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Serious maternal complications after early preterm delivery (24–33 weeks'gestation)

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Abstract

OBJECTIVE—To describe the prevalence of serious maternal complications following early preterm birth by gestational age (GA), delivery route and type of cesarean incision.

STUDY DESIGN—Trained personnel abstracted data from maternal and neonatal charts for all deliveries on randomly selected days representing 1/3 of deliveries across 25 US hospitals over 3 years (n=115,502). All women delivering non-anomalous singletons between 23 and 33 weeks' gestation were included. Women were excluded for antepartum stillbirth and highly morbid conditions for which route of delivery would not likely impact morbidity including non-reassuring fetal status, cord prolapse, placenta previa, placenta accreta, placental abruption, and severe,

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unstable maternal conditions (cardiopulmonary collapse, acute respiratory distress syndrome, seizures). Serious maternal complications were defined as: hemorrhage (blood loss ≥1500 mL, blood transfusion, or hysterectomy for hemorrhage); infection (endometritis, wound dehiscence, or wound infection requiring antibiotics, reopening or unexpected procedure); ICU admission; or death. Delivery route was categorized as classical cesarean delivery (CCD), low transverse cesarean delivery (LTCD), low vertical cesarean delivery (LVCD), and vaginal delivery (VD). Association of delivery route with complications was estimated using multivariable regression models yielding adjusted relative risks (aRR) controlling for maternal age, race, body mass index, hypertension, diabetes, preterm premature rupture of membranes, preterm labor, GA, and hospital of delivery.

RESULTS—Of 2659 women who met criteria for inclusion in this analysis, 8.6% of women experienced serious maternal complications. Complications were associated with GA and were highest between 23–27 weeks of gestation. The frequency of complications was associated with delivery route; compared with 3.5% of SVD, 23.0% of CCD (aRR 3.54, 95%CI 2.29–5.48), 12.1% of LTCD (aRR 2.59, 95%CI 1.77–3.77), and 10.3% of LVCD (aRR 2.27, 95%CI 0.68–7.55) experienced complications. There was no significant difference in complication rates between CCD and LTCD (aRR 1.37, 95%CI 0.95–1.97) or between CCD and LVCD (aRR 1.56, 95%CI 0.48–5.07).

CONCLUSION—The risk of maternal complications after early preterm delivery is substantial, particularly in women who undergo cesarean delivery. Obstetricians need to be prepared to manage potential hemorrhage, infection and ICU admission for early preterm births requiring cesarean delivery.

Keywords

maternal morbidity; early preterm delivery; classical cesarean delivery; hemorrhage; infection; ICU admission

INTRODUCTION

Improved neonatal survival has led to an increase in the number of cesarean deliveries being performed preterm, especially at the border of viability.[1,2] Use of a vertical incision in the upper uterine segment is often required and is referred to as a classical cesarean delivery. Classical cesarean deliveries are usually performed for indications such as an inadequately formed or inaccessible lower segment and/or fetal malpresentation, conditions that occur more commonly in preterm pregnancies.

The increased neonatal morbidity with early preterm birth (23–33 weeks of gestation) is well described. However, there is a paucity of data on maternal morbidity associated with early preterm delivery and in fact this has been identified as a key area requiring further research.[3] Classical cesarean delivery has been associated with an increased risk of uterine rupture and uterine scar dehiscence in subsequent pregnancies[4,5] and, in some studies, with an increased risk of acute complications such as hemorrhage and infection.[6–10] Several mostly small studies have evaluated the relationship of preterm delivery (including variation across gestational age) and route of delivery to postpartum maternal morbidity.[5,8,9,11] The data

comparing postoperative morbidity in classical versus low segment cesarean delivery in the early preterm period are also extremely limited.[5,8,9,11] The objectives of this analysis were to determine the prevalence of serious maternal complications associated with early preterm delivery by gestational age (GA) and to determine rates of serious maternal complications by route of delivery (vaginal delivery (VD); classical cesarean delivery (CCD), low transverse cesarean delivery (LTCD) and low vertical cesarean delivery (LVCD) by using highly detailed data obtained by chart abstraction by trained research personnel.

MATERIALS AND METHODS

Between 2008 and 2011, investigators at 25 medical centers of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units (MFMU) Network assembled an observational obstetric cohort (i.e., the Assessment of Perinatal EXcellence (APEX) study) that included detailed information on patient characteristics, intrapartum events, and pregnancy outcomes that was collected by trained and certified nurses. Patients eligible for data collection were those who delivered within the institution, were at least 23 weeks of gestation, had a live fetus on admission and delivered during the 24-hour period of randomly selected days representing one-third of deliveries over this 3-year period (hence approximating the number of deliveries in one year in the MFMU Network). Days were chosen via computer-generated random selection, stratified by weekdays, weekends and holidays and generated separately for each hospital. On selected days, the labor and delivery logbook at each participating center was screened to identify all eligible women. Data from maternal and neonatal charts for all eligible deliveries were abstracted as soon as the delivery and nursery medical records became available (n= 115,502). Institutional review board approval for the study and a waiver of informed consent was obtained at all centers. Full details of the technique of data collection have been described previously.[12]

This secondary analysis included women delivering a non-anomalous singleton between 23 weeks and 0 days and 33 weeks and 6 days of gestation. Women with an antepartum stillbirth and women who were admitted with non-reassuring fetal status, cord prolapse, placenta previa, placenta accreta, placental abruption, unstable and severe maternal condition (cardiopulmonary collapse, acute respiratory distress syndrome, seizures) were excluded from the main analysis due to the extremely high maternal morbidity associated with these indications for delivery by themselves and in order to understand the effect of the route of delivery on serious maternal postpartum complications. Serious maternal complications were defined as the occurrence of one of the following: hemorrhage (blood loss ≥1500 mL, blood transfusion, or hysterectomy for hemorrhage); infection (endometritis, wound dehiscence, or wound infection requiring antibiotics, reopening or unexpected procedure); ICU admission; or death.[12]

The delivery route was classified as vaginal delivery (VD), classical cesarean delivery (CCD), low transverse cesarean delivery (LTCD) and low vertical cesarean delivery (LVCD). Uterine incisions that were started as low segment incisions but were extended into the upper uterine segment - “J” or inverted “T” incisions -were included as part of the CCD group.

Univariate analyses used the chi-square or Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. The association of delivery route (CCD, LTCD, LVCD, VD) with the occurrence of serious maternal complications was determined using multivariable log Poisson regression yielding adjusted relative risks (aRR) and 95% confidence intervals after controlling for maternal age, race, body mass index (kg/m^2), hypertension (chronic, gestational or preeclampsia), diabetes (pregestational or gestational), preterm premature rupture of membranes (PPROM), preterm labor, gestational age (GA), and hospital. We also sought to describe the association between delivery route and maternal morbidity by categories of gestational age and conducted a post-hoc analysis that included a multivariable model with an interaction term between delivery route and gestational age. SAS software (SAS Institute, Cary, NC), was used for the analyses. All tests were two-tailed and $p<.01$ was used to define statistical significance to account for multiple univariate and multivariate analyses. No imputation for missing data was performed.

RESULTS

Of 3390 women delivering a non-anomalous singleton between 23 weeks and 0 days and 33 weeks and 6 days of gestation, 712 women were excluded from the main analysis and evaluated separately due to the presence of the following: antepartum stillbirth (n=11); non-reassuring fetal status or cord prolapse (n=374); an adverse placental condition (previa, accreta or abruption) (n=324); or an unstable and severe maternal condition on admission (n=3). An additional 19 were excluded because they were delivered by cesarean and had missing type of incision or were missing data regarding type of fetal presentation, leaving 2659 women who are the subject of the main analysis. All 2659 women had complete data to define the outcomes of infection, ICU admission, and death; however, 63 women had missing data to define hemorrhage and 61 had missing data to define the composite of serious maternal complication. There were 272 women in the CCD group (248 with vertical incision in the upper uterine segment and 24 with T and J incisions), 904 women in the LTCD group and 29 women in the LVCD group.

Patient characteristics differed significantly by route of delivery. Women in the CCD, LTCD and LVCD groups had a higher BMI, were more likely to have had a prior cesarean delivery and hypertension, less likely to have PPROM and preterm labor, and more likely to have a non-vertex fetal presentation and a lower birth weight and small for gestational age neonate than the VD group, $p< 0.01$. (Table 1) Women in the CCD group were more likely to be black, less likely to have private insurance, more likely to have a non-vertex fetal presentation and a lower birth weight neonate, and deliver at an earlier gestational age than the LTCD group, $p < 0.01$. (Table 1)

Overall, 8.6% of women experienced a serious maternal complication. The composite of serious maternal complications also captured other serious outcomes such as disseminated intravascular coagulation (n=5), idiopathic thrombocytopenic purpura (n=1), cardiopulmonary arrest (n=1), cardiac dysfunction (n=8), adult respiratory distress (n=6), renal failure (n=2), sepsis (n=6) and hysterectomy (n=2) which were classified under ICU admission. The occurrence of serious maternal complications was associated with gestational age and highest in the earliest gestational age range (23–27 weeks of gestation).

The rate of CCD also was associated with gestational age and highest in the earliest gestational age range. (Table 2) The frequency of complications was associated with route of delivery, with 23.0% of those undergoing classical CD, 12.1% of those undergoing LTCD and 10.3% of those undergoing LVCD experiencing serious maternal complications compared with 3.5% of women delivering vaginally (p<0.001, Table 3). Hemorrhage, infection, and ICU admission also were increased among women undergoing CCD or LTCD compared with VD (p<0.001, Table 3). In multivariable analyses, CCD (aRR 3.54, 95%CI 2.29–5.48) and LTCD (aRR 2.59, 95%CI 1.77–3.77) were associated with significantly more serious maternal complications than VD when adjusting for characteristics affecting maternal outcome (Table 4; bold indicates RRs significant at P<.01). There was no significant difference in serious maternal complications between CCD and LTCD (aRR 1.37, 95%CI 0.95–1.97) or between CCD and LVCD (aRR 1.56, 95%CI 0.48–5.07).

Frequencies of serious maternal complications are summarized in the supplemental table on the cases who were excluded from the current analysis because of non-reassuring fetal status, cord prolapse or an adverse placental condition (previa, accreta or abruption).

COMMENT

In this study, using detailed recent data we found that 8.6% of women undergoing early preterm delivery experience serious maternal complications. The clinical implications of these findings are that the risk of maternal postpartum complications in early preterm delivery is substantial, particularly in women who undergo cesarean delivery. Of women undergoing classical cesarean delivery, 23.0% experienced serious maternal complications whereas the rate was 3.5% for women delivering vaginally. Given the effect on immediate maternal morbidity as well as increased risk associated with subsequent pregnancies, it is important that providers caring for women who deliver in the early preterm period be cognizant of these complications and be prepared to manage them.

Our results are similar to previous smaller case series of classical cesarean delivery. Greene et al. studied classical CD at a single institution in Ireland between 1983–1995 (35 preterm, 27 term). There were no maternal deaths; 49% and 19% were complicated by infection and hemorrhage, respectively, and 2 women required hysterectomy.[6] Bethune et al. studied a total of 123 classical CD at a single institution in Melbourne, Australia from 1986–1994. The incidence of CCD declined with increasing gestational age. At 24 weeks of gestation, 20% of all cesarean deliveries were classical, decreasing to 5% by 30 weeks of gestation. Complications after classical CD were related to the indication for performing the CD and not specifically to the classical incision itself. For example, 5 women required a cesarean hysterectomy because of uncontrolled hemorrhage in association with placenta accreta (N = 4) and uterine rupture (N = 1).[7]

Prior literature on this topic is limited, conflicting, and has included heterogeneous groups of women (term vs. preterm, placenta accreta/emergency CD) making it difficult to distinguish the association of the indications from delivery route in maternal outcomes. Blanco et al. compared 89 CCD matched to 89 LTCD between 1970 and 1977. The authors found no significant difference between the groups in endometritis, wound infection, UTI or

pulmonary infection. The incidence of operative site infection and major infectious complications was comparable for LTCD and CCD refuting, according to the authors, the widely held belief that women undergoing CCD have a much higher morbidity and mortality than those having LTCD.[13] Halperin et al. examined 163 classical and 163 low-transverse primary CD at 24–35 weeks gestation between 1978 and 1984. Postpartum fever occurred significantly more often after a classical CD (16% vs. 6%) than after a LTCD. However, more serious complications such as blood loss >1000 mL or need for blood transfusion, endometritis, sepsis, wound infection or dehiscence, paralytic ileus, and thromboembolism were not significantly different between the 2 groups. Of note, the women in this series experienced a relatively high postoperative morbidity (31%).[5] Shah et al. studied 178 women undergoing cesarean delivery (77 CCD and 101 LTCD) for a preterm delivery at a single institution between 1983 and 1985 and found that there was no difference in acute maternal morbidity (blood loss, infection, and intestinal obstruction) associated with the type of uterine incision in the preterm gestation.[11]

In contrast, there are studies that have shown a difference in maternal morbidity when comparing classical to low transverse cesarean delivery. Lao et al. compared 31 women delivered by classical CD in a retrospective case-control study to 31 women delivered by LTCD between 25 and 34 weeks of gestation. Excluded from the study were women who had antepartum hemorrhage or placenta previa. There was a significantly greater reduction in maternal hemoglobin and a higher incidence of severe bleeding in the CCD group compared to the LTCD group ($P < 0.05$). The authors concluded that for preterm cesarean delivery, the classical incision was associated with increased blood loss compared to the lower segment incision.[8] In a retrospective study of singleton cesarean delivery between 23–34 weeks of gestation from 2002–2009 at a single institution, Luthra et el. found an increased odds of blood transfusion in 187 CCD compared with 586 LTCD (OR=2.17, 95% CI 1.0–4.67).[9] Patterson et al. in a 19-year review of all cesarean deliveries in the Nova Scotia Atlee Provincial Database (1980–1998) found that puerperal infection, blood transfusion, hysterectomy, intensive care unit admission, death) were each significantly higher in 221 CCD compared with 19,422 LTCD. However, the mean gestational age at delivery was significantly higher in the LTCD group (38.8 weeks of gestation) than the CCD group (31.6 weeks of gestation).[10] The analyses did not account for indications for delivery such as preeclampsia and PPROM which by themselves are associated with increased maternal morbidity and are more frequent in preterm deliveries.

Although our study has a larger sample size than previous studies, there are a few limitations. With an even larger sample size in our study, the difference in serious maternal complications between classical and low transverse cesarean delivery was not statistically significant (aRR 1.37, 95% CI 0.95–1.97). This may be due to inadequate sample size. In addition, we accounted for baseline characteristics of women (e.g. BMI) as well as conditions that would affect maternal outcome such as hypertension in the multivariable analyses, but there may have been other conditions present that were not adjusted for that could have influenced maternal outcomes.

There are several strengths of this study. The use of trained chart abstractors to obtain detailed medical information, uniform and rigorous definitions used for outcomes, and the

relatively large sample size of early preterm births compared with previous studies allowed for comparison of maternal morbidity by delivery route and gestational age. We excluded women with indications for early preterm delivery morbidity (eg accreta, abruption, cardiopulmonary collapse) which could be responsible for the increased complications seen after delivery to allow for better understanding of the association of delivery route itself with maternal morbidity. Furthermore, we were able to adjust for important covariates influencing maternal morbidity given the detailed medical record abstraction.

In conclusion, women undergoing an early preterm delivery are at substantially increased risk of having a serious maternal complication, particularly in those who undergo cesarean delivery. Given the relatively high rates of maternal complications after early preterm delivery, obstetricians need to be prepared to manage potential hemorrhage, infection and ICU admission. There has been a substantial improvement in neonatal outcomes after early preterm delivery. It is time to focus on the concomitant improvement of maternal outcomes after early preterm delivery. Determination of the optimal antepartum, intrapartum and postpartum management of women who require early preterm delivery will be needed in order to decrease the high rates of maternal complications observed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

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Table 1

Baseline characteristics by delivery route

Characteristic, n (%) or mean ± SD	Delivery route				P-value CCD vs. VD*	P-value LTCD vs. VD*	P-value LVCD vs. VD*	P-value CCD vs. LTCD*	P-value CCD vs. LVCD*	P-value LTCD vs. LVCD*
	Classical cesarean (CCD) n=272	Low transverse cesarean (LTCD) n=904	Low vertical cesarean (LVCD) n=29	Vaginal (VD) n=1454						
Age, y	28.4±6.7	28.0±6.5	28.4±6.8	26.5±6.5	<.001	<.001	.13	.45	.90	.73
Race/ethnicity					.001	.01	.27	<.001	.18	.41
Non-Hispanic white	71 (26.1)	394 (43.6)	11 (37.9)	559 (38.5)						
Non-Hispanic black	122 (44.9)	268 (29.7)	8 (27.6)	522 (35.9)						
Non-Hispanic other	25 (9.2)	75 (8.3)	5 (17.2)	111 (7.6)						
Hispanic	54 (19.9)	167 (18.5)	5 (17.2)	262 (18.0)						
Private insurance	83 (30.6)	363 (40.4)	10 (34.5)	486 (33.7)	.32	.001	.93	.004	.67	.52
Obstetric history					<.001	<.001	<.001	.02	.43	.51
Nulliparous	100 (36.8)	411 (45.5)	11 (39.3)	682 (46.9)						
Prior vaginal delivery only	89 (32.7)	229 (25.3)	6 (21.4)	671 (46.2)						
Prior cesarean	83 (30.5)	264 (29.2)	11 (39.3)	100 (6.9)						
Diabetes					.64	<.001	.03	.14	.03	.04
None	246 (90.4)	778 (86.3)	22 (75.9)	1302 (89.9)						
Pregestational	10 (3.7)	59 (6.5)	1 (3.5)	43 (3.0)						
Gestational	16 (5.9)	65 (7.2)	6 (20.7)	103 (7.1)						
Hypertension†	135 (49.6)	501 (55.4)	16 (55.2)	313 (21.6)	<.001	<.001	<.001	.09	.57	.98
Body mass index, kg/m2	33.5±9.3	32.1±7.4	34.6±8.4	29.8±7.2	<.001	<.001	.001	.11	.35	.10
Smoked during pregnancy	48 (17.7)	147 (16.3)	5 (17.2)	288 (19.9)	.40	.03	.73	.59	.96	.80
PPROM	82 (30.2)	252 (27.9)	7 (24.1)	709 (48.8)	<.001	<.001	.009	.47	.50	.66
Preterm labor	115 (42.3)	336 (37.2)	10 (34.5)	1137 (78.2)	<.001	<.001	<.001	.13	.42	.77
Presentation at delivery					<.001	<.001	<.001	<.001	.76	.09
Vertex	94 (34.6)	545 (60.3)	12 (41.4)	1411 (97.0)						
Breech	155 (57.0)	333 (36.8)	15 (51.7)	42 (2.9)						
Non-breech malpresentation	23 (8.5)	26 (2.9)	2 (6.9)	1 (0.1)						

Characteristic, n (%) or mean ± SD	Delivery route				P-value CCD vs. VD*	P-value LTCD vs. VD*	P-value LVCD vs. VD*	P-value CCD vs. LTCD*	P-value CCD vs. LVCD*	P-value LTCD vs. LVCD*
	Classical cesarean (CCD) n=272	Low transverse cesarean (LTCD) n=904	Low vertical cesarean (LVCD) n=29	Vaginal (VD) n=1454						
Gestational age at delivery, weeks	27.8±2.8	30.8±2.5	29.0±2.8	30.7±3.0	<.001	.30	.002	<.001	.02	<.001
Birthweight, grams	1007.2±439.2	1517.8±564.5	1171.9±516.8	1634.6±580.5	<.001	<.001	<.001	<.001	.05	<.001
Size for gestational age‡					<.001	<.001	<.001	.34	.26	.12
Small	49 (18.0)	130 (14.4)	7 (24.1)	70 (4.8)						
Appropriate	220 (80.9)	763 (84.4)	21 (72.4)	1365 (93.9)						
Large	3 (1.1)	11 (1.2)	1 (3.5)	18 (1.2)						

*based on the chi-square or Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables

†includes chronic, gestational or preeclampsia

‡estimated per the methods of Alexander et al (Alexander GR, Kogan MD, Himes JH. 1994–1996 U.S. singleton birth weight percentiles for gestational age by race, Hispanic origin, and gender. Matern Child Health J. 1999;3(4):225-31.) using neonatal gestational age at delivery, birthweight and sex and maternal race/ethnicity; small defined as < 10^{th} percentile for sex and race/ethnicity; appropriate defined as 10^{th}–90^{th} percentile for sex and race/ethnicity; large defined as > 90^{th} percentile for sex and race/ethnicity

Table 2

Serious maternal complications and delivery route, by gestational age at delivery

Outcome, n (%)*	Gestational age at delivery			P-value†
	23–27 weeks n=597	28–31 weeks n=919	32–33 weeks n=1143	
Composite serious maternal complications	67 (11.5)	86 (9.5)	70 (6.3)	<.001
Hemorrhage	41 (7.0)	46 (5.1)	34 (3.1)	<.001
Infection	16 (2.7)	27 (2.9)	15 (1.3)	.03
ICU admission	20 (3.4)	36 (3.9)	33 (2.9)	.43
Death	1 (0.2)	1 (0.1)	0 (0.0)	.33
Delivery route				<.001
Classical cesarean (CCD)	154 (25.8)	89 (9.7)	29 (2.5)	
Low transverse cesarean (LTCD)	145 (24.3)	365 (39.7)	394 (34.5)	
Low vertical cesarean (LVCD)	13 (2.2)	10 (1.1)	6 (0.5)	
Vaginal (VD)	285 (47.7)	455 (49.5)	714 (62.5)	

*all 2659 women had complete data to define the outcomes of infection, ICU admission, and death; 63 had missing data to define hemorrhage; 61 had missing data to define MM

†based on the chi-square or Fisher's exact test

Table 3

Serious maternal complications by delivery route

	Delivery route				
Outcome, n (%)*	**Classical cesarean (CCD) n=272**	**Low transverse cesarean (LTCD) n=904**	**Low vertical cesarean (LVCD) n=29**	**Vaginal (VD) n=1454**	**P-value†**
Composite serious maternal complications	62 (23.0)	109 (12.1)	3 (10.3)	49 (3.5)	<.001
Hemorrhage	39 (14.4)	56 (6.2)	2 (6.9)	24 (1.7)	<.001
Infection	14 (5.2)	33 (3.7)	1 (3.5)	10 (0.7)	<.001
ICU admission	18 (6.6)	45 (5.0)	0 (0.0)	26 (1.8)	<.001
Death	1 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)	.10

* all 2659 women had complete data to define the outcomes of infection, ICU admission, and death; 63 had missing data to define hemorrhage; 61 had missing data to define MM

† based on the chi-square or Fisher's exact test

Table 4

Adjusted* relative risk (95%CI) for association between route of delivery and serious maternal complications, overall and by gestational age at delivery

	Delivery route			
	Classical cesarean (CCD) n=272	**Low transverse cesarean (LTCD) n=904**	**Low vertical cesarean (LVCD) n=29**	**Vaginal (VD) n=1454**
Overall, 23–33 weeks gestation	**3.54 (2.29–5.48)**	**2.59 (1.77–3.77)**	2.27 (0.68–7.55)	1.0 (referent)
23–27 weeks gestation†	**3.22 (1.62–6.38)**	**2.86 (1.35–6.05)**	4.20 (0.90–19.55)	1.0 (referent)
28–31 weeks gestation†	**2.69 (1.39–5.21)**	1.86 (1.06–3.26)	1.16 (0.15–8.94)	1.0 (referent)
32–33 weeks gestation†	**8.16 (3.44–19.40)**	**3.48 (1.91–6.32)**	‡	1.0 (referent)

Bold indicates RR significant at P<.01

*adjusted for maternal age, race, body mass index, hypertension (chronic, gestational or preeclampsia), diabetes (pregestational or gestational), preterm premature rupture of membranes, preterm labor, gestational age at delivery, and hospital

†based on model with interaction terms; interaction p=.09

‡not computed due to small cell sizes