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Investigating potential hard materials: the case of tetragonal TaMoN

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Title Page

Comparative study of changes in maternal and perinatal morbidity inequalities among migrant and native women over time, between 2008 and 2014 in France.

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Short title: Changes in maternal and perinatal morbidity between women born in France and migrants

Abstract

Background: An increased risk of severe maternal morbidity and mortality has been described in migrant women, particularly in those born in sub-Saharan Africa. The mechanisms in question are poorly identified and rarely studied specifically.

Objective: To compare changes in maternal and perinatal morbidity inequalities among migrant and native women over time, between 2008 and 2014.

Material and Method: A retrospective, single-centre study carried out at the Maternity Unit of the University of Caen Hospital in France. All women who gave birth in 2008 or 2014 were included. Twin pregnancies and delivery before reaching 22 weeks of pregnancy were excluded. Pre-pregnancy characteristics and maternal and perinatal morbidities were collected from the university hospital's medical and administrative database. We compared the maternal and perinatal morbidity in 2008 and 2014 of women born in France to the morbidity of women born abroad. Secondly, we compared these migrant women between 2008 and 2014 to see if changes in the characteristics of migrant women were associated with a change in the type of maternal and perinatal complications.

Results: Of the 3,038 and 3,001 women included in 2008 and 2014, respectively, 272 (9.0%) and 385 (12.8%) women were migrants. Compared to women born in France, we found two times more severe postpartum hemorrhages in women born in sub-Saharan Africa (aOR=2.1[1.1-3.9]) and a significant increase in the risk of gestational diabetes in women born in North Africa (aOR=1.9[1.2-2.9]). We found a significant increase in the risk of severe postpartum hemorrhage (aOR=2.1[1.5-3.0]) and gestational diabetes (aOR=3.0[2.5-3.7]) in 2014 compared to 2008. We did not find a significant difference in perinatal morbidity between 2008 and 2014.

Conclusion: We noted a significant increase in the risk of severe postpartum hemorrhage in women born in sub-Saharan Africa and gestational diabetes in women born in North Africa compared to those born in France, and these risks increase in 2014 relative to 2008.

Keywords: Pregnancy, Maternal morbidity, Perinatal morbidity, Migrant women.

Main body of text

Introduction

Europe has been experiencing a migrant and humanitarian crisis for the past several years (1). From 2004 to 2009, entries into France remained relatively stable (2) before increasing between 2009 and 2015 (3). According to France's National Institute of Statistics and Economic Studies, 20.9% of women giving birth in France in 2014 were born outside of France, with the main countries of origin being African countries, followed by European countries (4).

Migrant women have a higher risk of adverse pregnancy outcomes with an increase in severe maternal morbidity (SMM), mainly involving pregnancy-related hypertensive diseases (OR 1.67 [CI 95% 1.43 – 1.95]) (5). The subgroup of migrant women from sub-Saharan Africa seems to be at a higher risk of SMM (adjusted OR: 1.8 [1.4-2.4]) compared to non-migrant women, mainly involving hypertensive complications, sepsis and severe obstetric hemorrhage (5–14). Migrant women also have an increased risk of giving birth prematurely or delivering low birth weight babies (15–17).

Explanations for these health-related inequalities remain limited. Potential explanations that have been proposed include a constitutional genetic hypothesis (18) and a higher prevalence of other individual risk factors, such as advanced age, obesity, pre-existing high blood pressure, diabetes, anemia (19). Other reported explanations are the biological effects of social stress, discrimination with differentiated care, lack of interaction with the healthcare system (leading to insufficient care) and the lack of health literacy (20–26). It is essential to identify and understand the mechanisms behind this increase in perinatal and maternal morbidity in order to guide policies for public health and the organisation of care. Identification and understanding are also essential for designing prevention and monitoring measures in the current national setting.

To better understand these health-related inequalities, the primary objective of this study was to study changes in maternal and perinatal morbidity inequalities among migrant and native women over time, between 2008 and 2014, within the Maternity Unit of the University of Caen Hospital. The secondary objective was to try to evaluate whether the change in the characteristics of migrant women between 2008 and 2014 could explain this trend.

Methods

This retrospective, observational, single-centre study was carried out at the Maternity Unit of the University of Caen Hospital in France. All women who gave birth in 2008 or 2014 were identified and included. The only two exclusion criteria were delivery before 22 weeks of pregnancy and twin pregnancies. We excluded only the births in question. So if a mother gave birth to twins in 2008, then she was not excluded from the study if she gave birth after 22 weeks of pregnancy again in 2014. In accordance with French legislation regarding data-based studies, it was not necessary to obtain consent from women but to ensure that they did not object. Women were informed through a booklet and were given the opportunity to object to the use of their data for research purposes. A favourable opinion was obtained from the Nord-Ouest III institutional review board on 28 September 2016 (Reference: A16-D43-VOL.29).

The exposure variable was in five categories corresponding to the most often described geographical areas (7,9,14,24): France (metropolitan France and French overseas), Europe (outside of France), North Africa (Egypt, Libya, Tunisia, Algeria, Morocco and Western Sahara), sub-Saharan Africa (the 48 African countries more southern than Sahara), and "Other". We opted to use a woman's country of birth as an indicator of their migration status because it is more reflective of migrant status (27).

We looked for elements of severe maternal morbidity, including severe preeclampsia (systolic blood pressure ≥ 160 mmHg, diastolic blood pressure ≥ 110 mmHg, oliguria < 500 mL/24 hours, serum creatinine > 135 $\mu\text{mol/L}$, proteinuria > 3 g/24 hours, acute pulmonary oedema, persistent epigastric pain, HELLP syndrome, persistent neurological signs (visual impairments, headaches, strong or exaggerated deep tendon reflexes or convulsions) or retroplacental haematomas) (28), eclampsia, HELLP syndrome, placenta abruption, uterine rupture and severe postpartum hemorrhage (blood loss $\geq 1,000$ mL) (29). Elements of non-severe maternal morbidity were also studied, including gestational diabetes, pregnancy cholestasis, placenta previa and postpartum infections. With regard to perinatal morbidity, we selected severe morbidity criteria (severe prematurity before 32 weeks of pregnancy, intrauterine growth restriction below the third percentile, a five-minute Apgar score of less than 7, blood pH of less than 7.1 at birth and foetal death in utero) and macrosomia.

We also selected maternal characteristics such as age at the beginning of pregnancy, prepregnancy body mass index (BMI), the mother's socio-professional category from six classes at the beginning of pregnancy (craftsmen, tradesmen and general managers; managerial staff or higher intellectual professions; middle-level professions; employees; manual workers; unemployed), social coverage from five categories (standard health insurance, universal health coverage, supplementary universal health coverage, state medical assistance, or none), smoking during pregnancy collected in early pregnancy, notable medical history outside of pregnancy (arterial hypertension, pre-existing diabetes, or the presence of myomas), obstetrical history (parity, uterine scarring in the event of multiparity, personal history of postpartum hemorrhage, gestational diabetes or hypertensive disorders during a previous pregnancy). In France, employed women are automatically covered by the standard health insurance. The universal health coverage (CMU) is awarded to unemployed women residing in France for more than 3 months with a legal status. The supplementary universal health coverage is granted to unemployed women residing in France for more than 3 months with a legal status and with resources below a level depending on their place of residence and the composition of the household. The state medical assistance (AME) is awarded to undocumented women residing in France for more than 3 months and with resources below a level depending on place of residence and household composition.

Midwives and obstetricians collected prospectively the data during women's follow-up using our medical software. It was not possible to close a file without filling in all information. So we did not have missing data. Then we extracted data retrospectively from the university hospital's medical and administrative database. We were unable to extract from our data base the gestational age at initiation of prenatal care and the number of prenatal visit to assess the prenatal care utilization.

First, we compared the five categories of women based on their place of birth for the pre-pregnancy characteristics and the maternal and perinatal morbidities for the years 2008 and 2014. Second, we compared the 2008 and 2014 data for women born abroad to evaluate whether the change in migrant characteristics between 2008 and 2014 could explain a change in maternal and perinatal morbidity inequalities.

Categorical variables were expressed as percentages, and continuous variables were expressed by their mean and standard deviation. The statistical tests used were the analysis of variance (ANOVA and Bonferroni post-hoc test) for the

quantitative variables after verifying the equality of variances hypothesis (Levene's test) and the chi-square test (or Fisher's exact test, if necessary) for the qualitative variables. Logistic regression models were used to assess maternal and perinatal morbidity inequalities among migrant and native women over time, between 2008 and 2014. We selected adjustment variables using a stepwise top-down procedure. The main regression model adjusted for the year of delivery when comparing the maternal birth place and adjusted for the maternal birth place when comparing the year of delivery. The alpha value was fixed at 0.05. The statistical analysis was conducted by the Biostatistics and Clinical Research Unit of the University of Caen Hospital with IBM®-SPSS® 22.0 software.

Results

Of the 3,038 and 3,001 women included in 2008 and 2014, respectively, 272 (9.0%) and 385 (12.8%) women were migrants.

The characteristics of women who gave birth in 2008 and 2014 are described in Tables 1 and 2, respectively. We found that the woman's place of birth was associated with their social situation. Women born in sub-Saharan Africa were more frequently in a precarious situation compared to other migrant and non-migrant women. The migrant women, including those born in sub-Saharan Africa, had significantly more uterine scarring, a history of gestational diabetes and uterine myomas in 2008 and 2014 (Tables 1 and 2).

The compared prevalence of maternal and perinatal morbidities in women who gave birth in 2008 and 2014 is shown in Table 3. For 2008, we observed a significant difference in the number of gestational diabetes cases ($p = 0.01$) among the five groups, with a lower prevalence in non-migrant women (Table 3). We did not find any significant difference either in moderate or in severe preeclampsia both in 2008 and in 2014 (Table 3).

In the multivariate analysis, compared to women born in France, we found two times more severe postpartum hemorrhages in women born in sub-Saharan Africa ($aOR=2.1[1.1-3.9]$) and a significant increase in the risk of gestational diabetes in women born in North Africa ($aOR=1.9[1.2-2.9]$) compared to the non-migrant women (Table 4).

If we compare the migrant women in 2008 and 2014, we noted that these women in 2014 were significantly less "unemployed", with more managerial staff and higher intellectual professions, but with more women with supplementary universal health coverage ($p < 0.001$), a higher BMI ($p = 0.04$) and a greater history of hypertensive pathology ($p = 0.04$) (Table 5).

In the multivariate analysis, we found a significant increase in the risk of severe postpartum hemorrhage ($aOR=2.1[1.5-3.0]$) and gestational diabetes ($aOR=3.0[2.5-3.7]$) in 2014 compared to 2008 (Table 4).

We did not find a significant difference in perinatal morbidity between 2008 and 2014 (Table 3). However, we noted a significant difference in the prevalence of macrosomia in migrant women between 2008 and 2014 (Table 6).

Discussion

We noted a significant increase in the risk of severe postpartum hemorrhage in women born in sub-Saharan Africa and gestational diabetes in women born in North Africa compared to those born in France. This risk increased in 2014 relative to 2008, unlike the prevalence of macrosomia, which decreased.

This study, to our knowledge, is the first to compare two different years in order to study changes in characteristics and morbidities in migrant women compared to non-migrant women. Its greatest strength is its large sample of 6,039 women, including 657 migrant women. Yet, it has some limitations. This is a retrospective study with a risk of information bias because the data was collected from the university hospital's medical and administrative databases. It is also possible that data was missing from the files of the women born abroad due to the language barrier and less frequent monitoring, resulting in an under-identification of variables and data input errors. The collection is exhaustive, however, since all 2008 and 2014 births were included, it rules out the possibility of selection bias. Another limitation is the time period between the two selected years. It is possible that there were significant changes in practices in those six years, leading to potential alterations in the diagnosis and especially in the treatment of certain pathologies. Specifically, screening methods and the diagnostic criteria for gestational diabetes changed after the publication of recommendations for clinical practice from the French Board of Gynaecologists and Obstetricians (CNGOF) in 2010 (30). The low prevalence of certain morbidities and the low number of women born abroad (8.9% in 2008 and 12.8% in 2014) may lead to the lack of statistical power. Our results are difficult to extrapolate to the population of mainland France, making it difficult to compare with studies on the same subject. The percentage of women born abroad during the two study years, 2008 and 2014, was much lower than in the national perinatal survey report from 2016 (18.6%), which is the average for France, with wide variance across the different regions (4).

Concerning gestational diabetes, the lack of significant difference between the five groups in 2014 versus 2008 may be surprising. This could be explained by the increase in the number of cases of gestational diabetes in 2008 and 2014 among women born in France (Table 3). The increase is linked to changes in our diagnostic criteria following the publication of recommendations for clinical practice by the CNGOF in 2010 (30). It may also be related to the significant decrease in the number

of “unemployed” women and the significant increase in managerial women and women with higher intellectual professions. This improvement in their socio-professional category, possibly due to a better understanding of the French language, would suggest better pregnancy monitoring, including the screening for gestational diabetes, and a lower prevalence of macrosomia. The significant increase in the severe postpartum hemorrhage rate in women born in sub-Saharan Africa may be secondary to a significantly higher prevalence of myomas, inductions, and caesarean deliveries before or during labour (31). An increased risk of severe postpartum hemorrhage in these women (raw OR=1.8 [1.4-2.4]) was highlighted in the French EPIMOMS study, for both vaginal and caesarean delivery alike. This increased risk persisted after adjusting for the pre-existing characteristics of the women and factors related to the pregnancy, labour and delivery (aOR=1.8 [1.2-2.6]) (8). It has also been shown that women from sub-Saharan Africa have a three times higher risk of hypertensive disorders (OR = 2.8, CI 95% [2.1-3.8]) and a four times higher rate of severe sepsis (OR = 3.6, CI 95% [1.5-8.4]). The increased risk of hypertensive disorders in pregnancy was lower after adjusted for the women’s pre-existing characteristics and factors related to their pregnancy (aOR=1.8 [1.1-2.9]). The risk of severe sepsis disappeared after adjusting for these same factors, particularly prenatal care (8). These results suggest the role of inadequate prenatal care. The persistence of the risk of hypertensive complications and severe hemorrhage may be explained by a genetic mechanism or by differentiated or suboptimal care leading to a later diagnosis and a more common progression to severity (8). In our study, the absence of a significant difference in hypertensive complications among all of the migrant women compared to the non-migrant women may be secondary to a lack of statistical power due to the low prevalence of such events. The same applies for perinatal morbidity, which is reported in the literature (8,13,14).

The factors and mechanisms involved in aggravating these risks are complex and unclear. The difficulty in understanding them is partly due to the significant heterogeneity of the group of migrant women, in terms of both their socioeconomic characteristics and their maternal/perinatal risk profile. For this reason, it is difficult to study the so-called “other” group, which includes women of highly heterogenic geographical origins, socioeconomic backgrounds and migratory routes. In addition to changes in practices over the six years in question, there has probably also been a

changes in migrant flows to France. Adding to the fact that migrant flows shift over years, it is difficult to explore these mechanisms when we study migrant women related to the place of birth. Indeed, administrative status could also be a key determinant of medical risk. Only asylum seekers and refugees have been covered in published studies. It has been shown that these groups are at an increased risk of severe maternal and perinatal morbidity (32). In addition, such women whose status provides them a level of social protection, the number of migrant women without a legal residency permit is on the rise in European countries (33). So-called “undocumented” people are likely to be more exposed due to the many obstacles they face when interacting with the healthcare system, including individual and institutional discrimination and a lack of social protection (17,34). It may be interesting to study the specific impact of the migrant’s legal status, particularly that of undocumented migrants, on their risk of maternal and perinatal morbidity.

Conclusion

This retrospective study showed a significant increase in the risk of severe postpartum hemorrhage in women born in sub-Saharan Africa and gestational diabetes in women born in North Africa compared to those born in France. These risks were higher in 2014 compared to 2008.

To date, there is insufficient evidence to affirm that such differences are related to pre-pregnancy maternal characteristics. They may be secondary to the administrative background of these women. A study is currently underway to examine the association between the administrative background of migrant women and severe maternal and perinatal morbidity.

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Disclosure of Interests

The authors report no conflicts of interest

Contribution to Authorship

Eslier Maxime designed, analyzed, wrote and read over the article in collaboration with Dreyfus Michel.

Azria Elie read over the article.

Morello Rémy conducted the statistical analysis and actively helped develop and write this study.

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Table Caption List

Table 1. Characteristics of women who gave birth in 2008 according to maternal birth place

Table 2. Characteristics of women who gave birth in 2014 according to maternal birth place

Table 3. Comparison of maternal and perinatal morbidity among women who gave birth in 2008 or 2014 according to maternal birth place

Table 4. Association between maternal birth place and maternal morbidity among women who gave birth in 2008 or 2014

Table 5. Comparison of characteristics among migrant women who gave birth in 2008 to those who gave birth in 2014

Table 6. Comparison of maternal and perinatal morbidity among migrant women who gave birth in 2008 to those who gave birth in 2014