Maternal cerebrovascular accidents in pregnancy: incidence and outcomes

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Summary: Stroke occurring during pregnancy and the postnatal period is a rare but potentially catastrophic event. The aim of this study was to examine the incidence and outcomes of pregnancies complicated by maternal stroke in a single centre. This is a prospective study of over 35,000 consecutive pregnancies over a four-year period at the National Maternity Hospital in Dublin from 2004 to 2008; in addition we also retrospectively examined all cases of maternal mortality at our institution over a 50-year period from 1959 to 2009. We prospectively identified eight cases of strokes complicating pregnancy and the postnatal period giving an overall incidence of 22.34 per 100,000 pregnancies or 24.74 per 100,000 deliveries. There were no stroke-related mortalities during that time. Retrospective analysis of maternal mortality revealed 102 maternal deaths over a 50-year period, 19 (18.6%) of which were due to cerebrovascular accidents. In conclusion, strokes complicating pregnancy and the puerperium remain a rare event and though there appears to be evidence that the incidence is increasing, the associated maternal mortality appears to be falling.

Keywords: vascular accidents, stroke

INTRODUCTION

Stroke in pregnancy is a rare event but one with a potentially devastating outcome for both mother and baby. Maternal mortality rates are reported to be as high as 26%¹ with an estimated 42–63%^{2,3} of survivors having residual neurological deficit. Fetal mortality is also reported in up to 12% of cases.²

The true prevalence of stroke in pregnancy and the postnatal period is difficult to ascertain due both to the rarity of the occurrence and to variations in reporting. The incidence in the literature varies widely from three to 64 per 100,000 deliveries (Figure 1). Earlier reports quoted a lower incidence of 3–5 events per 100,000 deliveries.^{4,5} More recently in 1995 Sharshar *et al.*² reported an incidence of 4.6 haemorrhagic and an additional 4.3 ischaemic strokes per 100,000 deliveries. The highest incidence in the literature to date was published by Jaigobin *et al.*⁶ in 2000 from a series in Toronto. They quoted an overall incidence of 64 strokes per 100,000 deliveries. The authors did concede that, as a tertiary referral institution, their numbers were likely to be exaggerated; however, even following exclusion of cases of external referrals the authors still quoted an incidence of 26 per 100,000 maternities, a far higher incidence than earlier studies.

The literature suggests that the incidence of stroke in pregnancy is increasing. This would seem biologically plausible giving the changing demographics of most obstetric cohorts in the developed world. Obesity is a significant risk factor for both vascular and thrombotic disease⁷ and its incidence in pregnancy is increasing.⁸ Similarly, maternal age is also a risk

factor for stroke,⁹ and the predominant child-bearing cohort has now moved from 25–29 years to 30–34 years.¹⁰

We sought to clarify the incidence and outcomes of maternal stroke in pregnancy and the puerperium in our institution. Due to the rarity of the event we performed both a prospective analysis of cases over a four-year period and a retrospective review of maternal mortality in our institution from stroke in the last 50 years for comparison.

METHODS

We performed a prospective study of all cases of stroke during pregnancy and the first six weeks following delivery or miscarriage in the National Maternity Hospital, Dublin between January 2004 and January 2008. The National Maternity Hospital is a tertiary level referral institution delivering over 9000 women annually. All cases were identified as part of an ongoing audit of severe maternal morbidity at our institution.¹¹ We identified both cases which presented to our hospital at the time of stroke, and those who presented to general hospitals but were patients attending our institution for their maternity care. We also performed a retrospective analysis of all cases of maternal mortality at our institution from January 1959 to December 2008. Details of all maternal mortalities are contained and published annually in the hospital's annual clinical reports. Details of all mortalities during that time were recorded and the incidence and trends in maternal mortality from stroke were derived.

RESULTS

During the prospective study from January 2004 to January 2008, eight cases of maternal stroke during pregnancy or the

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Figure 1 Incidence of stroke in pregnancy in the literature. The quoted incidence over time of stroke in pregnancy in seven papers in the literature

postpartum period were identified from 35,803 pregnancies or 32,334 deliveries over 500 g, giving an overall incidence of 22.34 per 100,000 pregnancies or 24.74 per 100,000 deliveries. Of the eight cases, three were embolic and two were haemorrhagic; there were two cases of cerebral venous sinus thromboses and one internal carotid artery dissection.

Thrombotic infarcts

There were three cases of thrombotic stroke, all of whom had identifiable risk factors. The first case was a 26-year-old woman who was obese with a body mass index (BMI) at first antenatal consultation at 15 weeks gestation of 31 kg/m². Her mother had suffered a stroke at age 23 when she was three months postpartum, and the patient was a smoker of 10 cigarettes per day. She had regular and uncomplicated antenatal care. She attended a general hospital at 35 weeks gestation with a left sided hemiparesis and a magnetic resonance imaging (MRI) confirmed a vast diffuse area of infarction consistent with an embolic shower in the territory of the right middle cerebral artery. Neither transthoracic nor transoesophageal echocardiograms revealed any cardiac defect and both carotid and lower limb doppler studies were normal, as was a thrombophilia screen. She was treated with aspirin 75 mg once daily and enoxaparin 100 mg twice daily. Labour was induced at 38 weeks gestation. Low molecular weight heparin was stopped 12 hours prior to induction and she had an uncomplicated labour and delivery with epidural analgesia. A ventouse was performed to shorten the second stage and there were no postnatal complications. She received warfarin for three months postnatally and has a mild residual left upper limb weakness.

The second case of thrombotic stroke was in a woman with a prosthetic metal mitral valve secondary to a bacterial endocarditis. This case has been previously published.¹² In this case warfarin was stopped at six weeks gestation and low molecular weight heparin (tinzaparin 10,000 IU) commenced. At 10 weeks gestation she presented to another hospital with dysarthria and right upper limb paraesthesia. MRI brain demonstrated multiple infarcts in the cerebellar region and a cardiac echo confirmed thrombosis of the prosthetic mitral valve. Anti-Xa was subtherapeutic at 0.7 IU/mL. Warfarin was recommenced and the thrombosis resolved without need for valve replacement.

Warfarin was continued until 37 weeks gestation when low molecular weight heparin was recommenced. She was induced and delivered normally at 40 weeks gestation. Postnatally the patient was readmitted with a secondary postpartum haemorrhage related to an elevated international normalized ratio, but otherwise made a good recovery. She has no residual deficit.

The third case was in a 35-year-old woman who had had two previous uncomplicated term deliveries. Her family history was significant for a half sister with a heterozygous Factor V Leiden deficiency, her father had a myocardial infarction age 50 and her grandmother had suffered a stroke in her 50s. She presented to a general hospital with left arm weakness at five weeks gestation prior to finding out she was pregnant. A computed tomography (CT) brain was normal but MRI confirmed a right parietal lobe infarct. Transoesophageal echocardiogram was normal. She was treated with aspirin 75 mg once daily and prophylactic low molecular weight heparin and had a spontaneous delivery at term with no complications. She has no residual deficit.

Haemorrhagic strokes

There were two cases of haemorrhagic stroke in our series, neither of whom had any identifiable risk factors.

The first case was in a 32-year-old woman in her second pregnancy. She had an uncomplicated antenatal course. She attended in spontaneous labour at 41 weeks gestation. She had an eight-hour labour of which 90 minutes was in the second stage. Two hours following delivery she complained of nausea and a headache. She was normotensive throughout. She became agitated and then progressively weak and ultimately comatose. She was transferred to a tertiary referral general hospital where a CT brain revealed a large intracerebral bleed in the basal ganglion with extension into both lateral, third and fourth ventricles. MRI angiogram was performed, which did not reveal any intracranial aneurysm or vascular malformation. Following discharge from intensive care she was transferred to a rehabilitation unit. She has a residual hemiplegia. The second case of haemorrhagic stroke was in a 31-year-old woman who had had two previous uncomplicated term deliveries. She had an uneventful pregnancy until 33 weeks gestation when she had a sudden collapse at home and was brought by ambulance to a tertiary level general hospital with neurosurgical expertise. CT brain confirmed a subarachnoid haemorrhage. She was delivered by emergency caesarean section. She has some residual deficit but is able to care for her child independently.

Cerebral venous sinus thromboses

There were two cases of stroke secondary to cerebral venous sinus thromboses in two women with remarkably similar risk factor profiles.

The first case was in a 37-year-old in her third pregnancy. Both of her previous pregnancies had been complicated by pregnancy-induced hypertension. She was morbidly obese with a BMI at first antenatal consultation of 40.5 kg/m². She was an ex-smoker having discontinued six months previously. She presented at five weeks gestation with a severe headache and left lower limb paraesthesia. MRI confirmed a left thalamic infarct. An MR venogram demonstrated a widespread venous

sinus thrombosis. She was initially anticoagulated with unfractionated heparin with good clinical result. She was treated with low molecular weight heparin for the remainder of her pregnancy. She developed preeclampsia at 36 weeks gestation and had an uncomplicated delivery at 38 weeks following induction of labour. She has no residual defect.

The second case related to venous sinus thrombosis was in a 34-year-old with a history of preeclampsia in two previous pregnancies. She had a BMI of 40 kg/m². She presented to a general hospital at nine weeks gestation with a severe headache. MRI brain confirmed a large left lateral venous sinus thrombosis. She was anticoagulated with low molecular weight heparin with good result. She had a spontaneous vaginal delivery at 39 weeks following induction of labour and received warfarin for three months postnatally. She made a full recovery.

Internal carotid artery dissection

There was one case of internal carotid artery dissection. This was in a 34-year-old attending our high-risk antenatal clinic due to a poor obstetric history. Her first pregnancy was complicated by severe preeclampsia necessitating preterm delivery at 33 weeks. In her second pregnancy she had an intrauterine demise at 20 weeks. In her third pregnancy she had hypertension and a placental abruption. She had no known thrombophilia. In this pregnancy she was commenced on aspirin 75 mg once daily which was discontinued at 34 weeks gestation. She was delivered at 35 weeks gestation by emergency caesarean section for suspected fetal distress. She presented 10 days following delivery reporting an episode of left arm weakness which had resolved. She reattended within hours with a similar episode and was transferred to a general hospital where a dissection of the internal carotid artery was confirmed.

Retrospective review of cases of maternal mortality

We performed a retrospective review of all cases of maternal mortality in our institution over the 50-year period from January 1959 to December 2008. During that time there were 102 maternal mortalities reported, of which 19 (18.6%) were due to cerebrovascular accidents.

There was a trend toward a reducing mortality from cerebrovascular accident with an incidence of 0.2 per 1000 deliveries in the five-year epoch from 1959 to 1963 compared with 0.025 from 1999 to 2003 and 0 in the epoch from 2004 to 2008 (Figure 2).

DISCUSSION

Stroke occurring during pregnancy or the postnatal period is an uncommon phenomenon. However, the incidence is increased in the pregnant compared with the non-pregnant population. The incidence of stroke in non-pregnant women aged 15–44 years has been reported to be 10.7 per 100,000 women years.¹³ In this age group it is more common in women than in men and women also have reportedly poorer outcomes in terms of long-term neurological outcome.¹⁴ There is also evidence that the incidence is increasing and the incidence in our series of 22.34 per 100,000 pregnancies would be in keeping with the series from Toronto by Jaigobin *et al.* At

Figure 2 Mortality from cerebrovascular accident per 1000 deliveries from 1959 to 2008. The mortality per 1000 deliveries from cerebrovascular accidents in five-year epochs from 1959 to 2008 inclusive

these rates, average maternity units delivering around 4000 women annually should expect to deal with at least one case of stroke in pregnancy annually, and obstetricians need to be prepared for the appropriate multidisciplinary management of such cases. The data from our retrospective analysis would suggest that the incidence of maternal mortality secondary to stroke appears to be reducing with no maternal death from stroke reported at our institution in the last eight years, or over 70,000 maternities. This is probably due to improvements in diagnostic imaging techniques and intensive multidisciplinary team management rather than to improvements in the obstetric management of these cases. However, it highlights the importance of easy access to multidisciplinary team input. Our addition of the 50-year retrospective analysis of over 400,000 maternities is useful in examining trends in mortality from stroke; however, our study is limited by our lack of morbidity data for this time period. Therefore, we are unable to comment on the incidence of stroke in pregnancy during this time period. As stroke in pregnancy is such a rare event with just eight cases identified in our prospective series of over 35,000 maternities, we feel the addition of this retrospective data worthy of inclusion.

Our series highlights important points for clinical practice. The majority of women in our case series had significant, identifiable risk factors for both coronary and cerebrovascular disease. Such cases should not only be managed as high risk for adverse obstetric outcome but should also be counselled about their risk both during pregnancy and beyond, of potentially serious vascular complications. Our series has highlighted that this may be of particular relevance in women with a history of hypertensive disease in pregnancy. Preeclampsia has been reported as a risk factor for both cerebral haemorrhage and non-haemorrhagic stroke.² Indeed, the Stroke Prevention in Young Women Study concluded that women with a history of preeclampsia are 60% more likely to have a non-pregnancy-related ischaemic stroke.¹⁵

Similarly our series has highlighted once more the maternal risk associated with the discontinuation of warfarin in women with prosthetic metal heart valves. This case highlights the importance of close monitoring of anticoagulation in pregnant women with metal heart valves. Pregnant women with mechanical prosthetic heart valves represent a very high risk. All metal valves are thrombogenic and pregnancy heightens this risk. Warfarin, which is the optimal treatment for the mother, is teratogenic, but unfractionated heparin has been

associated with a greater risk of thromboembolic events, thus making anticoagulation management a fine balance between what is best for mother versus what is best for baby. It is important to note that the pharmacokinetics of low molecular weight heparin change in pregnancy, so that doses appropriate outside of pregnancy may not reach therapeutic levels in pregnancy. Other pregnancy-specific risk factors for stroke have been described including postpartum cerebral angiopathy, characterized by reversible multifocal vasoconstriction of the cerebral arteries and amniotic fluid embolism. These were not encountered in our series.

CONCLUSION

In conclusion, stroke in pregnancy is a rare event. It is associated with a number of risk factors that are known, and, for the most part, are modifiable. Despite the potential for a devastating outcome, when appropriately managed, it can be associated with both good maternal and perinatal outcome.

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Ethical approval: Ethical approval was not required as this was an analysis of existing hospital data.

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