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Title: Pregnant Women with Inflammatory Bowel Disease are at Increased Risk of Vitamin D Insufficiency: A Cross-Sectional Study

Short Title: Vitamin D Insufficiency in Pregnant Women with IBD

Authors:

Sangmin Lee (sarahlee@ucalgary.ca)

Amy Metcalfe (Amy.Metcalfe@albertahealthservices.ca)

Maitreyi Raman (mkothand@ucalgary.ca)

Yvette Leung (leungyvette@hotmail.com)

Fariba Aghajafari (fariba.aghajafari@ucalgary.ca)

Nicole Letourneau (nicole.letourneau@ucalgary.ca)

Remo Panaccione (rpanacci@ucalgary.ca)

Gilaad G. Kaplan (ggkaplan@ucalgary.ca)

Cynthia H. Seow (cseow@ucalgary.ca)

1Community Health Sciences, University of Calgary, Alberta, Canada

2Obstetrics & Gynecology, University of Calgary, Alberta, Canada

3Cumming School of Medicine, University of Calgary, Alberta, Canada

4Pediatrics & Psychiatry, University of Calgary, Alberta, Canada

5Department of Family Medicine, University of Calgary, Alberta, Canada

Manuscript Doi: 10.1093/ecco-jcc/jjy030

6Faculty of Nursing, University of Calgary

Institution Where the Work was Performed: University of Calgary, Alberta, Canada

Corresponding Author: Dr. Cynthia H. Seow

Email: cseow@ucalgary.ca

Address: TRW building, Rm 6D18, 3280 Hospital Drive NW, Calgary, Alberta, Canada, T2N 4Z6

Authors' Contributions:

- *Sangmin Lee:* Data management, analysis of data, interpretation of data, preparation of manuscript, review of manuscript, approval of final manuscript
- *Amy Metcalfe:* Study design/concept, interpretation of data, review of manuscript, approval of final manuscript.
- *Maitreyi Raman:* Study design/concept, interpretation of data, review of manuscript, approval of final manuscript.
- *Yvette Leung:* Data collection, approval of final manuscript.
- *Fariba Aghajafari:* Data collection, data management, approval of final manuscript.
- *Nicole Letourneau:* Data collection, data cleaning, coding and validation, data access and explanation, approval of final manuscript.
- *Remo Panaccione:* Interpretation of data, approval of final manuscript.
- *Gilaad G. Kaplan:* Study design/concept, interpretation of data, review of manuscript, approval of final manuscript.

- *Cynthia H. Seow:* Study design/concept, data collection, interpretation of data, preparation of manuscript, review of manuscript, approval of final manuscript.

Ethics:

1. Alberta Pregnancy Outcomes and Nutrition (APrON): The Impact of Maternal Nutrient Status During Pregnancy on Maternal Health and Child Development (REB14_1702)
2. Materno-Fetal Outcomes in Inflammatory Bowel Disease (REB15-1871)

Abbreviations: (define those that are non-standard in the field)

IBD: inflammatory bowel disease

CD: crohn's disease

UC: ulcerative colitis

D3: cholecalciferol

BMI: body mass index

APrON: Alberta Pregnancy Outcomes and Nutrition

CHREB: Conjoint Health Research Ethics Board (CHREB)

LC-MS/MS: liquid chromatography mass spectrometry

WHO: World Health Organization

USES: US Endocrine Society

HBI: Harvey-Bradshaw Index

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ABSTRACT

BACKGROUND AND AIMS: Vitamin D insufficiency is prevalent in individuals with inflammatory bowel disease, as well as in pregnant women; however, the prevalence of vitamin D insufficiency in pregnant women with IBD is unknown. This study assessed the prevalence of vitamin D insufficiency in pregnant women with IBD and the adequacy of recommended supplementation.

METHODS: A cross-sectional study was conducted in pregnant women with inflammatory bowel disease (Crohn's disease=61, ulcerative colitis=41) and without inflammatory bowel disease (n=574). Chi-square tests and log binomial regression were used to examine the prevalence of vitamin D insufficiency. Covariates included ethnicity and season. Adequacy of vitamin D supplementation during pregnancy was also assessed.

RESULTS: The prevalence of vitamin D insufficiency (25-OHD ≤75 nmol/L) in those with Crohn's disease was 50.8% (95% CI: 38.4%-63.2%) and 60.9% (95% CI: 45.3%-74.7%) with ulcerative colitis compared to 17.4% (95% CI: 14.6%-20.8%) without inflammatory bowel disease. Women with inflammatory bowel disease were more likely to be vitamin D insufficient after adjusting for ethnicity and season (Crohn's disease – adjusted relative risk [aRR]=2.98, 95% CI: 2.19-4.04; ulcerative colitis – aRR=3.61, 95% CI: 2.65-4.93). Despite vitamin D supplementation, 32.3% (95% CI: 17.8%-51.2%) with Crohn's disease, 58.3% (95% CI: 37.1%-76.9%) with ulcerative colitis and 10.8% (95% CI: 6.9%-16.6%) without inflammatory bowel disease were still vitamin D insufficient.

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CONCLUSIONS: Pregnant women with inflammatory bowel disease are at increased risk of vitamin D insufficiency compared with those without inflammatory bowel disease. The current guidelines for vitamin D supplementation may be inadequate for pregnant women with inflammatory bowel disease.

KEYWORDS: vitamin D, pregnancy, inflammatory bowel disease.

INTRODUCTION

The incidence and prevalence of inflammatory bowel disease (IBD), consisting of Crohn's disease (CD) and ulcerative colitis (UC), is increasing worldwide.[1–3] Europe has one of the highest reported prevalence of IBD with 322 per 100,000 persons affected with CD in Germany and 505 per 100,000 persons affected with UC in Norway.[1–4] Similarly to Europe, North America has also has the highest prevalence of IBD with 319 per 100,000 persons affected with CD in Canada and 286 per 100,000 persons affected with UC in USA.[1–4] Given that the onset and diagnosis peaks between 18 and 35 years of age,[5] IBD may be of a greater concern for females as the peak coincides with their prime reproductive years. Studies have consistently demonstrated an association between disease activity (particularly at conception) and adverse pregnancy outcomes including preterm birth and delivery of small for gestational age infants.[6–8] Since these adverse pregnancy outcomes can predispose infants to morbidity later in life such as type 2 diabetes and cardiovascular disease,[9,10] studying potential preventable factors for adverse pregnancy outcomes, apart from disease control, in the IBD population is important.

One such modifiable risk factor for adverse pregnancy outcomes is vitamin D insufficiency. Lower levels of vitamin D have been independently associated with increased maternofetal-related morbidity in the general population including preeclampsia, preterm birth, and delivery of small for gestational age infants.[11–14] Vitamin D, a micronutrient, can be obtained through exposure to sunlight as

cholecalciferol (D3) or through a natural and fortified diet in the form of ergocalciferol (D2).[15,16] Individuals who are unable to obtain sufficient vitamin D through these sources can increase their vitamin D concentrations with exogenous supplementation of D2 or D3.[15,16] Vitamin D2 and D3 is absorbed in the proximal part of the small intestine and goes through a chain of metabolic reactions starting at the liver, then the kidney.[16]

Vitamin D insufficiency is common with varying prevalence of vitamin D insufficiency globally, depending on various factors including geographic location, season, time of day, skin pigmentation, sunscreen use, smoking status, calcium intake or body mass index (BMI).[17–20] Pregnant women who are vitamin D insufficient are at increased risk of numerous pregnancy-related health issues including preeclampsia, gestational diabetes and preterm birth.[21] The prevalence of vitamin D insufficiency in the general population of pregnant women ranges between 20%-65%.[22–26] However, non-pregnant individuals with IBD have a higher prevalence of vitamin D insufficiency than the general population for various reasons, including inflammation or surgical resection leading to malabsorption, decreased oral intake or inadequate sunlight exposure.[16,19,27] The prevalence of vitamin D insufficiency in individuals with CD ranges from 22%-83% and between 15%-55% for those with UC.[28–32] However, the prevalence of vitamin D insufficiency has not been established in pregnant women with IBD.

As vitamin D insufficiency is treatable with supplementation, documenting the prevalence of vitamin D insufficiency in pregnant women with IBD and examining the adequacy of supplementing with vitamin D using current guideline is crucial in optimizing care of this vulnerable population. Therefore, we set out to compare the vitamin D status in pregnant women with and without IBD.

MATERIALS AND METHODS

This cross-sectional study utilized two pregnancy cohorts from Alberta, Canada: the research registry of the IBD Pregnancy Clinic at the University of Calgary and the Alberta Pregnancy Outcomes

and Nutrition (APrON) cohort (a longitudinal cohort study on nutrition and mental health of pregnant women, full details of this study are found elsewhere).[33] We used the STROBE statement checklist for cross-sectional studies (**See Supplementary Table 1**). Ethics for APrON study and materno-fetal outcomes cohort of the University of Calgary IBD Pregnancy Clinic was approved by the Conjoint Health Research Ethics Board (CHREB).

Study Population

All women with available second and third trimester intrapartum measurements of vitamin D reported as nmol/L from the IBD Pregnancy Clinic (2012–2016) and APrON study (2009–2010) were included resulting in 102 pregnant women with IBD and 574 pregnant women without IBD. The IBD pregnancy clinic utilized a chemiluminescent assay from Calgary Laboratory Services, Alberta for their vitamin D measurements, while the APrON study used liquid chromatography tandem mass spectrometry (LC-MS/MS) at the laboratory of Doctor's Data Inc., Illnois,[34] Validation studies have shown good comparability between the two vitamin D assays ($r \geq 0.87$).[35,36]

Demographic data and information on vitamin D supplementation were obtained through self-reported questionnaires and surveys. Formalized quantification of dietary intake of vitamin D through food frequency questionnaires was not available for the IBD cohort. IBD phenotypic and clinical details were obtained through detailed chart reviews. Guidelines of vitamin D supplementation for pregnant women did not change between the years of 2009 and 2016.

The primary outcome was the prevalence of vitamin D insufficiency, which was defined by the World Health Organization (WHO) and the US Endocrine Society's (USES) Clinical Practice Guidelines (25-OHD ≤75 nmol/L).[37,38] The secondary outcome was the prevalence of vitamin D deficiency (25-OHD ≤50 nmol/L). The vitamin D insufficient cohort therefore included individuals that were vitamin D deficient. Potential confounders including maternal age at the time of conception (<30 vs. ≥30 years of age), ethnicity (Caucasian vs. non-Caucasian), household income (≥$100 000 CAD vs. <$100 000 CAD),

level of education (post-secondary vs. high school) and season of blood work (spring, summer, fall, winter) were considered.

Clinical characteristics including disease severity, location/extent, duration and behaviour were captured in women with CD and UC. Disease severity was defined using the validated clinical indices for IBD (the Harvey-Bradshaw Index (HBI)[39] for those with CD; the Simple Clinical Colitis Activity Index (SCCAI)[40] for those with UC). Clinical remission was defined as HBI <5 or SCCAI <3 and clinical relapse as HBI ≥5 or SCCAI ≥3. Phenotyping for disease location, extent and behaviour was based on the Montreal Classification of IBD.[41] Disease duration was defined as the period from first diagnosis of IBD to the date of blood work during pregnancy (<10 vs. ≥10 years).

Vitamin D dosing was based on supplementation guidelines authored by The Institute of Medicine,[42,43] Health Canada[44] and Dietitians of Canada[45], which recommends daily vitamin D supplementation of ≥400 IU/day for all pregnant women. This is based on the Recommended Daily Allowance of vitamin D level of 600 IU/day and with the assumption that individuals obtain 200 IU of vitamin D per day from diet. The Institute of Medicine[42,43] and the USES Guideline Committee[37] recommend a daily dosage of vitamin D supplementation of 2000 IU/day for pregnant women at risk of vitamin D deficiency, which is defined by the current literature describing risk factors for vitamin D deficiency.

Statistical Analysis

All statistical analyses were performed using STATA/IC 14.1© (StataCorp LLC, College Station, Texas, USA). Chi-square tests were used to determine the distribution and association of vitamin D status with; 1) the absence or presence of IBD; 2) potential confounders including maternal age, ethnicity, income, education, and season; 3) vitamin D supplementation and 4) clinical characteristics of IBD. A p-value of <0.05 indicated statistical significance. Log-binomial multivariate logistic regression modelling with a Poisson distribution was used to assess the relative risk of vitamin D insufficiency adjusting for

ethnicity and season. Subgroup analyses were conducted for women with CD and UC to determine whether clinical characteristics of IBD were associated with vitamin D insufficiency. Sensitivity analyses were conducted on women who reported the level of vitamin D supplementation separately for those with and without IBD, using cut offs of 400 IU/day and 2000 IU/day. Listwise deletion was used to exclude missing data.

RESULTS

Population

The study population of 676 women with singleton pregnancies consisted of 574 (84.9%) without IBD, 61 (9.02%) with CD and 41 (6.07%) with UC. Demographic details are shown in **Table 1.** The study population primarily consisted of Caucasian (88.0%) women (mean age[SD]=32.0[4.3] years) with a total household income greater or equal to $100 000 CAD ($77 640 USD) (58.1%) and who had completed a post-secondary degree/diploma (89.8%). Overall, 23.1% of women were vitamin D insufficient (25-OHD ≤75 nmol/L) and 3.25% of women were vitamin D deficient (25-OHD ≤50 nmol/L).

Prevalence of Vitamin D Insufficiency (25-OHD ≤75 nmol/L)

There was a significant association (p <0.01) between the presence of IBD and vitamin D insufficiency. The prevalence of vitamin D insufficiency in women with CD was 50.8% (95% CI: 38.4%-63.2%) and 60.9% (95% CI: 45.3%-74.7%) with UC compared to 17.4% (95% CI: 14.5%-20.8%) without IBD. While there were numerically more women with UC with vitamin D insufficiency than women with CD, this was not statistically significant (p=0.31).

Pregnant women with CD were 2.92 (95% CI: 2.15-3.96) times more likely to be vitamin D insufficiency than those without IBD and those with UC had 3.50 (95% CI: 2.58-4.74) times the risk of

being vitamin D insufficient than those without IBD (**Table 2.**). Similarly, women with IBD were more likely to be vitamin D insufficient even after adjusting for the covariates of ethnicity and season (**Table 2.**). There was no statistical difference between UC and CD patients in the crude (relative risk (RR)=1.20, 95% CI: 0.85-1.70) or the adjusted RR (adjusted RR (aRR)=1.18, 95% CI: 0.82-1.69).

Prevalence of Vitamin D Deficiency (25-OHD≤50nmol/L)

The prevalence of vitamin D deficiency in women with UC was 14.6% (95% CI: 6.65%-29.2%) compared to 6.56% (95% CI: 2.4%-16.3%) with CD and 2.09% (95% CI: 1.19%-3.65%) without IBD. Women with UC had a significantly greater prevalence of vitamin D deficiency when compared to the women without IBD (p <0.01), but the prevalence of vitamin D deficiency was not significantly greater for those with CD (p=0.06) when compared to those without IBD. There was no statistical difference in the prevalence of vitamin D deficiency between women with UC and CD (p=0.20).

Clinical Characteristics

Phenotypic data of the women with CD and UC can be found in **Supplementary Table 2 and 3**. Generally, women had well-controlled disease. Disease severity (p=0.08), disease location (p=0.69), disease behaviour (p=0.47), medical therapy for IBD (p=0.20), nor the presence of the perianal disease (p=0.24) in women with CD influenced vitamin D status (**Table 3**). Individuals with CD of longer disease duration (≥10 years) were more likely to be vitamin D insufficient (64.5%; 95% CI: 45.9%-79.6%; p <0.01) than those with CD for less than 10 years (63.3%; 95% CI: 44.4%-78.9%). Disease severity (p=0.92), disease extent (p=0.50), disease duration (p=0.94), and medical therapy for IBD (p=0.20) were not significantly associated with vitamin D status in pregnant women with UC (**Table 3**).

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Vitamin D Supplementation for Pregnant Women

In women without IBD, vitamin D status (vitamin D insufficient vs. vitamin D sufficient) was significantly influenced by whether or not individuals met the recommended minimum daily dosage of 400 IU/day of vitamin D supplementation ($p < 0.01$; **Table 4**). Despite meeting the recommended 400 IU of vitamin D supplementation per day, 10.8% (95% CI: 6.9%-16.6%) of women without IBD were vitamin D insufficient.

There was no statistically significant difference in the proportion of women with CD or UC taking vitamin D supplements (400 IU/day ($p=0.44$); 2000 IU/day ($p=0.40$)). The majority of pregnant women with IBD consumed the minimum daily vitamin D supplementation of 400 IU/day (CD: 72%; UC: 80%). Despite this, 32.3% (95% CI: 17.8%-51.2%) of those with CD and 58.3% (95% CI: 37.1%-76.9%) with UC were still vitamin D insufficient (**Table 4.**). Women with CD were responsive to the 400 IU/day of vitamin D supplementation in achieving vitamin D sufficiency (67.8%, 95% CI: 48.8%-82.2%, $p=0.04$), while 400 IU/day of vitamin D supplementation did not influence achieving vitamin D sufficiency for those with UC (41.7%, 95% CI: 23.1%-62.9%, $p=0.26$).

Only 39% of pregnant women with CD and 30% of those with UC were taking greater than 2000 IU of vitamin D/day. Even with these higher doses, the prevalence of vitamin D insufficiency was 29.4% (95% CI: 12.1%-55.8%) in those with CD and 44.4% (95% CI: 15.7%-77.4%) with UC. Vitamin D sufficiency did not appear to be associated with this higher degree of supplementation (UC: $p=0.16$; CD: $p=0.18$) (**Table 7**).

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DISCUSSION

In this cross-sectional observational study, we demonstrated that pregnant women with IBD were at a greater risk for vitamin D insufficiency than pregnant women without IBD. The majority of the literature reports a higher prevalence of vitamin D insufficiency in the non-pregnant cohort with IBD compared to the general population.[16,29,32,46–48] However, a few studies have not supported this suggesting that the prevalence of vitamin D insufficiency is not statistically different between non-pregnant individuals with IBD and healthy controls.[38,49,50] The differences in these findings may be due to a variety of confounding factors including the definition of vitamin D insufficiency (i.e. different thresholds) and differences in the geographic locations of the studies. Irrespective of this, the existing literature only presents data on non-pregnant individuals with IBD, while our study is the first to assess the prevalence of vitamin D insufficiency in pregnant women with IBD. There was a numerical but non-significant increased prevalence of vitamin D insufficiency in pregnant women with UC compared to those with CD. Our findings may be influenced by detection bias, where physicians were more likely to screen and subsequently supplement individuals with CD, based on the premise that vitamin D absorption occurs predominantly in the proximal small intestine.[16,28–32]

The current guidelines for vitamin D supplementation recommends vitamin D supplementation of 400 IU/day for all pregnant women.[42–45] However, the guidelines relating to vitamin D supplementation for pregnant women with IBD are as clear. Our study determined that 72.1% of pregnant women with CD and 80.0% of pregnant women with UC were compliant in meeting the minimum daily dosage of 400 IU of vitamin D per day; however, a large proportion of women with IBD were still vitamin D insufficient. This was congruent with a study conducted by Suibhne et. al.[50] of non-pregnant individuals with IBD, where vitamin D supplements of 200-400 IU/day were inadequate in treating vitamin D deficiency. The findings from this study suggest that the current guideline for vitamin D supplementation for all pregnant women of 400 IU/day may be inadequate for pregnant women with IBD.

The USES Practice Guideline Committee[37] recommends a 2000 IU daily vitamin D supplement for pregnant women at risk of vitamin D deficiency defined by literature. However, only 39.5% of pregnant women with CD and 22.5% with UC were taking more than 2000 IU vitamin D/day suggesting that knowledge of the 'at risk' population may not be well understood. Further, even in those taking greater than 2000 IU/day of vitamin D supplements, 29.4% with CD and 44.4% with UC remained vitamin D insufficient. As vitamin D insufficiency has been associated with adverse pregnancy outcomes in the general population,[34,51,52] it is important that health care professionals are aware that despite taking either greater than 400 IU/day or 2000 IU/day of vitamin D supplements, a significant proportion of pregnant women with IBD remain vitamin D insufficient. The current guidelines should change accordingly to be more explicit in their recommendations, and even higher recommended doses may be required.

This cross-sectional study design utilising two defined pregnancy cohorts was appropriate and adequately powered to determine the prevalence of vitamin D insufficiency. Further, the cohorts were obtained from the same geographic region, which allowed for consistency in the sunlight exposure throughout each season. A limitation was the inability to adjust for individual outdoor exposure. Further, the cross-sectional study design did not allow for an association between vitamin D status and pregnancy outcomes to be made and an alternate study design utilizing population-based administrative data may better answer whether increasing vitamin D supplementation will improve pregnancy or clinical outcomes. Future studies may prospectively assess the optimal daily dosage of vitamin D supplementation for pregnant women with IBD and capture data on pregnancy outcomes.

It is acknowledged that our study's findings may only be generalizable to Caucasian pregnant women >30 years of age with a higher socio-economic status (SES). However, the existing literature shows that Caucasian pregnant women and those of higher SES are more likely to be vitamin D sufficient,[53,54] therefore, the risk calculated in this study may be lower than the true value of the

association. This makes our findings more important as the risk for vitamin D insufficiency may be even greater in pregnant women with IBD.

Potential residual confounding includes cigarette smoking status and pre-pregnancy BMI. Cigarette smoking is associated with lower circulating vitamin D levels, increasing the risk of vitamin D insufficiency.[20,55–57] Further, non-pregnant individuals with CD that are smokers are more likely to have active IBD,[58,59] though smoking has controversially been associated with protective effects in those with UC.[58,60] We were unable to assess for the potential confounder of smoking as the total number of current (n=1) and former (n=56) smokers in this pregnant cohort was too small to model. This was not unexpected as smoking is less common in the pregnancy state.[61]

Further, we were limited to assessing changes in vitamin D levels during pregnancy. Women are found to be more vitamin D insufficient during the first trimester than the third trimester,[62] however our cross-sectional study only measured the vitamin D levels at trimester two or three. This makes our findings even more important as there was a high prevalence of vitamin D insufficiency in women with IBD that had their vitamin D measured during trimester two or three.

Our study concludes that pregnant women with IBD have a higher prevalence of vitamin D insufficiency (25-OHD ≤75 nmol/L) than those without IBD. The implications of these findings raise awareness and build a foundation for understanding the magnitude of vitamin D insufficiency in pregnant women with IBD, a critical first step in developing appropriate clinical care pathways to address vitamin D in this population. There is a need for greater awareness of vitamin D status in pregnant women with IBD during prenatal and intrapartum care, as vitamin D insufficiency during pregnancy in the general population has been associated with adverse pregnancy outcomes. Further, current protocols and guidelines for vitamin D supplementation should be updated and made appropriate for pregnant women with IBD, who are more likely to be vitamin D insufficient. Future studies should build from our findings to better understand the role of vitamin D insufficiency in pregnant women with IBD. Vitamin D

supplementation is an easy treatment to improve one's vitamin D status and as such, research should focus on determining the optimal daily dosage of vitamin D supplementation without increasing adverse pregnancy outcomes in pregnant women with IBD. Further, researchers should determine whether improving one's vitamin D status will improve pregnancy outcomes for pregnant women with IBD. These future studies have implications for developing appropriate protocols and guidelines for vitamin D insufficiency in hopes to provide equal and consistent treatment for pregnant women with IBD during their prenatal and intrapartum visit.

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CONFLICT OF INTEREST

There were no potential competing interests.

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TABLES

Table 1. Demographics and vitamin D status of the study population.

	Without IBD		**CD**		**UC**	
Study Population (n)	574		61		41	
Mean age (sd)	32.1 (4.35)		31.2 (3.72)		31.7 (3.56)	
	n	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**
Vitamin D insufficiency	100	17.4 (14.5 to 20.8)	31	50.8 (38.4 to 63.2)	25	61.0 (45.3 to 74.7)
Vitamin D deficiency	12	2.1 (1.2 to 3.6)	4	6.6 (2.5 to 16.3)	6	14.6 (6.6 to 29.2)
Ethnicity						
Caucasian	505	88.0 (85.0 to 90.4)	57	93.4 (83.7 to 97.5)	33	80.5 (65.3 to 90.0)
Non-Caucasian	69	12.0 (9.6 to 15.0)	4	6.6 (2.5 to 16.3)	8	19.5 (10.0 to 34.7)
Income ($)						
≥ 100 000 CAD	325	56.6 (52.5 to 60.6)	40	65.6 (52.8 to 76.5)	28	68.3 (52.5 to 80.8)
< 100 000 CAD	325	56.6 (52.5 to 60.6)	40	65.6 (52.8 to 76.5)	28	68.3 (52.5 to 80.8)
Education						
≥ Post-secondary	517	90.1 (87.3 to 92.3)	52	85.2 (73.9 to 92.2)	38	92.7 (79.4 to 97.7)
≤ High school	57	9.9 (7.7 to 12.7)	9	14.8 (7.8 to 26.1)	3	7.3 (2.3 to 20.6)
Season of blood work						
Spring (Mar 20 to Jun 19)	86	15.0 (12.3 to 18.2)	18	29.5 (19.4 to 42.2)	11	26.8 (15.4 to 42.5)
Summer (Jun 20 to Sept 21)	135	23.5 (20.2 to 27.2)	7	11.5 (5.5 to 22.3)	10	24.4 (13.5 to 39.9)

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Fall (Sept 22 to Dec 20)	192	33.4 (29.7 to 37.4)	17	27.9 (18.0 to 40.5)	11	26.8 (15.4 to 42.5)
Winter (Dec 21 to Mar 19)	161	28.0 (24.5 to 31.9)	19	31.1 (20.7 to 43.9)	9	22.0 (11.7 to 37.3)

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Table 2. Log binomial regression for vitamin D insufficiency and disease status.

	Crude RR (95% CI)	**Adjusted RR (95% CI) for ethnicity and season**
Without IBD	Ref	Ref
Crohn's Disease	2.92 (2.15 to 3.96)	2.98 (2.19 to 4.04)
Ulcerative Colitis	3.50 (2.58 to 4.74)	3.61 (2.65 to 4.93)

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Table 3. Clinical characteristics and vitamin D status of pregnant women with IBD.

	Crohn's Disease					**Ulcerative Colitis**				
	Vitamin D Sufficient		**Vitamin D Insufficient**			**Vitamin D Sufficient**		**Vitamin D Insufficient**		
	n	**%(95%CI)**	**n**	**%(95%CI)**	**p**	**n**	**%(95%CI)**	**n**	**%(95%CI)**	**p**
Severity										
Remission (CD:HBI<5; UC:SCCAI≤2)	28	54.8 (40.0 to 67.2)	24	46.2 (32.8 to 60.1)	-	13	39.4 (23.8 to 57.5)	20	60.6 (42.5 to 76.2)	-
Relapse (CD:HBI≥5; UC:SCCAI>2)	n<5		7	77.8 (39.0 to 95.0)	0.08	n<5		5	62.5 (25.6 to 89.0)	0.92
Location										
Ileal	8	42.1 (21.9 to 65.4)	11	57.9 (34.6 to 78.1)	-	N/A		N/A		
Colonic	8	57.1 (30.3 to 80.4)	6	42.9 (19.6 to 69.7)	0.39	N/A		N/A		
Ileocolonic	14	50.0 (31.6 to 68.4)	14	50.0 (31.6 to 68.4)	0.60	N/A		N/A		
Behaviour[a]										
B1	21	55.3 (38.9 to 70.5)	17	44.7 (29.5 to 61.1)	-	N/A		N/A		
B2	n<5		6	60.0 (27.8 to 85.4)	0.39	N/A		N/A		
B3	5	38.5 (16.0 to 67.2)	8	61.5 (32.8 to 84.0)	0.30	N/A		N/A		
Perianal										
No	20	54.1 (37.6 to 69.7)	17	45.9 (30.3 to 62.4)	-	N/A		N/A		

Yes	8	38.1 (19.7 to 60.7)	13	61.9 (39.3 to 80.3)	0.24	N/A		N/A		
Extent										
Ulcerative Proctitis	N/A		N/A			n<5		n<5		-
Left sided UC	N/A		N/A			5	31.3 (12.8 to 58.4)	11	68.8 (41.6 to 87.2)	0.81
Extensive UC	N/A		N/A			10	47.6 (26.9 to 69.2)	11	52.4 (30.8 to 73.1)	0.40
Duration										
<10 years	19	63.3 (44.4 to 78.9)	11	36.7 (21.1 to 55.6)	-	12	38.7 (22.8 to 57.4)	19	61.3 (42.6 to 77.2)	-
≥10 years	11	35.5 (20.4 to 54.1)	20	64.5 (45.9 to 79.6)	0.03	n<5		6	60.0 (27.5 to 85.6)	0.94
Medications										
No IBD Therapies	6	46.2 (19.5 to 75.2)	7	53.8 (24.8 to 80.5)	-	n<5		n<5		-
Non-Biologic Therapy	10	66.7 (37,2 to 87.1)	5	33.3 (12.9 to 62.8)	0.27	5	25.0 (9.9 to 50.3)	15	75.0 (49.7 to 90.1)	1.00
Biologic Therapy	12	38.7 (22.7 to 57.6)	19	61.3 (42.4 to 77.3)	0.65	7	58.3 (26.7 to 84.3)	5	41.7 (15.7 to 73.3)	0.620

[a] B1: non-stricturing, non-penetrating; B2: stricturing; B3: penetrating

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Table 4. Effect of Vitamin D supplementation on vitamin D status in pregnant women with and without Inflammatory Bowel Disease (Crohn's Disease and Ulcerative Colitis).

		Without IBD				**Crohn's Disease**				**Ulcerative colitis**			
		VD(+)		**VD(-)**		**VD(+)**		**VD(-)**		**VD(+)**		**VD(-)**	
		n	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**
Recommended for All Pregnant Women (IU/day)	≥400	148	89.2 (83.4 to 93.1)	18	10.8 (6.9 to 16.6)	21	67.7 (48.8 to 82.2)	10	32.3 (17.8 to 51.2)	10	41.7 (23.1 to 62.9)	14	58.3 (37.1 to 76.9)
	<400	240	78.7 (73.7 to 82.9)	65	21.3 (17.1 to 26.3)	4	33.3 (12.1 to 64.5)	8	66.7 (35.5 to 87.9)	1	16.7 (1.7 to 70.0)	5	83.3 (30.1 to 98.3)
Recommended for Pregnant Women at Risk of Vitamin D Insufficiency (IU/day)	≥2000					12	70.6 (44.2 to 87.9)	5	29.4 (12.1 to 55.8)	5	55.6 (22.6 to 84.3)	4	44.4 (15.7 to 77.4)
	<2000					13	50.0 (30.8 to 69.2)	13	50.0 (30.8 to 69.2)	6	28.6 (12.7 to 52.4)	16	71.4 (47.6 to 87.3)

*Abbreviation: VD(+): vitamin D sufficient; VD(-): vitamin D insufficient