

ORIGINAL RESEARCH ARTICLE

Maternal age and risk of cesarean section in women with induced labor at term—A Nordic register-based study

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Abstract

Introduction: Over the last decades, induction of labor has increased in many countries along with increasing maternal age. We assessed the effects of maternal age and labor induction on cesarean section at term among nulliparous and multiparous women without previous cesarean section.

Material and methods: We performed a retrospective national registry-based study from Denmark, Finland, Iceland, Norway, and Sweden including 3 398 586 deliveries between 2000 and 2011. We investigated the impact of age on cesarean section among 196 220 nulliparous and 188 158 multiparous women whose labor was induced, had single cephalic presentation at term, and no previous cesarean section. Confounders comprised country, time-period, and gestational age.

Results: In nulliparous women with induced labor the rate of cesarean section increased from 14.0% in women less than 20 years of age to 39.9% in women 40 years and older. Compared with women aged 25-29 years, the corresponding relative risks

were 0.60 (95% confidence interval [95% CI] 0.57 to 0.64) and 1.72 (95% CI 1.66 to 1.79). In multiparous induced women the risk of cesarean section was 3.9% in women less than 20 years rising to 9.1% in women 40 years and older. Compared with women aged 25-29 years, the relative risks were 0.86 (95% CI 0.54 to 1.37) and 1.98 (95% CI 1.84 to 2.12), respectively. There were minimal confounding effects of country, time-period, and gestational age on risk for cesarean section.

Conclusions: Advanced maternal age is associated with increased risk of cesarean section in women undergoing labor induction with a single cephalic presentation at term without a previous cesarean section. The absolute risk of cesarean section is 3-5 times higher across 5-year age groups in nulliparous relative to multiparous women having induced labor.

KEYWORDS

birth register, cesarean section, induction of labor, maternal age

1 | INTRODUCTION

For many decades maternal age at childbirth has increased in Europe¹ and the USA.² Data from Nordic Perinatal Statistics confirms the international trends of increasing maternal age in all the Nordic countries.³ Along with increasing maternal age, the overall rate of labor inductions has doubled from 2000 to 2012 in Denmark⁴ and from 2003 to 2013 in Norway.⁵ In Sweden, induction of post-term pregnancies increased from 28% in 1992 to 46% in 2006.⁴

A systematic review of randomized controlled trials comparing post-term spontaneous onset of labor with induction at or beyond term concluded on a significantly decreased risk of perinatal death as well as a reduction in cesarean section (CS) among women having an induced labor.⁵ Furthermore, randomized controlled trials have found induction of labor associated with improved maternal outcomes for women with mild hypertensive disorders beyond 37 weeks of gestation,⁶ and with reduced risk of shoulder dystocia and related morbidity in large-for-dates fetuses compared with expectant management.⁷

There is a general concern about increasing CS rates worldwide.⁸ Delivery by CS has implications for postoperative maternal morbidity and complications in subsequent pregnancies.^{9,10} The World Health Organization has recently re-evaluated their strategy regarding the optimal CS rate. They state that CS should only be performed in pregnancies that benefit fetal and maternal health, and this may vary around the world according to obstetric competence and organization of labor care.¹¹ Physiological changes in the pregnant population including increasing maternal age^{1,12} and body mass index,^{13,14} combined with an increasing proportion of women with previous CS,¹⁵ and multiple pregnancies,¹⁶ have been associated with increasing risk for CS in subsequent pregnancies. CS rates have been reported from 3.5% in Africa to 29.2% in Latin America and the Caribbean,¹⁷ and 32.0% in the USA.¹⁸ The overall CS rate in the Nordic countries was 17.0% from 2000 to 2011, ranging from 15.7%

Key message

Induction and cesarean section rates increased by age in both nulliparous and multiparous women in all Nordic countries over the years 2001 through 2011.

in Norway to 19.2% in Denmark.¹⁵ National variation in CS rates in the Nordic countries was far less than reported elsewhere.¹⁹

The aims of the present study were to assess the effects of maternal age and labor induction on risk of CS at term among nulliparous and multiparous women without previous CS in the Nordic countries over a 12-year period.

2 | MATERIAL AND METHODS

The study was initiated by the Nordic Robson Research collaboration^{15,20} based on national medical register data from the 5 Nordic countries, merged and processed in Statistics Denmark, Copenhagen. Selected variables were harmonized across birth register in the merged database. Maternal age was defined as the difference in completed years between date of delivery and maternal date of birth, and categorized into 6 groups (<20, 20-24, 25-29, 30-34, 35-39, ≥40 years). Parity and previous CS were defined as the highest number based on information in the register or maternal information provided at first delivery. Gestational age was with few exceptions estimated from ultrasound screening of biparietal diameter in second trimester and categorized into 3 categories (37-38, 39-41, ≥42 weeks). Included in the original database were women who delivered after the 22nd gestational week, or, if gestational age was missing, women who gave birth to infants with a birthweight of ≥500 g. Start of delivery was defined

as spontaneous onset of birth, induction, or CS. Emergency CS encompassed all CS not reported as elective. Mode of delivery comprised spontaneous vaginal delivery, instrumental vaginal delivery (vacuum extraction or forceps), or CS. Data on presenting part of the baby at delivery was categorized into cephalic, breech presentation, or transverse lie. We categorized 3-year periods as 2000-02, 2003-05, 2006-08 and 2009-11.

We have used the Robson classification system, a method of stratifying delivering women into 10 clinically relevant groups, making comparison of interventions and outcomes within groups more clinically relevant. In the Robson system, groups are mutually exclusive.²¹ In this study, we have included Robson groups 1-4. Groups 1 and 2 comprise nulliparous women with a baby in single cephalic presentation after 36 weeks of gestation. Group 1 includes women in spontaneous labor (R1) and group 2 comprises women having labor induced (R2a) or pre-labor CS (R2b). Groups 3 and 4 comprise multiparous women with a baby in single cephalic presentation after 36 weeks of gestation and no history of CS. Group 3 includes multiparous women in spontaneous labor (R3) and group 4 includes multiparous women having labor induced (R4a) or pre-labor CS (R4b).

2.1 | Statistical analyses

We estimated proportions of nulliparous women having pre-labor CS ($R2b/[R1+R2]$), proportion of women having induction of labor ($R2a/[R1+R2]$), and overall CS rate in nulliparous women (CS in $[R1+R2a]/[R1+R2]$). Similarly, proportions of multiparous women having pre-labor CS ($R4b/[R3+R4]$), induction of labor ($R4a/[R3+R4]$), and overall CS rate in multiparous women with no history of CS (CS in $[R3+R4a]/[R3+R4]$) were calculated.

We performed multiple unconditioned logistics regressions models to estimate odds ratio of CS in induced nulliparous (R2a) and multiparous (R4a) women, and in nulliparous (R1) and multiparous (R3) women having spontaneous onset of labor. Maternal age was the main exposure, while country, time-period, and gestational age were considered confounding factors. Results are presented as proportions (rates) in percentages and in relative risks (RRs) with 95% confidence intervals (95% CI). IBM SPSS Statistics Version 24 (IBM Corp., Armonk, NY, USA) was used for the statistical analyses.

2.2 | Ethical approval

The Danish Data protection Agency administered the Danish participation in the study (reference NOH-2016-006), and the Regional Committee for Medical and Health Research Ethics South-East C (REK Sør-Øst 2010/3256) assessed the Norwegian participation. The Directorate of Health in Iceland, THL Finnish Institute of Health and Welfare in Finland, and the Swedish National Board of Health and Welfare gave their authorizations for using anonymized data.

3 | RESULTS

From January 2000 to December 2011 there were in total 3 398 586 deliveries in the 5 Nordic countries. Nulliparous women with a single baby in cephalic presentation at term included 1 294 452 mothers (R1+R2). Of these, 40 572 (3.1%) women had pre-labor CS (R2b), 196 220 (15.2%) had labor induced (R2a), and 1 057 660 (81.7%) had spontaneous onset of labor (R1). Multiparous women with a single baby in cephalic presentation at term, with no previous CS, included 1 471 057 mothers (R3+R4). Of these, 40 885 (2.8%) women had pre-labor CS (R4b), 188 158 (12.8%) had labor induced (R4a), and 1 242 014 (84.4%) had spontaneous onset of labor (R3).

Over the 12-year study period the proportion of women having labor induction increased from 11.8% to 20.1% in nulliparous women and from 9.9% to 16.8% in multiparous women. The increases among nulliparous as well as multiparous women were consistent across countries and age groups.

In the multivariate unconditional logistic regression analysis, country, time-period, and gestational age had no confounding effect on the age-specific or overall estimates of CS in nulliparous and multiparous women having labor induced (data not presented). Consequently, we only presented crude estimates and RR in Table 3. The age-specific estimates of induction on CS were consistent and relatively robust in almost all analyses of time-period and country (no interactions).

The temporal relations between proportions of women having pre-labor CS, induction of labor, and overall CS rates by parity are displayed in Figure 1. The proportions of nulliparous as well as multiparous women having pre-labor CS were relatively low and stable over time with estimates varying from 2.0% to 3.4%. The overall CS rate in nulliparous women (CS/R1+R2) increased from 12.4% in 2000 to 14.9% in 2006 and remained stable thereafter. In the multiparous women (CS/R3+R4) the CS rate varied from 4.2% in 2000, with a peak of 5.6% in 2007, to 5.1% in 2011.

Crude rates of CS in induced nulliparous women at term (R2a) by age and overall (R2a) are displayed in Table 1. The overall CS rate was 25.0%, increasing consistently from 14% in the youngest to 40% in the oldest age group. There were small variations in the crude CS rates by age and in total between nulliparous women in R2a in the 5 Nordic countries. Age-stratified analysis by time-period and gestational age found consistently increasing CS rates from the youngest to the oldest age group across all subsets of analyses.

In the same manner, the number of women under risk and the crude rates of CS in induced multiparous women with no previous CS (Robson 4a) are shown in Table 2. The overall CS rate in the Robson 4a group was 5.5%. The risk of CS increased with age in all countries. Finland had lower age-specific CS rates and a lower overall crude CS compared with the other Nordic countries. Moreover, the crude CS rates ranged from 2.4% (Finland) to 4.7% (Iceland) in women 20-24 years of age, and from 5.2% (Finland) and 10.9% (Sweden) in women 40 years or older.

Across age groups, the RR of CS in nulliparous women with induced labor (R2a) increased significantly by 5-fold from 0.60 (95% CI

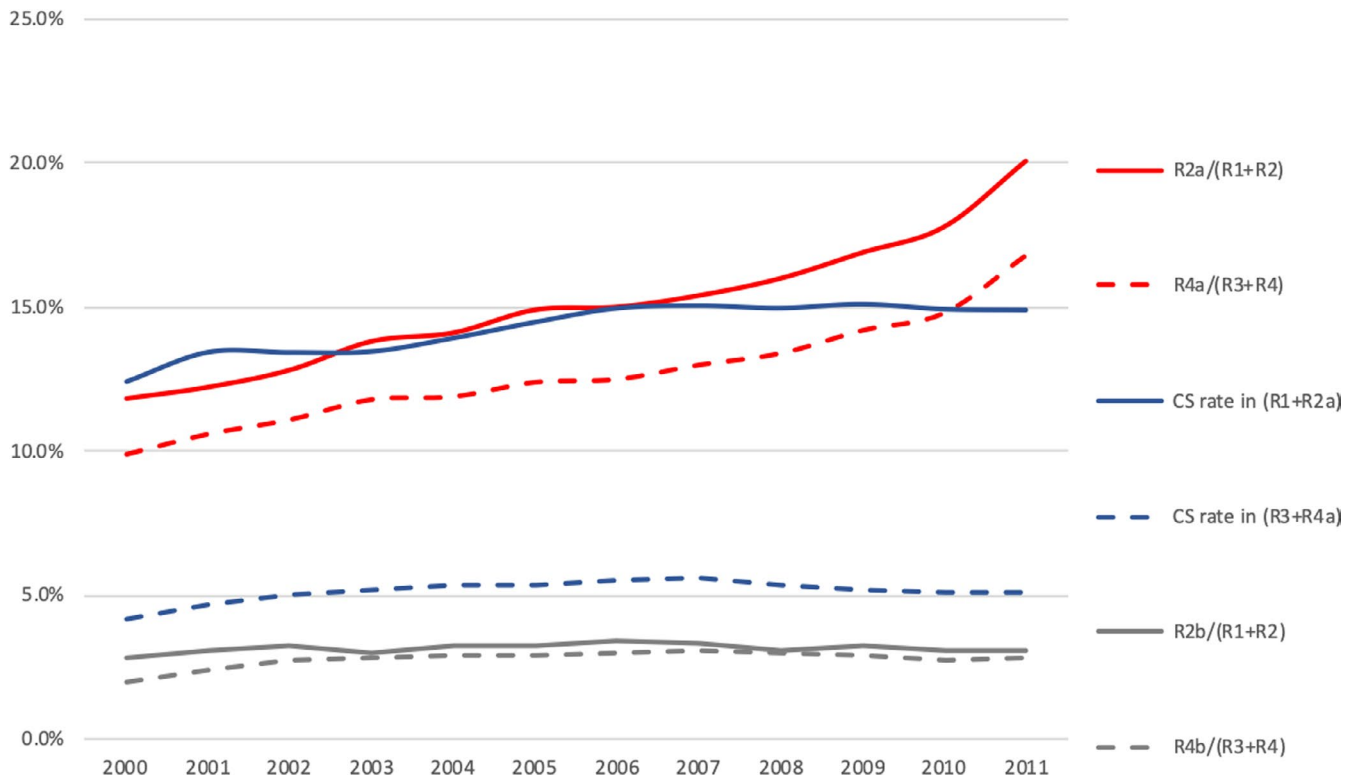


FIGURE 1 The proportion of women having cesarean section (CS) before onset of labor R2b/(R1+R2) and R4b/(R3+R4), having labor induced R2a/(R1+R2) and R4a/(R3+R4), and CS rates in women with spontaneous and induced labor CS/(R1+R2a) and CS/(R3+R4a) by parity. Nordic countries, 2000-2011 [Colour figure can be viewed at wileyonlinelibrary.com]

0.57 to 0.64) in women below 20 years of age to 1.72 (95% CI 1.66 to 1.79) in women 40 years or above (Table 3). The same pattern was observed in nulliparous women with spontaneous onset of labor (R1) with RRs increasing from 0.57 (95% CI 0.55 to 0.60) in the youngest group to 2.50 (95% CI 2.37 to 2.64) in women 40 years or older.

In the 432 multiparous women, younger than 20 years, with induced labor (R4a) the crude CS rate was 3.9%. The CS rate increased from 3.2% in women aged 20-24 years to 9.1% in women 40 years or above. The RR increased from 0.70 (95% CI 0.63 to 0.77) in women 20-24 years to 1.98 (95% CI 1.84 to 2.12) in women 40 years or above.

The absolute risk of CS in both nulliparous and multiparous women with induced labor (R2a/R4a) compared with the respective women with spontaneous onset of labor (R1/R3) was 1.90-2.98 times higher among nulliparous and 2.28-2.80 higher among multiparous women (Table 3).

4 | DISCUSSION

The main findings from this study were an increasing incidence of induction of labor and stable rates of CS before onset of labor in the Nordic countries, from 2000 to 2011 in both nulliparous and multiparous women, with a single baby in single cephalic presentation at term, and no previous CS. In addition, we found that increasing maternal age was associated with increasing RR of CS in both nulliparous and multiparous women. The RR of CS was 2-3 times higher

in each age group among women having induced relative spontaneous onset of labor. These estimates enable Nordic obstetricians and midwives to inform pregnant women at term, with a single baby in cephalic presentation and no previous CS, about their average risk of CS if they are having labor induced.

Furthermore, we found an association between rising induction rates to 15% in nulliparous women (R1+R2) and 13% in multiparous women (R3+R4) from 2000 to 2007, and an increasing risk of overall CS to 15.0% and 5.1%, respectively, during the same period. When the induction rates increased further to 20.1% and 16.8% in 2011, the respective overall CS rates remained stable at 14.9% and 5.1%. These findings indicate that the risk of CS might be unaffected above a certain proportion of women having labor induced among nulliparous as well as multiparous women without a previous CS. Our findings among nulliparous women are supported by the findings of a large randomized controlled trial of induction of labor in 6104 American low-risk women between 39⁺⁰ and 39⁺⁴ weeks of gestation, the ARRIVE study.²² The authors found a decreased RR of CS (RR 0.84; 95% CI 0.76 to 0.93) in women randomized to labor induction compared with women awaiting spontaneous onset of labor. Low-risk nulliparous women are currently not having labor induced before term in the Nordic countries, but if they are going to be in the future, the results from the ARRIVE suggests that there may be an associated reduced overall CS rate.

A major strength of the study is the large sample size with national data from the 5 Nordic countries. Limitations of the study

TABLE 1 Total number of nulliparous women with a singleton infant in cephalic presentation at term and with induced labor (Robson group 2a), displayed with the cesarean section (CS) rate (%), by maternal age, country, time-period, and gestational age. Nordic countries, 2000-2011

Maternal age	<20		20-24		25-29		30-34		35-39		>40		Total	
	n	CS %	n	CS %	n	CS %	n	CS %	n	CS %	n	CS %	n	CS %
Total	7285	14.0	38 932	18.7	68 987	23.2	54 752	28.2	21 484	34.3	4780	39.9	196 220	25.0
Country														
Denmark	1222	13.5	7478	17.9	16 530	23.3	12 023	27.4	4298	32.9	873	38.3	42 424	24.5
Finland	2418	12.4	10 593	17.0	15 460	20.4	11 097	25.5	4446	31.4	1034	38.8	45 048	21.9
Iceland	280	14.6	1092	23.9	1277	25.7	576	32.3	248	35.1	70	35.7	3543	26.2
Norway	1668	14.6	8683	18.6	14 532	22.4	10 707	25.7	3935	32.2	809	37.2	40 334	23.4
Sweden	1697	15.9	11 086	20.4	21 188	25.5	20 349	31.3	8557	37.5	1994	42.4	64 871	28.3
Time-period														
2000-2002	1654	12.9	8052	16.8	13 986	22.6	9577	26.7	3317	33.3	574	36.6	37 160	23.2
2003-2005	1669	12.4	8753	18.8	16 310	23.0	12 889	28.3	4768	33.7	883	40.7	45 272	24.8
2006-2008	1863	15.2	9834	19.6	17 603	24.3	15 019	29.8	6003	35.5	1399	40.2	51 721	26.4
2009-2011	2099	14.9	12 293	19.2	21 088	22.7	17 267	27.4	7396	34.3	1924	40.3	62 067	25.0
Gestational age														
37 ⁺⁰ to 38 ⁺⁶	1477	13.4	7575	15.6	12 492	19.4	8987	22.6	3312	27.2	665	37.0	34 508	20.2
39 ⁺⁰ to 41 ⁺⁶	4016	12.8	21 300	17.8	36 604	21.8	28 584	26.5	11 756	33.2	3132	38.5	105 392	23.7
>41 ⁺⁶	1792	17.0	10 057	22.9	19 891	28.2	17 181	33.9	6416	40.2	983	46.4	56 320	30.3

are the observational design combined with lack of data for body mass index, more detailed information of indications for induction, and the Bishop score at time for induction. However, a systematic review from 2013 concluded that Bishop score is a poor predictor of outcome of induced labor, including risk of CS, and the authors

advocated not to use the Bishop score to decide whether to induce labor or not.²³

Cheng and colleagues published an observational study of 442 003 low-risk nulliparous women with a baby in single cephalic presentation delivering between 39 and 42 weeks of gestation

TABLE 2 Total number of multiparous women without previous cesarean section (CS), with a singleton infant in cephalic presentation at term and with induced labor (Robson group 4a), displayed with the CS rate (%), by maternal age, country, time-period, and gestational age. Nordic countries, 2000-2011

Maternal age	<20		20-24		25-29		30-34		35-39		>40		Total	
	n	CS %	n	CS %	n	CS %	n	CS %	n	CS %	n	CS %	n	CS %
Total	432	3.9	13 329	3.2	47 629	4.6	71 500	5.2	43 931	6.9	11 337	9.1	188 158	5.5
Country														
Denmark	78	5.1	2326	3.9	10 267	5.5	16 772	5.6	9495	7.3	2116	10.1	41 054	6.1
Finland	165	1.2	4928	2.2	13 802	2.9	17 773	3.3	10 783	4.6	3084	5.2	50 535	3.4
Iceland	9	11.1	256	4.7	1049	3.2	1392	5.6	827	7.0	236	8.5	3769	5.4
Norway	83	2.4	2555	4.3	9915	5.4	15 179	5.8	9004	7.9	2080	10.6	38 816	6.3
Sweden	97	8.2	3264	3.5	12 596	5.1	20 384	6.1	13 822	7.8	3821	10.9	53 984	6.5
Time-period														
2000-2002	75	4.0	2856	3.2	10 389	5.1	14 562	5.2	8214	6.5	1901	9.0	37 997	5.5
2003-2005	112	4.5	3089	3.0	11 399	4.7	16 753	5.5	10 098	7.5	2454	8.9	43 905	5.8
2006-2008	119	4.2	3356	3.6	11 605	4.6	18 591	5.4	11 522	7.1	3151	10.0	48 344	5.8
2009-2011	126	3.2	4028	3.2	14 236	4.1	21 594	4.8	14 097	6.6	3831	8.6	57 912	5.2
Gestational age														
37 ⁺⁰ to 38 ⁺⁶	117	4.3	3630	3.0	11 779	4.5	16 798	5.2	10 278	7.1	2654	9.0	45 256	5.5
39 ⁺⁰ to 41 ⁺⁶	252	4.4	7436	3.0	26 706	4.2	39 959	4.9	25 010	6.3	6899	8.5	106 262	5.2
>41 ⁺⁶	63	1.6	2263	4.6	9144	5.7	14 743	6.0	8643	8.4	1784	11.7	36 640	6.7

TABLE 3 Total number of women with a singleton infant in cephalic presentation at term, no previous cesarean section (CS) and with induced or spontaneous onset of labor (Robson group 1 + 2a and Robson group 3 + 4a), displayed with number (N), CS rate (%) and relative risk (RR) with 95% confidence intervals (95% CI), by maternal age and parity. In addition, RR with 95% CI of CS in women having induced labor compared with women with spontaneous onset of labor is presented. Nordic countries, 2000-2011

Maternal age (y)	Induced labor (R2a)					Spontaneous labor (R1)					Induced/spontaneous	
	Total	N	CS rate %	RR	95% CI	Total	N	CS rate %	RR	95% CI	RR	95% CI
Nulliparous women												
<20	7285	1020	14.0	0.60	(0.57 to 0.64)	48 463	2278	4.7	0.57	(0.55 to 0.60)	2.98	(2.78 to 3.19)
20-24	38 932	7280	18.7	0.81	(0.79 to 0.83)	239 336	15 317	6.4	0.78	(0.77 to 0.80)	2.92	(2.85 to 3.00)
25-29	68 987	16 005	23.2	1.00		409 618	33 591	8.2	1.00		2.83	(2.78 to 2.88)
30-34	54 752	15 440	28.2	1.22	(1.19 to 1.24)	271 596	29 877	11.0	1.34	(1.32 to 1.36)	2.56	(2.52 to 2.61)
35-39	21 484	7369	34.3	1.48	(1.44 to 1.51)	77 338	11 678	15.1	1.84	(1.81 to 1.88)	2.27	(2.21 to 2.32)
>40	4780	1907	39.9	1.72	(1.66 to 1.79)	11 309	2375	21.0	2.50	(2.37 to 2.64)	1.90	(1.81 to 2.00)
Multiparous women												
<20	432	17	3.9	0.86	(0.54 to 1.37)	3701	52	1.4	0.88	(0.67 to 1.15)	2.80	(1.63 to 4.80)
20-24	13 329	432	3.2	0.70	(0.63 to 0.77)	104 917	1364	1.3	0.81	(0.77 to 0.86)	2.49	(2.24 to 2.77)
25-29	47 569	2174	4.6	1.00		357 208	5716	1.6	1.00		2.86	(2.72 to 3.00)
30-34	71 500	3721	5.2	1.13	(1.07 to 1.19)	494 883	9403	1.9	1.19	(1.15 to 1.23)	2.74	(2.64 to 2.84)
35-39	43 931	3040	6.9	1.50	(1.42 to 1.58)	245 197	6375	2.6	1.63	(1.57 to 1.68)	2.66	(2.55 to 2.78)
>40	11 337	1032	9.1	1.98	(1.84 to 2.12)	43 575	1743	4.0	2.50	(2.37 to 2.64)	2.28	(2.11 to 2.45)

comparing induction of labor with expectant management. They found a lower risk of CS (odds ratio 0.90; 95% CI 0.88 to 0.91) if induced at 39 weeks of gestation compared with expectant management.²⁴ In their low-risk nulliparous population the proportion aged 35 years or more, was 7.3% compared with 13.4% in our population. As high maternal age is associated with CS and assisted vaginal delivery,^{25,26} these findings underline the importance of maternal age differences in study populations when comparing the results of obstetric operative intervention in obstetrics across studies. In a randomized controlled trial of induction of labor relative expectant management in nulliparous women 35 years or older, no significant differences in CS rates were found (32.2% relative to 32.8%).²⁷ Their CS rate in the induction group was similar to the CS rate of 34.3% in nulliparous women 35-39 years of age in the present study. In a meta-analysis of randomized controlled trials of induction of labor at full term in uncomplicated singleton gestations, Saccone and Berghella reported a CS rate of 25.5% among nulliparous women with labor induced,²⁸ which was similar to our findings (25.0%).

Beside the increased use of induction of labor in post-term and hypertensive pregnancies, other factors, such as institutional culture in obstetric practice and growing patient involvement in the decision-making process, can influence the use of induction of labor. In a qualitative study, midwives and doctors from 10 Australian hospitals expressed a large variation in clinical decision-making

for induction of labor.²⁹ In addition, the authors found that hospitals having senior midwives or midwife managers, serving as gatekeepers with the authority to question the indication for induction, had lower rates of induction of labor. A Dutch interview study of doctors and midwives found that medical indications, such as preeclampsia and post-term pregnancy, were the most important factors in the decision for induction of labor.³⁰ Together, these findings indicate the need for continuous audit of the rates and indications for induction of labor and CS at each delivery unit. This is important for surveillance of institutional standards regarding induction of labor and to provide institutional data for information to the pregnant women.

5 | CONCLUSION

The risk of CS increases with increasing maternal age after both induced and spontaneous onset of labor in nulliparous and multiparous women without previous CS. In all age groups, the risk of CS is considerably higher following induced labor. The findings provide a knowledge basis that can help to inform women at term about their average risk of CS associated with induction of labor and help these women in the decision-making process. Women are entitled to be informed of benefits and risks related to the procedure, including risk of CS, when induction of labor is considered.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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