Perinatal health epidemiology in multi-ethnic Amsterdam: psychobiological processes

de Wolf, G.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)

Download date: 10 Jan 2020
Chapter 1

General introduction
Background

A healthy mother and child is the most precious outcome of human reproduction. Although medical focus and public’s concern is on unhealthy outcomes, the startling fact is that at a superficial level human reproduction rarely goes wrong despite its complexity. The development of a fetus is a mysterious but astonishing process. Growing evidence points towards a strong interaction with the maternal environment, preparing the fetus for the living conditions outside the womb.\textsuperscript{1-3} Many believe this to be an extremely ‘clever’, ‘efficient’, ultimately ‘selfish’ process, which supports the survival of human race.

Perinatal health epidemiology studies the health status of a mother and her baby during pregnancy, birth and the early postpartum period, and identifies causes and consequences of perinatal health problems. Main conventional indicators of perinatal health problems include on the one hand maternal mortality and morbidity (e.g. eclampsia), and on the other hand perinatal (fetal and neonatal) mortality and morbidity. Perinatal morbidity is mostly indicated by the following outcome measures: congenital anomalies, low birthweight or small-for-gestational-age (SGA), preterm birth (PTB) and a low Apgar score.\textsuperscript{4} Although the overall perinatal mortality rate decreased over the last decades due to improved living conditions and perinatal health care, the mortality rate in the Netherlands, and especially in its four largest cities (including Amsterdam), is high (10.0 per 1000 births) compared to other European countries.\textsuperscript{5,6} Partly as a consequence of the higher survival rate, perinatal morbidity rates increased over the last decades.\textsuperscript{4,7-9} Perinatal morbidity can be seen as a short-term marker of a poor intrauterine

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{chart}
\caption{Conceptual model for the emergence and persistence of health problems over the life course and across generations [sources: Kuzawa, 2008; Gravlee, 2009]}
\end{figure}
environment, which is not without long-term consequences. Pioneering research by Barker and colleagues strongly suggest a connection between perinatal morbidity and adult diseases like type 2 diabetes or cardiovascular disease; this is now known as the fetal programming hypothesis. Following this hypothesis, health problems may become a reinforcing circle over the life course and over generations (Figure 1.1). Increasing awareness on the multigenerational dimension of the reproductive cycle, and on the underlying genetic and epigenetic pathways, has made the field of perinatal health epidemiology more important than ever.

**Ethnicity and perinatal health epidemiology**

Worldwide, large differences in perinatal health outcomes exist between ethnic groups. In the United States (USA), for example, black infants are more than twice as likely to die as white infants, and in the United Kingdom (UK), Asian infants are more than twice as likely to have a low birthweight (<2500 g) as white infants. Also in the Netherlands ethnic differences in perinatal health outcomes exist, with the ethnic minority groups (e.g. Surinamese, Turkish or Moroccan groups) often having the worst outcomes. After years of research, the etiology of ethnic differences in perinatal health outcomes is still hardly understood. Ethnic inequalities in socioeconomic position or genetic differences between races are often held responsible, yet they lack explanatory exclusiveness and moreover, they lack preventive possibilities. Evidence is growing for an explanatory model in which ‘distal’ factors like socioeconomic position and genetic environment place pregnant women at greater susceptibility to ‘proximal’ risk factors, i.e. behavioral and physiological factors that directly influence maternal and fetal health. Potential proximal risk factors include stress, nutrition, infections, working conditions, living conditions, substance use, parity, maternal age, medical conditions and obstetric problems. In case of multiple (distal and/or proximal) risk factors, potential interaction effects could substantially increase the risk for perinatal health problems. These risk factors could, in theory, be mediators in the association between ethnic background and perinatal health outcomes. If confirmed, this will have huge implications for reducing ethnic differences in perinatal health outcomes. Below, we will expand on one of the potential mediating factors: maternal psychosocial stress.

**Psychobiological processes in perinatal health epidemiology**

As the overall prevalence of mental illnesses and stress-related problems is rising, the psychosocial health status of mother and child becomes more and more important in the field of perinatal health epidemiology. Women are two to three times more likely to experience mental health problems than men, particularly in the reproductive age. The prevalence of antenatal depression is, for example, estimated to be as high as 20%, although some claim the prevalence is not much unlike the prevalence in a comparable female population. While psychosocial problems in general already have a large impact on a woman’s life and that of her environment, psychosocial problems during pregnancy even have a much larger impact as it also affects the health of the fetus.

The commonly used term ‘psychosocial problems’ or ‘psychosocial stress’ covers a broad range of psychosocial indicators including emotional problems and disorders (e.g. depression,
anxiety), social stress, life events, work and household stress, domestic violence, racism and, in the case of pregnancy, pregnancy-related anxiety.\textsuperscript{25} Although it is not really appropriate to combine mental health problems with stress-related problems, for several reasons it is not uncommon in the field of perinatal health research. First, most studies measure mental health through self-report scales like the Center for Epidemiologic Studies Depression scale (CES-D)\textsuperscript{26} or the State-Trait Anxiety Inventory Questionnaire (STAI),\textsuperscript{27} which are not sufficiently valid to diagnose mental illness; they describe a mood state rather than a clinical entity or an etiologically coherent disease. Second, both mental health problems and stress-related problems share part of their symptoms and often appear as comorbid disorders.\textsuperscript{28} Third and most important, they probably share the same psychopathological mechanisms into perinatal health outcomes.\textsuperscript{25,28}

Numerous studies have examined the potentially negative effects of maternal psychosocial problems during pregnancy on perinatal health outcomes. Higher prevalences of PTB, low birthweight, SGA, certain congenital anomalies and a low Apgar score have been observed among infants born to mothers with psychosocial problems.\textsuperscript{8,25,28-39} Nevertheless, evidence on a causal contribution is far from consistent; to a large part this can be attributed to methodological differences between studies. Psychosocial problems, for instance, are operationalized by a wide variety of self-report scales; furthermore, they are measured during different time windows of pregnancy. In addition, studies differ in their consideration of potential confounding or mediating factors, such as maternal smoking behavior or nutritional intake.\textsuperscript{24,28,35,40-42} Besides the search for distinct evidence on the negative effects of maternal psychosocial problems on perinatal health outcomes, it is even more important to explore the psychopathological framework through which psychosocial stress affects fetal growth and development. Several psychopathological mechanisms have been proposed, with on top the involvement of the hypothalamic-pituitary-adrenal (HPA) axis. When a pregnant woman is exposed to a stressor, the HPA-axis releases, among others, cortisol, also called the ‘stress-hormone’, in order to help the body to recover. Normally, a placental barrier (including the enzyme 11β-hydroxysteroid-dehydrogenase type 2) protects the fetus from large amounts of maternal cortisol, however, in case of exposure to excess levels of cortisol the placental barrier may be too weak to protect the fetus any longer.\textsuperscript{2,25} This may result in reduced fetal growth, preterm parturition or teratogenic effects.\textsuperscript{28,37,38,43} Yet evidence for such a psychopathological mechanism is, so far, mainly provided by animal rather than human research.\textsuperscript{44-48}

The prevalence of maternal psychosocial problems during pregnancy is higher among ethnic minority groups. Turkish and Moroccan groups in Amsterdam had, for example, a higher prevalence of depressive and anxiety disorders (respectively 18.7\% and 9.8\%) compared to the Dutch group (6.6\%).\textsuperscript{49} This higher prevalence of maternal psychosocial problems could, in theory, be responsible for the higher prevalence of adverse perinatal health outcomes among the ethnic minority groups.\textsuperscript{50,51}

Psychobiological processes involved in fetal and infant health outcomes also include fetal origins of infant psychosocial health. In the first months of life, excessive crying behavior is a reasonable indicator of infant psychosocial stress. While many theories exist on the etiology of excessive infant crying, there is no general agreement.\textsuperscript{52} As a result, preventive measures are scarce and treatment of infants with excessive crying behavior is, so far, limited to advice parents to reduce stimulation or to
try hypoallergenic formula milk. Recently, the role of maternal nutrients in fetal neurodevelopment and, ultimately, infant behavior has gained interest. An early nutritional origin in infant crying behavior has, however, not yet been explored. Vitamin B-12 and folate seem to be good candidates because of their involvement in essential neuroendocrinological processes.

Aims and objectives of this thesis

The main aims of this thesis are (I) to explore perinatal health epidemiology in the multi-ethnic city of Amsterdam, the Netherlands, by examining (a) the perinatal health outcomes among the main ethnic groups in Amsterdam, and (b) to what extent ethnic disparities in perinatal health outcomes can be explained by ethnic differences in maternal risk factors during pregnancy; and (II) to elucidate psychobiological processes involved in (ethnic disparities in) perinatal health outcomes, by examining (c) the association between maternal psychosocial well-being during pregnancy (as indicated by self-report scales and the biomarker cortisol) and perinatal health outcomes, and vice versa, (d) the association between maternal risk factors during pregnancy, in particular maternal nutritional status, and infant psychosocial well-being (as indicated by infant crying behavior).

General Methods: ABCD study

To explore the association between (ethnic differences in) maternal risk factors during pregnancy and (ethnic disparities in) perinatal and infant health outcomes, a large prospective multi-ethnic cohort study among pregnant women in Amsterdam, the Netherlands, was initiated: the Amsterdam Born Children and their Development (ABCD) study. Initiators were the Public Health Service and Academic Medical Center in Amsterdam. Approval of the study was obtained from the Central Committee on Research involving Human Subjects in the Netherlands, the Medical Ethical Committees of participating hospitals and the Registration Committee of Amsterdam.

In the period from January 2003 until March 2004, all pregnant women living in Amsterdam were invited to enroll in the ABCD study at their first prenatal visit (median 13 pregnancy weeks, interquartile range 3 weeks) to participating obstetric care providers (general practitioners, midwives and gynecologists; overall participation rate 96%). For all approached women, the care provider completed a registration form with personal data such as name, address and country of birth. Based on this information, a pregnancy-questionnaire was sent to the pregnant woman's home address within two weeks, to be returned by prepaid mail. Reminders were sent two weeks after the initial mailing. Questionnaires were in Dutch and accompanied by an English, Turkish or Arabic copy depending on the woman's country of birth. Furthermore, Turkish and Moroccan women had the opportunity to contact Turkish- or Arabic-speaking trained female interviewers for oral administration of the questionnaire. This approach enhanced the inclusion of pregnant women from the main ethnic groups in Amsterdam: the Dutch, Surinamese, Antillean/Aruban, Turkish, Moroccan and Ghanaian group.
The pregnancy-questionnaire covered sociodemographic characteristics, (psychosocial) health status, lifestyle and obstetric history. Maternal psychosocial well-being during pregnancy was operationalized with several self-report scales. Depressive symptoms were measured by the Dutch version of the Center for Epidemiologic Studies Depression scale (CES-D); the 20-item CES-D scale assesses the self-reported frequency of depressive symptoms experienced over the past week. Anxiety was measured by the Dutch version of the state-scale of the State-Trait Anxiety Inventory (STAI); the 20-item state-scale asks subjects how they felt in the past week. State anxiety is conceptualized as a transient emotional condition. Pregnancy-related anxiety was measured by three scales (‘fear of giving birth’, ‘fear of bearing a handicapped child’, ‘concern about one’s appearance’) based on the Pregnancy Related Anxiety Questionnaire – Revised version (PRAQ-R). Parenting stress was measured by the Dutch version of the frequency scale of the Parenting Daily Hassles (PDH); the PDH scale lists 20 typical everyday events in parenting young children. Job strain was measured by four scales (‘pace of work’, ‘mental workload’, ‘physical workload’, ‘job control’) of the Dutch Work Experience and Appreciation Questionnaire (VBBA), based on the Job Content Questionnaire.

Pregnant women were also asked to participate in the ABCD biomarker study. For this purpose, an extra blood sample was drawn during routine blood collection at the first prenatal visit. Blood samples were analyzed for nutrients (including vitamin B-12 and folate) and hormones (including cortisol) at the National Institute for Public Health and the Environment (RIVM), Bilthoven, and the Medical Laboratory Dr. Stein & Colleagues, Maastricht, the Netherlands.

Three months after delivery (median 13 weeks postpartum, interquartile range 1 week), a baby-questionnaire was sent to the women who had given consent for follow-up. The baby-questionnaire covered the delivery, maternal lifestyle, and (psychosocial) health of the mother and her baby, including infant crying behavior. Women were also retrospectively asked whether they were exposed to physical and/or sexual violence during pregnancy.

Perinatal health outcomes were obtained from the Youth Health Care registration at the Public Health Service in Amsterdam. According to Dutch law, all children born in Amsterdam after 24 weeks’ gestation (either stillborn or liveborn) must be registered at the municipality’s Registry Office, after which a report is sent to the Youth Health Care Department. Between the 4th and 7th day after delivery, nurses from this department visit the liveborn infants for screening purposes. At this visit, they also record the date of delivery, infant gender, birthweight and gestational age at birth as provided by the obstetric care provider. These data are close to complete except for migrating families. Additional perinatal outcome data was obtained from the Dutch Perinatal Registration (PRN), which includes the national obstetric database for midwives (LVR-1), the national obstetric database for gynecologists (LVR-2), and the national neonatal database for pediatricians and neonatologists (LNR). These national data cover 95% of pregnancies, in the larger cities close to 100%.

Of all approached pregnant women in Amsterdam (n = 12,373), 8,266 women returned the pregnancy-questionnaire (response rate 67%) and 4,398 women also participated in the biomarker study. Of the 7,050 women who had given permission for follow-up, 5,218 returned the baby-questionnaire (response rate 73%). An overview of the subsamples available for each of the chapters of this thesis is presented in a flowchart in Figure 1.2.
Research questions

The following research questions will be addressed in the remaining chapters of this thesis:

Ethnicity and perinatal health outcomes
1. (a) Do the birthweights of term-born infants differ between ethnic groups; and (b) to what extent can the ethnic differences in birthweight be explained by constitutional vs. environmental risk factors? (Chapter 2)

2. (a) Does the prevalence of preterm birth (PTB), divided into spontaneous and iatrogenic preterm births, differ between ethnic groups; (b) to what extent can ethnic differences in PTB prevalence be explained by conventional risk factors; and (c) to what extent can a cumulation of conventional risk factors explain ethnic differences in PTB prevalence? (Chapter 3)

Maternal psychosocial and behavioral health
3. How do levels of maternal psychosocial problems during pregnancy relate to whether or not a woman continues to smoke during pregnancy? (Chapter 4)

Psychobiological pathways into perinatal health outcomes
4. (a) How does maternal depressive symptomatology during pregnancy relate to the prevalence of four major perinatal health outcomes, i.e. PTB, small-for-gestational-age (SGA), child loss and a low Apgar score; (b) does maternal smoking during pregnancy mediate these associations; and (c) does ethnic background modify these associations? (Chapter 5)

5. (a) How does maternal cortisol concentration during pregnancy relate to fetal growth as measured by offspring birthweight and SGA risk at term; and (b) to what extent do maternal cortisol levels mediate the association between maternal psychosocial problems during pregnancy and fetal growth? (Chapter 6)

Psychobiological pathways into infant health outcomes
6. (a) How do maternal vitamin B-12 and folate concentrations during pregnancy relate to the prevalence of excessive infant crying; and (b) in what way are maternal psychological problems during pregnancy involved in the association of vitamin B-12 and folate status with excessive infant crying? (Chapter 7)

In the general discussion (Chapter 8), the answers to the abovementioned research questions are summarized and discussed. Furthermore, methodological considerations, implications for interventions and recommendations for future research are discussed.
12,373 pregnant women in Amsterdam approached

- 8,266 women filled out the pregnancy-questionnaire
  - 2,008 women smoked before pregnancy
    - 7,949 available data on birthweight and pregnancy duration
      - Chapter 4
      - Chapter 5
  - twins excluded

- 4,389 women participated in the ABCD biomarker study
  - 4,252 available data on cortisol
    - Chapter 2
  - 4,255 available data on vitamin B-12
  - 3,938 available data on folate
    - Chapter 6

- 5,218 women filled out the baby-questionnaire
  - 5,120 available data on infant crying behavior
    - twins excluded

Figure 1.2 Flowchart of this thesis.
References