Increased Risk of Pregnancy Complications After Stroke

The FUTURE Study (Follow-Up of Transient Ischemic Attack and Stroke Patients and Unelucidated Risk Factor Evaluation)

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Background and Purpose—The study goal was to investigate the prevalence of pregnancy complications and pregnancy loss in women before, during, and after young ischemic stroke/transient ischemic attack.

Methods—In the FUTURE study (Follow-Up of Transient Ischemic Attack and Stroke Patients and Unelucidated Risk Factor Evaluation), a prospective young stroke study, we assessed the occurrence of pregnancy, miscarriages, and pregnancy complications in 223 women aged 18 to 50 years with a first-ever ischemic stroke/transient ischemic attack. Pregnancy complications (gestational hypertension, diabetes mellitus, preeclampsia, and hemolysis, elevated liver enzymes, low platelet count syndrome) were assessed before, during, and after stroke using standardized questionnaires. Primary outcome was occurrence of pregnancy complications and the rate of pregnancy loss compared with the Dutch population. Secondary outcome was the risk of recurrent vascular events after stroke, stratified by a history of hypertensive disorder in pregnancy.

Results—Data were available for 213 patients. Mean age at event was 39.6 years (SD=7.8) and mean follow-up 9.5 years (SD=8.5). Miscarriages occurred in 35.2% and fetal death in 6.2% versus 13.5% and 0.9% in the Dutch population, respectively ($P<0.05$). In nulliparous women after stroke (n=22), in comparison with Dutch population, there was a high prevalence of hypertensive disorders in pregnancy (33.3 versus 12.2%; $P<0.05$), hemolysis, elevated liver enzymes, low platelet count syndrome (9.5 versus 0.5%; $P<0.05$), and early preterm delivery <32 weeks (9.0 versus 1.4%; $P<0.05$). In primi/multiparous women (n=141) after stroke, 29 events occurred (20-year cumulative risk 35.2%; 95% confidence interval, 21.3–49.0), none during subsequent pregnancies, and a history of a hypertensive disorder in pregnancy did not modify this risk (log-rank $P=0.62$).

Conclusions—When compared with the general population, women with young stroke show higher rates of pregnancy loss throughout their lives. Also, after stroke, nulliparous women more frequently experienced serious pregnancy complications. **(*Stroke*. 2018;49:877-883. DOI: 10.1161/STROKEAHA.117.019904.)**

Key Words: fetal death ■ hypertensive disorders in pregnancy ■ preeclampsia ■ pregnancy ■ stroke

Each year, 16 to 59 per 100 000 women of childbearing age are affected by stroke,[1] which amounts to an estimated 180 000 women with ischemic stroke per year in Europe. Apart from the acute disabling stroke symptoms, all of a sudden, these young women are confronted with lifelong consequences[2] and limitations occurring in a period of life during which plans about starting a family are being made. Difficulties in taking these decisions are fuelled by a lack of knowledge on the risks of future pregnancy complications after stroke in women. It is known that pregnancy and the puerperium itself are associated with an increased risk of cerebrovascular disease caused by pregnancy-related disorders such as gestational hypertension and preeclampsia.[3,4] Because of a clear relationship between hypertensive disease during pregnancy and the increased risk of maternal cardiovascular disease (CVD) later in life,[4–6] it has been speculated that a common cause such as endothelial dysfunction may play a role.[7,8] It is, therefore, our hypothesis that women with stroke

Received October 26, 2017; final revision received January 2, 2018; accepted January 29, 2018.

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have an increased risk of future pregnancy complications. We investigated the frequency of pregnancy complications, miscarriages, and fetal death before, during, and after a first-ever transient ischemic attack (TIA) of stroke at young age and compared this with the general Dutch population. As a secondary outcome, we investigated whether a history of serious pregnancy complications increases the risk of a recurrent vascular event after a first-ever ischemic stroke/TIA.

Methods

Study Design

This study is part of the FUTURE study (Follow-Up of Transient Ischemic Attack and Stroke Patients and Unelucidated Risk Factor Evaluation), a single-center prospective cohort study on risk factors and prognosis of young patients with TIA, ischemic stroke, and intracranial hemorrhage. We used the same methodology as used in our previously published study.[9] In short, the FUTURE study comprises all consecutive patients with a TIA, ischemic stroke, or intracranial hemorrhage, aged 18 to 50 years, admitted to the Radboud University Medical Center from January 1, 1980, until November 1, 2010. For the present study, we included only women with first-ever TIA or ischemic stroke who reported they had been pregnant at least once. Exclusion criteria were cerebral venous sinus thrombosis and retinal infarction. TIA was defined as rapidly evolving focal neurological deficit, without positive phenomena such as twitches, jerks, or myoclonus, with vascular cause only and persisting for <24 hours. Stroke was defined as focal neurological deficit persisting for >24 hours. The Medical Ethics Committee of Arnhem-Nijmegen, the Netherlands, approved the study. All participants gave written informed consent. The data that support the findings of this study are available from the corresponding author on reasonable request.

Baseline Assessment

Information on demographics, National Institutes of Health Stroke Scale score, and cardiovascular risk factors was collected in a structured manner. A history of cardiovascular risk factors was determined by information on medical history or diagnosis at the time of index event; definitions of risk factors have been described earlier.[2]

Assessment of Pregnancy Complications and Outcome

During follow-up in November 2015, all eligible patients were contacted by telephone by a trained investigator. Structured questionnaires were used to assess the number of children, date of birth, and the occurrence of pregnancy complications, for example, gestational hypertension, preeclampsia, hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, gestational diabetes mellitus, preterm delivery, miscarriages, and fetal death. Patients who could not be contacted by telephone were sent a questionnaire by mail or via general practitioner.

Primary outcome was the occurrence of any pregnancy complication, and these are defined as follows:

1. Gestational hypertension as an elevated blood pressure after 20 weeks of gestation (systolic ≥140 mm Hg and diastolic ≥90 mm Hg), measured at 2 different times in a woman with a normal blood pressure before pregnancy.[10]
2. Preeclampsia as the combination of gestational hypertension with proteinuria (≥300 mg/24 h).[10]
3. HELLP syndrome as the combination of hemolysis, elevated liver enzymes, and thrombocytopenia.
4. Preterm delivery as delivery before 37 weeks of gestation[11] and divided into iatrogenic (induction of labor or cesarean delivery for medical reasons because of fetal or maternal disease such as HELLP, preeclampsia, or growth restriction) and spontaneous (without an apparent cause).[12]
5. Gestational diabetes mellitus as hyperglycemia diagnosed during pregnancy.[13]
6. Miscarriage as spontaneous embryonic or fetal death <16 weeks of pregnancy, fetal death as spontaneous fetal death ≥16 weeks of pregnancy, or death within 24 hours after delivery.[14] Induced abortions were not taken into account.

Other Variables at Follow-Up

Secondary outcome was the risk of any vascular event after stroke, stratified by the occurrence of pregnancy complications. During the telephonic assessment, we identified the occurrence of recurrent vascular events (stroke or other arterial event, eg, myocardial infarction or cardiovascular procedure). In case of a reported vascular event, medical records were retrieved from their treating physicians and verified by a neurologist or a cardiologist.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows version 22.0 (IBM, Corp, Armonk, NY). Baseline characteristics were presented as means or medians for data with a normal or non-normal distribution, respectively. On the basis of the date of stroke/TIA and date of birth of the children, patients were divided into 3 groups: patients who experienced stroke/TIA before their first pregnancy of a live-born child (group 1, nulliparous); after ≥1 pregnancies (group 2, primi/multiparous); or during pregnancy or postpartum, defined as within 6 weeks after delivery (group 3, gravidas).[15] For population-based characteristics of pregnancy (such as mean age at first gravidity, number of children per woman), we consulted the Central Bureau of Statistics of the Netherlands.[16] Prevalence of pregnancy complications within the Dutch reference population was assessed with the aid of Perined—a registry annually describing the overall outcome, morbidity, and mortality of pregnancy between 1999 and 2012 in 2 517 916 women and 2 564 530 live and stillborn children.[17] For early miscarriages (which occur more often subclinical) and for HELLP syndrome, Perined has insufficient data; to allow for comparison of our data with population data, we used the most reliable epidemiological data from other, in part, Dutch large cohorts.[18–21] A Fisher exact test was used to compare the incidence of pregnancy complications in nulliparous women to the Dutch population.

As a secondary outcome, we assessed the cumulative risk of recurrent vascular events in women with a history of hypertensive disorders in pregnancy (preeclampsia and hypertension) and HELLP syndrome versus those with uncomplicated pregnancies using Kaplan–Meier survival analyses. Using the same analyses, we calculated the cumulative risks of any vascular event in 3 subgroups based on the severity of the complication: those with a history of a more severe pregnancy complication (preeclampsia and HELLP) versus those with gestational hypertension only versus women with uncomplicated pregnancies. P values <0.05 were considered significant.

Results

Two hundred and thirteen female patients completed follow-up assessment on vascular events and pregnancy complications (Figure). Baseline characteristics are shown in Table 1.

Of 210 women, 569 pregnancies resulted in 425 live births (in 3 women, the number of pregnancies was unknown). Maternal age at birth of a first child did not significantly differ between groups of primi/multiparous (n=163), nulliparous (n=22), or gravidas (n=20; Table 2). All pregnancy complications were equally reported in all groups. Overall, ≈40% of the women experienced at least one pregnancy complication (Table 3). Miscarriage was the most frequent complication (total n=75, 35.2 versus 13.5% in population;[19] P<0.05); 6.1% of women with a stroke (either before or after pregnancy) experienced a fetal death in their life, whereas this proportion was 0.9% in the Dutch population from 1999 to 2012, implicating a 6-fold higher incidence (P<0.05).[22,23] 5.5% of

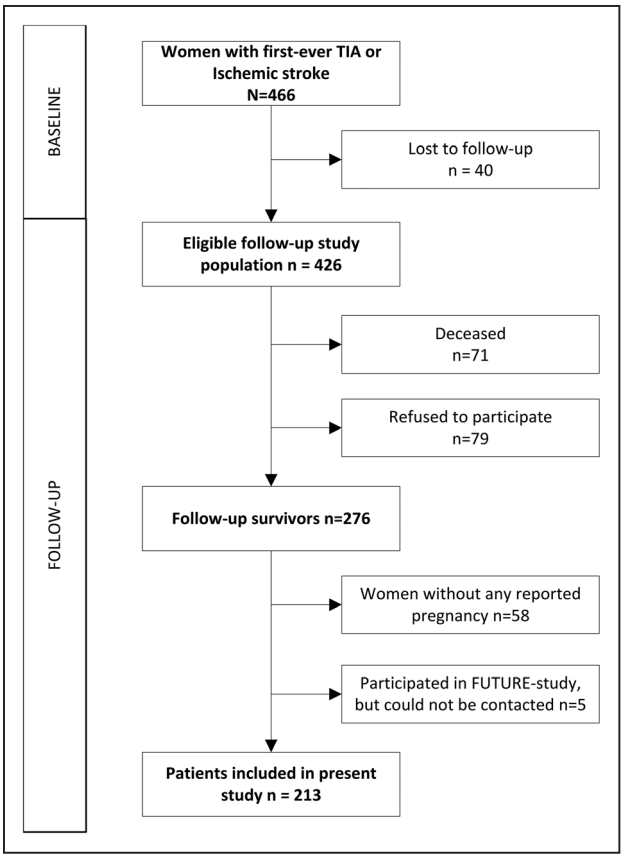

Figure. Flowchart of study population. FUTURE indicates Follow-Up of TIA and Stroke Patients and Unelucidated Risk Factor Evaluation; and TIA, transient ischemic attack.

women experienced ≥3 miscarriages, which is a 5-fold higher incidence compared with the estimated 1% among the general population (*P* value could not be calculated; only percentages are available).[17,21]

Pregnancy Complications After Stroke in Nulliparous Women

Thirty percent of nulliparous women experienced at least 1 complication during subsequent pregnancies after stroke (Table 3); 33.3% experienced hypertensive disorders in pregnancy as opposed to 12.2% in the general Dutch population, implicating a 3-fold higher incidence ($P<0.05$). Prevalence of HELLP was 20-fold higher (9.5 versus 0.5%; $P<0.05$) when compared with the general Dutch population.[10,20] Early preterm delivery <32 weeks occurred in 9.0% of all pregnancies compared with 1.4% in the general Dutch population ($P<0.05$),[23] with HELLP or preeclampsia being the cause in 50% of cases.

Recurrent Vascular Events

In primi/multiparous women after stroke, 29 recurrent vascular events occurred; 12 events (6 ischemic strokes and 6 other arterial event) in 46 women (26.0%), with hypertensive disorder/HELLP in pregnancy versus 17 events (11 ischemic strokes, 1 intracranial hemorrhage, and 6 other arterial event) in 95 women (17.9%) with uncomplicated pregnancies. The cumulative risk of recurrent cardiovascular events after

Table 1. Baseline Characteristics of Women With Young Stroke

	Total	Primi/ Multiparous*	Gravidas†	Nulliparous‡
N (%)	213§	163 (76.5)	20 (9.4)	22 (10.3)
Mean age at the time of event, y (SD)	39.6 (7.8)	42.2 (5.6)	33.1 (2.9)	24.8 (4.4)
Median NIHSS score at admission (IQR)‖	2 (0–5)	2 (0–5)	1 (0–8)	2 (0–3)
Mean follow-up time, y (SD)	12.7 (8.7)	11.8 (8.3)	14.8 (10.0)	17.9 (9.4)
mRS score at discharge, n (%)				
mRS 0–2	184 (86.4)	142 (87.1)	16 (80.0)	20 (90.9)
mRS 3–5	29 (13.6)	21 (12.9)	4 (20.0)	2 (9.1)
Stroke subtype, n (%)				
TIA	81 (38.0)	61 (37.4)	11 (55.0)	7 (31.8)
Ischemic stroke	132 (62.0)	102 (62.6)	9 (45.0)	15 (68.2)
Decade of event, n (%)				
1980–1989	36 (16.9)	23 (14.1)	5 (25.0)	7 (31.8)
1990–1999	42 (19.7)	28 (17.2)	6 (30.0)	6 (27.3)
2000–2010	135 (63.4)	112 (68.7)	9 (45.0)	9 (40.9)
TOAST, n (%)				
Atherothrombotic stroke	16 (7.5)	13 (8.0)	0 (0)	2(9.1)
Likely atherothrombotic stroke	33 (15.5)	31 (19.0)	0 (0)	1 (4.5)
Cardioembolic stroke	25 (11.7)	21 (12.9)	2 (10.0)	2 (9.1)
Lacunar stroke	17 (8.0)	13 (8.0)	1 (5.0)	2 (9.1)
Other defined	37 (17.4)	25 (15.3)	6 (30.0)	5 (22.7)
Multiple causes	3 (1.4)	2 (1.2)	1 (5.0)	0 (0)
Unknown cause	82 (38.5)	58 (35.6)	10 (50.0)	10 (45.5)
History of (cardiovascular) risk factors, n (%)				
Hypertension	66 (31.0)	54 (33.1)	7 (35.0)	4 (18.2)
Diabetes mellitus	9 (4.2)	8 (4.9)	1 (5.0)	0 (0)
Dyslipidemia¶	143 (67.1)	118 (81.4)	8 (66.7)	10 (62.5)
Smoking	98 (46.7)	72 (44.4)	6 (31.6)	13 (59.1)
Factor V Leiden	6 (2.8)	0 (0)	0 (0)	6 (3.7)
Systemic lupus erythematosus	6 (2.8)	1 (5.0)	2 (9.1)	3 (1.8)
Antiphospholipid syndrome	5 (2.3)	2 (10.0)	2 (9.1)	1 (0.6)

IQR indicates interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; and TOAST, Trial of ORG 10172 in Acute Stroke Treatment.

*Patients experiencing TIA/stroke after pregnancy.

†Patients with stroke during pregnancy or <6-wk postpartum.

‡Patients experiencing TIA/stroke before pregnancy of a live-born child.

§Eight patients (3.8%) never had a live birth and could not be placed in a group.

‖Range of scores between 0 and 21; in 1 patient NIHSS score was missing.

¶In 33 patients, information on hyperlipidemia was missing.

Table 2. Characteristics of Pregnancy and Pregnancy Loss Stratified by Parous Status at the Time of Stroke

Characteristics of Pregnancy	Total	Primi/Multiparous	Gravidas	Nulliparous	Dutch Population*
N	213†	163	20	22	2 517 916
Mean maternal age at first live-born child, y (SD)	27.4 (5.0)	26.6 (5.0)	30.5 (3.7)	30.1 (4.2)	30.6 (4.6)–31.0 (5.0)‡
Mean time from stroke to first pregnancy, y (SD)	N/A	N/A	N/A	5.6 (2.7)	N/A
No. of pregnancies per woman, median (range)§	2 (1–10)	2 (1–7)	3.5 (1–10)	2 (1–6)	N/A
No. of children per woman, mean (SD)	2.0 (0.9)	2.1 (0.9)	2.1 (0.9)	1.7 (0.7)	1.8–1.9
Twin pregnancies, % (n)	5.4 (11)	6.7 (11)	0 (0)	0 (0)	1.9–2.1
≥1 miscarriage, % of patients (n)‖,¶	35.2 (75)#	34.2 (55)	50.0 (10)	22.7 (5)	13.5**
2 times	8.5 (18)††	6.2 (10)	20.0 (4)	4.5 (1)	3.0††
≥3 times	5.5 (12)††	3.7 (6)	15.0 (3)	4.5 (1)	1.0††
≥1 fetal death, % of patients (n)‖,¶	6.1 (13)#	4.9 (8)	5.0 (1)	13.6 (3)	0.9
≥2 times	1.9 (4)	1.2 (2)	5.0 (1)	4.5 (1)	N/A

N/A indicates not available; NHG, Nederlands Huisarts Genootschap (translated: The Dutch College of General Pratitioners); and NVOG, Nederlandse Vereniging voor Obstetrie en Gynaecologie, (translated: Dutch Society of Obstetrics and Gynecology).

*Data from the Dutch Perinatal Registry or Dutch guidelines (NVOG/NHG) and the Central Bureau of Statistics of the Netherlands.[16]

†Eight patients never had a live birth and could not be placed in a group.

‡From 1999 to 2012.

§Of 1 woman, the number of pregnancies was unknown.

‖In primi/multiparous group, information on miscarriage was missing in 2 women and of fetal death in 1 woman.

¶Timing of pregnancy loss in relation to stroke was unknown.

#$P<0.05$: total group compared with Dutch population.

**Data from large Danish population-based registry (n=634 272).[19]

††Missing P values, χ^2 not applicable because of unavailable population-based absolute numbers.

stroke was 35.2% (95% confidence interval, 21.3–49.0) after 20 years, and a history of a hypertensive disorder/HELLP in pregnancy did not modify this risk (log-rank P=0.62). Those with a history of preeclampsia or HELLP (eg, a more severe pregnancy complication) had a higher, though not significant, cumulative risk of a recurrent event (74.4%, n=13) after 20 years of follow-up when compared with women with a history of gestational hypertension only (33.7%, n=33) or no complications during pregnancy (27.2%, n=95; P=0.086). Of those who experienced stroke/TIA during pregnancy or the postpartum period (n=20), 3 women had a recurrent ischemic stroke (20-year cumulative risk: 15.6%). Of women who were nulliparous at time of stroke (n=22), 4 women experienced a recurrent vascular event (20-year cumulative risk: 19.6%). None of abovementioned vascular events occurred during subsequent pregnancies.

Discussion

We found that obstetric prognosis after stroke is less favorable compared with the general population, as we found a higher prevalence of serious pregnancy-related complications such as (severe) hypertensive disorders in pregnancy and HELLP syndrome with consequently a high rate of early preterm delivery. Also, women who experienced a stroke/TIA at a fertile age showed high rates of (recurrent) miscarriages or fetal death throughout their lives, compared with the general population.

This is the first study that addressed risk of pregnancy complications in a large group of women after their stroke. Main strengths are an exceptional long-term follow-up and a high response rate with consequently detailed information on the course of pregnancy in these patients. However, there are some methodological considerations. First, because of the retrospective and patient-reported collection of pregnancy data, recall bias may have played a role. However, pregnancy and its complications such as birth (or loss) of a child are important life events that are generally remembered remarkably well. Also, it was previously demonstrated that using self-report versus professional reported outcome in pregnancy did not influence the outcome of the analyses performed.[24] Second, retrospectively collected data on pregnancy loss prevented us from collecting specific dates of miscarriages, which resulted in a lifetime prevalence. Third, as a consequence of the long-term follow-up, diagnostic guidelines and medication protocols may have changed over time. It is already known that secondary prevention lowers the risk of developing preeclampsia with 15%,[10] and because most patients likely received secondary prevention after stroke, this may have led to an underestimation of preeclampsia after experiencing stroke in comparison with the Dutch (untreated) population. Fourth, some of the population-based data we used from Perined should be interpreted with caution as Perined makes note of possible under-reporting of especially gestational diabetes mellitus (1.8%) and preeclampsia (0.5%). Current population-based Dutch cohorts suggest that the incidence of these conditions is estimated at 1.4 to 3.5% for preeclampsia[25,26] and 3.0 to 4.9% for gestational diabetes mellitus,[13,27] which is in accordance with our data. Finally, although our study is the largest of its kind, the absolute numbers of patients eligible to answer our outcome measures was small, and, therefore, the power is limited. This possibly results in an underestimation of the prevalence of pregnancy complications. Especially for our secondary outcome, our findings

Table 3. Frequency of Pregnancy Complications Stratified by Parity at the Time of Young Stroke

Pregnancy Complications*	Total†	Primi/Multiparous	Gravidas	Nulliparous	Dutch Population, %‡
N	205	163	20	22	1033649
Hypertensive disorders in pregnancy, % (n)§	30.3 (60)‖	29.3 (46)	35.0 (7)	33.3 (7)¶	12.2
Chronic hypertension persisting in pregnancy, % (n)	3.5 (7)‖	3.2 (5)	0 (0)	9.5 (2)¶	0.4
Gestational hypertension, % (n)	22.7 (45)‖	22.9 (36)	25.0 (5)	19.0 (4)	11.7
Preeclampsia, % (n)	7.3 (15)‖	6.4 (10)	20.0 (4)	4.8 (1)¶	0.5
HELLP syndrome, % (n)	6.1 (12)‖	3.8 (6)	20.0 (4)	9.5 (2)¶	0.5#
Gestational diabetes mellitus, % (n)	6.0 (12)‖	5.7 (9)	10.0 (2)	4.8 (1)	1.8‡‡
Preterm delivery, % (n)					
<37 wk	14.2 (29)‖	13.0 (21)	20.0 (4)	18.2 (4)	7.7
<32 wk	4.4 (9)	2.5 (4)	1.5 (3)	9.0 (2)¶	1.4
Cause of preterm delivery, % (n)					N/A
Iatrogenic	55.2 (16)	…	…	…	…
Intrauterine growth restriction	6.9 (2)	9.5 (2)	0 (0)	0 (0)	…
HELLP/preeclampsia	41.4 (12)	33.3 (7)	75.0 (3)	50.0 (2)	…
Hypertension	6.9 (2)	4.8 (1)	25.0 (1)	0 (0)	…
Spontaneous	10.3 (3)	…	…	…	…
Premature rupture of membranes	6.9 (2)	4.8 (1)	0 (0)	25.0 (1)	…
Premature labor with intact membranes	3.4 (1)	4.8 (1)	0 (0)	0 (0)	…
Other**	10.3 (3)	14.3 (3)	0 (0)	0 (0)	…
Unknown	24.1 (7)	28.6 (6)	0 (0)	25.0 (1)	…
Any complication, % (n)††	38.7 (77)	39.2 (62)	45.0 (9)	28.6 (6)	N/A

HELLP syndrome indicates hemolysis, elevated liver enzymes, low platelet count; and N/A, not available.

*Information on complications was missing in 1 nulliparous woman, except for preterm delivery, on hypertensive disorders in pregnancy in 6 women, on HELLP syndrome in 7, gestational diabetes mellitus in 5, and preterm delivery in 1 woman.

†Eight patients never had a live birth and were excluded from this table.

‡Data from Dutch Perinatal Registry.[17]

§Hypertensive disorders in pregnancy: preeclampsia and gestational hypertension.

‖$P<0.05$: total group compared with Dutch population.

¶$P<0.05$: nulliparous compared with Dutch population.

#Based on data from the Dutch HELLP foundation (https://www.hellp.nl/wat-is-hellppe/).

**Other: twin, scarring from previous caesarean section, and trauma.

††Any complication: gestational hypertension, preeclampsia, HELLP syndrome, gestational diabetes mellitus, and preterm delivery.

‡‡n=705838.

suggest that there may be a higher risk of recurrent vascular events after stroke for those who experienced preeclampsia or HELLP, but we were unable to reach significance (P=0.086). We found that 1 out of 3 women experience a serious pregnancy complication after stroke. Although there are no comparable studies focusing on prognosis of pregnancies after stroke in women, there is growing evidence that pregnancy complications such as gestational hypertension or preeclampsia are significantly associated with a doubled risk of CVD such as stroke.[6,28] Conversely, we now build on this notion by showing that a stroke preceding pregnancy is also related to higher frequency of pregnancy complications.

There are several explanations for this; one explanation is that the stroke and pregnancy complications share common risk factors, such as the classical cardiovascular risk factors such as dyslipidemia and hypertension.[7] In our cohort, 18% of nulliparous women were diagnosed with hypertension and 62.5% with dyslipidemia at the time of stroke. The antiphospholipid syndrome is also considered as a shared risk factor; this is supported by one other study that found an increased risk of pregnancy complications after stroke in patients with antiphospholipid syndrome.[29] They also found a high risk of pregnancy complications (8.7% fetal deaths, 34.8% preeclampsia, and 42.9% preterm delivery) after stroke and a nonsignificant higher risk of recurrent events in women with antiphospholipid syndrome and preeclampsia. Another explanation linking these conditions might be an unelucidated shared pathophysiology. Although the pathological processes involved in both pregnancy complications and CVD are still largely unknown, most studies focus on endothelial damage as a common denominator; in preeclampsia, for example, the inadequate maternal uterine spiral artery remodeling leads to inadequate uteroplacental circulation with oxidative stress, with not only local but also systemic inflammatory response

and endothelial dysfunction as a result.[7,30] It has been suggested that this leads to early-in-life (irreversible) endothelial damage to the systemic vascular system, which persists after pregnancy. This in turn might ultimately contribute to an increased risk of maternal CVD such as ischemic stroke later in life.[4,5] Vice versa, we found that women who experience stroke also have an increased risk of future pregnancy complications, which might be because of the same proposed endothelial dysfunction as common denominator, although more studies are needed to confirm this hypothesis. Not all pregnancy complications related to CVD are hypertensive disorders per se; other complications such as preterm delivery and fetal loss also have been associated with a higher risk of CVD. A recent study showed that preterm delivery increased the risk of CVD by a 2-fold, even when the preterm delivery was not preceded by hypertensive pregnancy complications.[31] Therefore, multiple miscarriages are also found closely linked to placental endothelial dysfunction,[32] and multiple pregnancy loss or fetal death doubles the risk of ischemic stroke.[33,34] Our cohort shows high rates of miscarriages (35.2%), multiple miscarriages (5.5%), and extreme high rates of fetal death (6.1%). Besides involvement of endothelial damage also shared risk factors play a role: late miscarriages >12 weeks are mostly because of maternal (usually vascular) risk factors,[18] and, therefore, in our cohort, 17 women experienced antiphospholipid syndrome, Factor V Leiden, or systemic lupus erythematosus, which are also risk factors for having (multiple) miscarriages.[35,36]

Our study provides insight in the frequency of pregnancy complications in women who experience a stroke at young age. Our data can be used to inform women with stroke who are seeking personalized advice on future pregnancies. We hereby addressed an important but yet underexposed topic of a higher frequency of serious pregnancy complications after a stroke at a young age. This may imply that women with a history of stroke should be put under intensive control of a gynecologist during pregnancy to prevent serious and possibly life-threatening pregnancy complications.

Sources of Funding

Professor de Leeuw received a clinical established investigator grant from the Dutch Heart Foundation (2014 T060); a VIDI innovational grant from the Netherlands Organization for Health Research and Development ZonMw [016-126-351]; and a research support from the Dutch Epilepsy Fund (2010–18).

Disclosures

None.

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Stroke. 2018;49:877-883; originally published online March 6, 2018;
doi: 10.1161/STROKEAHA.117.019904
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628