Received: 10 August 2021 | Revised: 13 November 2021 | Accepted: 24 November 2021

DOI: 10.1111/ppe.12847

Paediatric and Perinatal Epidemiology WILEY

ORIGINAL ARTICLE

Antepartum severe maternal morbidity: A population-based study of risk factors and delivery outcomes

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Funding information
The EPIMOMS study was funded with support from the French National Research Agency (*Agence Nationale de la Recherche* (ANR), Paris France; grant no. ANR-10-BLAN-1134-01) and the Ile de France Regional Health Agency (*Agence Régionale de Santé Ile de France*, Paris, France; grant no. PPS784)

Abstract

Background: Severe maternal morbidity (SMM) is a key indicator of maternal health. Generally explored without distinction by the timing of the event, it mainly reflects postpartum SMM. Although antepartum (pre-labour) SMM presents specific challenges in its need to optimise the risk-benefit balance for both mother and foetus, its features remain inadequately explored.

Objectives: We explored risk factors of antepartum SMM and described adverse delivery and neonatal outcomes associated with antepartum SMM.

Methods: We designed a population-based nested case-control study based on data from the EPIMOMS study (119 maternity hospitals of 6 French regions, 2012–2013, $N = 182{,}309$ deliveries in the source cohort). This study included all women with antepartum SMM (cases, $n = 601$) compared to a randomly selected sample of women who gave birth without SMM in the same hospitals (controls, $n = 3651$). Antepartum SMM risk factors were identified with multivariable logistic regression following imputations for missing data.

Results: Antepartum SMM complicated 0.33% (95% confidence interval [CI] 0.30, 0.36) of pregnancies. Antepartum SMM risk factors were maternal age ≥35 years (adjusted odds ratio [OR] 1.55, 95% CI 1.22, 1.97), increased body mass index (OR for 5 kg/m^2 increase, 1.24, 95% CI 1.14, 1.36), maternal birth in sub-Saharan Africa (OR 1.80, 95% CI 1.29, 2.53), pre-existing medical condition (OR 2.56, 95% CI 1.99, 3.30), nulliparity (OR 2.26, 95% CI 1.83, 2.80), previous pregnancy-related hypertensive disorders (OR 4.94, 95% CI 3.36, 7.26), multiple pregnancy (OR 5.79, 95% CI 3.75, 7.26), irregular prenatal care (OR 1.86, 95% CI 1.27, 2.72). For women with antepartum SMM, preterm delivery, neonatal mortality and transfer to the neonatal intensive care unit were 10 times more frequent than for controls. Emergency caesarean and general anaesthesia were more frequent in women with antepartum SMM.

Conclusions: Antepartum SMM is rare but associated with increased rates of adverse delivery and neonatal outcomes.

KEYWORDS
perinatal morbidity, pregnancy-related hypertensive disorders, preterm delivery, severe maternal morbidity, antepartum

1 | BACKGROUND

Severe maternal morbidity (SMM), defined as a potentially life-threatening complication occurring during pregnancy or just afterwards, is a major indicator of maternal health. Data about the incidence of SMM are increasingly available: it ranges from 0.5 to 1.5% of deliveries in the most recent population-based studies.[1–4] SMM is generally explored globally, without consideration of the timing of the morbid event relative to the delivery. But as the most frequent cause of SMM is postpartum haemorrhage (at least half of all SMM events),[5,6] results from studies exploring SMM mostly reflect postpartum SMM and postpartum haemorrhage. Indeed, the main risk factors for SMM are related to an increased risk of bleeding, such as caesarean delivery, abnormal placenta implantation or multiple pregnancy and may not be associated with SMM unrelated to postpartum haemorrhage.[7,8] On the contrary, some individual characteristics are also reported as risk factors for SMM overall, such as maternal age, ethnicity, obesity and parity, that could also be associated with SMM unrelated to haemorrhage, but these associations remain poorly explored.[8,9] The study of antepartum SMM—before labour—remains inadequate, as information about the timing of the morbid event is rarely available. It may, however, have specific characteristics, with a different profile of causes, risk factors and adverse consequences. Additionally, its management presents a unique challenge, in its need to optimise the risk-benefit balance for both mother and the child.[10] Better knowledge of antepartum SMM might help to anticipate the occurrence of this complex situation and prevent its adverse outcomes.

EPIMOMS is a French population-based study specifically designed to explore SMM.[11] Its prospective inclusion of women with SMM allows the exploration of antepartum SMM separately from intra and postpartum SMM. The objectives of this study were to explore causes and risk factors of antepartum SMM, and to describe the adverse delivery and neonatal outcomes associated with antepartum SMM.

Synopsis

Study question

Antepartum severe maternal morbidity (SMM), that is before labour, presents specific challenges in its need to optimise the risk-benefit balance for mother and child, but its specific features remain inadequately explored. We explored risk factors of antepartum SMM and described adverse delivery and neonatal outcomes associated with antepartum SMM.

What's already known

Often explored without distinction by the timing of the morbid event, previous studies of SMM are mostly confined to risk assessments in the postpartum period.

What this study adds

This study highlights antepartum SMM risk factors and the magnitude of its associated adverse maternal and neonatal outcomes.

2 | METHODS

2.1 | Study population

We conducted a population-based nested case-control study. Data came from the EPIMOMS population-based study, conducted in 6 French regions (May 2012 - November 2013).[12] The EPIMOMS study was funded with support from the French National Research Agency (*Agence Nationale de la Recherche* (ANR), Paris France; grant no. ANR-10-BLAN-1134–01) and the Ile de France Regional Health Agency (*Agence Régionale de Santé Ile de France*, Paris, France; grant no. PPS784). The first step of EPIMOMS was to define SMM through an extensive national Delphi expert consensus process. This definition of SMM combined 6 diagnostic criteria (major obstetric bleeding, eclampsia, severe preeclampsia, pulmonary embolism, stroke or psychiatric disorder), 6 organ dysfunction criteria (cardiovascular, respiratory, renal, neurologic, hepatic or hematologic) and 2 intervention criteria (admission to an intensive care unit (ICU) or laparotomy after delivery), as well as maternal death (Table S1).

The source population included all women (N = 182,309) who gave birth in the 119 maternity units of 6 French regions, during the study period, which account for one fifth of all deliveries in France. The characteristics of women and maternity units were similar to the national profile.[13] All women who experienced a morbid event meeting the EPIMOMS SMM definition between 22 weeks of gestation and 42 days after delivery were prospectively included (n = 2540). The prospective inclusion of women with SMM allowed to take into account the timing of the morbid event relative to the delivery, and to make the distinction between antepartum, intrapartum and postpartum SMM. Besides, a 2% unmatched control sample of women without SMM was randomly selected among women who gave birth in the same maternity units during the same time period retrospectively from delivery logbooks (control group, n = 3651 women). In the EPIMOMS study, detailed data were collected not for all the women who delivered in the 119 maternity units, but for all the women with SMM and for all the women included in the random sample.

This analysis excludes among the women with SMM those for whom the date of the morbid event was missing (n = 3) and those with intrapartum or postpartum (or both) SMM only (n = 1936). Finally, we included all women who experienced SMM in the antepartum

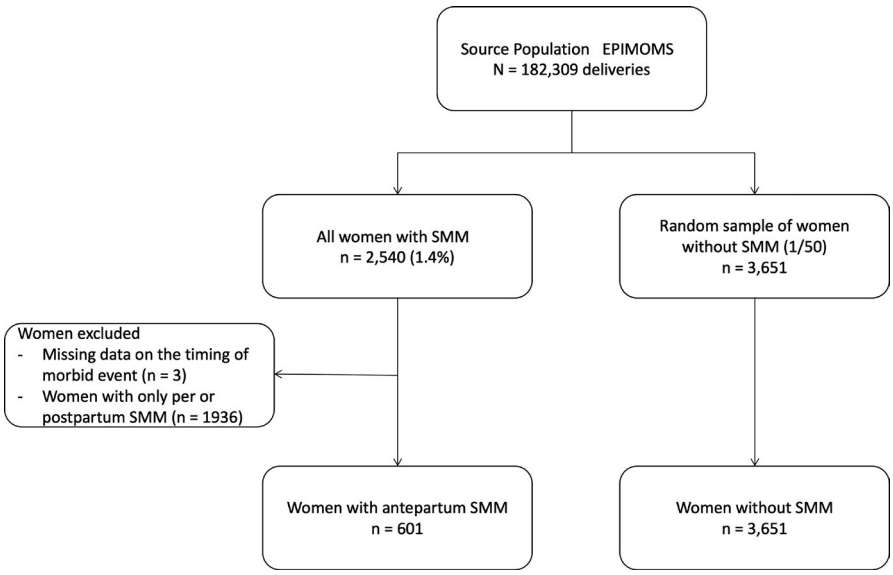

FIGURE 1 Flow Chart of the study population. The source population included all women ($N = 182,309$) who gave birth in the 119 maternity units of 6 French regions, during the study period. All women who experienced a morbid event between 22 weeks of gestation and 42 days after delivery were prospectively included ($n = 2540$). The analysis excluded among the women with SMM those for whom the date of the morbid event was missing ($n = 3$) and those with intrapartum or postpartum (or both) SMM only ($n = 1936$). Finally, we included all women who experienced SMM in the antepartum period, defined as a morbid event occurring from 22 weeks of gestation and before the onset of labour ($n = 601$). Besides, a 2% unmatched control sample of women without SMM was randomly selected among women who gave birth in the same maternity units during the same period (control group, $n = 3651$ women)

period, defined as a morbid event occurring from 22 weeks of gestation and before the onset of labour. Women with antepartum SMM but also intrapartum and/or postpartum SMM were included in the study population. Furthermore, this analysis included the entire group of control women ($n = 3651$) (Figure 1).

2.2 | Outcomes

The primary outcome was antepartum SMM, defined according to the EPIMOMS definition as a morbid event occurring from 22 weeks of gestation and before the onset of labour. The causes of antepartum SMM, gestational age at occurrence of the morbid event and at delivery (in weeks) were prospectively collected by the clinician responsible for the woman.

2.3 | Characteristics studied

Data were collected from a manual review of all available medical files by research midwives trained for this study similarly for cases and controls. They included women's social and demographic characteristics (age, pre-pregnancy BMI, maternal place of birth, living alone), pre-existing medical and obstetric conditions (parity, prior pregnancy-related hypertensive disorders, prior caesarean, prior postpartum haemorrhage), pregnancy (in vitro fertilisation, multiple pregnancy, irregular prenatal follow-up) and delivery characteristics (mode of delivery, anaesthesia for delivery), and neonatal outcomes (gestational age at birth, status at birth, birthweight, arterial umbilical pH, Apgar score, transfer to NICU, neonatal death <7 days); they were entered into an electronic case report form specifically designed for this study and used for the women in both the case and control groups.

2.4 | Statistical analysis

We calculated the incidence of antepartum SMM among all deliveries and the proportion of antepartum SMM among all women with SMM. We described causes of antepartum SMM and the characteristics of cases and controls. Using logistic regression models, we explored risk factors for antepartum SMM in relation to social and demographic characteristics, medical and obstetric pre-existing conditions, and features of current pregnancy. The linearity of the association between quantitative variables and antepartum SMM was tested using fractional polynomials. Pre-pregnancy BMI did not show any deviation from linearity and was then entered as a continuous variable in the multivariable model. The selection of the variables included in the multivariable model was based first a priori on the available literature and secondly on the results of the bivariate analysis. We repeated the model for most frequent causes of antepartum SMM.

We then described and compared the characteristics of delivery and neonatal outcomes for cases and controls. Gestational age at onset of the morbid event and at delivery was described for cases. STATA software was used for all analyses (Version 13; Stata Corp).

2.5 | Missing data

The proportion of women with missing data in the multivariable model was 32.1%. As the comparison of the characteristics of women with and without missing data supported the missing-at-random hypothesis, we performed multiple imputation with chained equations for missing data according to Rubin's rule (30 datasets, Table S2).[14] Results of multivariable analysis are all presented with imputed data.

2.6 | Ethics approval

The *Commission Nationale de l'Informatique et des Libertés* (CNIL, no 912210), the French data protection agency, approved the EPIMOMS study. The requirement for written informed consent was waived, in accordance with French legislation at that time, because all women received standard care and all data were anonymised.

3 | RESULTS

Among the source population of 182,109 deliveries, 601 women experienced antepartum SMM (0.33% of all deliveries, 95% CI 0.30, 0.36). They accounted for 23.1% (95% CI 23.1, 24.1) of all women with SMM (601/2,540). Severe pregnancy-related hypertensive disorders were the leading cause of antepartum SMM (52.1%), followed by exacerbation of chronic somatic conditions, psychiatric disorders (de novo or decompensation of a chronic psychiatric condition), and obstetric haemorrhage, each accounting for 8.7% to 9.6% of the cases (Table 1).

Characteristics of cases and controls are presented in Table 2. In the multivariable analysis with imputed data, risk factors for antepartum SMM were maternal age ≥35 years, higher pre-pregnancy BMI, maternal birth in sub-Saharan Africa, pre-existing medical condition, nulliparity, prior pregnancy-related hypertensive disorders, multiple pregnancy and irregular prenatal care (Table 3). The same risk factors were found for antepartum SMM due to pregnancy-related hypertensive disorders (Table S3).

Compared with controls, women with antepartum SMM gave birth significantly more frequently by emergency caesarean (69.4% vs. 13.6%) and with general anaesthesia (29.7% vs. 1.2%), as well as before 37 weeks (73.0% vs. 7.3%) and before 32 weeks (50.3% vs. 1.4%). The proportion of induced preterm delivery among infants born to mothers with antepartum SMM was also higher than among controls (93.3% vs. 49.6%) (Table 4).

Adverse neonatal outcomes occurred more frequently among women with antepartum SMM than controls, with higher rates of stillbirths (9.6% vs. 0.8%); among live births, higher rates of transfer to the NICU (65.4% vs. 4.8%) and of neonatal mortality within the first 7 days of life (2.7% vs. 0.1%) were also seen among SMM cases than controls. Gestational age at occurrence of the morbid event and at delivery differed according to the cause of SMM. In women with antepartum SMM due to pregnancy-related hypertensive disorders, both morbid event and delivery occurred before 32 weeks in more than 80% of the women. In contrast, among women with antepartum SMM from psychiatric disorders, the morbid event occurred before 28 weeks in 50% of women, but 80% of them gave birth after 37 weeks (Table 5).

TABLE 1 Causes of antepartum severe maternal morbidity

Causes*	Women with antepartum SMM ($N = 601$)	
	n	%
Any severe pregnancy-related hypertensive disorder	313	52.1
Severe preeclampsia	272	45.3
Eclampsia	24	4.0
HELLP associated with splenic rupture or hematoma	79	13.1
Exacerbation of a chronic somatic disease[a]	58	9.6
Hematologic disease	14	2.3
Nephropathy	8	1.3
Cardiopathy	7	1.1
Diabetes	5	0.8
Chronic infection	5	0.8
Neurologic disease	5	0.8
Other	14	2.3
Psychiatric disorder	52	8.7
De novo	30	5.0
Exacerbation of chronic disease	22	3.7
Severe antepartum obstetrical haemorrhage	52	8.7
Severe hepatic disease	33	5.5
Sepsis	24	4.0
Stroke	14	2.3
Pulmonary embolism	11	1.8
Other[c]	47	7.8

[a]Women may have had more than one SMM and the proportions reported may exceed 100%.

[b]thromboembolic disease, autoimmune disease, inflammatory bowel disease, pulmonary disease, neoplasia.

[c]Gestational thrombopaenia, thrombotic thrombocytopenic purpura, trauma, acute pulmonary oedema, PRESS, peripartum cardiomyopathy, cardiac arrhythmia, hypoglycaemic coma, hyperemesis gravidarum, acute undernutrition, acute intoxication, Guillain-Barre syndrome.

4 | COMMENT

4.1 | Principal findings

In this population-based nested case-control study, antepartum SMM complicated 0.33% of pregnancies and accounted for a quarter of all SMM cases. Half of the antepartum SMM cases were secondary to pregnancy-related hypertensive disorders. The other main causes of antepartum SMM were exacerbation of chronic somatic conditions,

TABLE 2 Characteristics of cases and controls

	Women with antepartum SMM *N* = 601		Controls *N* = 3651	
	n	%	*n*	%
Maternal age (years)				
<35	426	70.9	2915	79.9
35–39	130	21.6	599	16.4
≥40	45	7.5	137	3.7
Pre-pregnancy BMI (per 5 kg/m^2)	25.6	6.2	23,9	5.0
Maternal place of birth				
France or other European country	369	70.3	2419	79.0
North Africa	71	13.5	353	11.5
Sub-Saharan Africa	69	13.1	172	5.6
Other[a]	16	3.0	119	3.9
Living alone	41	7.5	135	4.0
Pre-existing medical condition[b]	127	21.7	274	7.5
Nulliparous	301	50.9	1517	41.8
Previous pregnancies[c]				
Prior pregnancy-related-hypertensive disorder	66	23.9[c]	102	4.8[c]
Prior caesarean	87	31.4[c]	441	21.2[c]
In vitro fertilisation	30	5.1	76	2.1
Multiple pregnancy	47	8.0	59	1.6
Irregular prenatal follow-up	40	8.4	151	4.6

[a]Asia (Japan, China, India, Southeast Asia) and North, Central and South America.

[b]Pre-existing medical condition were defined as a binary variable by the presence of at least one of the following conditions: chronic hypertension, diabetes, dyslipidaemia, constitutional bleeding disorders, asthma, allergy, psychiatric disorder, thromboembolic disease, stroke, transient ischemic attack, coronary heart disease, severe trauma, heart disease, epilepsy, haemoglobinopathy, hepatopathy, thyroid dysfunction, systemic lupus erythematosus, autoimmune disease, inflammatory bowel disease, nephropathy, cancer, myasthenia gravis, myopathy, multiple sclerosis, respiratory disease.

[c]Among multiparae pregnant women.

psychiatric disorders and obstetrical haemorrhages. The risk factors associated with antepartum SMM included multiple pregnancy, previous pregnancy-related hypertensive disorders, pre-existing medical conditions, nulliparity, increased maternal age, higher pre-pregnancy BMI, maternal birth in sub-Saharan Africa and irregular prenatal care. Women with antepartum SMM had more severe and higher rates of adverse neonatal outcomes than women without SMM; their preterm birth rate was 10 times higher, and half of their babies were born before 32 weeks. Moreover, their prevalence of interventions at risk of postpartum maternal morbidity, such as emergency caesareans and general anaesthesia for delivery, was also higher.

4.2 | Strengths of the study

The prospective inclusion of women with SMM in the EPIMOMS study provided detailed information, particularly on the timing of both the antepartum morbid event and the delivery and neonatal outcomes. We did not use a diagnosis code-based algorithm for identifying SMM, but a standardised definition based on a national expert consensus. This method was chosen because it permitted to include all criteria considered to be relevant to define SMM and not to be dependent on codes availability from routine databases. It can, however, alter the comparability of our results with others.[15] However, interestingly, based on the EPIMOMS definition, the overall incidence of SMM was found to be close to the one reported in studies using the CDC code-based definition.[16] Additionally, this comprehensive definition is not limited to interventions or diagnostic criteria that might be influenced by local practices but also includes severe clinical presentations such as organ dysfunctions. Consequently, the selection bias of women with antepartum SMM was minimised. The population-based design and the large source population, with characteristics similar to the national profile,[13] provided good external validity.

TABLE 3 Risk factors for antepartum severe maternal morbidity

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Maternal age (years)		
<35	1.00 (Reference)	1.00 (Reference)
35–39	1.49 (1.20,1.84)	1.55 (1.22,1.97)
≥40	2.25 (1.58,3.19)	2.01 (1.35,3.00)
Pre-pregnancy BMI (/5 kg/m^2)	1.29 (1.20,1.40)	1.24 (1.14,1.36)
Maternal place of birth		
France or other European country	1.00 (Reference)	1.00 (Reference)
North Africa	1.27 (0.96,1.68)	1.30 (0.97,1.73)
Sub-Saharan Africa	2.43 (1.81,3.26)	1.80 (1.29,2.53)
Other[a]	0.89 (0.51,1.57)	0.90 (0.49,1.62)
Living alone	1.88 (1.30,2.71)	1.34 (0.89,2.01)
Pre-existing medical condition[b]	3.31 (2.62,4.17)	2.56 (1.99,3.30)
Nulliparous	1.49 (1.25,1.77)	2.26 (1.83,2.80)
Previous pregnancies[c]		
Prior pregnancy-related-hypertensive disorder	4.47 (3.23,6.17)	4.94 (3.36,7.26)
Prior caesarean	1.26 (0.99,1.63)	1.01 (0.73,1.38)
In vitro fertilisation	2.51 (1.64,3.87)	1.34 (0.81,2.22)
Multiple pregnancy	5.20 (3.51,7.72)	5.79 (3.75,7.26)
Irregular prenatal follow-up	1.72 (1.22,2.44)	1.86 (1.27,2.72)

Note: Bivariate and multivariable logistic regression models with multiple imputation, including all variables listed in the table except prior postpartum haemorrhage.

Abbbreviations: 95% CI, 95% confidence interval; aOR, adjusted odds ratio; BMI, body mass index.

[a]Asia (Japan, China, India, Southeast Asia) and North, Central and South America.

[b]Pre-existing medical condition were defined as a binary variable by the presence of at least one of the following conditions: chronic hypertension, diabetes, dyslipidaemia, constitutional bleeding disorders, asthma, allergy, psychiatric disorder, thromboembolic disease, stroke, transient ischemic attack, coronary heart disease, severe trauma, heart disease, epilepsy, haemoglobinopathy, hepatopathy, thyroid dysfunction, systemic lupus erythematosus, autoimmune disease, inflammatory bowel disease, nephropathy, cancer, myasthenia gravis, myopathy, multiple sclerosis, respiratory disease.

[c]Among parous pregnant women.

4.3 | Limitations of the data

This study also has some limitations. The data used were collected in 2012–2013. However, as no significant change occurred in the content or organisation of maternal care during the last 10 years, our findings are still relevant. For the study of antepartum SMM risk factors, controls should have included all the women without antepartum SMM, that is, not only women without SMM overall, but also women with intrapartum or postpartum SMM. These women were not included in the EPIMOMS' control group. However, as they accounted for 1.1% of all deliveries,[4] their omission from the control group probably had little, if any, impact on the associations we observed. The incidence of antepartum SMM we report does not include severe morbidity before 22 weeks, which may result in an underestimate for the entire duration of pregnancy. Data were missing for at least one variable included in the multivariable analysis in 32% of women. But because the characteristics of women with and without missing data were similar, we were able to apply multiple imputations.

4.4 | Interpretation

Only one previous study, a retrospective population-based study from Canada, reported data about the incidence of antepartum SMM. Using national hospital database (2004–2015), the authors reported that antepartum SMM concerned 0.30% of all deliveries, very close to our results.[9]

The profile of causes of antepartum SMM we report here differs from that of causes of SMM globally. As expected, pregnancy-related hypertensive disorders were the main cause of antepartum SMM. However, non-obstetric diseases, such as exacerbation of a chronic disease or psychiatric disorders, also account for significant proportions of antepartum SMM. France is a high-resource country, where obstetric transition towards non-obstetric maternal pathology has already occurred. As the prevalence of chronic diseases among pregnant women is increasing over time,[17] this result highlights the importance of multidisciplinary care for these women, including in the pre-conceptional and antenatal periods, to prevent acute decompensation and antepartum SMM.[18] Similarly, recent studies reported that antepartum psychiatric disorders, severe or not, concern 5% to 10% of pregnant women.[19] Our study, specifically focusing on the severe end of the continuum of psychiatric disorders, emphasises their contribution to SMM. It highlights the need for women with psychiatric disease to receive multidisciplinary care, as well as the importance of regularly assessing maternal mental health during prenatal care for those with de novo psychiatric disorders.

In our study, risk factors for antepartum SMM and for antepartum SMM from severe pregnancy-related hypertensive disorders were very similar. These results may be explained by the fact that severe pregnancy-related hypertensive disorders are the most frequent cause of antepartum SMM. Interestingly, these risk factors for SMM due to pregnancy-related hypertensive disorders are also quite similar to those described for pregnancy-related hypertensive disorders overall, that is, severe or not severe.[20–22] These results suggest that, among these disorders, the specific phenotype of severe maternal complications is associated with the same at risk subgroups, such as multiple pregnancy and previous hypertensive disorder. Yet, due to the limited number of women with SMM from severe pregnancy-related hypertensive disorders, our

TABLE 4 Delivery characteristics and neonatal outcomes among women with antepartum severe maternal morbidity and controls

	Women with antepartum SMM *N* = 601		Controls *N* = 3651	
	n	%	*n*	%
Delivery mode				
Vaginal delivery	131	22.7	2906	79.6
Caesarean during labour	48	8.3	357	9.8
Caesarean before labour	399	69.0	386	10.6
Emergency caesarean	353	88.5	139	36.0
General anaesthesia for delivery	171	29.7	43	1.2
Gestational age at birth (weeks)				
22–27	84	14.6	26	0.7
28–31	206	35.7	26	0.7
32–36	131	22.7	214	5.9
37–42	156	27.0	3382	92.7
Induced preterm delivery	393	93.3	132	49.6
Status at birth[a]				
Alive	562	90.5	3680	99.2
Intrapartum death	10	1.6	4	0.1
Intrauterine foetal death	49	7.9	25	0.7
Birthweight (mean, SD), g[b]	1889.7	1025.0	3265.8	580.3
<1500	264	46.2	55	1.5
1500–2499	134	23.4	207	5.7
≥2500	174	30.4	3385	92.8
Apgar <7 at 5 min [a,c]	92	16.4	52	1.4
Arterial umbilical pH <7.0[a,c]	22	3.9	13	0.3
Neonatal ICU transfer[a,c]	376	66.9	187	5.1
Neonatal death <7 days[a,c]	17	3.0	3	0.1

[a]For multiple pregnancy, one event was counted if at least one baby was concerned.

[b]For multiple collected, the birthweight of the first baby was collected.

[c]Among live births.

results remain exploratory. Antepartum SMM from hypertensive disorders would deserve a specific study.

Finally, women with non-obstetric risk factors, as well as those with obstetric risk factors for antepartum SMM we reported here, such as multiple pregnancy, deserve to receive prenatal care and to give birth in a maternity unit with all appropriate resources for mother and child.

Our study shows that severe adverse neonatal outcomes, mostly severe preterm delivery and perinatal mortality, were much higher among babies of women with antepartum SMM. High rates of preterm birth have previously been noted in studies focusing on pregnancy-related hypertensive disorders,[23,24] not among women with antepartum SMM overall and with non-obstetric conditions. Additionally, we were able to describe specifically other adverse outcomes, such as neonatal death <7 days, low birthweight, low pH, low Apgar score and NICU admission. Preterm births were particularly prevalent in our study among women with antepartum SMM from pregnancy-related hypertensive disorders (94.6%), but not only: exacerbation of chronic diseases or antepartum obstetrical haemorrhage also led to preterm birth very frequently (63.6% and 70.6%, respectively). Our approach also added information to the current literature about antepartum SMM from pregnancy-related hypertensive disorders, because the EPIMOMS definition of SMM focused on the severity of maternal outcomes. Women with severe preeclampsia and delivery before 32 weeks were included only if the preterm delivery was performed for a main maternal indication.

Our study reports a high proportion of at-risk interventions for delivery among women with antepartum SMM, including caesarean deliveries, in particular emergency caesareans, and general anaesthesia. Although these interventions may be indicated in this context to improve maternal condition, they also constitute well-known risk factors for SMM.[25] Caesarean delivery is an independent risk factor for intrapartum and postpartum SMM[11] and for severe postpartum haemorrhage.[26,27] A recent population-based study with propensity score analysis reported that the risk of serious maternal complications rose quite significantly among women who had general

TABLE 5 Gestational age at the occurrence of the morbid event and at delivery in women with antepartum severe maternal morbidity, overall and by causes

Gestational age (weeks)	Antepartum SMM overall ($n = 601$)		Antepartum SMM from pregnancy-related hypertensive disorder ($n = 313$)		Antepartum SMM from exacerbation of chronic somatic disease ($n = 58$)		Antepartum SMM from psychiatric disorder ($n = 52$)		Antepartum SMM from obstetrical haemorrhage ($n = 52$)	
	SMM event	Delivery	SMM event	Delivery	SMM event	Delivery	SMM event	Delivery	SMM event	Delivery
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
22–27	147 (25.1)	84 (14.6)	80 (25.7)	73 (23.5)	14 (24.1)	3 (5.5)	20 (47.6)	0 (0.0)	8 (16.7)	7 (13.7)
28–31	234 (40.0)	206 (35.7)	173 (55.6)	176 (56.6)	17 (29.3)	8 (14.5)	3 (7.1)	0 (0.0)	13 (25.5)	11 (21.6)
32–36	148 (25.3)	131 (22.7)	43 (13.8)	45 (14.5)	19 (32.8)	24 (43.6)	16 (38.1)	8 (19.1)	16 (31.4)	18 (35.3)
37–42	56 (9.6)	156 (27.0)	15 (4.8)	17 (5.5)	8 (13.8)	20 (36.4)	3 (7.1)	34 (80.9)	14 (27.4)	15 (29.4)

anaesthesia without clinical indication for a caesarean as compared to women who had neuraxial anesthesia.[28] Preventing the occurrence of the antepartum SMM event may also prevent these interventions at risk for intra/postpartum morbidity.

5 | CONCLUSIONS

Antepartum severe maternal morbidity presents a specific profile of causes dominated by pregnancy-related hypertensive disorders, but non-obstetric conditions also make a notable contribution and should be taken into account in the management of pregnant women. Although antepartum SMM is rare, it is frequently associated with severe outcomes for both mother and children, dominated by severe induced preterm delivery. Better knowledge of antepartum SMM would help to prevent, or at least anticipate, these adverse events and their harmful consequences, probably by optimising pre-conceptional and prenatal care. Additionally, the identification of antepartum SMM risk factors should permit to focus on women or subgroups at risk of antepartum SMM. Then, individualised risk stratification could be applied to these groups and improve their care.

Further research, with a prospective design, is needed to explore the morbidity continuum and identify the specific individual and care-related factors associated with the occurrence of antepartum SMM among women with chronic conditions or non-severe pregnancy-related hypertensive disorders. Moreover, even though caesarean delivery or general anaesthesia are often justified in an antepartum SMM, careful assessment of the clear indications of these interventions and decision-making processes should improve perinatal care and help optimise clinical decisions in these complex situations.

ACKNOWLEDGEMENTS

The authors thank the coordinators of the participating regional perinatal networks: Alsace, Aurore, Auvergne, Basse-Normandie, Maternité Yvelines et Paris (MYPA), Naître dans l'Est Francilien (NEF), Paris Nord, 92 Nord, Lorraine; and the following individuals: Chloé Barasinski (R.M., Ph.D., Auvergne perinatal network, Clermont-Ferrand), Sophie Bedel (R.M., Lorraine perinatal network, Nancy), Aline Cline D'Amour (R.M., National Institute for Health and Medical Research (INSERM) Unit 1153 Obstetrical, Perinatal and Paediatric Epidemiology Research Team (EPOPé), Paris), Laurent Gaucher (R.M., Aurore perinatal network, Lyon), Isabelle Lecreff (R.M., 92 Nord perinatal network, Colombes), Blandine Masson (R.M., Aurore perinatal network, Lyon), Carole Ramousset (B.S., Alsace perinatal network, Strasbourg), Mathias Rossignol (M.D., Assistance-Publique-Hôpitaux de Paris (AP-HP), Paris), Zelda Stewart (M.D., M. Sc., Caen University Hospital, Caen), Dalila Talaourar (R.M., National Institute for Health and Medical Research (INSERM) Unit 1153 Obstetrical, Perinatal and Paediatric Epidemiology Research Team (EPOPé), Paris), Yacine Toure (B.S., Basse Normandie perinatal network, Caen), Nicole Wirth (R.M.,

Lorraine perinatal network, Nancy) for their contribution to the implementation of the EPIMOMS study in their region; the obstetricians, midwives and anaesthesiologists who contributed to case identification and documentation in their hospital, and the research assistants who collected the data. The authors also thank J.A. Cahn for editorial assistance.

CONFLICT OF INTEREST

MPB, who works in Armand-Trousseau Hospital, (AP-HP, Paris), reports personal fees from Ferring outside the submitted work. No other external funding or competing interests declared.

AUTHOR CONTRIBUTION

CDT, MPB, MR had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. CDT, MPB and MG conceptualized the study and wrote the manuscript. MR and AS performed the statistical analysis. CDT obtained funding and supervised the study. All authors contributed to the analysis plan and interpretation of the results and reviewed and approved the final manuscript. All authors accept responsibility for the papers as published. CDT is the guarantor.

DATA AVAILABILITY STATEMENT

The procedures carried out with the French data privacy authority (CNIL, *Commission national de l'informatique et des libertés*) do not provide for the transmission of the database. Consultation by the editorial board or interested researchers may nevertheless be considered, subject to prior determination of the terms and conditions of such consultation and in respect for compliance with the applicable regulations.

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How to cite this article: Raineau M, Deneux-Tharaux C, Seco A, Bonnet M-P; the EPIMOMS Study Group. Antepartum severe maternal morbidity: A population-based study of risk factors and delivery outcomes. *Paediatr Perinat Epidemiol*. 2022;36:171–180. doi:10.1111/ppe.12847