



Original Article

The association between epidural labor analgesia and the fetal outcome and mode of delivery of the second twin: a nationwide register-based cohort study in Finland



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ABSTRACT

Background: The aim of this study was to assess the association between epidural labor analgesia and the mode of delivery for the second twin and to analyze the health outcomes of the second twin.

Methods: In this nationwide, retrospective, register-based cohort study, data from the National Medical Birth Register (MBR) of Finland (2004–2018) were used to analyze the association between epidural analgesia and delivery mode (emergency and urgent cesarean section, and assisted vaginal delivery) and fetal outcomes (neonatal mortality and need for intensive care unit admission) for the second twin. Multivariable logistic regression was used to assess the delivery mode and fetal outcomes of the second twin.

Results: A total of 3242 twin pregnancies with epidural analgesia were compared with a control group consisting of 2780 twin pregnancies without epidural analgesia. Epidural analgesia was associated with lower odds for all cesarean delivery (aOR 0.64, 95% CI 0.44 to 0.92) for the second twin and for emergency cesarean delivery (aOR 0.52, 95% CI 0.33 to 0.79) when compared with the odds for the second twin in the control group. Epidural analgesia was associated with lower odds of neonatal mortality for the second twin (aOR 0.61, 95% CI 0.73 to 0.90).

Conclusion: This study found epidural labor analgesia was associated with a lower rate of emergency cesarean delivery and neonatal mortality for the second twin. These results should be acknowledged by obstetricians and anesthesiologists when planning optimal peripartum management for mothers with twin pregnancies.

Introduction

Multiple pregnancies have a higher risk of maternal and fetal morbidity and mortality compared with singleton pregnancies. Fortunately, the rate of perinatal mortality is decreasing.^{1,2} In Finland, perinatal and early neonatal mortality in twins has decreased during recent decades to 0.7% for the first twin, and 1.2% for the second twin.² Generally, a trial of vaginal birth is a safe option for women with twin pregnancy.^{3,4} However, twin deliveries, especially the delivery of the second twin, are still associated with a higher complication rate than are singleton deliveries, and research on minimizing these challenges is warranted.^{2,5}

Epidural analgesia is beneficial in certain deliveries, such as trial of labor after cesarean and twin delivery, because it allows obstetric procedures to be performed without additional anesthesia.^{6–9} In addition, according to the 2019 UK National Institute for Health and Care Excellence (NICE) guidelines, epidural analgesia reduces the risk of emergency delivery (CD) for the second twin.¹⁰ Furthermore, a 2021 study investigating the association of epidural analgesia with delivery mode and health of the second twin reported a reduced risk of CD after vaginal birth of the first twin among women who used epidural analgesia compared with women who did not use epidural analgesia.¹¹ However, there are also disadvantages of epidural analgesia, it being associated with a greater risk of operative vaginal delivery and in some cases a longer duration of labor.^{9,12,13}

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The aim of this study was to assess the association between epidural analgesia and the mode of delivery for the second twin and to analyze the health outcomes of the second twin.

Methods

In this nationwide retrospective register-based cohort study, data from the National Medical Birth Register (MBR) of Finland were used to analyze the association of epidural analgesia and maternal and fetal outcomes. The MBR is maintained by the Finnish Institute for Health and Welfare and contains information on pregnancies, delivery statistics, and the perinatal outcomes of all births with a birthweight of ≥ 500 g or a gestational age of ≥ 22 weeks. The MBR has high coverage and quality (current coverage nearly 100%).^{14,15} All twin pregnancies in which the first twin was born vaginally were included from the period January 1, 2004 to December 31, 2018. These pregnancies were divided into two cohorts based on the use of epidural analgesia, this information being collected routinely in the register as a categorized dichotomous (yes or no) variable.

The Ethical Committee of Tampere University hospital waived the ethical committee evaluation of this retrospective study utilizing routinely collected healthcare data, based on the law of medical research 488/1999 and the law of patient rights 785/1992. The MBR uses a pseudonymized identification number for each patient. The pseudonymization was done by the Finnish data authority, Findata, and the authors did not have access to the pseudonymization key. In accordance with Finnish regulations (the law of secondary use of routinely collected healthcare data 552/2019), no informed written consent was required. Permission to use these data was granted by Findata after the evaluation of the study protocol (permission number THL/1756/14.02.00/2020).

The time interval chosen for this study was 2004–2018 because the register had minimal changes in the content during this interval; major modifications to data collection were made in 2004 and 2019. Data were compared between women with and without epidural labor analgesia. Continuous variables are summarized as mean with standard deviation or median with interquartile range, based on variable distribution. Categorical variables are summarized as absolute numbers and percentages with 95% confidence intervals (CIs). The CI for rates was calculated using Poisson regression. Multivariable logistic regression was used to assess the delivery mode and fetal outcomes of the second twin. Mode of delivery was analyzed separately for assisted vaginal deliveries (including vaginal breech deliveries, breech extractions, vacuum, and forceps deliveries), all CDs (emergency and urgent CD), and emergency CD. Fetal outcomes included intensive care unit (ICU) treatment and neonatal mortality from birth to seven days of age. The analyses were adjusted for maternal age and smoking during pregnancy, maternal gestational diabetes, maternal pre-gestational body mass index (BMI), birthweight, and gestational age, as these factors are known to increase the risk of CD and adverse neonatal outcomes.^{16–23} Analyses were also adjusted for year of the delivery as the use of labor analgesia has increased during past decades.²³ Due to the good quality and coverage of the MBR, the proportion of missing values for these variables was low ($< 7.5\%$), so complete case analysis was used. Adjusted odds ratios (aOR) with 95% CI were calculated for the main outcomes. The results of this study are reported according to the STROBE guidelines.²⁴ Statistical analysis was performed using R version 4.2.2.

Results

A total of 6022 twin pregnancies with the first twin born vaginally were included in this study. Of these, 3242 twin pregnancies with epidural analgesia were included in the epidural group. The control group consisted of 2780 twin pregnancies without epidural analgesia

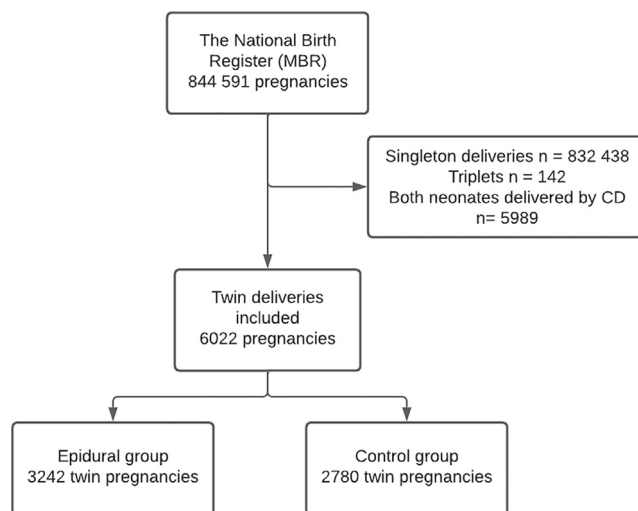


Fig. 1. Flowchart of the study groups. CD: cesarean delivery.

(Fig. 1). There was a higher proportion of nulliparous women, labor induction, and a lower rate of preterm deliveries and spinal anesthesia in the epidural group compared with the control group. Baseline characteristics are shown in Table 1.

Spontaneous vaginal birth with cephalic presentation occurred for 1876 (58%) second twins in the epidural group and 1882 (68%) second twins in the control group. Epidural analgesia was associated with lower odds for all CD of the second twin (aOR 0.64, CI 0.44 to 0.92) and for emergency CD of the second twin (aOR 0.52, CI 0.33 to 0.79) compared with second twins in the control group (Table 2). However, epidural analgesia was associated with greater odds of assisted vaginal delivery, primarily vacuum-assisted deliveries. In addition, epidural analgesia was associated with lower odds of neonatal mortality for the second twin compared with the control group. Neonatal ICU admission was not significantly different between groups (Table 2).

Discussion

The main finding of this study was that epidural analgesia was associated with a lower rate of emergency CD and neonatal mortality for the second twin, but a higher rate of vacuum-assisted vaginal deliveries.

The overall risk of CD for the second twin was low and similar to that previously reported.²⁵ The most recent study investigating the relationship between the use of epidural analgesia and the delivery mode of the second twin found a reduced risk for CD after vaginal birth of the first twin among women with epidural analgesia.¹¹ The authors concluded that future studies were needed to confirm their findings and our results support this association. Also, in previous studies, epidural analgesia was associated with a higher success rate of vaginal birth after CD.^{6,7} In our study, women in the epidural group had a slightly higher rate of previous CD. The higher odds for assisted vaginal delivery in the epidural group may be partly related to the lower rate of CD.

We found that neonates in the epidural group had a lower rate of neonatal mortality than those in the control group, which is partly explained by the higher rate of deliveries before 32 weeks of gestation in the control group. However, after analysis was adjusted by gestational age, the odds for neonatal mortality remained lower. It is also possible that neonates in the control group had a higher rate of fetal distress or malpresentation, resulting in a higher CD rate. However, no conclusions can be drawn as to reasons for the lower CD rate and

Table 1
Baseline characteristics of patients with and without (control) epidural labor analgesia.

Total number of patients	Epidural group n = 3242		Control group n = 2780	
		% (CI)		% (CI)
Age (y), mean (SD)	30.1 (5.0)		31.2 (4.9)	
Nulliparous	1717	53.0 (50.5 to 55.5)	559	20.1 (18.5 to 21.9)
Previous CD	178	5.5 (4.7 to 6.4)	132	4.7 (4.0 to 5.6)
Maternal smoking status				
smoker	448	13.8 (12.6 to 15.2)	369	13.3 (12.0 to 14.7)
unknown	64	2.0 (1.5 to 2.5)	203	7.3 (6.3 to 8.4)
Maternal BMI (kg/m ²) ^a , mean (SD)	24.3 (4.6)		24.7 (5.0)	
BMI missing	190	5.9 (5.1 to 6.8)	130	4.7 (3.9 to 5.5)
Gestational diabetes	492	15.2 (13.9 to 16.6)	407	14.6 (13.3 to 16.1)
Gestational age <32 weeks	105	3.2 (2.6 to 3.9)	250	9.0 (7.9 to 10.2)
Labor induction	1840	56.8 (54.2 to 59.4)	1278	45.6 (43.5 to 48.6)
Spinal analgesia	134	4.1 (3.5 to 4.9)	534	19.2 (17.6 to 20.9)

BMI: body mass index. CD: cesarean delivery.

^a Pre-pregnancy body mass index.

Table 2

Absolute numbers, rates, and adjusted odds ratios (aORs) with 95% confidence intervals (CI) for the delivery mode, and neonatal health outcomes for the second twin in pregnancies when the first twin was born vaginally.

Total number of patients	Epidural group 3242		Control group 2780		aOR	CI
	n	%	n	%		
Delivery mode ^a						
Assisted vaginal ^b	1302	40.2	823	29.6	1.45	1.29 to 1.62
breech extraction	611	18.9	511	18.4		
vacuum	683	21.1	312	11.2		
forceps	8	0.2	0	0.0		
All CD ^c	64	2.0	75	2.7	0.64	0.44 to 0.92
Emergency CD	36	1.1	59	2.1	0.52	0.33 to 0.79
Neonatal outcome ^d						
Neonatal mortality	48	1.5	81	2.9	0.61	0.73 to 0.90
Intensive care unit admission	1190	36.7	1088	39.2	1.05	0.93 to 1.18

CD: cesarean delivery.

^a Adjusted for maternal age, smoking status, gestational diabetes, maternal body mass index, gestational age, birthweight, and year of the delivery.

^b Includes breech extraction, vacuum delivery, and forceps delivery.

^c Includes urgent and emergency cesarean delivery.

^d Adjusted by maternal age, smoking status, gestational diabetes, and maternal body mass index, gestational age, and year of the delivery.

improved neonatal mortality in the epidural group because data regarding labor complications were not available. The rate of breech delivery for the second twin was similar in both groups and we did not have information about the proportion of spontaneous vaginal breech delivery and breech extraction as these are coded together in the MBR.

Some women having epidural analgesia also had spinal analgesia. The use of spinal analgesia was higher among women without epidural analgesia, with one-fifth of this cohort receiving spinal analgesia. In Finland, this method is most often used by multiparous women in cases when analgesia is required shortly before delivery, or if epidural analgesia is insufficient. The effects of spinal analgesia remain unknown, but it might have decreased the differences between the groups.

The main strength of this study is the nationwide register coverage including almost all deliveries in Finland, and the high validity and precision of the register data.¹⁵ The sample size in our study is larger than that of the previous studies but limitations include the lack of data on unsuccessful attempts to provide epidural analgesia and information on analgesic drug doses. However, based on our experience, the rate of unsuccessful labor analgesia attempts is likely low. Also, the regional variability in the availability of labor analgesia remains unknown and access to neuraxial techniques might have had greater variation during the first years of our study period. The centralization of births to larger hospitals since 2010 has most likely reduced any differences in the availability of neuraxial analgesia among hospitals. In

addition, we do not have information on the total duration of labor or the twin-twin delivery interval, the indications for CD or the causes of neonatal death, as these are not reported to the register.

In conclusion, this study found that successful vaginal delivery of both twins is usually possible. Epidural analgesia was associated with a lower rate of emergency CD and neonatal mortality of the second twin. The results of this study should be acknowledged by obstetricians and anesthesiologists when planning peripartum management for mothers with twin pregnancies, and will hopefully encourage researchers to further investigate the reasons for the findings.

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Declaration of interests

The authors declare no conflicts of interest.

References

1. Perinatal mortality rate in multiple pregnancies: a 20-year retrospective study from a tertiary obstetric unit in Hong Kong. HKMJ. October 12, 2022. Available at: <https://www.hkmj.org/abstracts/v28n5/347.htm>. Accessed February, 13, 2023.
2. Rissanen ARS, Jermman RM, Gissler M, Nupponen IK, Nuutila ME. Perinatal outcomes in Finnish twins: a retrospective study. *BMC Pregn Childbirth*. 2019;20:2. <https://doi.org/10.1186/s12884-019-2670-3>.

3. Ylilehto E, Palomäki O, Huhtala H, Uotila J. Term twin birth – impact of mode of delivery on outcome. *Acta Obstet Gynecol Scand.* 2017;96:589–596. <https://doi.org/10.1111/aogs.13122>.
4. Ylilehto E, Palomäki O, Korhonen P, Huhtala H, Uotila J. Impact of mode of delivery on perinatal outcome in moderately and late preterm twin birth. *Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet.* 2021;153:106–112. <https://doi.org/10.1002/ijgo.13418>.
5. Hayata E, Nakata M, Morita M. Time trend analysis of perinatal mortality, stillbirth, and early neonatal mortality of multiple pregnancies for each gestational week from the year 2000 to 2019: a population-based study in Japan. *PLoS One.* 2022;17. <https://doi.org/10.1371/journal.pone.0272075> e0272075.
6. Sun J, Yan X, Yuan A, et al. Effect of epidural analgesia in trial of labor after cesarean on maternal and neonatal outcomes in China: a multicenter, prospective cohort study. *BMC Pregn Childbirth.* 2019;19:498. <https://doi.org/10.1186/s12884-019-2648-1>.
7. Peled T, Sela HY, Joseph J, Martinotti T, Grisaru-Granovsky S, Rottenstreich M. Factors associated with failed trial of labor after cesarean, among women with twin gestation—a multicenter retrospective cohort study. *J Clin Med.* 2022;11:4256. <https://doi.org/10.3390/jcm11154256>.
8. Jaschevatzky OE, Shalit A, Levy Y, Grünstein S. Epidural analgesia during labour in twin pregnancy. *Brit J Obstet Gynaecol.* 1977;84:327–331. <https://doi.org/10.1111/j.1471-0528.1977.tb12592.x>.
9. Rottenstreich M, Rotem R, Ehrlich Z, Rottenstreich A, Grisaru-Granovsky S, Shen O. Vacuum extraction in twin deliveries—maternal and neonatal consequences: a retrospective cohort study. *Arch Gynecol Obstet.* 2020;302:845–852. <https://doi.org/10.1007/s00404-020-05668-2>.
10. National Guideline Alliance (UK). Evidence review for the optimal method of analgesia and anaesthesia during labour and birth: twin and triplet pregnancy: evidence review H. National Institute for Health and Care Excellence (NICE); 2019. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK578071/>. Accessed February, 17, 2023
11. Farghali MM, Ibrahim AS, Farrag WS. Effect of labor epidural analgesia on delivery of second twin: a prospective observational study. *Ginekol Poloznictwo.* 2021;16:1–6.
12. Gullestad S, Sagen N. Epidural block in twin labour and delivery. *Acta Anaesthesiol Scand.* 1977;21:504–508. <https://doi.org/10.1111/j.1399-6576.1977.tb01252.x>.
13. Weekes AR, Cheridjian VE, Mwanje DK. Lumbar epidural analgesia in labour in twin pregnancy. *Brit Med J.* 1977;2:730–732. <https://doi.org/10.1136/bmj.2.6089.730>.
14. Gissler M, Teperi J, Hemminki E, Meriläinen J. Data quality after restructuring a national medical registry. *Scand J Soc Med.* 1995;23:75–80. <https://doi.org/10.1177/140349489502300113> [doi].
15. Gissler M, Shelley J. Quality of data on subsequent events in a routine Medical Birth Register. *Med Inform Internet Med.* 2002;27:33–38. doi:0UB69R4X61VDGCGDA [pii].
16. Bergholt T, Skjeldestad FE, Pyykönen A, et al. Maternal age and risk of cesarean section in women with induced labor at term—a Nordic register-based study. *Acta Obstet Gynecol Scand.* 2020;99:283–289. <https://doi.org/10.1111/aogs.13743>.
17. McLennan AS, Gyamfi-Bannerman C, Ananth CV, et al. The role of maternal age in twin pregnancy outcomes. *Am J Obstet Gynecol.* 2017;217:80.e1–80.e8. <https://doi.org/10.1016/j.ajog.2017.03.002>.
18. Lurie S, Ribenzafit S, Boaz M, Golan A, Sadan O. The effect of cigarette smoking during pregnancy on mode of delivery in uncomplicated term singleton pregnancies. *J Maternal-Fetal Neonatal Med.* 2014;27:812–815. <https://doi.org/10.3109/14767058.2013.842551>.
19. Knopik VS. Maternal smoking during pregnancy and child outcomes: real or spurious effect? *Develop Neuropsychol.* 2009;34:1–36. <https://doi.org/10.1080/87565640802564366>.
20. Jain U, Singhal K, Jain S, Jain D. Risk factor for gestational diabetes mellitus and impact of gestational diabetes mellitus on maternal and fetal health during the antenatal period. *Int J Reproduct Contracept Obstet Gynecol.* 2021;10:3455–3461. <https://doi.org/10.18203/2320-1770.ijrcog20213169>.
21. Ye W, Luo C, Huang J, Li C, Liu Z, Liu F. Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and meta-analysis. *BMJ.* 2022;377:e067946.
22. Machado LS. Cesarean section in morbidly obese parturients: practical implications and complications. *North Am J Med Sci.* 2012;4:13–18. <https://doi.org/10.4103/1947-2714.92895>.
23. Kuitunen I, Kekki M, Ponkilainen V, Huttunen T. Labor analgesia in obese and morbidly obese parturients: a nationwide register analysis in Finland from 2004 to 2018. *Obstetric Anesthesia Digest.* 2023;43:40. <https://doi.org/10.1097/01.aoa.0000912372.35322.e1>.
24. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol.* 2008;61:344–349. <https://doi.org/10.1016/j.jclinepi.2007.11.008>.
25. Schmitz T, Prunet C, Azria E, et al. Association between planned cesarean delivery and neonatal mortality and morbidity in twin pregnancies. *Obstet Gynecol.* 2017;129:986–995. <https://doi.org/10.1097/AOG.0000000000002048>.