



Full length article

Pregnancy outcome in women after total hip replacement: A population-based study



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ABSTRACT

Objective: Only a few small studies have been published on pregnancies after total hip replacement (THR), and they have reported no adverse pregnancy outcomes after THR. The aim of our study was to evaluate whether maternal THR affects pregnancy outcomes on a population-based level.

Study Design: Data for this nationwide register-based cohort study have been collected from four national registries in Finland from 1980 to 2007. All females who had undergone THR during that period formed the patient group, and three controls for each patient without THR were selected. Patient group comprised 2429 women, 719 (29.6%) of whom had 1190 pregnancies ending in singleton deliveries. Of those births, 986 were before THR and 204 after THR. The control group comprised 7276 women, 2805 (38.6%) of whom had 5112 pregnancies ending in singleton deliveries, 3695 occurred before the index date (time point when THR took place within the patient group) and 1417 after. Logistic regression model was used to analyze univariable and adjusted odds ratios (aOR) for adverse neonatal outcomes after maternal THR compared with controls. Data were adjusted using the following variables: maternal age, smoking, rheumatoid arthritis.

Results: Stillbirth was more common in the patient group compared with control group 4 (2.0%) vs 8 (0.6%) $p = 0.02$. Moreover, neonates in the patient group were more likely to be born preterm (aOR 3.58, $p < 0.001$), small for gestational age (aOR 2.83, $p = 0.006$) and low birthweight (aOR 4.79, $p < 0.001$), compared to control group. Trial of labor more likely ended in emergency cesarean section in the patient group than in the control group 39 (28.9%) vs 150 (11.6%), $p < 0.001$. Adverse pregnancy outcome was more common after THR also when compared to pregnancies before THR.

Conclusions: Neonates born after maternal total hip replacement have an increased risk of stillbirth, small for gestational age, low birthweight and preterm birth. Trial of labor is more likely to end in emergency cesarean section.

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Introduction

Total hip replacement (THR) is a highly effective operation for decreasing pain and improving quality of life in affected individuals [1]. The most common indications for THR in fertile-aged patients are rheumatoid arthritis (RA), avascular necrosis of the femoral head and developmental dysplasia of the hip [2,3]. In Finland, the annual incidence of primary THR among 30–39 year

olds was 59.5 per 100 000 person years in 2007 [4]. The prevalence of THR in Sweden in 1999 was 12 per 100 000 women aged under 40 years and 19 per 100 000 in 2012 [5]. In the United States, it has been estimated that the annual primary THR rate in the less than 45 years old group could possibly increase 3-fold by 2030 compared with 2006 rates [6].

There have only been a few studies that have evaluated the effect of previous THR on later pregnancy and delivery or vice versa. The results of these previous studies have not shown an increased risk for complications in delivery after THR, although the numbers of included patients in these studies have been small ($n = 10–50$) [7–14]. Interestingly, some of these studies have

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reported an increased rate of cesarean sections (CS) after THR [10,13,15].

Some studies have raised concerns regarding elevated fetal blood metal ion (chromium and cobalt) levels in women with metal-on-metal hip replacements and the possible passage of the metal ions to the fetus via the placenta [16–18]. Most of the case reports, however, have not shown any teratogenic impact, despite elevated placental blood metal ion levels [18–20]. Two case reports have described a neonate with high metal ion levels combined with congenital anomalies [21]. Considering the previous literature, women may still have concerns regarding pregnancy and vaginal delivery after THR operation [11].

The aim of this present study was to evaluate the effect of THR on the delivery and health of neonates on a population-based level using data routinely recorded into national health registers in Finland.

Materials and methods

The study population in this register-based nationwide cohort study was gathered from four different national registers in Finland. Information on all women aged 15 to 45 years who had undergone primary THR between 1980 and 2007 was retrieved from the Finnish Arthroplasty Register and included in this study ($n = 2429$ women with primary THRs). The register was established in 1980 and is maintained by the National Institute for Health and Welfare. The coverage of the register has been high over the years, especially with regard to primary THR (approximately 95%), and it matches well with the hospital discharge register data [22]. Based on the bearing material, the type of implant was categorized as either metal-on-metal or not metal-on-metal.

For each patient included in the patient group, three control women without THR matched by age at the time of THR and place of residence were obtained from the Finnish Population Information System maintained by the Population Register Centre and formed the control group ($n = 7276$ control women without THR). The start of the follow-up was the date of THR operation in the THR group and the operation date was the index date for the matching controls. The common closing date for this study was 31st December 2007.

In this study, information on singleton pregnancies and deliveries for both groups was gathered from the national Medical

Birth Register, which was established in 1987. The register is maintained by the National Institute for Health and Welfare and contains information on all pregnancies ending in birth or stillbirth after gestational week 22 and neonates weighing over 500 g. The Medical Birth Register also contains the background characteristics of the pregnancies and basic information on deliveries and neonate outcome up to hospital discharge or seven days postpartum [23].

Of the 2429 women in the patient group, 719 (29.6%) had 1190 pregnancies ending in singleton deliveries. Of these, 575 women had 986 singleton deliveries prior to THR, and 144 women had 204 singleton deliveries after THR. The control group comprised 7276 women, 2805 (38.6%) of whom had 5112 pregnancies ending in singleton deliveries. Of these, a total of 1893 women had 3695 singleton deliveries before the index date, and 912 women had 1417 singleton deliveries after the index date. The deliveries after THR/index date were included in the analysis. In addition, a subgroup comparison in the patient group was performed for before and after THR deliveries (Fig. 1).

Information on long-term chronic diseases was obtained from the Register of Medical Reimbursements that is maintained by the Social Insurance Institution of Finland and contains information on reimbursable medical costs for chronic diseases. Reimbursements for medical costs are granted with a medical certificate issued by a licensed doctor. Information on the most common long-term disease, RA, among the study population was obtained, and those persons who did not have a reimbursement for RA medication in the register were classified as not having RA.

Standard deviations (SD) for birth weight and birth length were calculated by using the new Finnish growth references for male and female children and adolescents [24]. A SD of less than -2.0 from mean was considered as small for gestational age (SGA), and a SD greater than $+2.0$ from mean was considered as large for gestational age (LGA). Standard deviations were calculated for all neonates. Neonates born before gestational week 37+0 were defined as preterm. Neonates weighing less than 2500 g were defined as low birthweight (LBW).

All the singleton pregnancies were observed and compared between the groups. Chi-squared test was used to analyze intergroup differences in the categorical variables between the patient group and the control group. A p -value under 0.05 was considered statistically significant. Confidence intervals (95% CI) for the difference of the two proportions were used when

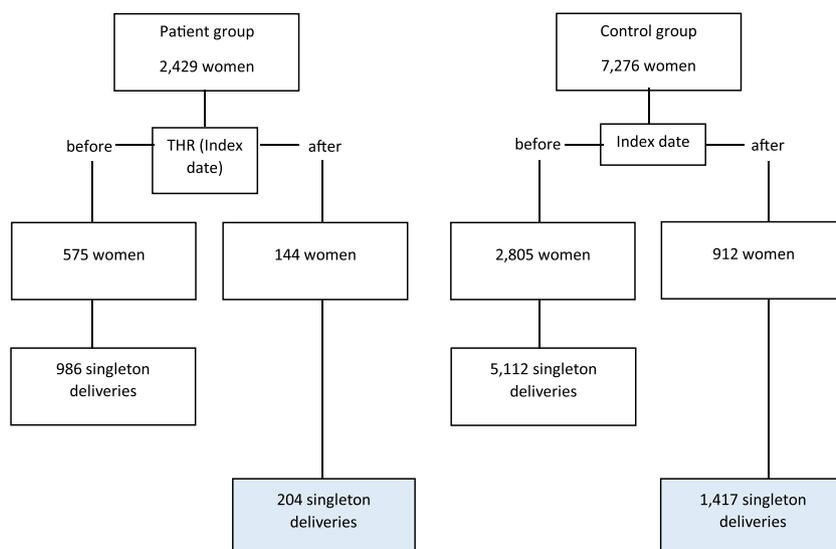


Fig. 1. Flow chart of study population. Index date is the date of THR. Deliveries of the patient group were classified as taking place before or after THR, and likewise the deliveries of the control group were matched according to the index date.

comparing before and after THR proportions in the patient group. Means with SDs were calculated for normally distributed variables and medians with interquartile ranges for non-normally distributed variables. Logistic regression model was used to calculate odds ratios (OR) with 95% CI to compare adverse pregnancy outcomes between the patient and control groups. The following covariates from the available variates in the registers were included and selected based on the previous literature in the adjusted model: maternal age, smoking during pregnancy and maternal RA. Statistical analyses were performed using IBM SPSS for Windows, version 24.0 software.

All the data were linked by using the individual personal identification code that is issued to all permanent residents of Finland. No written consent was required since none of the participants were contacted, and hence no approval from the local ethical committee was required. However, our study protocol did undergo ethical evaluation by the National Institute for Health and Welfare in order to gain access to register data, permission number: THL/599/5.05.00/2010.

Results

Women in the patient group were older at the time of delivery compared with the control group. A higher proportion of women had their first pregnancy after THR in the patient group. In 42% of the deliveries in the patient group, the mother had RA. Baseline information and background characteristics of the pregnant women are presented in Table 1.

Stillbirth was more common in the patient group compared with the control group (Table 2). In the patient group, neonates had a lower birthweight and birth length. The neonates born in this group were also more likely to be born preterm compared with the control group. In addition, neonates born after THR also had higher LBW and SGA proportions and needed more neonatal intensive care treatment and phototherapy compared with the control group (Table 2). When these findings were adjusted with potential confounders, THR remained an independent risk factor in the patient group for preterm birth, LBW and SGA, but not for stillbirth (Table 3).

The pregnancies in the patient group were also compared to pregnancies before THR. Our findings showed adverse pregnancy outcomes were more common after THR than before THR. Moreover, the rates of stillbirth (2.0% vs 0.3%, $p = 0.004$), SGA neonates (8.3% vs 3.3%, $p = 0.001$) and preterm births (13.7% vs 7.1%, $p = 0.001$) were all found to be higher after THR.

In subgroup analysis, deliveries with maternal metal-on-metal THRs ($n = 16$) were compared with deliveries with non-metal-on-metal THRs ($n = 188$). The groups had similar rates of stillbirths

Table 1

Background characteristics of women having singleton pregnancies ending in delivery in the patient group and in the control group.

	Patient group		Control group		P
	n	%	n	%	
Total number	204		1417		
Age at birth (years, mean SD)	33.4	5.2	32.6	5.2	0.046
Nulliparous	80	39.2	438	31.0	0.02
Previous cesarean section	37	18.1	161	11.4	0.006
Marital status					
never married	28	13.7	205	14.5	0.78
ever married	176	86.3	1212	85.5	
Maternal smoking					
non-smoker	173	84.1	1191	84.1	0.63
quit during 1 st trimester	4	2.0	43	3.0	
Smoker	25	12.3	142	10.0	
unknown	2	1.0	41	2.9	
Rheumatoid arthritis	86	42.2	6	0.4	<0.001

Table 2

Perinatal characteristics and outcome in the patient group after THR and the control group.

	Patient group		Control group		p
	n	%	n	%	
Total number	204		1417		
Intended mode of delivery					
Elective CS	69	33.8	124	8.8	<0.001
Trial of labor	135	66.2	1293	91.2	
Fetal gender male	103	50.5	730	51.5	0.78
Birth length (cm) (mean; SD)	48.7	2.8	50.3	2.6	<0.001
Birth weight (grams) (mean; SD)	3240	670	3580	560	<0.001
LBW <2500g	25	12.3	41	2.9	<0.001
SGA	17	8.3	39	2.8	<0.001
LGA	3	1.5	57	4.0	0.04
Preterm, <37 + 0 weeks	28	13.7	65	4.6	<0.001
Perinatal mortality	4	2.0	10	0.7	0.09
Stillbirths	4	2.0	8	0.6	0.02
Neonatal deaths	0	0.0	2	0.1	0.99
1-minute Apgar score ≤ 6	13	6.4	73	5.2	0.47
Delivery related asphyxia	5	2.5	35	2.5	0.99
Phototherapy	19	9.3	63	4.4	0.003
Neonatal intensive-care unit	8	3.9	38	2.7	0.32
Neonatal status 7 days postpartum					
at home	169	82.8	1284	91.4	<0.001
in hospital	31	15.2	111	7.9	

THR = total hip replacement, SD = standard deviation, LBW = low birthweight, LGA = large for gestational age, SGA = small for gestational age.

(0.0% vs 2.1%, $p = 1.00$), preterm births (25.0% vs 12.8%, $p = 0.25$) and LBW neonates (18.8% vs 11.7%, $p = 0.42$). In addition, neonates born to mothers with metal-on-metal THR were more likely to be SGA compared with those born to mothers with non-metal-on-metal THR (25.0% vs 6.9%, $p = 0.03$).

The proportion of elective cesarean sections (CS) was higher in the patient group than in the control group (Table 2). The overall proportion of CS was 27% before THR and 53% after THR and trial of labor more often resulted in emergency CS. The use of epidural analgesia and amniotomies were more common in the control group (Table 4).

Discussion

The results of this study raise concerns over adverse pregnancy outcomes, such as preterm birth, LBW, SGA and stillbirth, that were found to be more common in women after THR than in the control group without THR.

In Finland, the national stillbirth rate has been between 3–5 per 1000 births for the last 30 years [23]. The stillbirth rate of the control group, as well as the patient group before THR, was similar to national levels, but in the patient group after THR it was four to five times higher. One reason for the increased stillbirth rate might be the underlying diseases of the THR patients. Two of the four women with stillbirth in the patient group had RA. RA has been shown to increase the risk of preterm birth and SGA neonate, but not for stillbirths or perinatal mortality in large cohort studies [25–27]. However, the prevalence of RA was also high in the patient group before THR.

Some studies have described the possible effects of the ion release of metal-on-metal implants on fetal health. Chromium and cobalt have been shown to be toxic, but it is believed that the increased blood metal ion concentration remains below teratogenic levels. The placenta also prevents a large proportion of the ions from entering the fetal circulation [18,20]. Although the concentrations of metal ions may remain below teratogenic levels, the slightly elevated fetal blood metal ion level might influence the growth of the fetus and be involved in preterm births or stillbirths. Metal-on-metal implants gained popularity in Finland in the year

Table 3
Univariable and adjusted Odds ratios (OR) with 95% confidence intervals (CI) for pregnancy outcomes. Data were adjusted by the following variables: maternal age at delivery, smoking during pregnancy and maternal rheumatoid arthritis.

	Stillbirth OR (95% CI)	Preterm OR (95% CI)	SGA OR (95% CI)	LBW OR (95% CI)
Univariable	3.52 (1.05–11.81)	3.31 (2.07–5.30)	3.21 (1.78–5.79)	4.67 (2.77–7.87)
Adjusted*	2.72 (0.58–12.67)	3.58 (2.03–6.30)	2.83 (1.35–5.93)	4.79 (2.56–8.97)

LBW = low birthweight, SGA = small for gestational age.

Table 4
proportions of obstetric variables in attempted vaginal deliveries for the patient group and the control group.

	Patient group		Control group		P
	n	%	n	%	
Total number	135		1293		
Mode of delivery					
spontaneous vaginal	93	68.9	1056	82.1	<0.001
vacuum or forceps extraction	3	2.2	84	6.5	0.05
emergency cesarean section	39	28.9	150	11.6	<0.001
labor analgesia					
epidural	23	17.0	334	25.8	0.03
spinal	2	1.5	30	2.3	0.53
paracervical	18	13.3	219	16.9	0.28
amniotomy	33	24.4	516	39.9	<0.001
oxytocin augmentation	39	28.9	467	36.1	0.10
episiotomy	28	20.7	372	28.8	0.05
manual placental removal	1	0.7	15	1.2	0.66
uterine curettage	1	0.7	18	1.4	0.53

2000 and were widely used for the following 10 years. In this study, only the rate of SGA was significantly higher among metal-on-metal implants compared with non-metal-on-metal implants, but the same trend was also noted in other outcome measures. However, the number of patients with metal-on-metal THR was low in this study. Furthermore, no information on maternal metal ion levels was available.

The intended modes of delivery differed between groups. Women in the THR group had more elective CS and fewer trials of labor. One explanation for the higher rate of elective CS could be that patients with a replaced hip opt to have elective CS because of a possible fear of damaging the THR implant and negatively affecting the delivery outcome in vaginal delivery [10,13,15]. Women in the THR group already had higher CS proportions before THR compared with the control group, which might be explained by their underlying diseases. A German cohort study showed that women with chronic diseases were more likely to deliver by CS than healthy referents [23].

The trials of labor were more likely to result in acute CS compared with the control group. It remains unclear whether this finding was because of abnormalities in cardiotocography or prolonged labor as this information was not available. It is also possible that not all THR patients classified as having a trial of labor were really opting for vaginal delivery. The small percentage of epidural analgesia and amniotomies after THR may be explained by the possibility that a considerable number of parturients in that group had actually planned elective CS, but it had been converted to emergency CS for reasons such as early onset of labor. Our results differ from those of the largest previous study by Sierra et al. who observed a total of 47 deliveries after THR and suggested that the percentage of CS (35.0%) in their patient series did not differ from national levels [11]. A couple of smaller patient series also reported similar CS rates compared to national rates in their studies [28–30], while some smaller studies have reported increased rates of CS (41.1%–100%) [10,13,15]. However, none of these previous studies have had control groups without THRs.

One of the main strengths of this study is the large, nationwide study population with long study period. A further strength is that this is also the first study to compare post-operative deliveries to both preoperative deliveries and matching controls. Moreover, a register-based study design further eliminates any possible recall-bias. One of the benefits of these registers is their good coverage so that the data represents well the defined population. The register data are routinely collected using structured forms with nationwide instructions that reduce possible reporting bias.

A long study period is one complicating factor when analyzing deliveries and neonatal outcomes. During the 20-year study period, delivery methods and neonatal care changed, as did the medications used for the treatment of RA. Moreover, there were some important missing variables in the MBR. For example, information on previous preterm deliveries or previous SGA children was not available. In addition, no information on body mass index was recorded before 2004, and the register data only had information on 1-minute Apgar-scores, since 5-minute scores only became part of the register in 2004. Also, durations of labor stages were not found in most of the cases, since they also became part of the register in 2004.

According to the findings of this study, adverse pregnancy outcome (preterm birth, LBW, SGA and stillbirth) are more common in women who have undergone THR. As a result, such women are more likely to have elective and emergency cesarean sections after THR. Further studies with combined multinational registries would be needed to confirm these novel findings.

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Conflict of interest statement

None of the authors have any potential conflicts of interests to declare

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