Upsala J Med Sci 83: 29–34, 1978

Studies on Toxaemia of Pregnancy with Special Reference to Blood Pressure

I. Incidence and Some Characteristic Features of the Mothers and Infants

H. ÅBERG, L. KARLSSON and S. MELANDER

From the Department of Internal Medicine and the Department of Obstetrics and Gynaecology, University Hospital, Uppsala, Sweden

ABSTRACT

An investigation was made of 150 women who were diagnosed at the Department of Obstetrics and Gynaecology, University Hospital, Uppsala in 1964–68 as having toxaemia of pregnancy. Eleven had eclampsia and the remainder pre-eclampsia. Toxaemia occurred in 0.88 % (average) of all parturients during the study period. Some characteristics of the mothers and their infants are reported. Thus, there were more instrumental deliveries in the toxaemia group than in the non-toxaemic patients delivered in the clinic. The maternal weight at delivery was also greater in the toxaemia group. The frequency of complications among the infants was higher in the group with toxaemia. There were more stillbirths, lower birth weights and more congenital malformations. With regard to blood pressure, almost identical pressures were noted in the eclamptic and pre-eclamptic groups, with one exception. The maximum blood pressure recorded during delivery was higher in the eclamptic than in the pre-eclamptic group (198/127 and 175/117).

INTRODUCTION

The term toxaemia of pregnancy includes the two disorders pre-eclampsia and eclampsia, which may be manifested during gestation or shortly after delivery. Pre-eclampsia is characterized by the appearance of two or all of the three conditions hypertension, oedema and proteinuria. In eclampsia, convulsions—and occasionally coma—occur in addition. The relation between pre-eclampsia and eclampsia is certainly in some cases a matter of degree rather than of different disorders (1). However, there are also differences between them (2). The pathogenesis is still not known in detail (3, 4, 5, 6).

These disorders have latterly attracted increasing interest—partly due to the association between contraceptive pills and hypertension. As early as in 1967 Laragh et al. reported on the occurrence of pill-induced hypertension (7). A further reason for interest in the long-term outcome of toxaemia of pregnancy is the effort in the community to find as many hypertensive individuals as possible and to treat them in order to improve cardiovascular health.

The purpose of the present investigation was mainly to evaluate the significance of toxaemia with regard to the future development of arterial hypertension. In this first report on our studies on this subject the incidence of toxaemia and some maternal and foetal findings at the time of delivery will be presented.

MATERIAL

The material comprised all women (total 150) with a diagnosis of pre-eclampsia or eclampsia and treated in the Department of Obstetrics and Gynaecology, University Hospital, Uppsala, in the period 1964–68. The criteria for the diagnosis of toxaemia were at least two of the three symptoms hypertension, oedema and proteinuria. Hypertension was diagnosed if several recordings above 140/90 mmHg were noted at rest in the supine position. The diagnosis of oedema was based on general swelling or oedema of the hands and/or face. Proteinuria was diagnosed if more than 1‰ (Esbach) protein was detected in the urine. A survey of the fulfilment of the various diagnostic criteria is given in Table I.

All diagnoses made during the period under study were checked by one of the authors (S. M.) at the time of diagnosis. He was not aware at that time, however, that the present investigation was to be carried out.

METHOD

The investigation was retrospective, which means that the cases under study were collected from the lists of

Table I. *The criteria for diagnosis of toxaemia of pregnancy, the incidence of toxaemia and the total number of births in 1964–68*

HT=hypertension, E=oedema and P=proteinuria

	Various criteria (*n*)					Cases with toxaemia *n*	Total no. of births *n*	Proportion toxaemia cases/total births (%)
	HT+P	HT+E	P+E	HT+P+E	Eclampsia			
1964	6	8	4	14	8	35	3 306	1.06
1965	8	6	5	10	0	30	3 274	0.92
1966	9	11	0	10	0	35	3 445	1.02
1967	5	4	1	15	1	26	3 450	0.75
1968	6	8	1	8	2	24	3 509	0.68
Total	34	37	11	57	11	150	16 984	0.88[a]

[a] Mean value for the period 1964–68.

diagnoses for the years in question. The chart for each woman with a relevant diagnosis was reviewed. For comparisons in some respects the total number of deliveries in the period 1964–68 was used, and in other respects a randomly selected material from the same Department in 1969. This latter control material was also used for another study (8). With regard to foetal malformations and congenital disorders the "normal" incidence was obtained from a special register in the Department of Paediatrics at this hospital. For statistical analyses the programs for means and standard deviations in a Hewlett-Packard (9100B) calculator were used.

RESULTS

During the period 1964–68 there was a falling trend in the incidence of toxaemia of pregnancy (Table I). Toxaemia occurred in an average of 0.88% of all parturients during the period under study. In 119 women only one episode of toxaemia had been recorded, and this occurred between 1964 and 1968. Of these women, 96 were primipara. Twenty-three women developed toxaemia after at least one normal pregnancy. The remaining 31 of the total 150 women with toxaemia had recurrent toxaemic pregnancies, one of them occurring within the study period (1964–68). Four women had toxaemia during three subsequent pregnancies. These figures must be considered as minimal, since not all women have been traced since 1968.

Table II gives some data from the toxaemia group in comparison with those of the randomly selected sample (8). The proportion of primiparas among the toxaemic women was almost twice as high as in the randomly selected sample. The mean age was almost the same for both groups. In spite of shorter gestation periods in the toxaemia group the maternal weights at delivery were higher than in the controls. Further, the mean duration of hospitalization was more than twice as long for the toxaemic women as for the women with a normal pregnancy.

In Table III the methods of delivery in the group of patients with toxaemia of pregnancy are compared with those used in the total deliveries at this hospital over the period 1964–68. It is seen that there were many more instrumental deliveries in the toxaemia group. Of the mothers with "vaginal" deliveries, many more received an oxytocin (Syntocinon®) infusion to initiate labour in the toxaemic group than in the controls.

Table IV shows the incidence of some concurrent diseases in the group of women with toxaemia.

Table II. *Some features of the toxaemia group compared with the randomly selected sample of women ("normals") registered at the maternity welfare clinic in Uppsala in 1969 (8)*

	n	Age (years)	Order of pregnancy		Duration of pregnancy (days)	Weight at delivery (kg)	Hospital stay (days)
			1	≥2			
Toxaemia group	150	26.4±6.1	96	54	273.0±16.4	75.9±14.8	17.9±11.0
Normals	299	25.6	159	140	283.3± 9.3	68.8[a]	7.3

[a] The body weight is calculated after 273 days (39 weeks) for the normals.

Table III. *Obstetrical data for the toxaemic women compared with those for the whole material of deliveries over the period 1964–68*

		Method of delivery, % of total		
	n	Vaginal	Vacuum	Caesarean section
Toxaemia group	150	72	15	13
Total material	16 984	94	4	2

Among symptoms considered typical for pre-eclampsia, it may be noted that fewer than one-third of the patients spontaneously reported headache or visual disturbances.

It is seen in Table V that there were more stillbirths, more congenital disorders and malformations and more infants with low birth weights among the infants of toxaemic mothers than among those of mothers in the total material. Only one malformation is given in the Table, but others also showed the same trend.

In Fig. 1 the mean blood pressures (BPs) are shown for all individual patients of the toxaemia group The BPs were almost identical in the eclampsia and pre-eclampsia groups except for the maximum BP recorded during the delivery, which was higher in the eclampsia group (198/127) than in the pre-eclampsia group (175/117).

Finally, in Table VI some laboratory results are given and compared with the normal limits for this hospital. Both the potassium and the sodium concentration may well have been influenced by the therapy given to some of these women (saluretics). In fact these laboratory reports should be viewed with great caution, collected as they are over a 5-year period.

Table IV. *A review of concurrent diseases complicating the toxaemia, and maternal symptoms*

Complicating diseases	No. of cases
Diabetes	4
Hypertension[a]	3
Renal disease	1
Epilepsy	2
Polio	1
Symptoms	
Headache[b]	33
Visual disturbances	4
Headache+visual disturbances	8

[a] Toxaemia superimposed on essential hypertension.
[b] Nine of 11 eclamptic women had headaches. These are not included here.

DISCUSSION

Differentiation between the various hypertensive states of pregnancy is difficult. The classification tends to be arbitrary. Therefore, data from different studies on toxaemia of pregnancy must be interpreted with some reservation when clinical criteria are the only bases for the differentiation. It is reasonable to assume that some contradictory data from studies on this disorder are attributable to heterogeneity of the materials in question.

The diagnostic shortcomings of the clinical criteria for the various types of hypertensive disorders during pregnancy have been well illustrated by kidney biopsies (9). These studies suggest that chronic renal diseases play a much more important role in the hypertensive states of pregnancy than has previously been believed.

The incidence of pre-eclampsia among obstetric patients admitted to hospitals in the United States is 6–7%. According to the same source of information (10) eclampsia is seen once in every 2000 pregnancies. In an earlier report by Pritchard & Stone

Table V. *Review of stillbirths, perinatal mortality (death within the first 7 days), number of infants with a low birth weight and infant malformations in the toxaemia group and in the total deliveries in the period 1964–68 (" normals")*

	Infants		Stillbirths		Perinatal mortality		Infant weight <2 500 g			Congenital malformations, CGS	
	Total	Twins	%	*n*	%	*n*	%	*n*	Mean (g)	%	*n*
Toxaemia group	157	7	1.3	2	1.9	3	16.6	26	3 172	1.3	2
Normals	17 132	148	1.0	176	0.8	133	4.4	754	3 487	0.1	21

CGS=Isolated cleft palate+cleft lip with or without cleft palate.

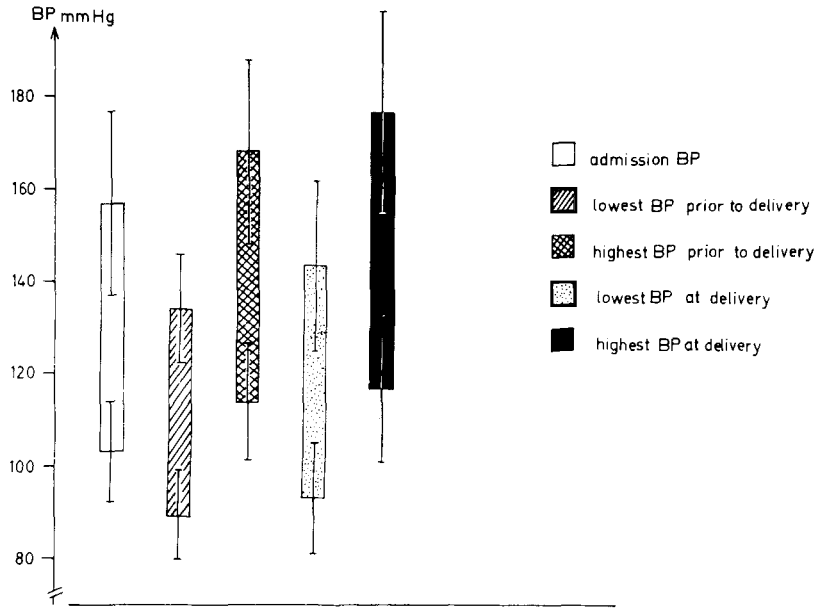

Fig. 1. The mean blood pressures of all women in the toxaemia group ($n=150$) at the time of the delivery.

(11) the incidence of eclampsia was stated to be 69 out of 67 000 pregnancies. However, their investigation period was 1955–66. The incidence of eclampsia in the present study, viz. 11 cases out of 17 000 pregnancies, lies almost mid-way between these two reported results. However, the incidence of pre-eclampsia in our material is far lower than in the other studies mentioned (9, 10).

It seems plausible that the difference between the incidence figures is due to different diagnostic criteria, in spite of the use of the same definitions [American College of Obstetricians and Gynecologists, Committee on Terminology (12)]. There are indications that the incidence of both eclampsia and pre-eclampsia has declined gradually over the years (10). In our series there was also a trend towards a lower incidence for the toxaemia group as a whole. However, a 5-year period with a limited number of cases each year is too short a time to allow of any conclusion as to whether a true change in incidence has taken place.

The mean age in the toxaemic patients was the same as in the control group. It is usually said that there is a preponderance of older women in a toxaemia material (13). The possibility exists that there is a skew age-distribution curve both to the right and to the left, eliminating any change in the mean age. However, no such distribution curve was found here. There might also be another reason to expect a higher mean age in the toxaemia material. Some cases could have been diagnosed erroneously as pre-eclampsia instead of essential hypertension with or without proteinuria and/or oedema. Since essential hypertension is usually manifested at the

Table VI. *Some laboratory data at the time of delivery for the women with toxaemic pregnancies*

	No. of cases with reported results	Results		Normal limits
		Mean±S.D.	Range	
Hemoglobin (g/l)	143	125±14	80–154	113–139
Serum creatinine (μmol/l)	129	82±24	44–185	64–106
Serum proteins (g/l)	125	60±0.8	37–79	61–81
Serum potassium (mmol/l)	126	4.2±0.4	3.1–5.7	3.0–4.9
Serum sodium (mmol/l)	128	139.5±6.3	113–158.8	134–146
Serum bicarbonate (mmol/l)	115	23.1±2.7	17–33	22–30

age of 35–40 years, such a fact would influence the mean age in the upward direction.

The higher maternal weight in the toxaemia group is pronounced. As correction was made for the longer gestation in the "normal" material, this difference must be real. In this connection Kidess et al. (14) have recently reported various early warning signs of pre-eclampsia in women with low and with high body weights. Hypertension occurs in both, but is more frequently associated with oedema in heavier women and proteinuria in those with a lower body weight.

The present findings also further stress the fact that toxaemia implies an increased risk not only for the mother but also for the infant. As seen in Table VI there was an increased frequency of stillbirths as well as of some reported malformations and congenital disorders. At present, a great deal of work is being devoted to selecting pregnancies attended by an increased risk of foetal death or neonatal asphyxia. In this connection various plasma hormone concentrations and urine–plasma ratios of various proteins have been measured (15, 16, 17).

In this regard the recent findings in the Collaborative American Project (18) are interesting. Thus it has been shown that pressures in excess of only 125/75 prior to the 32nd week of pregnancy and in excess of 125/85 at term are associated with a significantly increased foetal risk. The height of the BPs in the toxaemia group must be considered in the light of the reduced BP that is normally seen at the end of the gestational period (19). A BP of 140/90 is usually considered elevated in a pregnant woman. An interesting finding in the present series was that the mean BP was the same for the eclamptic as for the pre-eclamptic women. The only exception (Fig. 1) was the recorded maximum pressure during delivery, which was higher in the eclamptic women. However, this BP was still low, considering the severe symptoms of encephalopathy. The reason for this increased sensitivity to the elevated pressure is not known, but has been much discussed over the years (20).

In summary, the findings of the present investigation provide further evidence of a decreased incidence of toxaemia of pregnancy over the studied period. An annual mean incidence of just below 1 % was found. In spite of this fairly low figure it is still a condition of significance in view of the greatly increased frequency of perinatal infant mortality as well as of congenital anomalies and disorders. The great importance of an even moderate increase in BP for the encephalopathy symptoms and the foetal risk is evident. The reason for this, as well as the pathogenesis of the toxaemia of pregnancy, are unknown.

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Received July 18, 1976

Address for reprints:

Hans Åberg, M.D.
Department of Internal Medicine
University Hospital
S-750 14 Uppsala 14
Sweden