

MATERNAL DEATHS DUE TO CEREBRO-VASCULAR CAUSES*

by

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Although the 'obstetric' causes of maternal deaths have been very extensively studied by obstetricians, some 'medical' conditions causing maternal morbidity and mortality, such as cerebrovascular disease, have perhaps not received as much attention as they deserve.

The preliminary results of investigations conducted by the Medical Research Council and other organisations in the U.K., to examine the possible association of oral contraceptives and thromboembolism, have suggested that a woman taking oral contraceptives incurred 'a slightly increased risk of developing thromboembolic disorders, but that the risk is small and less than that which arises from the ordinary pregnancy and delivery which these contraceptives are intended to prevent' (Annotation, 1967). In order to ascertain whether such a statement is true also in India, where very widespread use of oral contraceptives is envisaged as a part of large-scale family planning programmes, it is necessary to esti-

mate the extent and nature of maternal mortality due to various acute vascular diseases under Indian conditions; among these, cerebrovascular accidents probably form the most important group.

It is not a very uncommon occurrence for a previously healthy woman, who has recently delivered, to present with a sudden onset of convulsions, headache, hemiplegia, coma or any combination of these symptoms. Indeed, Hippocrates is said to have been aware of this clinical problem (Stevens, 1954). The diagnosis considered first is usually eclampsia, but when the onset is more than 2 days after delivery, and when hypertension and albuminuria are absent, other conditions are likely: thrombosis of the cerebral veins or venous sinuses, subarachnoid or intracerebral hemorrhage, cerebral embolism, or thrombotic occlusion of a cerebral artery. An important aim of the present study was to ascertain the relative frequency of these different types of cerebrovascular accident as a cause of maternal deaths. Moreover, by concentrating mainly on those cases in which a definite diagnosis was obtained at autopsy, we hope to avoid the uncertainty inherent in purely clinical diagnosis.

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Thrombosis of Cerebral Veins or Venous Sinuses

The literature on this subject has recently been comprehensively reviewed (Carroll *et al*, 1966). They collected a total of 148 cases, 33% of which were fatal. The overall incidence of presenting symptoms were: paresis in 45%, severe headache in 34%, convulsions in 30%, speech disturbances in 24%, and drowsiness with confusion in 17%.

The reported incidence of cerebral venous thrombosis as a complication of pregnancy has varied from, 1 in 1966 pregnancies to 1 in 3000 (Goldman *et al*, 1964, Lorincz and Moore, 1962; Koller *et al*, 1958; Huggenberg and Kesslering, 1958). At the L.T.M.G. Hospital, 12 such cases were diagnosed over a 4 year period (1962-66). The condition is not uncommon in India; thus 21 cases (3 of them fatal) were seen at Patiala over a 4 year period (Prakash and Singh, 1960) and 40 cases (17 of them fatal) over a 4 year period in Kerala (Rao, 1966). The diagnosis was confirmed at autopsy in 3 of Rao's patients, while Prakash and Singh made no mention of autopsy findings in their fatal cases. Since, on an average, one-third of cases are fatal, the mortality of this condition could be expected to be of the order of 1 in 10,000 pregnancies.

Although some autopsy reports of cerebral venous thrombosis had appeared in the nineteenth century, (Tremoin, 1860; Behier, 1874; Virchow, 1883; Scougal, 1888; Collier, 1891), Carroll *et al* state that they could find no more than 34 autopsy

reports of the condition. In most instances the thrombosis affected the superior sagittal sinus, or the cerebral veins draining into it (particularly those in the vicinity of the precentral gyrus), or both. This was the case in the 3 autopsies reported by Martin and Sheehan (Martin and Sheehan, 1941), the 2 autopsies of Burt *et al* (Burt *et al*, 1951), and 2 of Rao's autopsied cases (Rao, 1966). However, in one of Rao's cases and one of ours (case 2) the lateral sinus was also affected.

The management of cerebral venous thrombosis is on medical lines, consisting of measures to reduce intracranial tension, such as concentrated magnesium sulphate enemas, intravenous infusions of mannitol or of hypertonic sucrose, and antibiotics. All our patients received these measures. The use of anticoagulants is controversial, and has been recently reviewed (Carroll *et al*, 1966). Although anticoagulants may possibly prevent extension of the thrombus in the affected veins or venous sinuses, on the other hand they could aggravate the focal hemorrhages so often seen in the infarcted areas of cerebral tissue.

Cerebral Hemorrhage

One of the main complications of eclampsia is intracranial hemorrhage. It caused 89 out of 533 deaths due to toxemia of pregnancy in one large series (Donnelly and Loch, 1954).

Only in recent years has it been realised that intracranial hemorrhage does occur also in non-eclamptic pregnant women. In one report of 16 cases of subarachnoid hemorrhage in

pregnant or puerperal women, only 2 patients had toxæmia of pregnancy (Cannell and Botterell, 1956). Nine of their patients had either cerebral arterial aneurysms or arterio-venous malformations, in 3 there was no obvious cause, and 2 other cases had superior sagittal sinus thrombosis and mycotic aneurysm due to bacterial endocarditis respectively. In another review of 34 instances of subarachnoid hemorrhage in non-eclamptic pregnancies, aneurysms and arterio-venous malformations caused 10, while 2 were due to neoplasms (Conley and Rand, 1951). It has been emphasised that in very few patients had intracranial hemorrhage occurred during labour; usually the onset had been either ante-partum or post-partum (Krieger, 1965). This suggests that the physical strain associated with labour has no direct role in precipitating the hemorrhage.

Cerebral Embolism

It is well known that cerebral emboli in young women are usually associated with mitral valve disease, with or without atrial fibrillation. We had one such patient (Case 14). Embolisation may also occur in women with congenital cardiac defects, either due to bacterial endocarditis or paradoxical embolisation, both of which hazards are more likely to occur during the puerperium than at other times. Both rheumatic valvular heart disease and congenital heart disease are usually easily diagnosed on auscultation of the heart, and thus cerebral embolism can be immediately differentiated from other cerebrovascular accidents. However, cerebral emboli can occur in puer-

peral cardiomyopathy (Walsh *et al*, 1965) which is not commonly associated with significant cardiac murmurs, and the embolic nature of the cerebral lesion in such patients is liable to be overlooked.

Cerebral Artery Thrombosis

Thrombotic occlusion of an artery supplying the brain (Carotid or vertebral-basilar or one of their major branches) seems to be excessively rare in association with pregnancy. Atherosclerosis is the commonest cause of such a lesion in elderly subjects, but in the child-bearing age group other conditions such as Takayasu's disease, polyarteritis nodosa, or occlusion of the cervical part of the internal or common carotid artery of obscure etiology, should be kept in mind. However, we have not come across such a case in pregnancy or puerperium. A few instances of Takayasu's disease in pregnancy have recently been reported (Burton, 1966; Emanuel *et al* 1966). An important recent study from Glasgow surprisingly shows that cerebral artery thrombosis is not uncommon in pregnancy and puerperium. They studied, by cerebral angiography, 23 pregnant or puerperal women over a 10 year period, who had "Carotid territory ischemia", defined by them as "any sudden dysfunction thought to involve the cerebral hemisphere". They demonstrated internal carotid artery occlusion in 5, middle cerebral artery occlusion in 10, other vascular abnormalities in 3, and no abnormality in 5. Seven of the 23 patients died, a mortality rate much higher than that of parallel series of non-pregnant women and of males stud-

ied by the same authors at the same hospital (Jennet and Goss; 1967.).

Meningitis, particularly tuberculous meningitis, has to be considered as an important differential diagnosis of cerebrovascular accidents in the puerperium, under Indian conditions. Meningitis is an extremely rare complication in pregnant or puerperal women in Western countries, and consequently is not generally mentioned in textbooks or review discussions on the diagnosis of puerperal cerebrovascular accidents. At the L.T.M.G. Hospital there were 4

deaths caused by pyogenic meningitis and 10 by tuberculous meningitis over a 6 year period (D'Cruz *et al*, 1967. Pyogenic meningitis is readily diagnosed by the turbid appearance and very high cell count of the cerebrospinal fluid. Tuberculous meningitis, however, can mimic thrombosis of the cerebral venous sinuses very closely, not only in its clinical picture of drowsiness, headache, neck rigidity, papilledema but also in the CSF picture. It is our experience that the history of severe headache and fever for several days preceeding the other

Case No.	Age	Diagnosis	Autopsy confirmation	Stage of pregnancy of death.	Associated conditions.
1.	30	Superior sagittal sinus thrombosis with infarction and hemorrhage in right temporal lobe.	Yes	Delivered 16 days previously.	
2.	20	Thrombosis of superior sagittal sinus and both lateral sinuses with secondary intracerebral hemorrhage.	Yes	Delivered 18 days previously.	
3.	25	Thrombosis of superior sagittal sinus and right lateral sinus.	Yes	Delivered 12 days previously.	
4.	28	Thrombosis of cerebral veins or venous sinus.	No	Delivered 20 days previously.	
5.	25	Thrombosis of cerebral veins or venous sinus.	No	Delivered 20 days previously.	
6.	25	Thrombosis of cerebral veins or venous sinus.	No	Delivered 17 days previously.	
7.	35	Right intracerebral hemorrhage, thrombosis of right cerebral vein.	Yes	Delivered 6½ weeks previously.	
8.	20	Subdural and subarachnoid hemorrhage left frontoparietal region.	Yes	8 months pregnant.	
9.	22	Subarachnoid hemorrhage right temporal region.	Yes	Delivered 7 months previously.	
10.	30	Subarachnoid hemorrhage right parietal region.	Yes	Delivered 16 days previously.	Pyometra.
11.	25	Subarachnoid and intracerebral hemorrhage right cerebrum; eclampsia.	Yes	Low forceps delivery still birth (7months) 1½ hrs. previously.	Eclampsia, brain abscess left cerebrum.
12.	24	Intracerebral hemorrhage right cerebral hemisphere.	Yes	Delivered 14 days previously	
13.	22	Cerebrovascular accident of uncertain etiology	No	Delivered 14 days previously.	Acute Nephritis.
14.	28	Cerebral embolism.	No	Spontaneous abortion (6 months) (8 days) previously.	Mitral Stenosis.

symptoms, and the presence of cranial nerve palsies, would favour the diagnosis of tuberculous meningitis. The incidence of maternal deaths due to cerebrovascular disease in various Indian and American series is shown in Table II. The relative frequency of the different types of cerebrovascular accidents cannot be definitely assessed in these series, since we do not know in how many instances the diagnosis of "Cerebral hemorrhage" Or "Cerebral thrombosis" was confirmed at autopsy.

Clinical Data

The case records of all hospital deaths in females between the ages of 12 to 50 years at the Lokmanya Tilak Municipal General Hospital over a 6 year period (1961-66) were scrutinised. The L. T. M. G. Hospital is a large charitable general hospital serving the north-eastern part of

Bombay city and adjacent suburbs. A total of 377 cases were classified as maternal deaths, having satisfied the following definition of maternal death (Klein *et al* 1958): "The death of any woman dying of any cause whatsoever, while pregnant or within 90 days of the termination of pregnancy, irrespective of the duration of the pregnancy at the time of the termination or the method by which it was terminated."

Fourteen of these deaths were due to cerebrovascular accidents, which thus constituted approximately 3.7% of all maternal deaths.

Cerebral Venous Thrombosis

Our 6 cases diagnosed as thrombosis of the cerebral veins or venous sinuses all manifested clinically in the second or third post-partum week. All passed through a stage of coma prior to death. The duration of

Authors.	Place	Period of observation	Total pregnancies	Maternal deaths.	Deaths due to Cerebrovascular causes.
Municipal Committee Report (1954).	Bombay	19½ Months	..	229	1 Cerebral hemorrhage.
Motashaw and Jadhav	Bombay	5 Years	..	218	1 Cortical thrombophlebitis. 1 Intracranial hemorrhage. 1 Pontine hemorrhage.
Kirlosker (1962)	Hyderabad	40½ Months	33,553	152	2 "Cerebral thrombosis".
Shastrakar and Devi (1962).	Nagpur	9 Years	14,564	550	2 Cerebral hemorrhage in toxemic women. 5 "Cerebral thrombosis".
Barno et al (1963)	U. S. A.	10 Years	..	493	23 Intracranial hemorrhage in non-toxemic women.
Lane and Andelman (1963)	U. S. A.	4 Years.	..	232	3 Cerebral hemorrhage in Toxemic women. 2 Cerebral hemorrhage in hypertensives of long standing. 8 Cerebral hemorrhages from aneurysms.
Llorens et al (1963)	U. S. A.	13 years	80,403	97	7 Cerebrovascular accidents in toxemic women. 5 Cerebrovascular accidents in non-toxemic women.

the illness and the clinical features that preceded loss of consciousness were variable. Mental confusion, together with abnormal speech and behaviour were prominent in 2 of our patients, while in the others fever, convulsions and headache were the chief presenting complaints. Pyramidal signs, as manifested by Babinski plantar response, rigidity of the limbs, ankle clonus, or exaggerated deep reflexes, were present in most patients, and were usually more marked unilaterally. Autopsy confirmation was available in 3 of the 6 cases:

Case 1: The superior sagittal sinus was thrombosed in the parietal region. The adjacent dura was inflamed and adherent to underlying brain tissue. There was subarachnoid as well as intracerebral hemorrhage in the right parietal region. The right parietal lobe showed many areas of softening.

Case 2: The superior sagittal sinus, both lateral sinuses, and some cortical veins were thrombosed. Small petechial hemorrhages were seen throughout the cerebral cortex. Clotted blood was seen in all the cerebral ventricles and aqueduct of Sylvius.

Case 3: Right sided lateral sinus and superior sagittal sinus showed thrombosis.

Our case 7 was unusual in that cortical venous thrombosis and massive cerebral hemorrhage were both present in the same patient. It is probable that the hemorrhage was secondary to the infarction and intense congestion produced by the cortical venous thrombosis. This patient presented with abnormal behaviour and convulsions. She became

progressively comatose and died 4 days later.

Autopsy: Cortical veins on the right cerebral hemisphere were thrombosed. Confluent areas of hemorrhage were seen in the right frontal and parietal lobes, and also in the midbrain. The hematoma in the substance of the right cerebrum was 4" x 3" in diameter.

Intracranial Hemorrhage

Cases 8, 9, 10, 11 and 12 were all between the ages of 20 and 30. Except for case 11, in whom a diagnosis of eclampsia was made because of the coexistence of hypertension (180/110 mm. Hg.) and massive albuminuria, all the 4 other patients were not hypertensive and did not suffer from toxæmia of pregnancy. In contrast to the patients with cerebral venous thrombosis, the onset of unconsciousness was very sudden in these 5 patients with intracranial hemorrhage. Inequality of the pupils and loss of the pupillary response to light were important clinical signs. Blood-stained cerebrospinal fluid was usually found on lumbar puncture. Neck rigidity may be present. Pyramidal signs might be bilateral or unilateral. Autopsies were performed in all 5 cases.

Case 8: A subdural haematoma 5" x 3" in diameter was seen in the left fronto-parietal region, and this had caused displacement of the cerebral hemisphere. Subarachnoid blood clots were present over the left cerebral surface. Within the uterus was a female foetus of 8 months gestation.

Case 9: Subarachnoid hemorrhage was seen over the right cerebral hemisphere, and had extended into

the substance of the cerebrum. There was softening in the right temporal lobe.

Case 10: Subarachnoid hemorrhage in the right parietal region was seen; the cerebral ventricles also contained blood. The right parietal lobe showed marked softening. The uterus was enlarged, with thickened walls and was filled with purulent matter.

Case 11: Subarachnoid hemorrhage over the right cerebral hemisphere extended into the substance of cerebrum. The ventricles of the brain were distended with blood clots. An abscess cavity 4" in diameter, containing necrotic matter mixed with blood clots, was found in the occipitoparietal region of the left cerebral hemisphere.

Case 12: Intracerebral hemorrhage was found in the right temporoparietal region, extending deep down towards the basal ganglia as well as posteriorly into the temporo-occipital region.

Case 13: had acute nephritis and severe hypertension. Ten days after delivery she had convulsions followed by unconsciousness and hemiplegia. The nature of the cerebrovascular episode is uncertain, since no autopsy was done.

Case 14: had mitral stenosis, and suddenly developed unconsciousness and hemiplegia 8 days after a spontaneous abortion. No autopsy was performed; the cerebrovascular lesion was probably embolic in nature.

Summary

Out of 377 maternal deaths at the Lokmanya Tilak Municipal General Hospital, 14 were diagnosed as cerebrovascular accidents. The diagnosis

was based on the autopsy findings in 8 cases. Thrombosis of cerebral veins and venous sinuses accounted for 6 instances, intracranial hemorrhage for 6, while in 1 patient, both the above conditions were present. One woman had cerebral embolism in association with mitral valve disease. The incidence of the various types of cerebrovascular accidents as a cause of maternal deaths is briefly discussed.

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