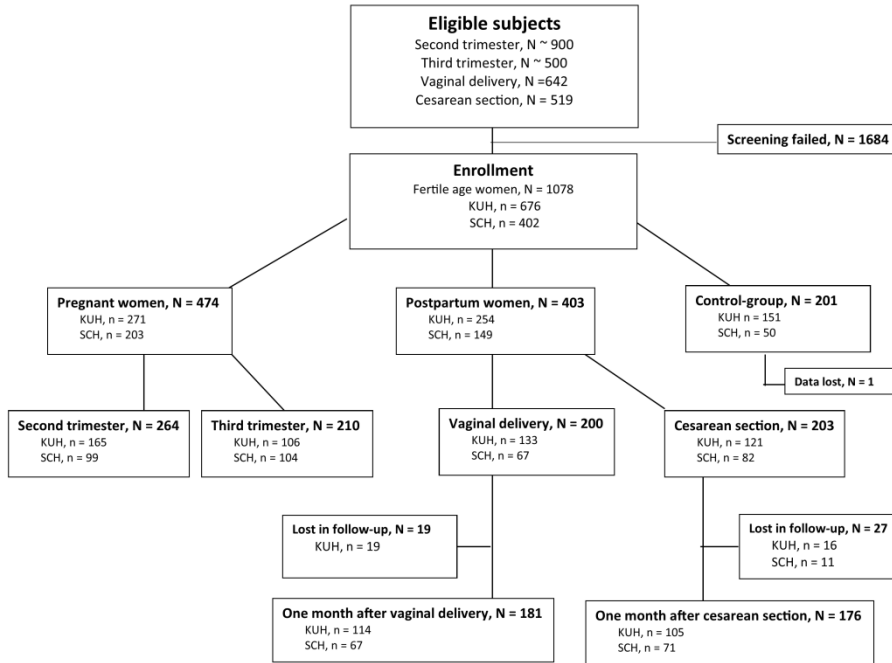
BFI = Bowel Function Index; BMI = body mass index; KUH = Kuopio University Hospital; NA = not available; SCH = Satakunta Central Hospital.

Table 2. Gastrointestinal symptoms in women during pregnancy, in postpartum women and in the control group. Data are presented as the number of cases (%).

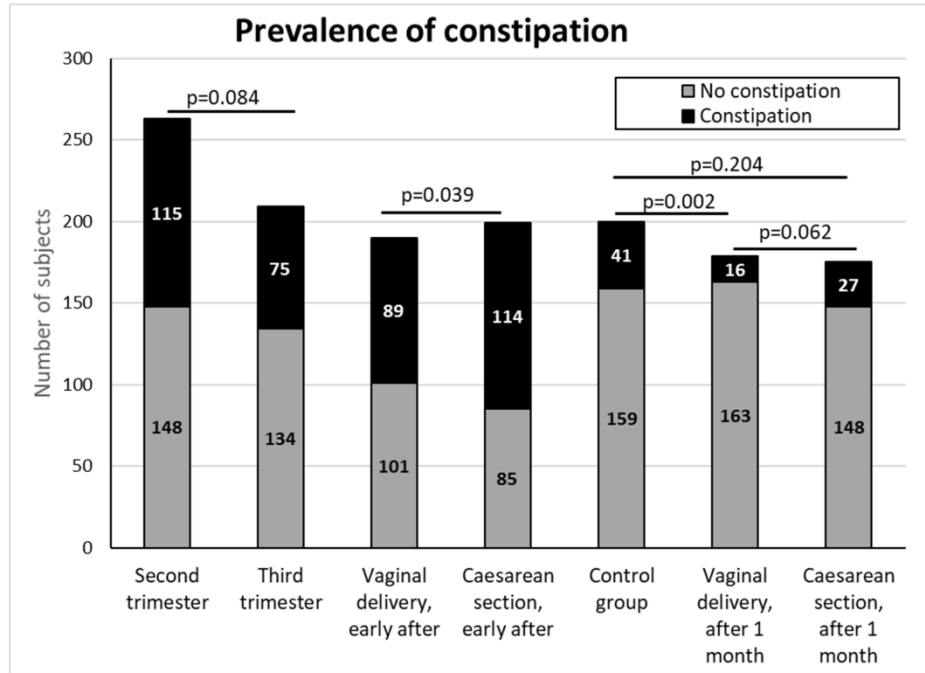
Parameter	Pregnant (N=474)	Early postpartum, a few days after delivery (N=403)	One month postpartum (N=356)	Control (N=201)	p-value, the Kruskal- Wallis test between the groups
Sense of pressure	268 (57%)	192 (48%)	41 (10%)	55 (27%)	<0.001
Feeling bloated	261 (55%)	238 (59%)	58 (14%)	127 (63%)	<0.001
Abdominal pain	212 (45%)	273 (68%)	64 (16%)	60 (30%)	<0.001
Stomach cramps	101 (21%)	89 (22%)	14 (4%)	33 (16%)	<0.001
Nausea	156 (33%)	60 (15%)	12 (3%)	26 (13%)	<0.001
Vomiting	37 (8%)	17 (4%)	3 (0.7%)	3 (3%)	<0.001
Burping	262 (55%)	84 (21%)	42 (10%)	67 (33%)	<0.001
Flatulence	300 (63%)	326 (81%)	121 (30%)	128 (64%)	<0.001
Loss of appetite	88 (19%)	66 (16%)	31 (8%)	24 (12%)	<0.001
Sleepiness	268 (57%)	218 (54%)	89 (22%)	98 (49%)	<0.001
Dizziness	116 (25%)	149 (37%)	40 (10%)	37 (18%)	<0.001
Headache	199 (42%)	83 (21%)	95 (24%)	99 (49%)	<0.001
Dry mouth	175 (37%)	215 (53%)	87 (22%)	44 (22%)	<0.001
Thirst	314 (66%)	331 (82%)	164 (46%)	103 (51%)	<0.001
Itching	93 (20%)	83 (21%)	23 (6%)	19 (10%)	<0.001
Difficulty to urinate	30 (6%)	53 (13%)	8 (2%)	3 (2%)	<0.001

Other	13 (3%)	39 (10%)	13 (3%)	9 (5%)	<0.001
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Accepted Article



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