Perinatal Mortality and Advanced Maternal Age

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Introduction

In industrialized countries a growing number of women delay reproduction until later in life \cite{1}. Consequently, the effect of advanced maternal age on perinatal mortality is becoming of increasing interest. However, the impact of maternal age on perinatal mortality is controversially discussed. While several studies \cite{2–6} have failed to find a higher risk for adverse pregnancy outcome in women older than 40 years, the adjusted ORs for perinatal mortality were 1.03 (95\% CI: 0.77–1.39) and 1.66 (95\% CI: 1.03–2.66) for age groups 35–39 and ≥40, respectively. Conclusions: Women older than 40 years carry an increased risk for stillbirth. Important amendable risk factors are obesity and poor antenatal care.

Key Message

- Women older than 40 years carry an increased risk for stillbirth which is particularly high at around 31 gestational weeks. Important amendable risk factors are obesity and poor antenatal care.

Key Words

Perinatal mortality · Maternal age · Stillbirth · Stillbirth risk

Abstract

Objective: To investigate the impact of advanced maternal age on the rate of perinatal mortality. Design: Retrospective cohort study including all 56,517 singleton hospital deliveries between 1999 and 2008. Methods: Data were analyzed according to maternal age at delivery in 3 groups of women, 25–34 years, 35–39 years and ≥40 years, using the youngest as the reference group. Results: Odds ratios (ORs) for antenatal deaths were 0.98 (CI: 0.67–1.43) and 2.57 (CI: 1.57–4.22) for age groups 35–39 years and ≥40 years, respectively. Significant differences in neonatal mortality rates between the age groups were not found. Significant amendable risk factors were attendance of <4 health care visits (OR = 15.55, CI: 9.47–25.51 in age group 35–39 years; OR = 16.38, CI: 9.78–27.43 in the age group ≥40 years). In the multivariate regression analysis, the adjusted ORs for perinatal mortality were 1.83 (CI: 1.22–2.74) in the age group 35–39 years; OR = 1.66, CI: 1.03–2.66 for age groups 35–39 and ≥40, respectively. Conclusions: Women older than 40 years carry an increased risk for stillbirth. Important amendable risk factors are obesity and poor antenatal care.
women older than 35 or 40 years, others have documented an increased rate of adverse perinatal outcome in these women [7–12].

This study aims to further investigate the impact of advanced maternal age on the rate of perinatal mortality in the state of Tyrol, Austria. This information should facilitate counselling women of advanced maternal age intending to become pregnant and allow them to improve on potential amendable risk factors.

**Patients and Methods**

This is a retrospective cohort study involving all 56,517 singleton hospital deliveries, which occurred in the state of Tyrol, Austria between January 1, 1999 and December 31, 2008 in women 25 years and older. In this time period the hospital deliveries accounted for 99.9% of all deliveries in Tyrol and 95.4% of women delivering were living in the state of Tyrol.

In Tyrol there are 10 district and council hospitals and one university hospital. The region is inhabited by a population of almost 700,000 people and characterized by a high economic standard. About 10% of the inhabitants are of foreign nationalities, comprising 25% from former Yugoslavia, 16% from Turkey and 44% from other countries of the European Union [13].

The data for this study were retrieved from the Perinatal Register of Tyrol. In this database, obstetricians and midwives of all the hospitals of the state of Tyrol provide data structured according to the German Quality Assurance Program (Datensatz Geburtshilfe 1G; specification 14.0 SR. AQUA Institute for Applied Quality Improvement and Research in Health Care, Göttingen, Germany) [14]. Besides demographic information, the data essentially consist of basic data on the course of pregnancy and delivery as well as the perinatal outcome. Information on perinatal mortality is completed by record linkage with the official mortality data for Tyrol (provided by the national statistical organization Statistics Austria) and the neonatal department of Innsbruck Medical University Hospital, which is the tertiary referring institution for all hospitals in Tyrol. Plausibility checks and checks for completeness of data are an integral part of the software, and quality checks are conducted on a regular basis. The deliveries were analyzed according to maternal age at delivery in 3 groups, namely of women 25–34 years, 35–39 years and ≥40 years or older. The group aged 25–34 years was used as reference group for the calculation of the perinatal mortality. In the Perinatal Register of Tyrol, the term housewife is used as a separate category. However, this is an inhomogeneous group regarding educational level and for this reason we summarized this group in the group ‘unknown educational status’.

Statistical analysis was done using STATA statistical software version 11 (StataCorp LP, College Station, Tex., USA). Univariate and age-adjusted odds ratios (OR) were calculated for perinatal mortality as the main endpoint unless otherwise specified. For the final analysis and in order to account for confounding, we applied a logistic regression model. A multivariate model was built starting with terms for age, postmiscarriage status, occupation, smoking, obesity, immigrant status, <4 prenatal care visits, mode of delivery, parity and SGA. Following a backward strategy, variables were tested for significance with the Wald test and dropped if they were not statistically significant. The variables maternal obesity, immigrant status, mode of delivery and SGA remained in the final multivariate model. Preterm birth was considered an outcome and therefore not included in the model. Different rates and medians in patient characteristics were tested with the χ² test and the Mann-Whitney U test. Values of p < 0.05 were considered statistically significant.

**Results**

Between 1999 and 2008 there were 56,517 singleton deliveries in women of 25 years of age or older in the 11 hospitals located in the Austrian state of Tyrol. The numbers and percentage of births of women aged 25–34 years, 35–39 years and ≥40 years were 43,313 (76.6%), 10,932 (19.3%) and 2,272 (4.0%), respectively. 18,666 (41.5%) of the mothers were nulliparous and 26,320 (58.5%) were multiparous.

Detailed patient characteristics are given in table 1. In comparison to the reference group, mothers aged 35–39 years and ≥40 years or older were significantly better educated, less often smokers, less often of immigrant status, more likely to be obese and presented more often with <4 healthcare visits during pregnancy than their younger counterparts. Cesarean section was to a markedly greater extent the mode of delivery in women age 40 years or older.

The rate of preterm delivery was significantly increased in the 35–39 years of age group and in the ≥40 group in comparison to the reference group, as was the rate of babies with a birth weight between 1,000 and 2,499 g. There was no statistical significant difference in the median birth weights between the 3 groups and also not in the fraction of neonates with SGA.

Median gestational age at stillbirth was 32, 34 and 31 gestational weeks in the reference group, in the group of women aged 35–39 years and in the group of women aged ≥40 years, respectively. No difference in the mean or median duration of delivery was noticed between the age groups, even when separated by parity.

Three hundred and eight perinatal deaths occurred during the study period (table 2). Women ≥40 years were
affected by a more than twofold increased rate of perinatal mortality than their younger counterparts. The OR for antenatal deaths were 0.98 (CI: 0.67–1.43) and 2.57 (CI: 1.57–4.22) for age groups 35–39 years and ≥40 years, respectively. No significant differences in neonatal mortality rates were found (fig. 1).

Perinatal mortality rates in the 3 age groups are shown in table 3 in detail. Smoking, obesity, immigrant status, <4 healthcare visits and cesarean section were significant risk factors for perinatal mortality in the age groups 35–39 years and ≥40 years, respectively. Low birth weight, preterm birth and SGA are the highest age-dependent risk factors for perinatal mortality.

The perinatal death rate in the SGA group was threefold higher in the ≥40 years of age group than in both younger age groups. Perinatal death in the preterm birth group occurred more often in the ≥40 years of age group than in the younger age groups. Birth weight below

<table>
<thead>
<tr>
<th>Table 1. Patient characteristics</th>
<th>Total (100%)</th>
<th>Age 25–34 years</th>
<th>Age 35–39 years</th>
<th>p</th>
<th>Age ≥40</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous miscarriage</td>
<td>11,543 (20.4)</td>
<td>7,791 (18.0)</td>
<td>2,955 (27.0)</td>
<td>&lt;0.001</td>
<td>802 (35.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Occupation/education</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Well educated</td>
<td>7,903 (14.0)</td>
<td>5,461 (12.6)</td>
<td>2,002 (18.3)</td>
<td>&lt;0.001</td>
<td>440 (19.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skilled</td>
<td>25,986 (46.0)</td>
<td>20,591 (47.5)</td>
<td>4,514 (41.3)</td>
<td>881 (38.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undergoing education</td>
<td>537 (1.0)</td>
<td>501 (1.2)</td>
<td>32 (0.3)</td>
<td>4 (0.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unskilled</td>
<td>6,255 (11.1)</td>
<td>4,936 (11.4)</td>
<td>1,091 (10.0)</td>
<td>228 (10.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>15,836 (28.0)</td>
<td>11,824 (27.3)</td>
<td>3,293 (30.1)</td>
<td>719 (31.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>5,728 (10.1)</td>
<td>4,523 (10.4)</td>
<td>996 (9.1)</td>
<td>209 (9.2)</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Obese (BMI &gt;30)</td>
<td>3,737 (6.7)</td>
<td>2,814 (6.6)</td>
<td>733 (6.8)</td>
<td>n.s.</td>
<td>190 (8.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unknown BMI</td>
<td>972 (1.7)</td>
<td>730 (1.7)</td>
<td>192 (1.8)</td>
<td>50 (2.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immigrant status</td>
<td>7,835 (13.9)</td>
<td>6,355 (14.6)</td>
<td>1,270 (11.6)</td>
<td>&lt;0.001</td>
<td>230 (10.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;4 prenatal care visits</td>
<td>294 (0.6)</td>
<td>198 (0.5)</td>
<td>72 (0.7)</td>
<td>0.007</td>
<td>24 (1.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>42,935 (76.0)</td>
<td>33,706 (77.8)</td>
<td>7,770 (71.1)</td>
<td>&lt;0.001</td>
<td>1,459 (64.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>13,566 (24.0)</td>
<td>9,596 (22.2)</td>
<td>3,157 (28.9)</td>
<td>813 (35.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Birth weight

| Median, g | 3,320 | 3,320 | 3,320 | 3,290 |
| Very low (<1,000 g) | 216 (0.4) | 159 (0.4) | 41 (0.4) | <0.001 | 16 (0.7) | <0.001 |
| Low (1,000–2,499 g) | 3,336 (5.9) | 2,384 (5.5) | 764 (6.8) | 206 (9.1) |     |      |
| Normal (2,500–3,999 g) | 48,809 (86.4) | 37,643 (86.9) | 9,294 (85.0) | 1,872 (82.4) |     |      |
| Macrosomia (>4,000 g) | 4,156 (7.4) | 3,127 (7.2) | 851 (7.8) | 178 (7.8) |     |      |
| SGA (<3rd percentile) | 1,722 (3.0) | 1,319 (3.1) | 325 (3.0) | n.s. | 78 (3.4) | n.s. |
| Preterm (<37th gestational week) | 4,534 (8.0) | 3,252 (7.5) | 995 (9.1) | <0.001 | 287 (12.6) | <0.001 |

Gestational age at stillbirth, weeks

| Median | 32 | 32 | 34 | 31 |
| Range | 20–42 | 20–42 | 23–39 | 23–40 |

Values represent number of women (%) unless otherwise indicated. n.s. = Not significant.

<table>
<thead>
<tr>
<th>Table 2. Peri-, ante- and neonatal mortality according to maternal age</th>
<th>Total</th>
<th>Age 25–34 years</th>
<th>Age 35–39 years</th>
<th>Age ≥40 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal deaths</td>
<td>308 (0.5%)</td>
<td>224 (0.5%)</td>
<td>59 (0.5%)</td>
<td>25 (1.1%)</td>
</tr>
<tr>
<td>Univariate OR (95% CI)</td>
<td>1 (reference)</td>
<td>1.04 (0.78–1.39)</td>
<td>3.14 (1.41–6.92)</td>
<td>3.34 (1.61–6.88)</td>
</tr>
<tr>
<td>Antenatal deaths</td>
<td>185 (0.3%)</td>
<td>134 (0.3%)</td>
<td>33 (0.3%)</td>
<td>18 (0.8%)</td>
</tr>
<tr>
<td>Univariate OR (95% CI)</td>
<td>1 (reference)</td>
<td>0.98 (0.67–1.43)</td>
<td>2.57 (1.57–4.22)</td>
<td>7 (0.3%)</td>
</tr>
<tr>
<td>Neonatal deaths</td>
<td>123 (0.2%)</td>
<td>90 (0.2%)</td>
<td>26 (0.2%)</td>
<td>7 (0.3%)</td>
</tr>
<tr>
<td>Univariate OR (95% CI)</td>
<td>1 (reference)</td>
<td>1.14 (0.74–1.77)</td>
<td>1.48 (0.69–3.21)</td>
<td>7 (0.3%)</td>
</tr>
</tbody>
</table>
1,000 g was the strongest risk factor for perinatal death with an age adjusted OR of 458.89. Macrosomia was not identified as a risk factor.

In the multivariate regression analysis for perinatal mortality only maternal obesity, immigrant status, mode of delivery and SGA remained statistically significant (table 4). Adjusted ORs for perinatal mortality were 1.03 (95% CI: 0.77–1.39) and 1.66 (95% CI: 1.03–2.66) for age the groups 35–39 years and ≥40 years, respectively (fig. 1).

### Table 3. Perinatal mortality rates according to maternal age

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 56,517; 100%)</th>
<th>Age 25–34 years (n = 43,313; 76.6%)</th>
<th>Age 35–39 years (n = 10,932; 19.3%)</th>
<th>Age-adjusted OR (95% CI)</th>
<th>p</th>
<th>Age ≥40 years (n = 2,272; 4.0%)</th>
<th>Age-adjusted OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous miscarriage</td>
<td>83 (0.7)</td>
<td>58 (0.7)</td>
<td>19 (0.6)</td>
<td>1.52 (1.17–1.98)</td>
<td>0.002</td>
<td>6 (0.7)</td>
<td>1.42 (1.06–1.89)</td>
<td>0.017</td>
</tr>
<tr>
<td>Occupation/education</td>
<td></td>
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<tr>
<td>Well educated</td>
<td>31 (0.4)</td>
<td>20 (0.4)</td>
<td>9 (0.4)</td>
<td>Reference</td>
<td></td>
<td>2 (0.5)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Skilled</td>
<td>119 (0.5)</td>
<td>87 (0.4)</td>
<td>21 (0.5)</td>
<td>1.11 (0.74–1.68)</td>
<td>0.609</td>
<td>11 (1.2)</td>
<td>1.20 (0.81–1.79)</td>
<td>0.363</td>
</tr>
<tr>
<td>In education</td>
<td>4 (0.7)</td>
<td>4 (0.8)</td>
<td>1 (0.5)</td>
<td>1.96 (0.69–5.61)</td>
<td>0.209</td>
<td>2 (0.7)</td>
<td>2.04 (0.71–5.80)</td>
<td>0.184</td>
</tr>
<tr>
<td>Unskilled</td>
<td>41 (0.7)</td>
<td>33 (0.7)</td>
<td>8 (0.5)</td>
<td>1.63 (1.01–2.66)</td>
<td>0.047</td>
<td>3 (1.3)</td>
<td>1.72 (1.08–2.75)</td>
<td>0.023</td>
</tr>
<tr>
<td>Housewife</td>
<td>69 (0.6)</td>
<td>46 (0.6)</td>
<td>17 (0.7)</td>
<td>1.52 (0.98–2.36)</td>
<td>0.063</td>
<td>6 (1.1)</td>
<td>1.58 (1.03–2.42)</td>
<td>0.035</td>
</tr>
<tr>
<td>Unknown</td>
<td>44 (1.0)</td>
<td>34 (0.9)</td>
<td>7 (0.9)</td>
<td>2.42 (1.50–3.90)</td>
<td>0.000</td>
<td>3 (1.8)</td>
<td>2.54 (1.60–4.02)</td>
<td>0.000</td>
</tr>
<tr>
<td>Lifestyle</td>
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</tr>
<tr>
<td>Smoker</td>
<td>42 (0.7)</td>
<td>32 (0.7)</td>
<td>6 (0.6)</td>
<td>1.37 (0.97–1.94)</td>
<td>0.070</td>
<td>4 (1.9)</td>
<td>1.47 (1.03–2.10)</td>
<td>0.032</td>
</tr>
<tr>
<td>Obese (BMI &gt;30)</td>
<td>34 (0.9)</td>
<td>24 (0.9)</td>
<td>7 (1.0)</td>
<td>1.85 (1.27–2.70)</td>
<td>0.001</td>
<td>3 (1.6)</td>
<td>1.83 (1.22–2.74)</td>
<td>0.003</td>
</tr>
<tr>
<td>Immigrant status</td>
<td>22 (2.3)</td>
<td>12 (1.6)</td>
<td>4 (2.1)</td>
<td>Reference</td>
<td></td>
<td>6 (1.2)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>&lt;4 prenatal care visits</td>
<td>68 (0.9)</td>
<td>56 (0.9)</td>
<td>10 (0.8)</td>
<td>1.88 (1.42–2.48)</td>
<td>&lt;0.001</td>
<td>2 (0.9)</td>
<td>1.85 (1.38–2.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
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</tr>
<tr>
<td>Vaginal delivery</td>
<td>213 (0.5)</td>
<td>152 (0.5)</td>
<td>44 (0.6)</td>
<td>Reference</td>
<td></td>
<td>17 (1.2)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Cesarean section</td>
<td>95 (0.7)</td>
<td>72 (0.8)</td>
<td>15 (0.5)</td>
<td>1.45 (1.12–1.86)</td>
<td>0.004</td>
<td>8 (1.0)</td>
<td>1.55 (1.18–2.03)</td>
<td>0.001</td>
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<tr>
<td>Birth weight</td>
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<td></td>
</tr>
<tr>
<td>Very low (&lt;1,000 g)</td>
<td>102 (47.2)</td>
<td>75 (47.2)</td>
<td>17 (41.5)</td>
<td>415.78 (295.15–585.73)</td>
<td>&lt;0.001</td>
<td>10 (62.5)</td>
<td>458.89 (317.17–663.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low (1,000–2,499 g)</td>
<td>102 (3.1)</td>
<td>69 (2.9)</td>
<td>22 (2.9)</td>
<td>14.63 (10.96–19.54)</td>
<td>&lt;0.001</td>
<td>11 (5.3)</td>
<td>15.44 (11.29–21.12)</td>
<td>&lt;0.001</td>
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<td>Normal (2,500–4,000 g)</td>
<td>98 (0.2)</td>
<td>76 (0.2)</td>
<td>18 (0.2)</td>
<td>Reference</td>
<td></td>
<td>2 (0.1)</td>
<td>Reference</td>
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<tr>
<td>SGA (&lt;3rd percentile)</td>
<td>6 (0.1)</td>
<td>2 (0.1)</td>
<td>2 (0.2)</td>
<td>0.49 (0.18–1.34)</td>
<td>0.164</td>
<td>2 (1.1)</td>
<td>0.60 (0.22–1.63)</td>
<td>0.311</td>
</tr>
<tr>
<td>Preterm (&lt;37th gestational week)</td>
<td>208 (4.6)</td>
<td>149 (4.6)</td>
<td>41 (4.1)</td>
<td>25.21 (19.63–32.38)</td>
<td>&lt;0.001</td>
<td>18 (6.3)</td>
<td>24.94 (19.09–32.58)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values represent number of women (%) unless otherwise indicated.

### Table 4. Multivariate logistic regression analysis of perinatal mortality

<table>
<thead>
<tr>
<th></th>
<th>Age-adjusted OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
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<tr>
<td>25–34</td>
<td>1</td>
</tr>
<tr>
<td>35–39</td>
<td>1.03</td>
</tr>
<tr>
<td>≥40</td>
<td>1.66</td>
</tr>
<tr>
<td>Maternal obesity</td>
<td>1.83</td>
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<tr>
<td>Immigrant status</td>
<td>1.72</td>
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<td>Mode of delivery</td>
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<tr>
<td>Vaginal delivery</td>
<td>1</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>1.3</td>
</tr>
<tr>
<td>SGA (weight below 3rd percentile)</td>
<td>5.57</td>
</tr>
</tbody>
</table>

Color version available online.

![Fig. 1. Antenatal and postnatal mortality in different age groups.](image-url)
Discussion

This study suggests that the risk for perinatal deaths in women aged ≥40 years is twice as high compared to the risk of women aged 25–34 years. This increment in risk is solely caused by an increased rate of stillbirths; the neonatal death rate is not significantly different between the age groups. Furthermore, we did not find an increased risk for perinatal mortality in the age group 35–39 years compared to women aged 25–34 years. We chose the women between 25 and 34 years of age to be the reference group, as the perinatal mortality in these women is particularly small [12].

This was a hospital-based study and involved all hospitals of all levels of care in the state of Tyrol, Austria. Due to the structure of the Austrian health system, the study population includes the vast majority of all women living in this region and therefore it reflects the characteristics of the Tyrolean population. Less than 5% of women who delivered in these hospitals live outside the state of Tyrol, and only a minority of women living in the region deliver outside of this area. Thus, in contrast to many other studies, our study depicts the perinatal outcome of nearly the complete population although the study was hospital based. Therefore, our study describes the impact of maternal age on perinatal mortality in a typical central European region with different ethnic groups and varying socioeconomic standards. Zancona- to et al. [16] previously demonstrated the impact of socioeconomic factors and ethnicity on the pregnancy outcome.

Our study includes all perinatal deaths regardless of the cause, and in particular includes also fetuses with malformations. In this way it reflects the age-related perinatal mortality rate of a typical central European state. To the best of our knowledge, studies covering perinatal mortality rates in women with advanced maternal age do not exist in Austria.

Several studies have investigated the impact of an increased maternal age on perinatal mortality. While the majority of studies show an increment in risk for perinatal death, the magnitude of this effect differs considerably (table 5). The differing results can partially be explained by differences in study design (hospital vs. community based), different definition of perinatal mortality, inclusion of different populations, adjusting for different risk factors, using different cutoff values for maternal age, etc. We limited this overview to recent studies as several studies [17–19] demonstrated that the risk of stillbirth has decreased.

In contrast to other studies [20] our population also included women who did not attend antenatal care. An important finding is the highly increased risk (OR = 15.92) for women who attended <4 antenatal health care visits. Inadequate antenatal care was also shown to be associated with stillbirth by Flenady et al. [21]. In Austria the management of pregnancy is highly standardized using an official document (Mutter-Kind-Pass) for recording the results of all examinations. Women, who attend at least 5 free-of-charge examinations including 2 ultrasound scans receive some financial incentive from the government. After the introduction of this approach in 1974, the perinatal mortality decreased significantly. However, 7.8% of women in our study attended <4 examinations. This is an important amendable risk factor that can improve the perinatal mortality rate.

Our study shows that in obese women of advanced maternal age, perinatal mortality is increased with an adjusted OR of 1.83 in the multivariate regression analysis. Whiteman et al. [22] found in women with increasing BMI in 2 subsequent pregnancies an elevated stillbirth risk with a hazard ratio between 1.2 and 1.5 depending on BMI before the first pregnancy and weight gain between the 2 consecutive pregnancies. Reyes et al. [23] showed that intense nutritional control in early pregnancy reduces the risk for perinatal adverse outcomes. Thus, obesity is an important risk factor for perinatal mortality, the impact of which can be diminished by control of maternal weight.

Biological mechanisms responsible for the increased risk for perinatal mortality are not yet known [24]. Myometrial underperfusion possibly due to sclerotic arterial lesions [25] and aging endothelium of older women are thought to be responsible for perinatal complications. Certainly, pregnancy-induced hypertension and gestational diabetes are observed more often in older pregnant women [26] and more than half of women experiencing stillbirth present with pregnancy-related complications [27]. Similar to other studies [5, 6, 28], we observed an increased rate of preterm deliveries and, hence, an increased rate of low birth weights in older women; however, the rate of SGA is not significantly different between the age groups. It is noteworthy that perinatal death in the SGA group occurred 3 times more frequently in the age group ≥40 years than in the younger age groups. This suggests that there is another pathogenic factor contributing to an increased perinatal death rate in older women besides myometrial underperfusion.

Perinatal Mortality and Advanced Maternal Age

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Table 5. Studies investigating the impact of maternal age on perinatal mortality published since 2000

<table>
<thead>
<tr>
<th>Study</th>
<th>Design and period of study</th>
<th>Study population n/nt; area; PNM/SB rate</th>
<th>I/E criteria</th>
<th>PNM or SB; definition</th>
<th>MA, years</th>
<th>Risk for PNM/SB</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jolly et al. [30], 2000</td>
<td>population-based cohort study 1988–1997</td>
<td>1,893/385,120 North West Thames Region, UK SB 4.9/1,000</td>
<td>I: consecutive singleton pregnancies in women ≥18 years; includes fetal malformations</td>
<td>SB; not defined</td>
<td>18–34 35–40 &gt;40</td>
<td>1.41 1.83</td>
<td>1.17–1.70 1.29–2.61</td>
</tr>
<tr>
<td>Nybo Andersen et al. [31], 2000</td>
<td>population based 1978–1992</td>
<td>2,230/519,050 Denmark SB 4.3/1,000</td>
<td>I: all women with reproductive outcome</td>
<td>SB; ≥28 GW</td>
<td>25–29 30–34 35–39 ≥40</td>
<td>1.09 1.28 1.65</td>
<td>1.00–1.20 1.11–1.48 1.14–2.31</td>
</tr>
<tr>
<td>Froen et al. [32], 2001</td>
<td>hospital-based case control study 1986–1995</td>
<td>582 controls 76 cases Oslo, Norway</td>
<td>I: sudden intrauterine unexplained fetal death in singleton pregnancies</td>
<td>SB; ≥500 g or ≥22 GW</td>
<td>&lt;25 ≥35</td>
<td>5.09</td>
<td>1.32–19.57</td>
</tr>
<tr>
<td>Ziadeh and Yahaya [5], 2001</td>
<td>hospital-based case control study 1997–1999</td>
<td>1,404 controls 468 cases Amman, Jordan PNM 4.3/1,000</td>
<td>not mentioned</td>
<td>PNM; not defined</td>
<td>20–29 ≥40</td>
<td>0.6 0.2</td>
<td>1.44 1.35–1.53</td>
</tr>
<tr>
<td>Astolfi et al. [33], 2002</td>
<td>population based 1993–1994</td>
<td>2,046/497,664 Italy SB 4.1/1,000</td>
<td>I: only legitimate singleton deliveries from whole of Italy (1994) and additionally Sardinia (1993)</td>
<td>SB; ≥26 GW</td>
<td>&lt;35 ≥35</td>
<td>1.0</td>
<td>1.44</td>
</tr>
<tr>
<td>Seoud et al. [34], 2002</td>
<td>hospital-based case control study 1992–1996</td>
<td>326 controls 319 cases Beirut, Lebanon</td>
<td>I: singleton pregnancies</td>
<td>SB; &gt;20 GW</td>
<td>20–30 ≥40</td>
<td>4.53</td>
<td>1.45–18.68</td>
</tr>
<tr>
<td>Tough et al. [35], 2002</td>
<td>population based 1990–1996</td>
<td>1,913/283,956 Alberta, USA SB 6.7/1,000</td>
<td>I: all deliveries including multiple births</td>
<td>SB; not defined</td>
<td>&lt;35 ≥35</td>
<td>1.43</td>
<td>1.26–1.63</td>
</tr>
<tr>
<td>Jacobsson et al. [36], 2004</td>
<td>population-based cohort study 1987–2001</td>
<td>5,032/909,228 Sweden PNM 5.5/1,000</td>
<td>I: all deliveries in the respective age groups</td>
<td>PNM; ≥28 GW up to 6 days of life</td>
<td>20–29 40–44 ≥45</td>
<td>1.67 2.45</td>
<td>1.48–1.88 1.51–3.98</td>
</tr>
<tr>
<td>Canterino et al. [37], 2004</td>
<td>population-based cohort study 1995–2000</td>
<td>23,238/7,910,679 USA SB 2.9/1,000</td>
<td>I: singleton pregnancies</td>
<td>SB; ≥24 GW</td>
<td>20–24 35–39 40–44 45–49</td>
<td>1.21 1.62 2.40</td>
<td>1.17–1.30 1.68–1.46 1.77–3.27</td>
</tr>
<tr>
<td>Astolfi et al. [38], 2005</td>
<td>population based 1990–1996</td>
<td>15,872/3,616,622 Italy 4.3/1,000</td>
<td>I: singleton births, maternal age ≥20; excluded large for gestational age</td>
<td>SB; ≥26 GW</td>
<td>20–29 ≥35</td>
<td>1.0</td>
<td>1.51–1.68</td>
</tr>
<tr>
<td>Cleary-Goldman et al. [20], 2005</td>
<td>hospital based 1999–2002</td>
<td>156/36,056 USA PNM 4.3/1,000</td>
<td>I: patients enrolled for the first trimester scan; AOR for pre-existing medical condition</td>
<td>PNM; intrauterine death ≥24 GW and NND up to 28 days</td>
<td>&lt;35 35–39 ≥40</td>
<td>1.0 1.1 1.1</td>
<td>0.6–1.9 1.1–4.5</td>
</tr>
<tr>
<td>Joseph et al. [26], 2005</td>
<td>population based 1988–2002</td>
<td>319/51,084 Nova Scotia, Canada PNM 6.2/1,000</td>
<td>E: fetal malformations and multiple pregnancies</td>
<td>PNM; SB; ≥500 g and ≥20 GW and neonatal death</td>
<td>20–24 35–39 ≥40</td>
<td>1.46 1.95</td>
<td>1.11–1.92 1.13–3.35</td>
</tr>
<tr>
<td>Bateman and Simpson [39], 2006</td>
<td>hospital based 1995–2002</td>
<td>n.p./5,874,203 USA n.p.</td>
<td>I: deliveries including multiple births; 20% stratified sample of hospital discharges in USA</td>
<td>SB; not defined</td>
<td>20–34 35–39 ≥40</td>
<td>1.0 1.28 1.72</td>
<td>1.24–1.32 1.63–1.81</td>
</tr>
<tr>
<td>Reddy et al. [29], 2006</td>
<td>population based 2001–2002</td>
<td>25,003/5,438,735 36 states of USA SB 6.5/1,000</td>
<td>E: fetal malformations and multiple pregnancies</td>
<td>SB; ≥20 GW</td>
<td>&lt;35 ≥35 ≥40</td>
<td>1.0 1.32 1.88</td>
<td>1.22–1.43 1.68–2.16</td>
</tr>
</tbody>
</table>

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Our study showed stillbirth to occur at a median gestational age of 31 weeks for the age group ≥40 years, 34 weeks for the age group 34–39 years and 32 weeks for the reference group. This is in contrast to previous studies [26, 29] that demonstrated higher rates of antenatal death in older women at the end of pregnancy, and has important implications for the provision of antenatal care.

One limitation of this study is that we were unable to control for maternal diseases except adiposity. Maternal diseases are not consistently reported in the Perinatal Register of Tyrol. However, our study provides information for counselling women of advanced age planning to get pregnant in a high-income country with generally good medical care.

In conclusion, this study demonstrates that women ≥40 years carry an increased risk for stillbirth, but not for neonatal death. This risk is particularly high at around 31 gestational weeks. Important amenable risk factors are high BMI and poor antenatal care. These findings have important implications for the provision of health services.

**Disclosure Statement**

All authors state that there are no conflicts of interest in connection with this article.
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