Epidemiology of pre-eclampsia and eclampsia at the KK Women's and Children's Hospital, Singapore

Tan K H, Kwek K, Yeo G S H

ABSTRACT

Introduction: The incidences and characteristics of pre-eclampsia (PE) and eclampsia in KK Women's and Children's Hospital (KKH), a tertiary obstetrical referral centre in Singapore, were studied.

Methods: The incidences and types of PE between July 1999 and June 2003 were derived from the pregnancy disease databases. The characteristics of women with PE in relation to the general obstetric population were analysed on the age, race, parity, types of delivery, gestation at delivery and mortality. Case records of eclampsia were analysed.

Results: A total of 2,213 (3.6 percent) out of 61,595 deliveries were complicated by PE between July 1999 and June 2003. Incidence rates for mild or unspecified PE, severe PE, eclampsia and PE superimposed on hypertension were 2.47 percent (1,518), 0.97 percent (599), 0.02 percent (10) and 0.14 percent (85), respectively. The incidence increased with multiple pregnancies: from 3.5 percent in singletons to 7.5 percent in twins, 19.4 percent in triplets and 25.0 percent in quadruplets. The Caesarean section rate for PE was 46.1 percent compared with 23.7 percent in the hospital population. The proportion of premature birth (<37 weeks) in PE was 31.0 percent and that of severe prematurity (<32 weeks) was 5.7 percent, while hospital population proportions were 9.8 percent and 1.3 percent, respectively. The perinatal mortality rate (PMR) of PE was 11.0/1,000 births (population PMR was 4.4/1,000 births). There were only ten cases of eclampsia out of 61,595 deliveries (1:6160) giving an incidence of eclampsia of 16.2/100,000 deliveries. There was no stillbirth, neonatal and maternal death among the eclamptic patients.

Conclusion: The incidence and outcome of eclampsia in KKH showed a significant reduction over the years due to improved obstetrical care. While PE is still common, eclampsia is now a very rare disease outcome.

Keywords: eclampsia, hypertension, maternal mortality, pre-eclampsia, pregnancy toxemia

Singapore Med J 2006; 47(1):48-53

Department of Maternal Foetal Medicine
KK Women's and Children's Hospital
100 Bukit Timah Road
Singapore 229899

Tan K H, MMed, FRCOG, FAMS
Senior Consultant

Kwek K, MMed, MRCOG, MRANZCOG
Consultant,

Yeo G S H, MBBS, FRCOG, FAMS
Chief of Obstetrics and Chairman, Division of Obstetrics & Gynaecology

Correspondence to:
Dr Kelvin Tan Kok Hian
Tel: (65) 6394 1011
Fax: (65) 6394 1017
Email: kh@tan.net

INTRODUCTION

Pre-eclampsia and eclampsia are diseases in pregnancy which contribute significantly to maternal and foetal mortality and morbidity. Pre-eclampsia decreases utero-placental perfusion, which puts the foetus at high risk for problems such as preterm birth and perinatal mortality. It may also lead to maternal hypertension and multisystemic organ dysfunction and damage, including eclampsia. We studied the incidences and characteristics of pre-eclampsia and eclampsia in KK Women's and Children's Hospital (KKH), a tertiary obstetrical referral centre in Singapore.

METHODS

Data from July 1999 to June 2003 were obtained from the KKH inpatient datawarehouse computer system (SAP/IS-H). In this system, each patient's details had been coded according to the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) at discharge. Hypertension was defined as a diastolic blood pressure of at least 90mmHg or a systolic blood pressure of at least 140mmHg, or a rise in the former of at least 15mmHg or in the latter of 30mmHg. These blood pressures must be manifested on at least two occasions six hours or more apart.

Pre-eclampsia (PE) was defined as the development of hypertension with proteinuria (presence of 300mg or more of protein in a 24-hour urine collection or a 1+ reaction on a standard urine dipstick) occurring after 20 weeks of gestation

Table I. Number of cases and incidence rates by types of pre-eclampsia for KK Women's and Children's Hospital from July 1999 to June 2003.

Preeclampsia and eclampsia	Jul-Dec 1999	2000	2001	2002	Jan-Jun 2003	Total
Types (No of cases)						
Mild PE	183	272	337	461	267	1,520
Severe PE	75	181	120	160	62	598
Eclampsia	0	3	4	3	0	10
PE superimposed on complicating pre-existing hypertension	8	3	19	40	15	85
Total PE cases	**266**	**459**	**480**	**664**	**344**	**2,213**
Total deliveries (KKH)	8,195	16,777	14,924	14,837	6,862	61,595
Type (Incidence %)						
Mild PE	2.23%	1.62%	2.26%	3.11%	3.89%	2.47%
Severe PE	0.92%	1.08%	0.80%	1.08%	0.90%	0.97%
Eclampsia	0.00%	0.02%	0.03%	0.02%	0.00%	0.02%
PE superimposed on complicating pre-existing hypertension	0.10%	0.02%	0.13%	0.27%	0.22%	0.14%
Total PE incidence	**3.25%**	**2.74%**	**3.22%**	**4.48%**	**5.01%**	**3.59%**

Table II. Comparison of pre-eclampsia cases with the general hospital population by age and incidence rates of different age groups.

Maternal Age (years)	PE population	%	Hospital population	%	Incidence rate (%)	Binomial 95% CI (%)
Unknown	0	0.00	9	0.0	–	
<20	40	1.80	2,481	4.0	1.6	1.2 - 2.2
20-24	201	9.10	9,156	14.9	2.2	1.9 - 2.5
25-29	558	25.20	21,249	34.5	2.6	2.4 - 2.9
30-34	705	31.90	18,739	30.4	3.8	3.5 - 4.0
35-39	551	24.90	8,333	13.5	6.6	6.1 - 7.2
40-44	149	6.70	1,573	2.6	9.5	8.1 - 11.0
>45	9	0.40	55	0.1	16.4	7.8 - 28.8
Total	**2,213**	**100.00**	**61,595**	**100.00**	**3.6**	**3.5 - 3.7**

CI: confidence interval.

in a woman whose blood pressure was previously normal. PE was categorised as either mild or severe. Severe PE was defined as PE with either a blood pressure greater than 160/110mmHg, or with severe biochemical and/or haematological disturbances. PE superimposed on pre-existing hypertension was defined as PE occurring in a woman with preexisting (before 20 weeks of gestation) hypertension. Eclampsia was defined as new-onset grand mal seizures in a pre-eclamptic patient.

An extraction of data on the general obstetric population and the PE cases, was done using the KK Hospital's datawarehouse computer program. The general population consisted of all women who delivered in KKH between July 1999 and June 2003. Incidence rates and trends for mild or unspecified PE (ICD-9 code 642.4), severe PE (ICD-9 code 642.5), eclampsia (ICD-9 code 642.6), and PE superimposed on pre-existing hypertension (ICD-9 code 642.7) were calculated. The characteristics of women with PE and the general obstetric population were analysed in relation to age, race, parity, types of delivery, gestation at delivery, birth weights and mortality.

Two-sided binominal 95% CI for the PE incidence rates in relation to age, race and parity were calculated. Chi-square test and p-value were calculated, when appropriate. Eclampsia cases derived from the database were further verified with the cases registered with KKH Eclampsia Registry

Table III. Comparison of pre-eclampsia cases with the general hospital population by ethnic groups and incidence rates of different races.

Race	PE population	%	Hospital population	%	Incidence rate (%)	Binomial 95% CI (%)
Chinese	1,155	52.2	32,958	53.5	3.5	3.3 - 3.7
Malay	760	34.3	17,953	29.1	4.2	3.9 - 4.5
Indian	164	7.4	6,266	10.2	2.6	2.2 - 3.0
Others	134	6.1	4,418	7.2	3.0	2.6 - 3.6
Total	**2,213**	**100.0**	**61,595**	**100.0**	**3.6**	**3.5 - 3.7**

CI: confidence interval.

Table IV. Comparison of pre-eclampsia cases with the general hospital population by parity and incidence rates of different parity.

Parity	PE population	%	Hospital population	%	Incidence rate (%)	Binomial 95% CI (%)
1	1,055	47.7	25,361	41.2	4.2	3.9 - 4.4
2	551	24.9	21,023	34.1	2.6	2.4 - 2.9
3	382	17.3	10,107	16.4	3.8	3.4 - 4.2
4	151	6.8	3,493	5.7	4.3	3.7 - 5.1
5	48	2.2	1,071	1.7	4.5	3.3 - 5.9
6	13	0.6	334	0.5	3.9	2.1 - 6.6
7	13	0.6	206	0.3	6.3	3.4 - 10.6
Total	**2,213**	**100.0**	**61,595**	**100.0**	**3.6**	**3.5 - 3.7**

CI: confidence interval.

(set up in 1995). The case records of eclampsia cases were traced and analysed. The incidences and outcomes of PE and eclampsia were derived from previous studies[1-8] and were compared.

RESULTS

A total of 2,213 (3.6%) out of 61,595 deliveries were complicated by PE between July 1999 and June 2003 (Table I). The annual rate of PE varied from 2.7% to 5.1% during this period. The incidence rate for mild or unspecified PE was 2.47% (1,518), while those for severe PE, eclampsia, and PE superimposed on pre-existing hypertension were 0.97% (599 cases), 0.02% (10 cases) and 0.14% (85 cases), respectively.

The risk of PE increased with maternal age from 1.6% below 20 years of age to 16.4% for 45 years and above ($p<0.0001$) (Table II). Malays had a higher PE rate (4.23%) than Chinese (3.50%), as shown in Table III ($p<0.0001$). The incidence of PE was high in primiparous patients (4.2%) with the lowest in patients of parity 2 (2.6%), as shown in Table IV ($p<0.0001$). The incidence of PE increased with multiple pregnancies from 3.5% in singletons (2,158 PE cases in the general singleton population of 60,917) to 7.5% in twins (48 PE cases in the general twin population of 643), 19.4% in triplets (six PE cases with general triplet population of 31 and 25.0% in quadruplets (one PE case out of four quadruplet deliveries).

The Caesarean section (CS) rate for PE cases was 46.1% (1,020 cases of 2,213) compared with the KKH general population CS rate of 23.7% (14,586 cases of 61,595) ($p<0.0001$). The instrumental (forceps and ventouse) vaginal delivery rate for PE cases was 14.8% (327 cases) compared with 9.0% (4937 cases) in KKH general population ($p<0.0001$). The proportion of prematurity (<37 weeks), severe prematurity (<32 weeks) and extreme prematurity (<28 weeks) in PE was 31.0% (686 cases), 5.7% (127 cases) and 1.1% (25 cases), respectively. In comparison, the population proportion was 9.8% (6,059 cases), 1.3% (822 cases) and 0.4% (267 cases), respectively, as shown in Table V.

There were 2,276 babies from all the PE cases of which 50 babies (2.2%) were less than 1,000g and 715 babies (31.4%) were less than 2,500g. In comparison, there were 62,311 babies in the general population of which 334 babies (0.5%) were less than 1,000g and 6,264 (10.1%) babies were less than 2,500g. The perinatal mortality rate (PMR) of PE was 11.0 per 1,000 births (25 cases) in contrast to population PMR of 4.4 per 1,000

Table V. Comparison of gestational age at delivery between pre-eclampsia cases and general hospital population.

Gestational age at delivery (weeks)	PE population	%	Hospital population	%
<24	0	0.0	16	0.0
24-27	25	1.1	251	0.4
28-33	205	9.3	1,170	1.9
34-36	456	20.6	4,622	7.5
>37	1,527	69.0	55,435	90.0
Unknown	0	0.0	101	0.2
Total	**2,213**	**100.0**	**61,595**	**100.0**

births (275 cases) (p<0.0001). Stillbirth rate was 8.3 per 1,000 births (19 cases), in contrast to population stillbirth rate of 3.3 per 1,000 births (204 cases) (p<0.0001).

There were only ten cases of eclampsia out of 61,595 deliveries (1:6,160) in KKH in 1999-2003 with the incidence of eclampsia in KKH at 16.2 per 100,000 deliveries in 1999-2003 (Tables VI and VII). The mean age of these ten cases was 28.4 years (range 22 to 39 years). Of these, eight patients were primiparae, one case of parity 2 and another of parity 4. Among the ten cases, there was a preponderance of Malays with six Malays (60%) (all antepartum cases) and four Chinese (40%) (one antepartum and three postpartum cases). Five of the ten cases (50%) did not have antenatal care in KK hospital. The mean gestation age for the six cases with antepartum eclampsia was 36.4 weeks (range 31 to 40 weeks). Of the seven antepartum cases, six had emergency lower segment Caesarian section (LSCS) and one had Neville Barns forceps delivery. Of the three postpartum cases, two cases had prior Caesarean section and one had a prior normal vaginal delivery. There was no stillbirth, neonatal and maternal death among the eclamptics in the most recent series.

DISCUSSION

There has been a number of Singapore studies of PE and eclampsia cases in KKH[1-8], which, as a tertiary referral hospital for obstetrics, is Singapore's largest maternity hospital (about 15,000 births annually) and was formerly the world's largest maternity hospital (more than 40,000 births in 1966). This current paper is the largest series of PE studied in Singapore. In a 1955 KKH study by Sheares[1], there were 501 cases of PE, essential hypertension and chronic nephritis accounting for 4.9% of deliveries. Exclusion of essential hypertension and chronic nephritis from Sheares'

Table VI. Outcome trends of eclampsia in KKH.

Period	1955		1990-1993		1994-1999		1999-2003	
	No	%	No	%	No	%	No	%
No of cases	77		27		63		10	
Incidence per 100,000 deliveries	338		45.3		67.2		16.2	
LSCS	23	29.9	24	88.9	44	71	8	80
Unbooked	74	96.1	9	33.3	24	38.7	5	50
Primiparity	45	58.4	16	59.3	40	64.5	8	80
Maternal Mortality	6	7.8	1	3.7	1	1.6	0	0
Stillbirths	4	5.2	0	0	6	9.7	0	0
Neonatal Deaths	16	20.8	0	0	0	0	0	0
Perinatal Mortality	20	26	0	0	6	9.7	0	0

Table VII. Trends of eclampsia in KKH.

Period	1955	1957	1968	1981	1990-1993	1994-1999	1999-2003
No. of cases	77	86	51	5	27	62	10
No. of deliveries	22,813	29,820	36,427	15,125	59,599	92,305	61,595
Incidence per 100,000 deliveries	3,37.5	288.4	140	33.1	45.3	67.2	16.2
Risk of eclampsia	1:296	1:348	1:715	1:3025	1:2207	1:1489	1:6160

Note: The 1981 study was confined only to the university unit of KKH.

study would mean that the actual incidence of PE was lower than 4.9%.

In the 1981 KKH study by Wong et al[6], there were 675 cases of hypertensive disorders out of 15,125 deliveries, accounting for an incidence of 4.5%. The criterion for inclusion in Wong et al's study was a diastolic blood pressure of 90mmHg during pregnancy, with or without proteinuria. Exclusion of cases without proteinuria (essential hypertension and non-proteinuric pregnancy-induced hypertension) from Wong et al's study would also mean that the actual incidence of PE was lower than 4.5%. These rates were comparable to the current rate of 3.6% for this series of PE cases in KKH (which excluded essential hypertension or transient hypertension) from 1999 to 2003. In contrast, the incidence of eclampsia in KKH showed a significant reduction trend (by 20-fold) from 337 per 100,000 deliveries in 1957 to 16.2 per 100,000 deliveries in 1999-2003. Eclampsia which used to occur more than once a week in KKH in the past, has become an extremely rare event in KKH, occurring only once or twice a year recently.

This is a large study based on the discharge diagnosis code (ICD-9-CM) of all 2,213 cases of PE (3.6%) out of 61,595 deliveries in our hospital between July 1999 and June 2003. A similar study[9] in United States (1979 to 1986), based on discharge diagnosis codes of sampled cases, showed a PE rate of 2.6% of all births. It is important to ensure the quality of discharge codes for such studies as a recent American study of 135 women[10] whose disease was coded as having PE or eclampsia, revealed that diagnostic (clinician) error was the most common reason for miscoding error in their centre.

In our hospital, regular audits and checks had been undertaken by senior staff relating to the quality of discharge summaries by junior doctors. There were also regular training for the doctors involved in these summaries and all new doctors, as part of routine orientation, were also briefed in detail on the topic of PE, including the definitions and diagnoses, as PE is a very important disease in our maternity hospital. This helped to ensure good quality of discharge diagnosis codes in our hospital. The discharge codes were also needed to be accurate as the codes affected the DRG and subvention payment system of the hospital. In addition, the PE discharge code data were cross-validated in audits with cases in our severe pre-eclampsia and eclampsia registries to ensure quality and accuracy.

Accurate ascertainment of eclampsia cases is necessary when documenting trends of PE care. KKH set up its Eclampsia Registry in November 1995, so as to accurately ascertain all eclampsia cases, and in particular, to avoid under-reporting of eclampsia cases. Prior to the setup of the Eclampsia Registry, cases might not have been judiciously reported or recorded. Cases for studies were culled retrospectively and manually from OT records and delivery records, and some eclampsia cases might be missed and not reported.

Thus the lower incidences of 33.1 per 100,000 deliveries in 1981 and of 45.3 per 100,000 deliveries from 1990 to 1993 compared to the higher rate of 67.2 per 100,000 deliveries from 1994 to 1999 (Chen et al[8]), were likely to be under-ascertainment. The 1981 study was also confined only to the university unit of KKH and thus would be subjected to further ascertainment bias.

The Eclampsia Registry, which was set up in November 1995, helped to ensure very accurate ascertainment of cases from 1995 onwards. Further analysis of the study of eclampsia cases from 1994 to 1999 by Chen et al revealed that a significant reduction in eclampsia incidence in KKH occurred after 1996[8]. The incidences (per 100,000 deliveries) were 101.3 (in 1995), 112.2 (in 1996), 56.4 (in 1997) and 19.1 (in 1998). There were only 10 cases of eclampsia (as confirmed by the Eclampsia Registry and also by the hospital database) out of 61,595 deliveries (incidence of 16.2 per 100,000 deliveries) in KKH between 1999 and 2003, reflecting a tremendous improvement in antenatal and perinatal care. We focused our attention on PE with the introduction of systematic audit, closer surveillance and increased medical education for doctors and staff involved in antenatal care of PE since 1996. The incidence has been brought down to the lowest ever level with adequate antenatal care (ensuring that pregnant women come for early and regular antenatal care), close surveillance using current prognostic tests judiciously and optimum timing of delivery with good neonatal care for premature babies.

In KKH, we have instituted the Perinatal High Risk Consult (HRC), which is a specialised service whereby maternal foetal medicine specialists, neonatalogists, obstetric physicians, social workers and obstetricians meet and discuss on the management of high-risk pregnancies on a twice-weekly basis. The HRC served as a focal point for the referral and the joint management of high-risk pregnancies, including PE, for over a decade from 1994 to 2004. Closer surveillance of PE cases, with the current prognostic tests as well as joint decision to determine the best time for delivery in the

interest of the foetus and the mother, coupled with the experience gained, has achieved very low rates of eclampsia while maintaining excellent perinatal and neonatal mortality and morbidity rates.

The outcome of eclampsia has also improved. Compared to earlier years where eclampsia was a major contributor to maternal and perinatal mortality, there was no stillbirth, neonatal and maternal deaths among the eclamptics in the most recent series. This eclampsia incidence rate of 16.2 per 100,000 deliveries is now among the lowest in reported literature for a tertiary maternity hospital. It is now rare for an obstetrics trainee to witness and manage an eclampsia case in our hospital. A concerted effort is now required to teach and maintain our trainees the necessary skills through frequent drills and various education modalities, so as to be able to optimally manage an eclampsia, should it occur.

There should be no room for complacency[11] in the management of PE. For example, despite modern obstetric care, the incidences of eclampsia in a Swedish tertiary hospital have steadily and significantly increased from 30/100,000 births (1973-79) to 62/100,000 births (1980-89) and to 109/100,000 births (1990-99)[12]. Continual audit and risk management strategies are needed to maintain optimal outcome. Malays, which formed 29.1% of KKH antenatal population, contributed to 34.3% of the PE cases and 60% of the eclampsia in this study. In Singapore, it is important to focus efforts on the Malay community and antenatal population to further improve antenatal care of PE and further reduce the eclampsia rate. Antenatal education needs to emphasise the necessity of early and regular antenatal follow-up.

In conclusion, the incidence of PE was 3.6% of total deliveries. PE risk was increased with age, primiparity, multiple pregnancy and Malay ethnicity. PE was associated with a higher CS rate, prematurity, low birth weight and higher perinatal mortality. The incidence of eclampsia was 16.2 per 100,000 deliveries in KKH in 1999-2003. While PE is still common with incidences remaining relatively static over the last half century, eclampsia has become a very rare outcome in Singapore with a 20-fold reduction in incidence. Concomitantly, the clinical outcome of eclampsia cases also showed significant improvement.

ACKNOWLEDGEMENT

We would like to acknowledge the support of Singhealth Cluster Research Project on High Risk Pregnancy Disease and Outcome Database SHS DD008/2001.

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