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## On perinatal pathology

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# CHAPTER 1

## **INTRODUCTION AND OUTLINE OF THESIS**



## **Introduction**

Death of a baby is one of the most painful and traumatic life events parents can experience. Perinatal mortality not only affects the parents but their relatives and the healthworkers involved as well. In the period just after death many issues have to be dealt with. In this thesis we address several of these issues and provide suggestions for obtaining permission for autopsy, for the use of placental examination, for improvement of placental reports, for better communication between pathologists and clinicians and for use of perinatal mortality classification systems. With these suggestions we hope to improve knowledge and care concerning perinatal mortality. Better knowledge and care will result in better analysis and hopefully contribute to preventive strategies for future cases.

## **Definition of perinatal mortality**

The perinatal period involves intrauterine life, the delivery and time after birth. In 1992 the World Health Organization (WHO) defined this perinatal period in the International Classification of Diseases version 10 (ICD 10) as: at least 22 completed weeks of gestation (154 days) or, if the gestational age is unknown, it includes infants with a birth weight of at least 500 grams or with a crown-heel length of at least 25 cm. This perinatal period lasts until 7 days after birth.<sup>1</sup> However, many different definitions have been used over time in- and between countries, thereby hampering (international) analysis of perinatal mortality figures.<sup>2</sup>

## **Perinatal mortality rates**

Perinatal mortality is an important problem and the perinatal mortality rate is among the most commonly used indicators for the health status of a population and for quality of obstetrical care. The perinatal mortality rate in developed countries, such as the Netherlands, is relatively low. The impact for the parents, family and also health workers however is enormous. Perinatal mortality rates have greatly declined over the past decades. The stillbirth rate halved between 1970 and 1998 and much of this decrease has occurred in (near) term babies.<sup>3</sup> The rate of early neonatal deaths fell even more.

A shift in stillbirths and neonatal deaths occurred. Preterm babies are delivered at an earlier gestational age in the case of expected intrauterine problems. Those babies die now in the neonatal period. On the other hand, the preterm neonates can be kept alive longer due to better neonatal intensive care facilities. Some of these babies will die after the neonatal period of seven days and therefore will be lost to the statistics of the perinatal period. At present, stillbirths account for almost half of perinatal mortality cases with an estimated 4 million stillbirths occurring worldwide every year. More than 97% of these take place in developing countries.<sup>4</sup> The intrapartum death rate in developed countries is a maximum 10% of stillbirth cases, while in the developing countries this rate can be up to 50%.<sup>5</sup>

## **Perinatal mortality in the Netherlands**

In 2003 the Peristat project revealed that the Netherlands is amongst the European countries with the highest perinatal mortality rates.<sup>6</sup> The Netherlands differ from other European countries because of the high percentage of home births. This, however, did not provide an explanation for the difference in mortality rates. Several other factors were considered responsible. First, in the Netherlands there is a reluctance to use

prenatal diagnosis and subsequent termination of pregnancy for congenital anomalies. These terminations of pregnancy usually occur before the perinatal period and accordingly would never appear in the perinatal statistics. Second, neonatologists are also more likely to refrain from treating very preterm newborns if their prospects are unfavourable. These untreated babies will die in the (early) neonatal period while treated babies may survive beyond the neonatal period. Third, the fact that more and more Dutch women have their first child when they are in their late twenties. The first time mothers in Holland are among the oldest mothers in the world, together with mothers in Greece and Spain.<sup>7</sup> This delay in childbearing also carries an increased risk of multiple pregnancies which forms an additional perinatal mortality risk. A fourth reason for the unfavourable mortality rates could be the relatively high percentage of non-western non-Dutch speaking women of low socio-economic background, from countries that carry relatively high risks of perinatal mortality, that have settled in the Netherlands. Consanguine relations are more frequent in some foreign groups, consanguinity results in more perinatal deaths caused by congenital anomalies. The final possible reason was a factor with unclear impact: the over-registration of perinatal deaths. The different registration systems (cause of death statistics and municipal population registration system) in the Netherlands are not linked with a unique linking key. The Peristat project used several registries, which can have resulted in double counting.<sup>8</sup> After publication of the Peristat a national feasibility study was initiated for audit of perinatal mortality (LPAS: Landelijke Perinatale Audit Studie) One of the elements of the perinatal audit is the determination of substandard factors in the care process and understanding its consequences for causality of mortality.

In 2008 the Peristat published results of the follow-up of the perinatal mortality rates in Europe and again the Netherlands was amongst the countries with the highest mortality rates in Europe.

## **Outline of the thesis**

The causes of perinatal mortality can be found in the mother, in the foetus, in the placenta and in their interaction. In order to determine the cause of death the, sometimes complex, processes can be analysed by thorough evaluation of the chain of events that eventually resulted in death.

## **Autopsy**

The analysis preferably involves an autopsy.<sup>10,11</sup> Perinatal autopsy rates however declined during the past decades for several reasons, the most recent being the “organ retention controversy” including the Alder Hey Scandal where pathologists retained organs without the consent or knowledge of the relatives.<sup>12</sup> The perinatal autopsy is the principal topic of the first chapters. In *Chapter 2* we assess the value of perinatal autopsy by reviewing the available literature on this subject. In *Chapter 3* we describe the topics concerning the autopsy that should be discussed with the parents, including differences in parental cultural and religious background.

## **Placenta**

Until recently the placenta has been a neglected source of information for establishing the diagnosis in case of perinatal mortality. This organ however forms the link between mother and foetus, it has been called the “diary” of pregnancy and should therefore always be submitted for pathological investigation in case of perinatal mortality. The next three chapters of this thesis focus on this special organ. In *Chapter 4* we address the quality of pathology reports of the placenta. We evaluate the reports for both their completeness and description of findings including the conclusion by the pathologist. For an estimation of the quality of the reports we use a selfdeveloped scoring system for evaluation of placental reports from four different hospitals. In *Chapter 5* we explain the rationale of evaluation of placentas. The importance of submission of placentas to the pathologist and communication between pathologist and obstetrician are illustrated. Some placental causes of foetal death are obvious and easy to diagnose by the clinician such as placental abruption (based mainly on the clinical diagnosis of vaginal bleeding and a “uterus en bois” resulting in foetal distress and death) other placental causes need to be diagnosed by the pathologist, for instance villous immaturity. This condition cannot be diagnosed on clinical history and macroscopic evaluation of the placenta alone, but requires histologic examination. We describe the evaluation of intrauterine foetal death cases caused by villous immaturity, either by villous immaturity alone or by villous immaturity in combination with other placental pathology, in our cohort of 1025 foetal deaths from the ZOBAS study (Zinnig Onderzoek bij Antepartum Sterfte) in *Chapter 6*.

## **Classification of perinatal mortality**

In the Netherlands, as in many other countries, the clinician enters the cause of death on a death certificate (the CBS B-form is used in the Netherlands) shortly after birth, despite unavailability of the results of autopsy, placental examination and other investigations. Reliable classification of perinatal mortality based on information from this death certificate is therefore not possible. Classification of perinatal mortality is essential to enable comparison of mortality figures; for audit of prenatal care and for determination of future preventive options.

In the last three chapters the aspects and results of a search for the ideal classification system are described. We aimed to find a classification system for perinatal mortality that classifies the underlying cause of death but also identifies the mechanism of death and risk factors. In our opinion none of the existing classifications was useful for our purpose. In *Chapter 7* we develop and test a new classification system for detecting the cause, mechanism and contributing factors of perinatal mortality: the Tulip classification. In *Chapter 8* we assess several classifications for their use in intrauterine foetal deaths, especially considering the placental causes of death. In *Chapter 9* we propose a systematic multilayered approach for the analysis of perinatal mortality that uses one or more of the previously published systems for classification of perinatal mortality.

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