Stillbirth and congenital anomalies in migrants in Europe

Anne-Marie Nybo Andersen, MD, PhD, Professor of Social Epidemiology *, Anna Gundlund, BA Med, Research Fellow, Sarah Fredsted Villadsen, MSc, PhD, Post Doc Research Fellow

Department of Public Health, University of Copenhagen, Denmark

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The risk of giving birth to a stillborn child or a child with severe congenital anomaly is higher for women who have immigrated to Europe as compared to the majority population in the receiving country. The literature, however, reveals great differences between migrant groups, even within migrants from low-income countries, although there is no clear pattern regarding refugee or non-refugee status. This heterogeneity argues against a particular migration-related explanation.

There are social disparities in stillbirth risk worldwide, and it has been suggested that the demonstrated ethnic disparity is a result of the socioeconomic disadvantage most migrants face. Consanguinity has been considered as another cause for the increased stillbirth risk and the high risk of congenital anomaly observed in many migrant groups. Utilization and quality of care during pregnancy and childbirth is the third major aspect. All three factors seem to contribute to stillbirth risk, and they should be considered in clinical practice and public health.

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* Corresponding author. Department of Public Health, University of Copenhagen, Oster Farimagsgade 5, Box 2099, DK-1014 Copenhagen K, Denmark. Tel.: +45 35326765.
E-mail address: amny@sund.ku.dk (A.-M. Nybo Andersen).

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Introduction

In a landmark systematic review and meta-analysis of perinatal health in migrants to Western countries, it was demonstrated that migrants from Africa, the Middle East, and Asia had higher feto-infant mortality than mothers in the receiving countries, although the picture was mixed in the case of gestational age at birth, fetal growth, and healthy lifestyle during pregnancy [1].

Stillbirth is a serious health outcome and an important health indicator. Even in high-income countries, the risk of intrauterine death in the third trimester is at the same level as the mortality risk for men and women above 80 years of age, and stillbirth is a traumatic experience for parents [2]. Huge variation in stillbirth risk between countries and populations indicates that a considerably large proportion of stillbirths are preventable [3]. Stillbirth rates are decreasing worldwide because of many reasons reflecting the complex causal nature of stillbirth. Some stillbirths are attributed to birth and antenatal care, some to poverty and individual risk factors, and some to the existing illness of the fetus (that may also be preventable), and a large proportion of stillbirths are still unexplained [4].

Between 10% and 20% of stillborn children have congenital anomalies [5], and the literature review indicated that migrant women had worse outcomes than majority populations in terms of congenital anomalies [1], but due to the heterogeneity of the outcome, congenital anomalies was not meta-analyzed. Congenital anomalies are among the three most common causes of infant and early child mortality [6,7], and in milder cases often a challenge for the individual, his/her family, and for the society.

Currently, a substantial proportion of women who give birth in Europe are not born in Europe; in fact, the proportion of women who are born outside the country in which they give birth exceeds 25% in most countries [8]. The concept of “migrants” covers a hugely diverse population, which differ from country to country and with great differences within each country. In Brussels, Belgium, around two-thirds of new mothers are migrants, many of whom are well-off migrant workers from other European countries. In most countries, however, the migrant groups are dominated by those from low- and middle-income countries and refugees from war zones.

In this paper, we address the contemporary reproductive health among migrants in Europe with respect to stillbirth and congenital anomalies. First, we describe the risk of stillbirth and congenital anomalies in offspring of migrant women, if possible as characterized by their country of origin, as reported in the literature. Then, we address some suggested causal factors with particular focus on the role of consanguinity. Finally, we briefly discuss possibilities for improvement of the situation in the future.

Stillbirth risk in migrants in Europe

In a study that covered birth in Norway between 1967 and 1993, Stoltenberg et al. reported that women from Pakistan had a high risk of stillbirth as compared to Norwegian women [9], and this tendency has been confirmed in a recent study, covering the period 1995–2010, where women who migrated to Norway from Pakistan had a 2.8 times higher risk of stillbirth than Norwegian women [10]. Women of non-Western background had even higher relative risks for stillbirth in twin pregnancies compared to Norwegian mothers [11]. In another study, it was reported that the other large migrant group in Norway, the Vietnamese, had a lower perinatal mortality than the Norwegian majority population [12]. The Danish nation-covering registers were used to assess risk of stillbirth according to maternal country of origin. The stillbirth risks in the five largest non-Western minority groups, defined by country of birth, were compared to the risk in the majority (Danish-born) population. Women from Pakistan, Somalia, and to a lesser extent Turkey had an increased risk of stillbirth, and this excess risk was not mediated through income or educational level [13]. In this study, the large Lebanese migrant group, vastly representing Palestinian refugees, had the same stillbirth risk as the majority population. A study from Flanders, Belgium, reported that migrants from low- and middle-income countries had, respectively, 2.7 and 1.5 times the native-born women’s risk of stillbirth during 2004–2008, while migrants from high-income countries had no such increased risk [14]. Another study from Brussels, Belgium, demonstrated that migrants from North Africa (the Maghreb), Egypt, Turkey, and sub-Saharan Africa had an almost doubled risk of stillbirth than Belgian-born women and the rest of the

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Europe-born women [15]. In Spain, in 2007–2010, it was reported that women born in Africa had an almost doubled risk of stillbirth as compared to Spanish women, while women who migrated from Europe, the Americas, and Asia to Spain had the same risk as Spanish-born women [16]. Analyses from the region of Valencia demonstrated a particularly high risk among women from sub-Saharan Africa and Eastern Europe, but not in the largest migrant group: women from Latin America [17]. A nation-covering study from Germany including all births from 2004–2007 demonstrated an increased risk of stillbirth for women from the Middle East and North Africa (RR = 1.3), while no statistically significant increased risks were found for women who migrated from Asia, Europe, or North America [18]. A register-based study from Sweden demonstrated that stillbirth risk was substantially increased in women from the Middle East and Africa, but not in women who migrated to Sweden from other parts of the world [19]. A study of deliveries in Malmö, Sweden, from the 1990s emphasized the particularly high rate of perinatal mortality in women from sub-Saharan Africa [20]. An older study from UK compared perinatal mortality in women with, respectively, UK, India, Bangladesh, and Pakistan as country of birth. Independently of maternal age and parity, the offspring of women of Pakistani origin had an approximately doubled risk of perinatal mortality as compared to UK mothers. The offspring of Indian and Bangladeshi mothers also showed increased mortality, but to a lesser degree [21].

A cross-country analysis of stillbirth risk in Turkish mothers compared to the majority population mothers demonstrated that in all of the eight European countries examined, the Turkish mothers had an increased risk of stillbirth, with odds ratios (ORs) within the range 1.1–1.6. The authors concluded that the variations in Turkish women’s stillbirth risk between countries indicated that preventable society-specific determinants contributed to the fetal mortality.

Overall, the studies reflect heterogeneity, in accordance with the conclusion of another review including all the industrialized countries in Europe [22]. We find most consistency in the following findings: mothers from refugee countries were not particularly vulnerable to stillbirth and many studies report increased stillbirth risk for migrants from Pakistan, Turkey, and sub-Saharan Africa.

Risk of congenital anomalies in children of migrants in Europe

A >25-year-old study of perinatal mortality among migrants to England and Wales from the Indian subcontinent demonstrated a three times higher risk of perinatal death from congenital anomalies in mothers from Pakistan, much higher than the likewise increased risk found for mothers from India and Bangladesh [21].

In a recent paper published in The Lancet, the risk of congenital anomalies was investigated in the multiethnic Born in Bradford cohort [23]. Compared to “White British” ethnicity, children of Pakistani origin had an almost twice as high risk and the heterogeneous “Other” group had a 22% higher risk of congenital anomalies. Children of Pakistani mothers also had a particularly high risk of infant death due to congenital anomalies [24].

In a Danish study, an excess risk of infant mortality due to congenital anomalies was found for offspring of Turkish-, Pakistani-, and Somali-born women [13] and this was also found in a study of mortality in children <5 years of age [7]. An analysis from Belgium, investigating the three largest non-European migrant groups, revealed that women from Morocco and Turkey, but not sub-Saharan Africa, had significantly increased risk of perinatal mortality due to congenital anomalies [25]. The study conducted in Valencia indicated that migrants as a large, heterogeneous group had an increased peri- and neonatal mortality due to congenital anomalies [17].

Essén’s study of all births in Malmö from 1990 to 1995 revealed no difference in severe congenital anomalies between offspring of Swedish- and foreign-born mothers, but the prevalence of severe congenital anomalies was very low (0.2%) and a very restrictive definition must have been used [20].

In an analysis of temporal changes in ethnic perinatal health disparities in Berlin, it was reported that Turkish women had an increased risk of giving birth to a child with a congenital anomaly in 1993–1997, but interestingly no increased risk during the period 2003–2007 [26].

A large nation-covering study from the Netherlands compared cause-specific infant mortality in offspring of Dutch and the four major immigrant group mothers: Turkish, Moroccan, Surinamese, and
Antillean/Aruban. Compared to offspring of Dutch mothers, children of Turkish and Moroccan mothers had a significantly increased risk of infant death from congenital anomalies, which was not the case for children with Surinamese and Antillean/Aruban origin [27].

In summary, the findings resemble those for stillbirth with respect to heterogeneity, but there may be a pattern indicating increased risk in women who migrated to Europe from the Middle East, North Africa, and Pakistan.

What are the reasons for the increased fetal mortality and congenital morbidity among migrants in Europe?

It is evident from the heterogeneity in risk that a number of factors contribute to this increased mortality and morbidity. Three main causative factors are at play. First, there are strong social inequalities in stillbirth risk, and the apparently ethnic disparity could in fact be a socioeconomic disparity. Consanguinity is also often mentioned as a causative factor, as marriage between people who have grandparents or great grandparents in common is frequent in many of the countries from where present-day migrants in Europe originate. Suboptimal pre- and perinatal health care for migrants is also often suspected to account for the increased mortality and morbidity.

Do we mix up the categories: migrants and poor social conditions?

This is a highly relevant question in terms of stillbirth. There are strong social inequalities in stillbirth risk in high-income countries [4,28], and migrants in European countries are, on average, socioeconomically disadvantaged.

A study of all births in Rotterdam in 2000–2007 addressed this issue by comparing pregnancy outcomes in Western and non-Western women according to a composite measure of neighborhood social index with four strata (SI). In Rotterdam, mothers of non-Western origin contribute to almost half of the births, and the distribution between Western and non-Western mothers by SI was markedly skewed. While perinatal mortality was higher in non-Western women, a strong social gradient in perinatal mortality was found in Western women with no such gradient in non-Western women [29].

In the Swedish study of stillbirth risk, it was concluded that the increased risk of stillbirth was unaffected by adjustment for socioeconomic factors and maternal morbidity [19], but the authors found that the duration of residence in Sweden was inversely related to stillbirth risk.

The Spanish study demonstrated that the stillbirth risk was almost twice as high in lower-educated women than in higher-educated women, and that the risk for the quartile of women living in the autonomous regions of Spain with the highest unemployment percentage was 2.6 times higher than the risk of the quartile of women living in the regions with the lowest unemployment. Adjustment for individual educational attainment and contextual unemployment did not, however, reduce the excess risk of stillbirth for African women [16], and an analysis of the multiplicative interaction between maternal educational attainment and country of origin confirmed this finding [30]. In the Danish study of stillbirth in different migrant groups in Denmark, we attempted to adjust for the socioeconomic situation of the parents (as measured by household income and educational attainment) to determine whether the ethnic differences in risk of stillbirth could be explained by differences in a socioeconomic situation. Notably, the adjusted risk estimates only attenuated marginally. We repeated the analyses, restricting the population to those in the upper 50 percentile of income and longest educational group, respectively, and found further increased risks of stillbirth in the migrant groups from Pakistan, Turkey, Lebanon, and Somalia [13].

This was in sharp contrast to the finding from Flanders, Belgium, where adjustment for maternal age, parity, and educational level eliminated the increased risk of stillbirth found in the crude analyses [14].

The risk of confounding from socioeconomically patterned factors is less when it comes to congenital anomalies. In contrast to the case of stillbirth, the evidence for social patterning of congenital anomalies is not very strong, although newer studies indicate a growing socioeconomic disparity in congenital anomalies [31,32]. This argument is in line with the study from Brussels that

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investigated the cause of mortality and reported that particularly congenital anomalies accounted for the excess perinatal mortality in Turkish and North African mothers, independent of socioeconomic status [15].

The role of consanguinity

Consanguinity, the situation where parents are related as second cousins or closer, is a widespread practice (except the majority of states in the USA, the People’s Republic of China, and the People’s Republic of Korea where first-cousin marriages or closer are banned). This is also a popular explanation for the increased risk of stillbirth and congenital anomaly in migrants in Europe. When we prepared and published our first paper, which demonstrated increased fetal mortality in some of the largest migrant groups in Denmark [13], our colleagues and friends first suggested “consanguinity” as a mechanism. Except from a couple of Norwegian studies [9,33], we were unable to find solid epidemiological evidence for the hypothesis, partly because data about consanguinity were so sparse.

Theoretically, the offspring of consanguineous parents are at a greater risk of known autosomal recessive diseases and congenital anomalies caused by recessive genes [34–36]. According to Garnica et al., the average human being carries three to five of such potentially harmful recessive genes [37], and comparison between related and unrelated parents shows a significantly increased risk of homozygosity in the offspring [34]. The risk of having a homozygote child for an aleatory autosomal recessive gene from the joint ancestor is, respectively, 3.13% for uncle–niece (aunt–nephew) and 1.56% for cousin–cousin unions; however, if consanguinity between parents exists in multiple generations, the risk may increase [38].

In the absence of consanguinity data, we used an indirect approach to assess any clinical significance of consanguinity on childhood morbidity in Denmark: We investigated how a number of selected congenital anomalies (and also four other disease categories), suspected to be of autosomal recessive origin, were distributed according to maternal country of birth [39]. Particularly, offspring of Turkish and Pakistani mothers had increased risks of the congenital anomalies (and even more for the other autosomal recessive diseases). These findings in combination with the Danish findings on fetal and infant mortality [7,13] support the contention that consanguinity plays an etiologic role in the increased risk of adverse reproductive outcomes observed in many studies conducted in Europe.

The authors of the Dutch study that showed a higher risk of lethal congenital anomalies in children of Moroccan and Turkish mothers, but not in Surinamese and Antillean/Aruban offspring, speculated that consanguinity could be of importance [27]. Information on consanguinity at the individual level is scarce, but the frequencies of consanguineous marriages in countries have been reported by Bittles et al. [40] This study confirms that consanguinity is very frequent (>30% of marriages) in Pakistan, Afghanistan, the Middle East, and many North African countries. It is indicative that the migrant populations from countries with a very high frequency of consanguineous marriages are also those with the highest risks of stillbirths and congenital anomalies. However, we must emphasize that the indication carries a risk of the ecologic fallacy: in most studies, we do not know the individual’s consanguinity status.

A recent study conducted in the Born in Bradford cohort demonstrated that the increased risk of congenital anomalies found in children of Pakistani mothers disappeared when the analyses were restricted to children of non-consanguineous couples [23].

Suboptimal health care for migrants

It is self-evident that socioeconomically challenged migrant women are at risk of suboptimal care in health-care systems based on direct payment for care. However, antenatal and birth care are free in most European countries. Universal and high-quality reproductive health care has been a cornerstone for the Swedish welfare state for decades, but even under such conditions substantial inequality in maternity care has been demonstrated: Rässjö et al. compared the health-care utilization among pregnant women of Swedish and Somali origin and found that Somali women had fewer antenatal care visits and started antenatal care later than the Swedish women [41]. Delayed antenatal care precludes prenatal screening or inhibits indicated terminations of pregnancies. The evidence regarding attitudes
toward and uptake of prenatal screening among contemporary migrant women is lacking, but this lack of knowledge should not be an argument for not providing migrant women with the same opportunities for screening and termination of pregnancies due to fetal abnormalities as pregnant women of the majority population get.

Another method of assessing whether migrant women’s increased risk of stillbirth is a result of suboptimal health care would be to compare the risk of intrapartum stillbirths with the risk for majority women [42]. A substantially higher risk of intrapartum stillbirths would indicate a need for better birth care for migrants. In an as yet unpublished study, we found a statistically nonsignificant higher intrapartum stillbirth frequency in non-Western migrant women as compared to Danish women. The study was a semi-qualitative assessment of 127 perinatal deaths, and better data materials may help address this issue.

In the same material, we identified examples of potentially fatal miscommunications between migrant women and health-care providers in the antenatal care. To improve health literacy, in the definition by Nutbeam [43], where the focus is on the cognitive and social skills needed to get access to, understand, and use information that promote and maintain good health, is a main goal for antenatal care and a great challenge for antenatal care providers.

Readers interested in challenges in optimal antenatal care for migrant women are encouraged to read the paper by Villadsen et al. in this issue of Best Practice, which addresses antenatal care [44].

How to reduce stillbirths and congenital anomalies in migrant women at increased risk in practice and research

The reasons for reduction in fetal mortality by providing antenatal care have never been completely understood [45]. Optimized utilization of the antenatal care and access to a migrant-friendly ante- and perinatal care are crucial and should be mentioned first.

A large proportion of late stillbirths are unexplained [46], many of these in socioeconomically disadvantaged women. It could be speculated whether emotional strain is related to late stillbirth. A growing field of research indicates that stressful life events increase the risk of stillbirth and congenital anomalies [47–49]. Many migrant women live under stressful living conditions. Whether discrimination is a stressor with detrimental health effects is not known, but it has been suggested as an explanation for the paradox that a migrant group that seemingly has a high socioeconomic status and a healthy lifestyle has a higher mortality rate than other migrant groups and indigenous populations with worse risk factor profile [50]. Research into the mechanisms underlying such relationships is encouraged.

Improved health care in relation to consanguinity is the next suggestion for improvement.

With the rapid development within medical genetics, it is likely that screening of consanguine couples for being carriers for known autosomal recessive disorders could be a routine procedure in the near future. There are indeed plenty of critical questions to address if this should be routine: what are the mitigation actions to be implemented? How frequent needs a condition to be to justify screening? This is a particularly difficult question as one of the main problems about consanguine parenthood is that extremely rare genetic variants have a substantial risk of being homozygote in the offspring. Currently, there are increasing opportunities for non-invasive prenatal testing beyond karyotype [51]; however, genomic arrays specifically for autosomal recessive disorders are — to our knowledge — yet to be developed.

Besides, a public health effort to ensure that the population is well informed of the health risks regarding consanguine parenting should be considered. An issue here is when and how? The antenatal care is an inconvenient place for this activity and preconception consultations, as has been suggested [34], is also difficult to promote given the few opportunities that are available at present for improving the health chances for the offspring of consanguineous marriages. Although autologous sperm insemination is a rather radical suggestion, some consanguineous couples have opted for this procedure. Any information campaign should be aware of the social advantages that accompany consanguineous marriages and the small absolute risk increases associated with consanguinity, and we advise that persons involved in such public health activities consult the insightful papers of one of the leading consanguinity experts in the world, AH Bittles [40,52].
There are signs of improvement in the situation: The large Turkish minority population in Berlin showed an increased risk of stillbirth and congenital anomalies in the mid-1990s, but this situation changed and the stillbirth and congenital anomaly rates were at the same level as for the German born a decade later [26]. In Norway, the proportion of new mothers of Pakistani origin in consanguine marriages was halved in less than a decade from the mid-1990s [53]. This substantial decrease occurred spontaneously, that is, without any governmental legislation. Reports from the Middle East also indicate the decrease in the proportion of consanguine marriages, but the reasons for these trends need to be studied by social scientists. Along the same optimistic lines, some migrant groups have a better reproductive outcome than the majority populations, as was the case for the Vietnamese group in Norway [12], or at the same level despite the detrimental socioeconomic situation as was the case with the Lebanese/Palestinian group in Denmark [13]. Studies of the mechanisms behind these favorable outcomes in some migrant groups may be of benefit for all women.

**Closing remarks**

An alternative framework to explain and understand the current high risk of stillbirth and congenital anomaly in some migrant women in Europe could be a life-course approach to health and disease. [54] A life-course framework would encompass the abovementioned three causative factors, and also the early-life experiences of the mothers who are now migrants. Increasing research supports that the life of grandmothers affects the health of individuals, through a programming of their offspring’s reproductive ability in fetal and infant life. [55] The life and health situations for the mothers of today’s migrants were often so severe that their daughters were persuaded to emigrate. If a programming through generations exists, this may also account for some of the reproductive disadvantages many women with migrant background have. There is, however, more to a life-course framework than programming: The social surroundings that affect the expecting mothers’ lifestyle, choice of partner, and emotional state before and during pregnancy, together with her socioeconomic position and her prepregnancy health, act in concert with utilization and quality of health care.

This is probably the complex causal network to be dealt with for optimizing the health-care system for children born to migrant women in Europe.

**Summary**

Pregnant women in Europe with a migrant background are at a particularly higher risk of giving birth to a stillborn child or a child with a congenital anomaly than indigenous women are. The heterogeneity in risk between different migrant groups, irrespective of the average socioeconomic position of the migrant group, points toward mechanisms beyond migration per se and socioeconomic.

In order to reduce the risk of stillbirth and having a child with a congenital anomaly in all women, the causes of such disparities have to be understood, and migrant groups with both adverse and favorable reproductive health outcomes have to be studied. Currently, the risk factor profile for stillbirth and congenital anomalies differs between different ethnic groups and the antenatal and birth care systems need to consider the risk evaluation conducted for the individual woman. Specific risk factors for migrant women including adverse socioeconomic position, consanguinity, emotional strain due to isolation, and hostility or discrimination, and, for refugees, PTSD victims in the household have to be considered. With regard to public health and the health-care system, efforts to begin antenatal care at an early stage, provision of early prenatal screening for congenital anomalies, and information to young people about risk factors for stillbirth and congenital anomalies including prepregnancy folic acid supplementation and consanguinity are needed, along with improvements in health literacy for women and professionals in antenatal and perinatal care.
Practice points

- Migrant women are at a particularly high risk of giving birth to a stillborn child or a child having a congenital anomaly.
- The indicators for increased risk of stillbirth and congenital anomalies differ between ethnic groups.
- Symptoms associated with fetal suffering may be communicated by migrant women in a different or less specific manner to the health-care providers, who should be aware of this.
- Migrant-friendly antenatal care includes access to interpreter service during antenatal care visits and birth.
- Women, who are in a consanguineous union, are at a small absolute, however high relative, risk of having children with an autosomal recessive congenital anomaly, and prepregnancy counseling and antenatal diagnostics should be offered.

Research agenda

- The teratogenic effect of emotional strain and the causal relation between stress and stillbirth are suspected, but more research-based evidence is needed.
- Reproductive health consequences of discrimination are an under-explored area in European public health research.
- Complex interventions and proper evaluations of migrant-friendly antenatal and birth care are needed.
- While array platforms for testing ill children who are known to have consanguineous parents exist, genomic array platforms to test couples for risk before establishing pregnancy or other technologies to prevent autosomal recessive disorders in offspring of consanguine couples are lacking.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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