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MATERNAL-FETAL MEDICINE

Contemporary epidemiology and novel predictors of uterine rupture: a nationwide population-based study

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Abstract
Purpose In spite of several policies aiming to decrease cesarean rates and related complications such as uterine rupture, data show that uterine rupture and associated morbidity are increasing along the years. Whether previously unidentified risk factors are currently playing an important role on these trends is unknown. We analyze current risks of uterine rupture and main preceding factors from more recent years compared to former data.
Methods All uterine rupture cases in the US from 2011–2012 were selected, with matched non-uterine rupture cases selected as controls. Variables considered for analysis included demographics, maternal morbidity, and obstetric complications. Likelihood forward selection was used to identify main risk factors of uterine rupture. Medians of main factors identified were used to simulate groups at risk and calculate odds ratios of uterine rupture.
Results From ~8 million births, 1925 presented uterine rupture. In patients with no prior cesarean delivery, multiple gestation, chronic hypertension and chorioamnionitis presented the highest odds of uterine rupture, with the combination of these factors increasing the odds of rupture 59 times (~1%). In women with prior cesarean delivery, induction/augmentation and chorioamnionitis were the most significant predictors, with the combination increasing the odds 33 times (~3%).
Conclusions Despite policies implemented and changes in clinical practice, uterine rupture remains an important issue. Previously unidentified risk factors are playing now an important role, information that should be considered during patient counseling and clinical practice. Combinations of some of these factors may increase the risk of uterine rupture significantly enough to modify clinical care.

Keywords Uterine rupture · Cesarean section · Pregnancy-induced hypertension · Chorioamnionitis · Induced labor · Pregnancy complications

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Introduction

Uterine rupture is one of the most serious obstetric emergencies and a life-threatening event. It is an important cause of morbidity and mortality for mothers and their newborns [1–3]. Based on reported risk factors from older studies, researchers have attempted to create predictive tools to avert this serious complication. Unfortunately, to date there is still no useful clinical tool for predicting this fearful complication [4–6]. Many institutions have created policies to decrease cesarean rates and consequently uterine rupture risk in future

pregnancies [7, 8]. However, despite all this research, economic investment and effort in creating policies, data suggests that uterine rupture rates have actually increased over the years [9]. It is unknown whether the increase in uterine rupture rates is due to effects of recent changes in obstetric practice or other preceding factors not previously identified in former studies.

Since uterine rupture is a rare event, analysis of national data from recent years may aid in the identification of new risk factors related to the increasing rates of this fearful complication. In this study, we analyze main risk factors for uterine rupture from more recent years after significant changes in policies and clinical practice have been implemented.

Methods

The study was approved by the Institutional Review Board of Wayne State University in Detroit, Michigan, USA. All reported obstetric deliveries in the United States from 2011 to 2012 complicated by uterine rupture were selected from the birth data files containing vital statistics data provided by The National Center for Health Statistics—Centers for Disease Control and Prevention. For each uterine rupture case identified, two non-uterine rupture cases matched by delivery in temporal and geographic proximity were selected as controls, using a methodology that has been previously described [10].

Variables selected for analysis included demographics (maternal age, maternal race, ethnicity, body mass index, socio-economic status, tobacco use), obstetric history (plurality, parity, interval since last birth, number of prior cesarean births), maternal morbidity (pregestational diabetes, gestational diabetes, chronic hypertension, gestational hypertension, eclampsia), and labor complications (induction/augmentation of labor, precipitous labor, prolonged labor, chorioamnionitis, fetal intolerance). Cases were categorized according to uterine rupture status and history of prior cesarean delivery. Rates were represented as number of cases per 10,000 deliveries. Categorical variables were represented as the number of cases with percentages, and compared with Pearson's Chi square test. Numerical variables were represented as means with standard deviation and compared with independent *t* test.

To isolate the main predictors of uterine rupture from variables containing information prior to delivery (preceding factors), likelihood ratio forward selection was used to regress specific variables against uterine rupture using multivariable logistic regression models. Using the medians of the variables that most significantly predict uterine rupture, the final logistic regression model was used to create simulated groups with an average- and high-risk of uterine rupture; and combined odds ratios of uterine rupture according to history of prior cesarean were calculated. A p value < 0.05 with confidence intervals not crossing one was used to indicate statistical significance.

Results

During 2011–2012, there were 7,922,016 births in the US Among these, 1925 were complicated by uterine rupture (baseline frequency of 2.4 × 10,000 births). Using these cases, the algorithm identified 3765 non-rupture cases (final case–control ratio 1:1–2). Cases according to history of previous cesarean delivery are shown in Fig. 1. The frequency of uterine rupture in cases without and with history of previous cesarean delivery was 1.8 and 8.9 per 10,000 births, respectively. For all cases, demographic information is shown in Table 1. Cases complicated by uterine rupture were predominantly older, African–American, had a lower socio-economic status, and had higher-order gestation, less interval since last birth, higher BMI and higher number of prior cesarean deliveries. There were no other demographic differences between groups.

For all cases, from all preceding risk factors analyzed, the model retained ten predictors, with chorioamnionitis, history of previous cesarean and pregestational diabetes as the most significant predictors of uterine rupture (Table 2). Using the medians of the most significant demographic

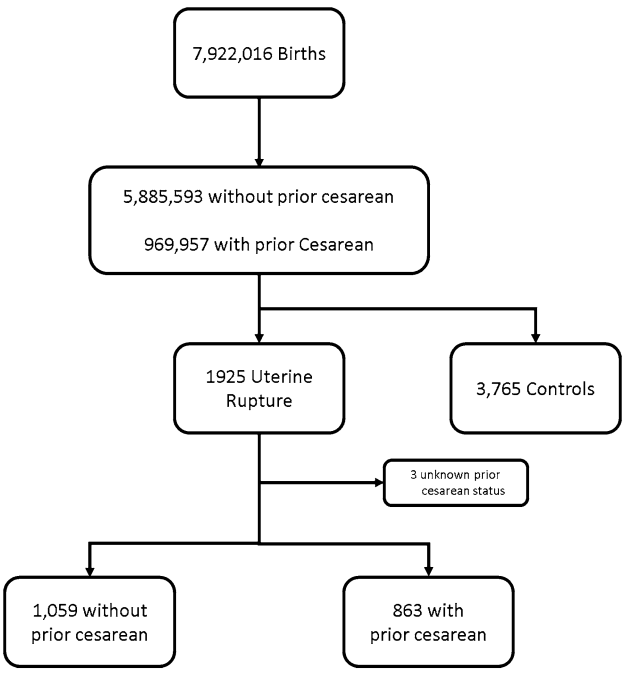

Fig. 1 Flowchart of cases complicated by uterine rupture and controls ($N = 7{,}925{,}781$). Flowchart of cases complicated by uterine rupture in the United States in the period from 2011 to 2012, with the number of control cases obtained

Table 1 Demographics of cases complicated by uterine rupture vs. controls ($N = 5690$)

Demographics	Mean (standard deviation)		
	Uterine rupture ($N = 1925$)	Non-uterine rupture ($N = 3765$)	p value[a]
Maternal age	29.72 (6.02)	28.09 (5.99)	<0.001
Plurality	1.06 (0.28)	1.02 (0.16)	<0.001
Body mass index	30.4 (17.51)	29.33 (15.47)	0.023
Parity	2.73 (1.64)	2.11 (1.33)	<0.001
Interval since last birth	299.07 (398.52)	432.6 (425.54)	<0.001
Number of previous cesarean	1.2 (7.14)	0.44 (4.86)	<0.001
	Number of cases (%)		p value[b]
Maternal race			<0.001
Caucasian	1344 (69.82)	2849 (75.67)	
African–American	428 (22.23)	639 (16.97)	
American–Indian	19 (0.99)	43 (1.14)	
Asian	134 (6.96)	234 (6.22)	
Ethnicity			
Hispanic	336 (17.66)	728 (19.45)	0.102
Smoking	193 (11.09)	337 (9.85)	0.167
Insurance			0.014
Medicaid	820 (43.52)	1519 (41.14)	
Private	865 (45.91)	1841 (49.86)	
Self-paid	68 (3.61)	132 (3.58)	
Other	131 (6.95)	200 (5.42)	

[a] Chi square test

[b] Student's t test

Table 2 Adjusted odds ratios for main preceding risk factors for uterine rupture ($N = 1925$)

Preceding risk factor[b]	Odds ratios[a] (95% CI)
Chorioamnionitis	6.60 (2.89–15.06)
Prior cesarean	5.27 (4.42–6.28)
Multiple pregnancy	2.49 (1.66–3.75)
Pregestational diabetes	2.29 (1.16–4.52)
African–American race	1.45 (1.17–1.79)
Induction/augmentation	1.44 (1.20–1.74)
Parity	1.26 (1.18–1.34)
Maternal age	1.03 (1.01–1.05)
Body mass index	0.98 (0.97–0.99)
Eclampsia	0.08 (0.01–0.71)

CI confidence interval

[a] Likelihood ratio forward selection

[c] Preceding factors included in the model included: demographics, obstetric history, maternal morbidity, labor outcomes

factors, an average-risk group for uterine rupture was defined as age = 25, BMI = 24, parity = 1; and a high-risk group as age = 25, BMI = 24, plurality >1, parity = 6, number of previous cesarean deliveries ≥1. The odds of uterine rupture in the high-risk group was 78.5 fold higher compared to an average-risk group, increasing the uterine rupture absolute risk from 2.4 to 189.2 per 10,000 births (Fig. 2).

In cases without a history of previous cesarean delivery, from all possible preceding risk factors analyzed, the model retained only seven factors, with multiple gestation, chronic hypertension and chorioamnionitis being the most significant predictors (Table 3). Compared to an average-risk patient (defined as cases of age = 27, parity = 2 without other risk factors), the combination of multiple gestation, chronic hypertension and chorioamnionitis increased the odds of uterine rupture in a high-risk group 59 fold, increasing the uterine rupture absolute risk from 1.8 to 107.0 per 10,000 births (Fig. 2).

In cases with history of previous cesarean delivery, from all possible preceding risk factors analyzed, the model retained only six factors, with induction and/or augmentation of labor and chorioamnionitis being the most significant predictors (Table 4). Compared to an average-risk patient (defined as cases of parity = 2, BMI = 26, interval since last birth 37 months), the combination of oxytocin use and chorioamnionitis increased the odds of uterine rupture in the high-risk group 33 fold (almost 3% of cases), increasing

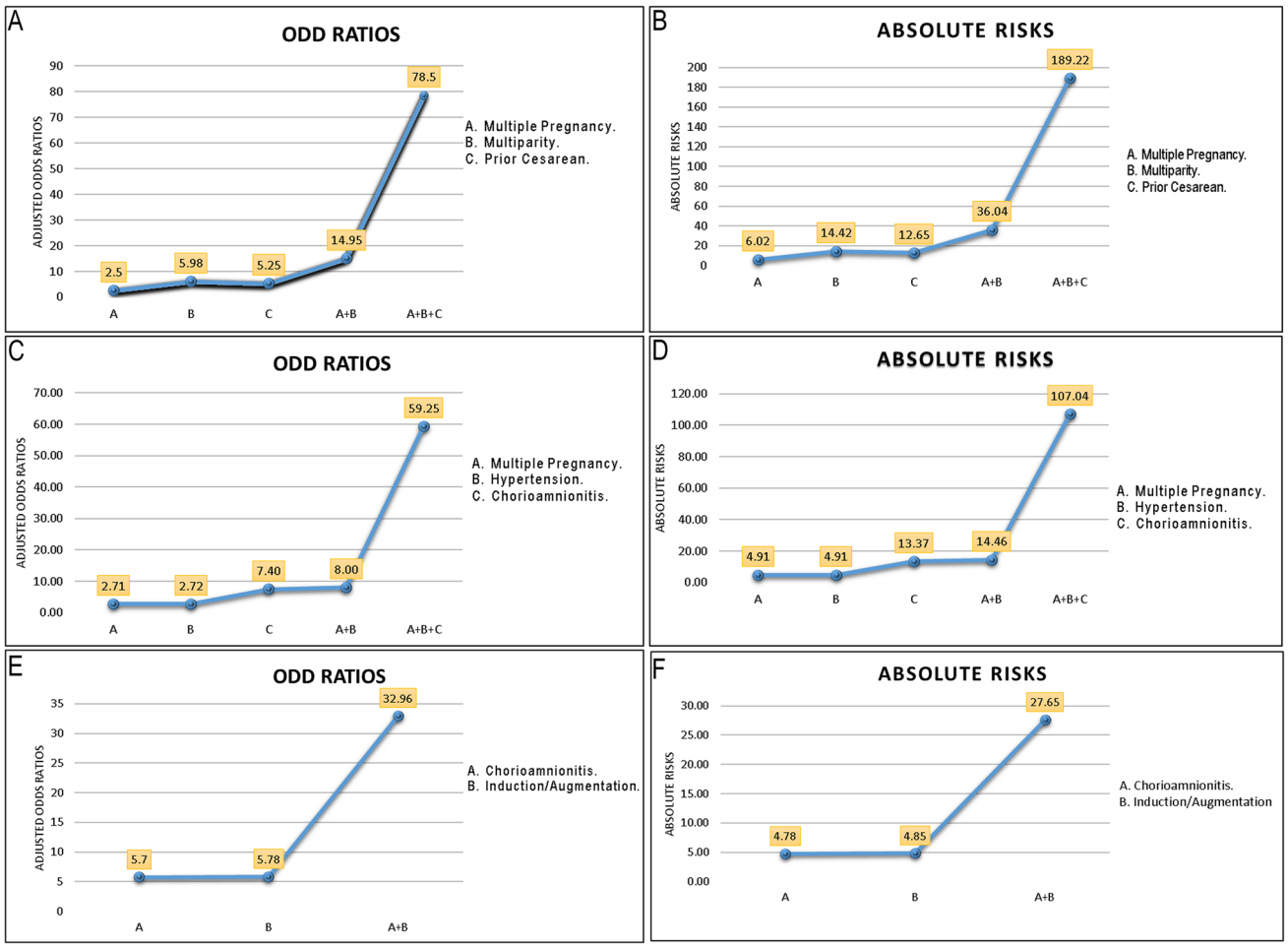

Fig. 2 Odds ratios and absolute risks of uterine rupture according to preceding risk factors ($N = 1925$). Combined odds ratios and absolute risks of uterine rupture according to the most significant preceding risk factors for all cases (**a** and **b**), in cases with no prior cesarean delivery (**c** and **d**), and in cases with prior cesarean delivery (**e** and **f**). The *letters* indicate the preceding factor. The *numbers* inside the *squares* indicate the odds ratios and absolute risks. The *lines* indicate the trend

Table 3 Adjusted odds ratios for main preceding risk factors for uterine rupture in cases with no prior cesarean delivery ($N = 1059$)

Preceding risk factor[b]	Odds ratios[a] (95% CI)
Chorioamnionitis	8.01 (3.00–21.35)
Multiple pregnancy	2.72 (1.72–4.30)
Chronic hypertension	2.72 (1.30–5.70)
African–American race	1.68 (1.27–2.22)
Parity	1.16 (1.07–1.26)
Maternal age	1.06 (1.04–1.08)
Eclampsia	0.11 (0.01–1.11)

CI confidence interval

[a] Likelihood ratio forward selection

[c] Preceding factors included in the model included: demographics, obstetric history, maternal morbidity, labor outcomes

Table 4 Adjusted odds ratios for main preceding risk factors for uterine rupture in cases with prior cesarean delivery ($N = 1925$)

Preceding risk factor[b]	Odds ratios[a] (95% CI)
Induction/augmentation	5.78 (3.71–9.01)
Chorioamnionitis	5.70 (1.28–25.47)
Multiparous	1.39 (1.24–1.57)
Private insurance	1.31 (1.01–1.71)
Interval since last birth	1.00 (0.99–1.00)
Body mass index	0.97 (0.95–0.99)

CI confidence interval

[a] Likelihood ratio forward selection

[c] Preceding factors included in the model included demographics, obstetric history, maternal morbidity, labor outcomes

the uterine rupture absolute risk from 0.8 to 27.6 per 10,000 births (Fig. 2).

Discussion

This study reveals that, although uterine rupture is a rare event, and in spite of numerous guidelines aiming to decrease cesarean rates, it is still a significant issue in obstetric practice. New risks factors, previously unrelated to uterine rupture, are now playing an important role in its occurrence. If some of these occur in combination, they may increase the risk of rupture significantly, and may be considered in the clinical evaluation of labor management and delivery route.

The frequency of uterine rupture depends on several factors such as gestational age, socio-economic status, geographic location, history of prior cesarean, type of prior incision, number of previous deliveries, and type of labor [11]. Former nationwide population-based studies reported an overall incidence of uterine rupture of 2.5 per 10,000 births [9]. In women without previous cesarean, a study reported an incidence of 0.7 per 10,000 births [12]. In patients with prior cesarean, another study reported an incidence of 37.1 per 10,000 births [9]. A study performed in Massachusetts reported incidences of 5.1 and 0.8 per 10,000 women with and without uterine scar, respectively [13]. Over the years, the rates have not decreased [9] and our results support those findings. In fact, a recent study reported an incidence of uterine rupture of 5.6/10,000 deliveries. [14] Thus, current guidelines on uterine rupture occurrence and its implications on maternal and neonatal morbidity–mortality may be revisited.

Changes in obstetric practice and rise in cesarean and induction of labor rates [15] suggest that analysis of previously unidentified risk factors [9] should be considered. In contrast to previous studies showing lower rates of uterine rupture in African–Americans [16], or no increased risk in higher-order gestations [17], we observed that these factors are now strongly associated with uterine rupture. The effect of race/ethnicity in perinatal outcomes after repeat cesarean or induction of labor has been previously demonstrated [18–20]. Further, we found that lower socio-economic status presents increased uterine rupture rates, similar to former studies [21]. Also, we found that short interpregnancy interval is still a significant risk factor as described before [22].

Although pregnancy complications such as diabetes and obesity are strongly related to adverse outcomes [10, 23] [24], their effect in the risk of uterine rupture has not been fully studied. Similarly, chorioamnionitis has not been previously associated uterine rupture. We found that these factors are significantly associated with uterine rupture, probably due to the association with protracted labor.

Uterine rupture in the unscarred uterus is rare [25]; therefore, it has been difficult to find significant risk factors [26]. We found that multiparity was significantly associated with uterine rupture, which conflicts with current evidence [27]. We also found chronic hypertension to be strongly associated with uterine rupture. Although former studies have showed increased risk of failed trial of labor in cases with chronic hypertension [28], research focusing on its effects in uterine rupture is limited. The relation of hypertension with protracted labor [29] might be a possible explanation.

Most of our findings agree with previous studies showing increased risk of uterine rupture in laboring women with prior cesarean having received oxytocin for either induction or augmentation of labor. The question is, therefore, whether to induce these patients at term or await for spontaneous labor. This issue was assessed in a study that showed increased risks of uterine rupture but higher chances of successful vaginal delivery [30].

The strengths of this study are rooted in its population-based methodology, being one of the largest series of uterine rupture in the literature. In addition, we were able to provide evidence of the strong association of formerly unrelated factors with uterine rupture. However, this study is not without limitations. Its retrospective nature, based on birth registry records, carries risks of potential coding errors.

In conclusion, based on national data, uterine rupture is still a major issue to be considered in pre-labor counseling and labor management. Due to changes in obstetric practice, previously unidentified risk factors may now be playing an important role. The combination of some of these risks factors may increase the risk enough to influence clinical practice and prevent potentially devastating complications, resulting in improved health of mothers and babies.

Author contribution GV: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing – original draft, writing—review and editing. SN: investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing—review and editing. KK: investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing—review and editing. MW: investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing—review and editing. JD: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing—original draft, writing—review and editing. RS: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing—original draft, writing—review and editing.

Compliance with ethical standards

Informed consent This is a retrospective population-based study of de-identified data so informed consent was not possible/required.

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Conflict of interest The authors report no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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