The impact of cardiovascular diseases on maternal deaths in the Nordic countries

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ORIGINAL RESEARCH ARTICLE

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Abstract
Introduction: Cardiovascular diseases have become increasingly important as a cause of maternal death in the Nordic countries. This is likely to be associated with a rising incidence of pregnant women with congenital and acquired cardiac diseases. Through audits, we aim to prevent future maternal deaths by identifying causes of death and suboptimal factors in the clinical management.

Material and methods: Maternal deaths in the Nordic countries from 2005 to 2017 were identified through linked registers. The national audit groups performed case assessments based on hospital records, classified the cause of death, and evaluated the standards of clinical care provided. Key messages were prepared to improve treatment.

Results: We identified 227 maternal deaths, giving a maternal mortality rate of 5.98 deaths per 100,000 live births. The most common cause of death was cardiovascular disease (n = 36 deaths). Aortic dissection/rupture, myocardial disease, and ischemic heart disease were the most common diagnoses. In nearly 60% of the cases, the disease was not recognized before death. In more than half of the deaths, substandard care was identified (59%). In 11 deaths (31%), improvements to care that may have made a difference to the outcome were identified.
1 | INTRODUCTION

The Nordic countries are among the safest places to give birth, with maternal mortality ratios (MMR) among the lowest in the world. The Organization for Economic Co-operation and Development (OECD) reported an average MMR of 4/100 000 live births for the Nordic countries in 2005-2017. Cardiovascular diseases (CVD) are becoming increasingly important as causes of maternal deaths in these countries. This is likely to be associated with a rising incidence of pregnant women with congenital and acquired CVD. In addition, a reduction in deaths from other causes has led to a relative increase in the proportion of cardiac deaths. Maternal mortality due to CVD is also rising in several other countries, and has become the leading cause of maternal deaths in countries like the USA and the UK. This has been found to be related to an increase in incidences of acquired heart diseases, probably due to increased incidence of key cardiovascular risk factors, such as delayed childbirth, diabetes, hypertension, and obesity, as well as to improvements in survival to reproductive age of women with congenital heart disease. Rates of maternal mortality or heart failure are reported to be high in pregnant women with CVD. In the UK, substandard care was prominent in almost half of the maternal cardiovascular deaths and nearly one-third of the cases were deemed potentially preventable with different care according to the last MBRRACE-UK report.

The Nordic Maternal Mortality Collaboration was initiated in 2010. The aim of the collaboration has been to collect information based on a large population that consists of about 27 million inhabitants in five countries with close historical and cultural connections and similarities in the healthcare and social welfare systems; for example, antenatal care is free of charge for all, generally of high quality, with easy access and a high uptake. We have strived to use uniform methods to identify all maternal deaths in the Nordic countries, to classify them based on common international criteria, and to review each case of maternal death to evaluate the care provided.

The aim of the current study was to provide contemporary information on the impact of maternal CVD on maternal deaths in the Nordic countries. Our objective was to describe the incidence and type of CVD as a cause of maternal mortality. Through case reviews, we also aimed to identify elements of substandard care to improve clinical management of CVD in pregnancy and reduce maternal deaths in the future.

Conclusions: Between 2005 and 2017, cardiovascular diseases were the most common causes of maternal deaths in the Nordic countries. There appears to be a clear potential for a further reduction in these maternal deaths. Increased awareness of cardiac symptoms in pregnant women seems warranted.

KEYWORDS
audit, cardiovascular disease, cause of death, high-risk pregnancy, maternal mortality

2 | MATERIAL AND METHODS

We used the maternal death definition given by the International Classification of Diseases, 10th revision: the death of a woman while pregnant or within 42 days of termination of a pregnancy, irrespective of the duration and the site of the pregnancy, caused by a disease related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes. We report maternal deaths from the period 2005-2017 (complete years), but for Finland up to the end of 2012 only. Register linkage (between births and deaths registers, and inpatient registers) was used in combination with direct reporting from hospitals. In Finland, an extensive register linkage between births, deaths, pregnancy terminations, and the inpatient register combined with linkage to hospital records was possible. Register linkage was facilitated by the unique personal identification numbers used in all the Nordic countries, based on date of birth and a four- or five-digit personal identification code. All residents in one of the study countries at the time of death were included. We were not able to identify deaths among visitors, migrants, or asylum seekers not yet registered with a personal identification number. We calculated the MMR with a 95% CI as the number of deaths by the number of live births in women of 15-49 years of age. The denominator was derived from the respective national birth registers, which all contain information about women giving birth to a liveborn child with a gestational age of ≥22 weeks and/or birthweight ≥500 g. Experienced clinicians, including obstetricians, anesthesiologists, pathologists, and cardiologists, constituted the national audit groups. To classify the cause of death and quality of care, we used a data form based on the form used by the Confidential Enquiry into Maternal and Child Health and maintained by the UK Maternal, Newborn and Infant Clinical Outcome Review Program (MBRRACE-UK). We classified the quality of care as: (a)
good care—no improvements identified, (b) improvements to care identified that would have made no difference to the outcome, and (c) improvements in care identified that may have made a difference to the outcome. Current clinical care guidelines for each country constituted the reference standard for good care.

2.1 Ethical approval

Ethical approval was sought in the respective countries according to national law stipulations. In Sweden and Denmark, according to the Swedish and Danish legislations, no ethical approval was required. The Danish Data Protection Agency for 2002-2017 (File no. 2001-41-1148) and the Danish Patient Safety Authority for 2002-2017 (File no. 3-3013-599), the Icelandic National Bioethics Committee as well as the Data Protection Authority, and the Finnish Institute for Health and Welfare (Ref: THL/1092/5.05/2012) and Statistics Finland (Ref: TK53-1273-11) gave their permissions to use the confidential health data imported for this study. The Regional Committee for Medical and Health Research Ethics—North Norway approved the study for Norway (Ref: 2010/2854-6, date of approval: December 16, 2010).

3 RESULTS

In total, we identified 227 maternal deaths. Based on 3 792 904 live births over the study period, the MMR was estimated to be 5.98/100 000 (95% CI 5.26-6.82). Inter-country MMR differences were small and insignificant.

The underlying causes of death are summarized in Figure 1 with a total of 215 deaths. We did not have any information on the causes of death from Finland after 2012, so these deaths were excluded (n = 12). The most frequent causes of maternal death were CVDs (n = 36), hypertensive diseases of pregnancy (n = 28), psychiatric disorders (n = 24), thromboembolic complications (n = 20), obstetric sepsis (n = 19), anamniotic fluid embolism (n = 15), central nervous system diseases (n = 15), hemorrhage (n = 15), early pregnancy complications (n = 7), and pregnancy-related cancer (n = 5). Fourteen deaths were due to other causes, including immunological disease (n = 2), diseases of the gastrointestinal tract (n = 2), anesthetic complications (n = 1), and obstetric air embolus (n = 1). CVD was the most frequent cause of death in Norway, Sweden, and Denmark. Before 2012, Finland had a slightly different pattern, with psychiatric disorders, anamniotic fluid embolism, and hemorrhage being the most prevalent causes. Iceland had only two deaths in the study period.

The MMR for deaths from CVD was 0.98/100 000 live births. The annual number of maternal deaths from CVDs has remained stable during the study period with one to four deaths each year.

Among the 36 cardiovascular deaths in our material, the most common cause was aortic dissection with a total of 10 maternal deaths (Figure 2). Ischemic disease caused nine maternal deaths, myocardial disease caused eight deaths, and non-gestational hypertensive disease caused four deaths. Valvular heart disease was the cause of three deaths, and sudden arrhythmia death syndromes and pulmonary hypertension caused one death each.

In Table 1, general characteristics are presented. Mean age at death was 32.1 years, ranging from 20 to 42 years. Fourteen women (39%) were ≥35 years of age, while three women (8%) were ≥40 years old at the time of death. Mean body mass index (BMI) was 24.5 kg/m$^2$, ranging from 18 to 46 kg/m$^2$. Nine out of 33 women (27%) were obese with a BMI ≥ 30. Moreover, acquired heart disease was reported more often (78%) than congenital heart disease (22%). Nine out of 36 women (25%) were not born in a Nordic country, but four out of the nine were from another high-income country. Certain vulnerability factors were reported in nine women; five women were newly arrived immigrants or asylum seekers with language barriers. Three were unemployed, and one had a late start of antenatal care.

Twenty-one women (58%) were not diagnosed with a CVD before they died (Table 2). Among these women, nine out of ten had an acquired disease (86%). Although no women with a known CVD were obese, nearly half of the women with an unknown CVD had a BMI ≥ 30 kg/m$^2$. There were no significant differences in age between the two groups or in gestational age at delivery.

A vaginal delivery was planned for 12 women. Six of these women had their labor induced; two due to hypertensive disease, two were postdates, one had premature rupture of membranes, and one woman was induced due to intrauterine fetal death. The majority of women were delivered by cesarean section (67%), but only four of these were scheduled. The indications for the cesarean deliveries are given in Table

![FIGURE 1 Causes of maternal deaths in the Nordic countries 2005-2017 (n = 215; Finland from 2005 to 2012) [Color figure can be viewed at wileyonlinelibrary.com](image-url)](image-url)

![FIGURE 2 Maternal deaths caused by cardiovascular diseases, 2005-2017 (n = 36). PAH, pulmonary arterial hypertension; SADS, sudden arrhythmia death syndrome [Color figure can be viewed at wileyonlinelibrary.com](image-url)](image-url)
There were 24 live births among 34 deliveries after gestational week 22+0. Four neonates died within the first 7 days.

Results from the case reviews using clinical management guidelines as the reference standard for good care are shown in Table 4. The care provided was deemed good in 42% of the cases. Suboptimal care was identified in 21 cases (59%), and improvements in care that may have led to a different outcome were identified in 31% of cardiovascular deaths.

4 | DISCUSSION

We identified 227 maternal deaths in the Nordic countries during the 12-year study period. The MMR was 5.98/100 000 live births, a very low MMR from an international perspective. Overall, CVD was the most common cause of death, with an incidence of 0.98/100 000 live births.

We found the MMR to be higher than in the official OECD statistics of 4/100 000 live births. According to the World Health Organization, official reports underestimate the true magnitude of maternal mortality worldwide, and previous studies have identified underreporting in official statistics in the Nordic countries.

There is no reason to believe that underreporting is more prevalent in the Nordic countries compared with other OECD countries. However, this indicates that official statistics alone are not sufficient for the identification of all maternal deaths. Accurate data on the number and causes of maternal deaths are essential to provide advice on improvements of care provided to pregnant women. To achieve better identification, we used multiple sources: extensive register linkages, direct reporting of maternal deaths from the hospitals to the audit groups, hospital records, death certificates, and autopsy data. We believe we have identified almost all maternal deaths within 42 days of delivery. However, we may have missed cases in which the delivery was not reported to any register and no obstetric diagnosis was reported to the Cause of Death Registers. Furthermore, unregistered deaths during early gestation, before the pregnancy was confirmed, may have occurred. The classification of maternal deaths is shown in Table 4.
is sometimes difficult. In a retrospective clinical audit study, the quality of the collected information is never optimal, as the audit is based on past clinical documentation. There is always a possibility of information bias due to misclassification of exposures. In each audit group, pathologists, cardiologists, and anesthesiologists were consulted to avoid misclassification. Cases that were difficult to classify were discussed in the Nordic group. As maternal deaths are rare in the Nordic countries, an international collaboration like The Nordic Maternal Mortality Collaboration is essential.

The women who died from CVD in the Nordic countries were older and more often obese (BMI ≥ 30 kg/m²) than the general pregnant population. In our material, 27% were obese at the start of pregnancy, compared with approximately 12% in the general pregnant population in the Nordic countries in the same time period. Likewise, 39% were ≥35 years of age, compared with 20% in the general pregnant population. An age of 40 years or more is related to increased risk of heart-related maternal deaths. Four women (11%) were diagnosed with hypertension before pregnancy. In Norway and Denmark, this applies to 0.5% of all pregnant women. Two women (5.5%) had type 1 diabetes, compared with 0.5% in the general pregnant population in the Nordic countries.

In a study from Norway, 25% of all pregnant women were born in a country outside the Nordic countries. Similarly, 25% of the women in our material were not born in a Nordic country. In the USA and the UK, ethnicity is reported to be an important risk factor for maternal cardiovascular deaths. In comparison, the impact of ethnicity seems to be less important in the Nordic countries. This may be a result of healthcare systems in the Nordic countries being free of charge for all and there is lower skewedness in the provision of health care in relation to ethnicity or migrant status. A recent study has reported a higher incidence of non-diagnosed heart disease in refugee populations in Australia and New Zealand, but this was not found to be reflected in the present Nordic study. However, it is worth mentioning that three out of the five women from a low- or middle-income country in our study were newly arrived immigrants with the associated inherent vulnerability.

Nearly 60% of the women with cardiac deaths had no known CVD before the tragic event. Similarly, 75% of the women with cardiac deaths in the UK did not have a known cardiac disease. Half of the women with an unknown disease were obese, probably reflecting the fact that 86% of these women had an acquired disease. None of the women in the known CVD group were obese.

To prevent deaths in pregnant women with an unknown heart disease, we need a higher awareness of cardiac symptoms in pregnant women. Presenting symptoms of a CVD may be sudden, with an acute onset of chest pain, breathlessness, and collapse. These women should be thoroughly investigated in the same way as nonpregnant women. The possibility of CVD in a woman of reproductive age is not at the front of many healthcare workers minds. In many cases, clear symptoms of cardiac problems were not recognized in a timely way, and this led to a delayed assessment of women with complaints such as chest pain, infrascapular pain, back pain, tachycardia, and dyspnea, and hence to a delay in diagnosis. Moreover, there seemed to be an inadequate use of maternal early warning scores in assessing the severity of their symptoms. Similar findings were reported in a Dutch study where the authors concluded that a high index of suspicion of cardiac problems when a woman presents with suggestive complaints may improve the prognosis for the woman and the fetus. Furthermore, appropriate investigative tools such as echocardiogram and blood tests, as well as more invasive techniques such as a coronary angiogram or a CT-angiogram, were rarely used. As more women with comorbidities, primarily with regard to age and obesity, appear in the pregnant population, there is an increased need for specialist obstetric care. Pregnant women with known moderate to severe CVD should be referred to a center with a multidisciplinary medical team with specific clinical competences, including access to heart surgery. Preconceptional counseling is advised for all women with a known CVD as this is associated with better clinical outcome.

### 4.1 Aortic dissection

Aortic dissection caused one-quarter of the deaths (26%), thus being the most common cause. In a recent Dutch publication on maternal cardiovascular deaths from the years 1983-2013, 21% of deaths were caused by aortic dissection. In the UK, aortic dissection caused 20% of maternal cardiac deaths in 2011-2013, declining to 11% in 2015-2017, possibly as the result of an increased awareness through campaigns such as “Think aorta” (www.thinkaorta.org). An estimated 50% of all cases of aortic dissection that occur in women younger than 40 years are associated with pregnancy, with most cases occurring in the third trimester or the early postpartum period. Both congenital and acquired factors, alone or in combination, can lead to aortic dissection and they carry a high risk of death. In our material, 60% had pre-existing risk factors such as obesity and hypertension, similar to what was found in a Dutch study on maternal deaths from vascular dissection. Awareness among clinicians of the increased risk and clinical presentations of aortic dissection in pregnancy were lacking when reviewing the Nordic deaths. A failing focus on family history was also reported, as post mortem information revealed that some of the women had family members who had died of aortic dissection. Known genetic aortopathy before pregnancy was reported in only two of these women, both diagnosed with Marfan syndrome. However, women with a family history or known genetically confirmed aortopathy should be referred for cardiac assessment before and during pregnancy to reduce the risk of adverse outcome and death.

### 4.2 Myocardial disease

Myocardial disease caused nine deaths (21%), similar to reports from other countries. The clinical presentation of myocarditis...
high incidence of histologically proven myocarditis in patients with cardiomyopathy, and several reports have demonstrated a relatively high incidence of histologically proven myocarditis in patients with peripartum cardiomyopathy. They all had an autopsy-verified diagnosis. Myocarditis has been suggested as a possible cause of peripartum cardiomyopathy. Among the cardiomyopathies, five women were diagnosed with myocarditis, whereas only two were diagnosed with peripartum cardiomyopathy, and several reports have demonstrated a relatively high incidence of histologically proven myocarditis in patients with peripartum cardiomyopathy. In addition, only deaths within 42 days postpartum were included and peripartum cardiomyopathy disease typically presents 1-3 months postpartum, with mortality rates up to 25% within 6 months.

The prevalence of coronary artery disease in pregnancy is reported to be rising due to the increasing prevalence of comorbid risk factors in pregnant women, such as delayed childbearing, obesity, and diabetes. This is similar to findings in our material, where 21% of the women died from ischemic heart disease, a prevalence very similar to other reports. Diagnostic delay has been proposed as a critical factor as many symptoms resemble physiological pregnancy signs, causing diagnostic measures to be insufficient and delayed; hence misdiagnosis. Besides, hesitance to perform diagnostic and interventional procedures in pregnancy still exists.

The Netherlands and the UK have reported a large proportion of deaths from sudden arrhythmia death syndromes (sudden arrhythmic death with a morphologically normal heart), with 20% and 18%, respectively. In the Nordic countries, only one death from sudden arrhythmia death syndromes was reported. This may be a result of how sudden unexplained maternal deaths are classified in the Nordic countries.

The majority of women (24/36) who died of CVD underwent cesarean section, of which only four were scheduled (17%). The fact that the majority were emergency cesareans may indicate that the recognition of the severity of, or the existence of, a CVD came too late. The indication for the cesarean delivery was cardiac arrest in 11 women. The perimortem cesarean sections (PMCS) were performed between 4 and 40 min after the cardiac arrest occurred, with only one PMCS performed within the recommended 5 min. To maximize the chance of survival, the urgency with which the PMCS can be performed after the onset of the cardiac arrest is highly important, and it should be undertaken at the site of the cardiac arrest. This will only be possible if the cardiac arrest happens inside the hospital. All but one woman arrested in the hospital, but three women were moved to the operating room before the cesarean section was performed. PMCS is an extremely rare event, and it is very unlikely that the obstetrician has experienced this before, and a prompt clinical decision can be difficult to make. However, multidisciplinary team training has been shown to be effective in reducing the time interval from the initial arrest to PMCS and should be undertaken in all units where care for obstetric patients is provided.

Substandard care was prominent in more than half of the maternal cardiovascular deaths in the Nordic countries. Similar to the UK, one-third of the cases were deemed potentially preventable with different care. The main topics were lack of prepregnancy counseling, delayed referrals to a cardiologist or to a hospital at the right level of specialty, delayed diagnosis, and delayed medical treatment of the cardiac condition. Based on assessment of the cases, we derived the following overall learning points to improve care in CVDs in pregnancy:

1. Pregnant women with known moderate to severe heart disease should receive care at a center with a multidisciplinary medical team encompassing special competences, including heart surgeons.
2. A detailed plan for the pregnancy and the delivery should be easily accessible in the medical records.
3. Preconceptional counseling should be offered to women with known CVD.
4. Increased focus on family history to obtain information on potential genetic predispositions, for example, deaths from arterial dissection in the family.
5. Raised awareness among clinicians on risk factors and clinical presentation of CVDs in pregnant women is warranted.
6. Symptoms such as chest pain or high back pain, persistent tachycardia, raised respiratory rate, or breathing difficulties in a pregnant woman should always lead to further investigations and a clinical review by a senior doctor.
7. Pregnancy is a major risk factor for vascular dissection or rupture and should always be considered in sudden unexplained back pain or chest pain.
8. Clinical investigations should not be withheld, due to pregnancy, when deemed necessary for the diagnosis of critical illness.
9. Autopsies by trained pathologists should be performed in all cases of unexplained maternal deaths.
10. Regular multidisciplinary team training in advanced life support for obstetric patients, maternal early warning score assessment, and perimortem cesarean sections should be undertaken regularly in all obstetric units to improve maternal survival in life-threatening emergencies.

5 | CONCLUSION

A proportion of maternal deaths caused by CVDs may be prevented in the future by a raised awareness of cardiovascular symptoms in pregnant women and by improved care.

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CONFLICT OF INTEREST
None.

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