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Caesarean birth in women with infertility: population-based cohort study

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Objective Caesarean section (CS) is more common following infertility treatment (IT) but the reasons why remain unclear and confounded. The Robson 10-Group Classification System (TGCS) may further explain variation in CS rates. We assessed the association between mode of conception and CS across Robson groups.

Design Population-based cohort study.

Setting Ontario, Canada, in a public healthcare system.

Population 921 023 births, 2006–2014.

Methods Modified Poisson regression produced relative risks (RR) and 95% confidence intervals, comparing the risk of CS among women with (1) subfertility without IT, (2) non-invasive IT (OI, IUI) or (3) invasive IT (IVF)—each relative to (4) spontaneous conception (SC).

Main outcome measures CS rate according to one of four modes of conception, overall and stratified by each of the TGCS groups.

Results Relative to SC (26.9%), the risk of CS increased in those with subfertility without IT (RR 1.17, 95% CI 1.16–1.18), non-invasive IT (RR 1.21, 95% CI 1.18–1.24) and invasive IT (RR 1.39, 95% CI 1.36–1.42). Within each Robson group, similar patterns of RRs were seen, but with markedly differing rates. For example, in Group 1 (nulliparous, singleton, cephalic at ≥37 weeks, with spontaneous labour), the respective rates were 15.0, 19.4, 18.7 and 21.9%; in Group 2 (nulliparous, singleton, cephalic at ≥37 weeks, without spontaneous labour), the rates were 35.9, 44.4, 43.2 and 54.1%; and in Group 8 (multiple pregnancy), they were 55.9, 67.5, 65.0 and 69.3%, respectively.

Conclusions CS is relatively more common in women with subfertility and those receiving IT, an effect that persists across Robson groups.

Keywords Caesarean section, infertility, Robson classification.

Tweetable abstract Caesarean delivery is more common in women with infertility independent of demographics and prenatal conditions.

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Introduction

Infertility, defined as the inability to conceive after 12 months of unprotected intercourse, affects an estimated 15% of Canadian couples.[1] Access to infertility treatment (IT) in Canada is on the rise,[2] and has been covered under Ontario's public health plan since 2015. Infertility, with or without IT, may result in adverse pregnancy outcomes and higher rates of birth by caesarean section (CS).[3–8] About 1/4 to 1/3 births in Canada are by CS.[9] CS is the most common in-patient surgery,[10] with a high cost to the healthcare system.[11] The reasons for the high rate of CS in IT pregnancies are not well documented, as prior studies were likely confounded by indication and none defined which specific characteristics lead to CS in women who access IT.[8] Providing clarity on this matter might help target potentially modifiable patient, provider and system factors.

In 2015, the World Health Organization recommended using the Robson 10-Group Classification System (TGCS) as a global standard for assessing and comparing the variation in CS rates between patient groups, hospitals or regions.[12,13] Doing so reduces study bias and confounding, by evaluating CS rates among similar groups of women nearer to the time of the expected birth.[14] Accordingly, this population-based cohort study was undertaken to assess

the association between mode of conception and CS rates, further stratified by like Robson classification groups.

Methods

Setting and design

This population-based cohort study comprised all liveborn or stillborn hospital births in Ontario from 1 April 2006 to 31 March 2014 through ICES (www.ices.on.ca). We obtained pregnancy and neonatal outcomes from the Better Outcomes Registry & Network (BORN) Ontario and Niday Legacy datasets (www.bornontario.ca/en/data/data-dictionary/legacy-datasets/). BORN captures more than 99% of hospital births in the province and has been previously validated for completeness and accuracy.[15] We included singleton and multiple births. Analyses were restricted to women aged 18–50 years. Maternal demographics and pre-existing health conditions were obtained from the Canadian Institute for Health Information Discharge Abstract Database (CIHI DAD), National Ambulatory Care Reporting System (NACRS), Ontario Health Insurance Plan Claims Database (OHIP), Registered Persons Database (RPDB), Postal Code Conversion File (PCCF), Linked Delivering Mothers and Newborns (MOMBABY), Ontario Hypertension Dataset (HYPER), Ontario Diabetes Dataset (ODD) and the Immigration, Refugees and Citizenship Canada dataset (IRCC) (Table S1). Patients were not involved in the development of the research.

Exposure and outcome variables

The exposure of interest was mode of conception as recorded in BORN, namely, (1) spontaneous conception (SC) (the reference group); (2) subfertility without IT (i.e. a history of an infertility consult with a physician, defined as an ICD-9 628 OHIP diagnosis in the 2 years prior to the estimated date of conception, and in the absence of receipt of IT); (3) non-invasive IT (i.e. ovulation induction [OI] or intrauterine insemination [IUI] alone); and (4) invasive IT (i.e. *in vitro* fertilisation [IVF] or intracytoplasmic sperm injection [ICSI]).

Each birth was further classified and then stratified into one of ten mutually exclusive Robson groups, based on six obstetric variables: parity, previous caesarean section, gestational age, onset of labour, fetal presentation and number of fetuses.[13]

The comparative outcome of interest was the CS rate according to one of four modes of conception, overall, and then stratified by each of the ten Robson groups.[13,16] As per the recommended Robson approach, we determined: the relative size of each Robson group, the CS rate in each group, the absolute contribution to the overall CS rate (i.e. the percentage contributed to the overall CS rate by a particular group), and the relative contribution to the overall CS rate (i.e. the absolute contribution expressed as a percentage of the overall rate).

Statistical analysis

Temporal trends in CS rates by mode of conception were quantified using the Cochran–Armitage test. The association between type of conception and CS was quantified by absolute rates and relative risks (RR), derived using modified Poisson regression with a robust error variance and a GEE component, which also accounts for correlated errors among potentially more than one birth in the same woman.[17] RRs were adjusted for maternal age at delivery, income quintile, rurality, immigration status, obesity (i.e. pre-pregnancy body mass index >30 kg/m^2 or presence of OHIP billing code for obesity – ICD-9 278 – if BMI was missing), pre-existing diabetes, gestational diabetes, chronic hypertension, gestational hypertension (including pre-eclampsia, eclampsia and HELLP syndrome), smoking status at first prenatal visit, and any substance use. Gestational age at birth was then further added to the latter model as it is correlated with multifetal pregnancy and also risk of caesarean birth (final model).

The same aforementioned final models were re-run but were further each stratified by the Robson TGCS.[12,13] In addition, two sensitivity analyses were conducted: (1) CS rates and RR by exposure were calculated for first pregnancies only, and (2) overall CS rates stratified by the Robson TGCS were calculated including all of Ontario births during the study period without exclusions, ($n = 1\,031\,536$) (Table S2).

Results

There were 921 023 births included among 670 333 women (Figure 1). Of these births, 807 164 (87.6%) were among women with SC, 92 117 (10%) among women with subfertility without IT, 10 632 (1.1%) among women with non-invasive IT, and 11 110 (1.2%) among women with invasive IT (Figure 1). In contrast to women with SC, those with subfertility without IT or who received IT tended to be older, resided in a higher income area, had higher rates of pre-existing health conditions, polycystic ovary syndrome (PCOS), endometriosis or fibroids (Table 1).

The overall rate of CS was 28.2% (259 928 of 921 023 births), slightly declining during the study period from 28.2% in 2006 to 27.4% in 2014 ($P < 0.001$). CS rates decreased in women with subfertility, from 37.0% in 2006 to 34.6% in 2014 ($P < 0.001$), and those with non-invasive IT, from 41.6% in 2006 to 33.6% in 2014 ($P = 0.002$), while remaining stable in those with invasive IT (50.2% in 2006 and 49.8% in 2014; $P = 0.13$) (Figure S1). Relative to women with SC (26.9%), the risk of CS increased in those with subfertility without IT (36.3%; RR 1.17, 95% CI

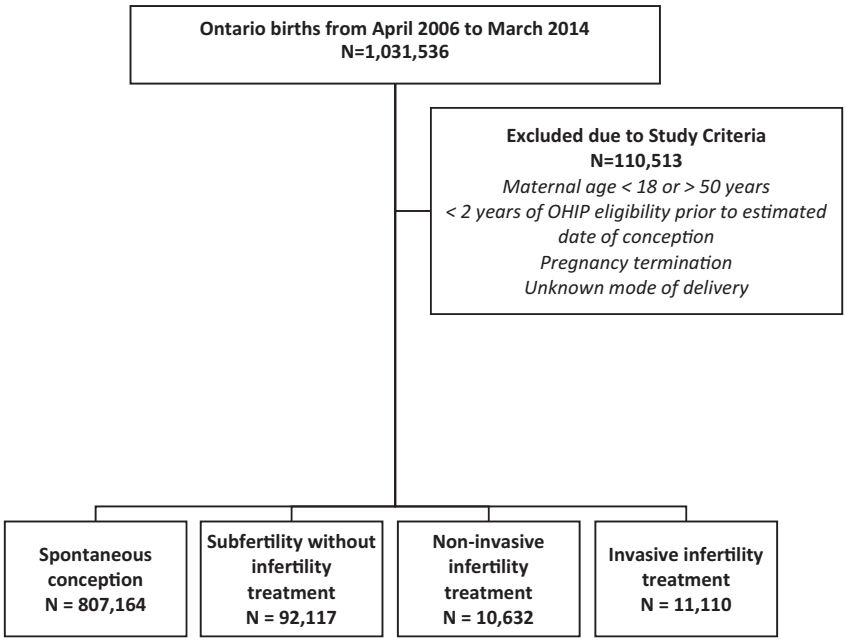

Figure 1. Study flow chart.

1.16–1.18), non-invasive IT (38.8%; RR 1.21, 95% CI 1.18–1.24) and invasive IT (50.6%; RR 1.39, 95% CI 1.36–1.42) (Figure 2). Similarly, in the sensitivity analysis including first pregnancies only, relative to SC (27.3%), the risk of CS increased in those with subfertility without IT (36.8%; RR 1.19, 95% CI 1.17–1.20), non-invasive IT (39.2%; RR 1.25, 95% CI 1.22–1.29, and invasive IT (51.6%; RR 1.52, 95% CI 1.49–1.55). When including all births without exclusions, the results were also unchanged (Table S2).

Women with a previous CS at ≥37 weeks with a single cephalic fetus (Robson Group 5) represent the largest single contributor to the overall CS rate, followed by nulliparous women (Groups 1 and 2) (Table 2). The contribution of each Robson group varied by type of conception (Tables S3–S6). For example, among women with SC, Robson Group 5 explained 9.0% of all births and 33.6% of all CS (Table S3), whereas, among those who conceived by invasive IT, Robson Group 5 described 5.2% of all births and 10.3% of all CS (Table S6). In contrast, in Robson Group 8 (multiple pregnancy), the respective proportion among women with SC was 0.7% of all births and 2.6% of all CS (Table S3), whereas among those who conceived by invasive IT, Robson Group 8 described 17.6% of all births and 34.9% of all CS (Table S6).

Upon stratifying by each Robson group, the pattern for the RRs for CS in relation to mode of conception was similar to those described above, but at markedly differing CS rates depending on the Robson group (Figure 2). For example, in Group 1 (nulliparous singleton women, cephalic presentation at ≥37 weeks, with spontaneous labour), the corresponding rates were 15.0, 19.4, 18.7 and 21.9% among those with SC, subfertility without IT, non-invasive IT and invasive IT, whereas in Group 2 (nulliparous singleton women, cephalic presentation at ≥37 weeks, without spontaneous labour), the rate of CS was 35.9, 44.4, 43 and 54.1%. In Group 8 (multiple pregnancy), the respective rates were the highest, at 55.9, 67.5, 65 and 69.3%.

We then stratified Robson Group 2 and Group 4 into (a) labour-induced, and (b) pre-labour CS—each relative to SC (Figure S2). Group 2 had higher rates of labour induction, whereas Group 4 had higher rates of pre-labour CS. In Group 2a, relative to SC, the associated risk of CS was not increased in those with subfertility (RR 1.02, 95% CI 0.99–1.05) or non-invasive IT (RR 1.02, 95% CI 0.96–1.08), but was increased in those with invasive IT (RR 1.10, 95% CI 1.03–1.16), each relative to SC. In Group 4a, the RR of CS was increased in those with subfertility (RR 1.29, 95% CI 1.18–1.42), non-invasive IT (RR 1.60, 1.24–2.05), and invasive IT (RR 1.66, 95% 1.25–2.20).

Upon removing gestational age at birth from the modified Poisson models, the adjusted RR did not change (data not shown).

Discussion

Main findings

This study observed an increased rate of CS in relation to use of IT and the degree of invasiveness of IT. After accounting for all Robson groups, having a previous CS contributed the most to the increased rate of CS in women

Table 1. Baseline characteristics of 921 023 births by mode of conception, 2006–2014. All data presented as a number (%) unless specified otherwise

Characteristic	Spontaneous conception ($n = 807\,164$)	Subfertility without infertility treatment ($n = 92\,117$)	Non-invasive infertility treatment ($n = 10\,632$)	Invasive infertility reatment ($n = 11\,110$)
Mean ± SD maternal age, years	29.9 ± 5.3	33.1 ± 4.7	32.9 ± 4.5	35.5 ± 4.8
Mean ± SD gestational age at birth, weeks	38.9 ± 1.9	38.5 ± 2.2	38.2 ± 2.6	37.6 ± 2.9
Rural residence	64 184 (7.9)	4010 (4.3)	623 (5.9)	402 (3.6)
Income quintile (Q)				
1 (lowest)	178 390 (22.1)	14 657 (15.9)	1352 (12.7)	1012 (9.1)
2	161 668 (20.0)	16 332 (17.7)	1779 (16.7)	1732 (15.6)
3	166 016 (20.6)	19 418 (21.1)	2272 (21.4)	2360 (21.2)
4	170 820 (21.2)	22 653 (24.6)	2925 (27.5)	2987 (26.9)
5 (highest)	130 270 (16.1)	19 057 (20.7)	2304 (21.7)	3019 (27.2)
Immigrant	186 090 (23.1)	27 371 (29.7)	2069 (19.5)	2851 (25.7)
History of polycystic ovary syndrome	4952 (0.6)	3304 (3.6)	649 (6.1)	302 (2.7)
History of fibroids	5088 (0.6)	2410 (2.6)	193 (1.8)	316 (2.8)
History of endometriosis	4766 (0.6)	2804 (3.0)	309 (2.9)	573 (5.2)
Nulliparity	333 384 (41.3)	46 849 (50.9)	6787 (63.8)	7713 (69.4)
Multi-fetal pregnancy	9951 (1.2)	3178 (3.5)	1272 (12.0)	2844 (25.6)
Obese	72 304 (9.0)	9109 (9.9)	1708 (16.1)	1026 (9.2)
Pre-pregnancy diabetes	20 264 (2.5)	4286 (4.7)	553 (5.2)	460 (4.1)
Gestational diabetes	33 999 (4.2)	6977 (7.6)	1009 (9.5)	948 (8.5)
Chronic hypertension	23 094 (2.9)	4006 (4.4)	515 (4.8)	520 (4.7)
Gestation hypertension	36 302 (4.5)	5150 (5.6)	918 (8.6)	969 (8.7)
Smoking	98 975 (12.3)	3946 (4.3)	407 (3.8)	220 (2.0)
Substance use*	12 150 (1.5)	402 (0.4)	71 (0.7)	56 (0.5)

IQR, interquartile range; SD, standard deviation.
*Includes any alcohol exposure, or marijuana, cocaine, gas/glue, hallucinogens, methadone, narcotics, opioids and other substance use.

with subfertility without IT, and a multiple pregnancy contributed the most to the CS rate in women with IT, especially invasive IT. In women with a singleton, term, cephalic pregnancy requiring labour induction, only nulliparous with invasive IT had a slight increased risk of CS relative to SC; nonetheless, in multiparous women the risk of CS increased by treatment invasiveness.

Strengths and limitations

The main strength of this study is its large sample size and population-based approach, with a cohort including 921 023 births. We acknowledge the possibility of misclassification of exposure status despite generally high accuracy of the datasets.[18] Such misclassification would be most likely in the group of women with subfertility without IT, as the 6.4% rate of multiple pregnancy among the latter group is higher than the 2–3% rate in the general population.[19] Data quality and misclassification of outcome status is also possible. Nearly 7% of births could not be classified by the Robson criteria because of missing details, which is high compared with other studies.[20,21] Another indicator of limited data quality is that the CS rates were lower than 100% in group 9 (fetus in transverse or oblique lie); however, it is reassuring that the size of group 9 (0.6% for the overall population) is within the expected range (0.4–0.6%) recommended by Robson and WHO.[16,22] Additional data quality criteria are within the expected ranges or differ only slightly, which is reassuring.[16] The size of Group 1 plus Group 2 (34.2%) is close to the expected range of 35–42%, whereas the size of Group 3 plus Group 4 (36.6%) is higher than the expected size of 30%.[16] The size of Group 5 (11%) is slightly higher than the recommended size of <10% in settings with low CS rates but lower than a size >15% seeing in settings with high CS rates.[16] The size of Group 6 plus Group 7 (3.7%) is within the expected range (3–4%).[16] The overall size of Group 8 (1.9%) is within the expected size of 1.5–2%, and the size of Group 10 (5%) is at the recommended limit of <5%.[16] In addition, the ratio Group 1/Group 2 of 1.8 in the overall population is slightly lower than the expected 2:1. However, the ratio Group

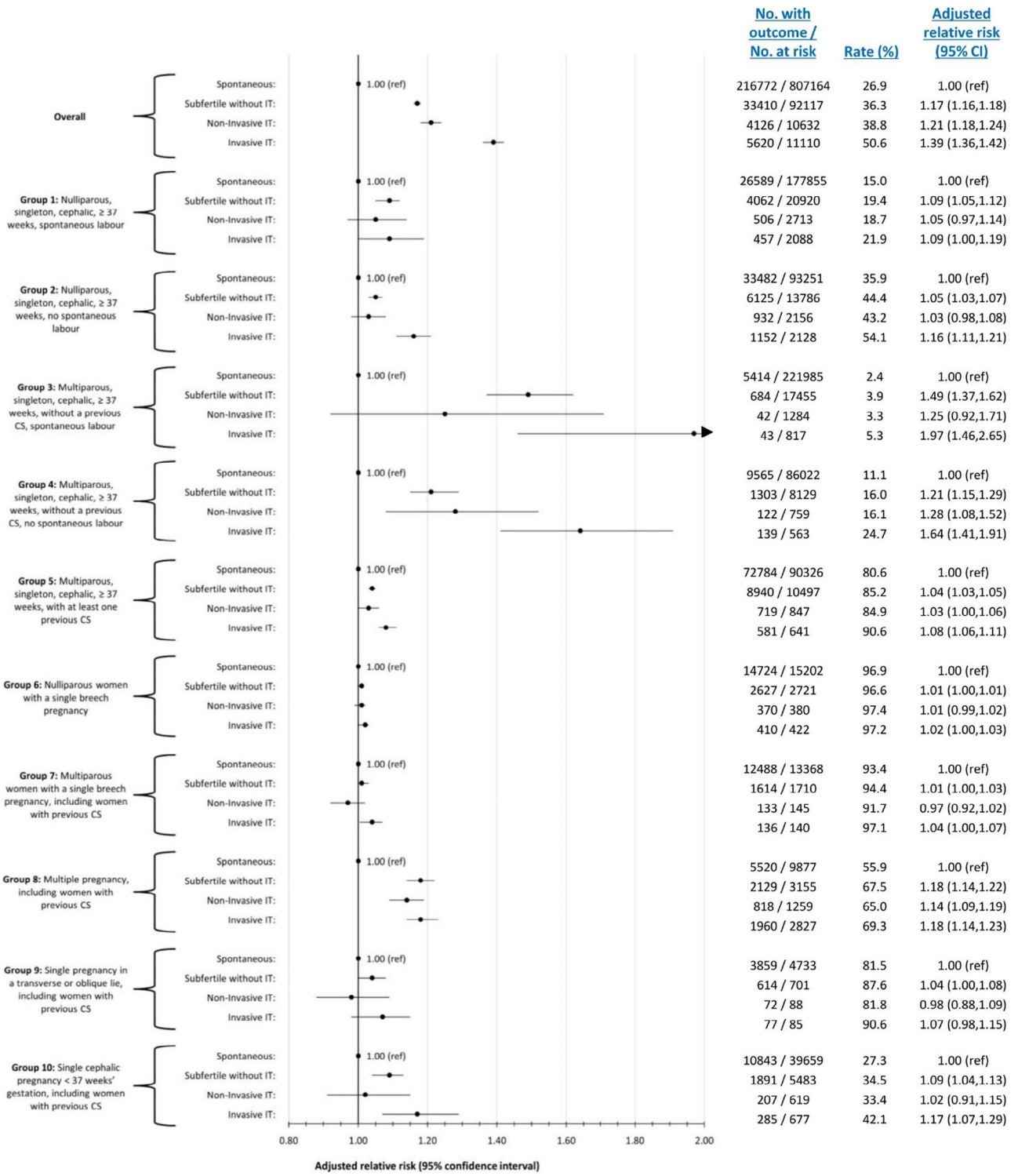

Figure 2. Risk of caesarean section by type of conception overall and further stratified by the Robson 10-Group classification.

3/Group 4 of 2.5 is higher than the recommended 2:1. Also, this research was based on data prior to the introduction of Ontario's publicly funded IT program in 2015. Since then, with more robust and granular data, more might be learned about the rate of CS by conception type, and according to Robson classification group. Finally,

Table 2. Ten group classification system table for the overall obstetrical population (n= 921 023)

Robson group	Number of CS in group	Number of women in group	Group size* (%)	Group CS rate** (%)	Absolute group contribution to overall CS rate*** (%)	Relative contribution of group to overall CS rate**** (%)
Group 1: Nulliparous, singleton, cephalic, ≥37 weeks, spontaneous labour	31 614	203 576	22.1	15.5	3.4	12.2
Group 2: Nulliparous, singleton, cephalic, ≥37 weeks, no spontaneous labour	41 691	111 321	12.1	37.5	4.5	16.0
Group 3: Multiparous, singleton, cephalic, ≥37 weeks, without a previous CS, spontaneous labour	6183	241 541	26.2	2.6	0.7	2.4
Group 4: Multiparous, singleton, cephalic, ≥37 weeks, without a previous CS, no spontaneous labour	11 129	95 473	10.4	11.7	1.2	4.3
Group 5: Multiparous, singleton, cephalic, ≥37 weeks, with at least one previous CS	83 024	102 311	11.1	81.2	9.0	31.9
Group 6: Nulliparous women with a single breech pregnancy	18 131	18 725	2.0	96.8	2.0	7.0
Group 7: Multiparous women with a single breech pregnancy, including women with previous CS	14 371	15 363	1.7	93.5	1.6	5.5
Group 8: Multiple pregnancy, including women with previous CS	10 427	17 118	1.9	60.9	1.1	4.0
Group 9: Single pregnancy in a transverse or oblique lie, including women with previous CS	4622	5607	0.6	82.4	0.5	1.8
Group 10: Single cephalic pregnancy <37 weeks' gestation, including women with previous CS	13 226	46 438	5.0	28.5	1.4	5.1
Unable to classify	25 510	63 550	6.9	40.1	2.8	9.8
Total	259 928	921 023	100.0	28.2	28.2	100.0

*Group size (%): n of women in the group/total number of women delivered in Ontario × 100.
**Group CS rate (%): n of CS in the group/total number of women in the group × 100.
***Absolute contribution (%): n of CS in the group/total number of women delivered in Ontario × 100.
****Relative contribution (%): n of CS in the group/total number of CS in the Ontario × 100.

information on the causes of infertility, including tubal factor, diminished ovarian reserve, unexplained infertility or male factor infertility, as well as the reasons for proceeding with caesarean section was not available.

Interpretation

Infertility, with or without IT, is known to be associated with several adverse pregnancy outcomes that heighten the risk of CS, such as pre-eclampsia, gestational diabetes, small-for-gestational age, and preterm labour.[3–7] Advanced maternal age and obesity are recognised risk factors for infertility,[23,24] and both are associated with a higher risk of CS.[25,26] In a prior Canadian study using BORN data from 2011 to 2012, there was a higher rate of CS among mothers of advanced age, rising from 26.2% in women under age 34 years to 43.1% in those over age 40 years.[27] Therein, women in Robson Groups 2 and 5 were the largest contributors to the overall CS rate among all age groups; prior CS, nulliparity and use of IT were associated with a higher risk of CS.[27] A recent French study reported a higher rate of CS in women with (28.1%) than without (14.2%) obesity, largely explained by those in Robson Group 5.[28] In the current study, we took into account similar factors, suggesting that maternal age, obesity, comorbidities and certain obstetrical complications do not completely explain the higher rate of CS observed in women with infertility.

Herein, multiple pregnancy contributed the most to the observed high rate of CS in women with non-invasive or invasive IT. A study performed in Singapore drew the same conclusion, with multiple pregnancy being the largest Robson group in IVF pregnancies and the largest contributor to overall caesarean section rate.[29] Despite current guidelines that support attempting vaginal delivery in a twin vertex pregnancy,[19] such births are commonly by CS. A recent Canadian population-based study reported a rate of CS of 60% in women with multiple pregnancy, but the relative contribution of Robson Group 8 to the overall CS rate was 3.6%.[30] While in the latter study, mode of conception was not evaluated, we noted large differences in the CS rate in Robson Group 8 by mode of conception: 55.9% with SC, 67.5% in women with subfertility without IT, 65.0% with non-invasive IT, and 69.3% with invasive IT. Although we did not possess direct information about the final decision to proceed to CS, increased access to highly specialised obstetrical care, prenatal surveillance and intrapartum monitoring,[31] along with the emotional and financial investment of an IT pregnancy,[32] might be other influential factors. There may also be provider aspects and bias that contribute to this phenomenon.

In the adjusted model, it appears that the elevated risks of CS mainly came from multiparous women. In Group 3 (spontaneous labour) women with subfertility and non-invasive IT were not at increased risk of CS; however, those with invasive IT had the highest adjusted RR (RR 1.97, 95% CI 1.46–2.65). Specific IT factors, not available in our study, could explain this increased risk. For example, in women returning to IVF/ICSI treatment in the hope of having a second child, over 70% will use a surplus frozen embryo from the cycle that resulted in their first IVF/ICSI-conceived live birth.[33] Frozen embryo transfer has higher odds of CS (OR 1.82, 95% CI 1.65–2.01) than fresh embryo transfer does (OR 1.55, 95% CI 1.41–1.69).[8] In Group 4 (no spontaneous labour), the increased risk of CS in women with subfertility, non-invasive IT and invasive IT is driven by a higher risk of failed induction of labour compared with SC, as well as a higher proportion of prelabour CS in the invasive IT group.

As access to IT intensifies in Canada and elsewhere, there is a pressing need to determine why CS is so common in women with infertility, with or without IT, and how the rate of CS can be safely reduced. The rate of CS is one important quality measure, but maternal satisfaction and choice, and locally available resource, are other considerations in choosing mode of delivery. Further research, both qualitative and qualitative, on both provider and patient beliefs and preferences will provide further insight into the drivers of these findings. The application of the Robson classification, as in the current study, might direct future research in the field.

Conclusion

The rate of CS in Ontario is highest in women who use IT to conceive. Care plans for pregnant women with infertility and IT are limited,[34] and strategies to decrease CS rates in this population are nonexistent. As demand and access to IT continues to increase, efforts are needed that aim to decrease the number of surgical interventions in women with subfertility or IT use. Certainly, one strategy should be a reduction in multiple pregnancy in women receiving IT.[2]

Disclosure of interests

None declared. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship

ER, MPV, JGR, JP: Study concept, analysis and interpretation of the data, drafting of manuscript, manuscript revision, approval of final version. MD: statistical analysis, manuscript revision, approval of final version. LG, MW, GS: Manuscript revision, interpretation and presentation of the data, approval of final version.

Details of ethics approval

This study was reviewed for ethical compliance by the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board and received initial clearance on 29 October 2019 (Reference number is 6028050).

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Data availability statement

The dataset from this study is held securely in coded form at ICES. Although data-sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS. The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programmes may rely upon coding templates or macros that are unique to ICES and therefore either inaccessible or requiring modification.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Annual rates of caesarean section by exposure in Ontario, 2006–2014.

Figure S2. Robson Group 2 and Group 4 stratified by subcategories.

Table S1. Datasets used in current study.

Table S2. Caesarean section rate and contribution to overall rates of each Robson group by exposure for Ontario, 2006–2014 ($n = 1\,031\,536$).

Table S3. Ten group classification system table among women with a spontaneous conceptions ($n = 807\,164$).

Table S4. Ten group classification system table among women with subfertility without IT ($n = 92\,117$).

Table S5. Ten group classification system table among women with non-invasive IT ($n = 10\,632$).

Table S6. Ten group classification system table among women with invasive IT ($n = 11\,110$). ■

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