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Perinatal Mortality and Advanced Maternal Age

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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) and obesity (OR = 1.85, CI: 1.27–2.70 in age group 35–39 years; OR = 1.83, CI: 1.22–2.74 in the age group ≥40 years). In the multivariate regression analysis, 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.

Introduction

In industrialized countries a growing number of women delay reproduction until later in life [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 [2–6] have failed to find a higher risk for adverse pregnancy outcome in

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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 16/1; 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. The group aged 25–34 years was used as reference group regarding age-related comparisons.

Perinatal death is defined as death of a child with a birth weight of at least 500 g occurring antenatally or within the first 7 days after delivery. Stillbirth is defined as intrauterine death of a child with a weight of at least 500 g. Preterm delivery is defined as delivery before 37 completed weeks of gestation. Small for gestational age (SGA) was defined as a birth weight below the 3rd percentile, according to published reference values in a German population [15]. Obesity is defined as a BMI ≥30.

Educational levels were reported in 5 categories: unskilled workers, undergoing education, skilled workers, well educated (holding a college degree) and housewives. The group with higher education was used as reference group for the calculation of the risk for 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 χ^2 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

Table 1. Patient characteristics

	Total (100%) (n = 56,517)	Age 25–34 years (n = 43,313)	Age 35–39 years (n = 10,932)	p	Age ≥40 (n = 2,272)	p
Previous miscarriage	11,543 (20.4)	7,791 (18.0)	2,955 (27.0)	<0.001	802 (35.3)	<0.001
Occupation/education						
Well educated	7,903 (14.0)	5,461 (12.6)	2,002 (18.3)	<0.001	440 (19.4)	<0.001
Skilled	25,986 (46.0)	20,591 (47.5)	4,514 (41.3)		881 (38.8)	
Undergoing education	537 (1.0)	501 (1.2)	32 (0.3)		4 (0.2)	
Unskilled	6,255 (11.1)	4,936 (11.4)	1,091 (10.0)		228 (10.0)	
Unknown	15,836 (28.0)	11,824 (27.3)	3,293 (30.1)		719 (31.7)	
Smoker	5,728 (10.1)	4,523 (10.4)	996 (9.1)	<0.001	209 (9.2)	n.s.
Obese (BMI >30)	3,737 (6.7)	2,814 (6.6)	733 (6.8)	n.s.	190 (8.6)	<0.001
Unknown BMI	972 (1.7)	730 (1.7)	192 (1.8)		50 (2.2)	
Immigrant status	7,835 (13.9)	6,335 (14.6)	1,270 (11.6)	<0.001	230 (10.1)	<0.001
<4 prenatal care visits	294 (0.6)	198 (0.5)	72 (0.7)	0.007	24 (1.1)	<0.001
Mode of delivery						
Vaginal delivery	42,935 (76.0)	33,706 (77.8)	7,770 (71.1)	<0.001	1,459 (64.2)	<0.001
Cesarean section	13,566 (24.0)	9,596 (22.2)	3,157 (28.9)		813 (35.8)	
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)	746 (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 2. Peri-, ante- and neonatal mortality according to maternal age

	Total	Age 25–34 years	Age 35–39 years	Age ≥40 years
Perinatal deaths	308 (0.5%)	224 (0.5%)	59 (0.5%)	25 (1.1%)
Univariate OR (95% CI)		1 (reference)	1.04 (0.78–1.39)	2.14 (1.41–3.24)
Antenatal deaths	185 (0.3%)	134 (0.3%)	33 (0.3%)	18 (0.8%)
Univariate OR (95% CI)		1 (reference)	0.98 (0.67–1.43)	2.57 (1.57–4.22)
Neonatal deaths	123 (0.2%)	90 (0.2%)	26 (0.2%)	7 (0.3%)
Univariate OR (95% CI)		1 (reference)	1.14 (0.74–1.77)	1.48 (0.69–3.21)

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).

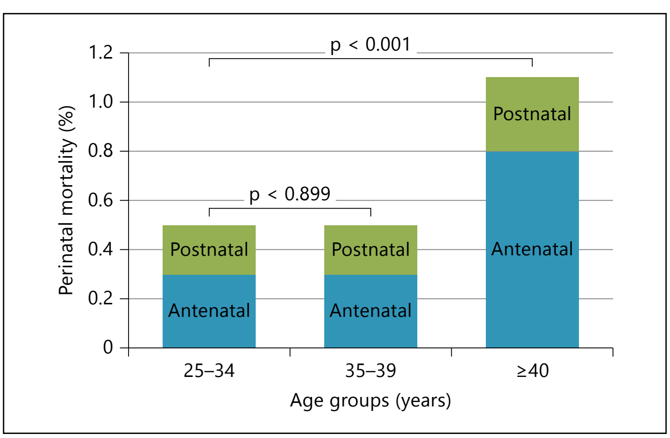
Perinatal mortality rates in the 3 age groups are shown in table 3 in detail. Smoking, obesity, immigrant status, <4 healthcare visits and cesarean section were significant risk factors for perinatal mortality in the age groups 35–39 years and ≥40 years, respectively. Low birth weight, preterm birth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

	Total (n = 56,517; 100%)	Age 25–34 years (n = 43,313; 76.6%)	Age 35–39 years (n = 10,932; 19.3%)	Age-adjusted OR (95% CI)	p	Age ≥40 years (n = 2,272; 4.0%)	Age-adjusted OR (95% CI)	p
Previous miscarriage	83 (0.7)	58 (0.7)	19 (0.6)	1.52 (1.17–1.98)	0.002	6 (0.7)	1.42 (1.06–1.89)	0.017
Occupation/education								
Well educated	31 (0.4)	20 (0.4)	9 (0.4)	Reference		2 (0.5)		
Skilled	119 (0.5)	87 (0.4)	21 (0.5)	1.11 (0.74–1.68)	0.609	11 (1.2)	1.20 (0.81–1.79)	0.363
In education	4 (0.7)	4 (0.8)		1.96 (0.69–5.61)	0.209		2.04 (0.71–5.80)	0.184
Unskilled	41 (0.7)	33 (0.7)	5 (0.5)	1.63 (1.01–2.66)	0.047	3 (1.3)	1.72 (1.08–2.75)	0.023
Housewife	69 (0.6)	46 (0.6)	17 (0.7)	1.52 (0.98–2.36)	0.063	6 (1.1)	1.58 (1.03–2.42)	0.035
Unknown	44 (1.0)	34 (0.9)	7 (0.9)	2.42 (1.50–3.90)	0.000	3 (1.8)	2.54 (1.60–4.02)	0.000
Lifestyle								
Smoker	42 (0.7)	32 (0.7)	6 (0.6)	1.37 (0.97–1.94)	0.070	4 (1.9)	1.47 (1.03–2.10)	0.032
Obese (BMI >30)	34 (0.9)	24 (0.9)	7 (1.0)	1.85 (1.27–2.70)	0.001	3 (1.6)	1.83 (1.22–2.74)	0.003
Unknown BMI	22 (2.3)	12 (1.6)	4 (2.1)			6 (12.0)		
Immigrant status	68 (0.9)	56 (0.9)	10 (0.8)	1.88 (1.42–2.48)	<0.001	2 (0.9)	1.85 (1.38–2.48)	<0.001
<4 prenatal care visits	23 (7.8)	12 (6.1)	6 (8.3)	15.55 (9.47–25.51)	<0.001	5 (20.8)	16.38 (9.78–27.43)	<0.001
Mode of delivery								
Vaginal delivery	213 (0.5)	152 (0.5)	44 (0.6)	Reference		17 (1.2)		
Cesarean section	95 (0.7)	72 (0.8)	15 (0.5)	1.45 (1.12–1.86)	0.004	8 (1.0)	1.55 (1.18–2.03)	0.001
Birth weight								
Very low (<1,000 g)	102 (47.2)	75 (47.2)	17 (41.5)	415.78 (295.15–585.73)	<0.001	10 (62.5)	458.89 (317.17–663.92)	<0.001
Low (1,000–2,499 g)	102 (3.1)	69 (2.9)	22 (2.9)	14.63 (10.96–19.54)	<0.001	11 (5.3)	15.44 (11.29–21.12)	<0.001
Normal (2,500–3,999 g)	98 (0.2)	78 (0.2)	18 (0.2)	Reference		2 (0.1)		
Macrosomia (>4,000 g)	6 (0.1)	2 (0.1)	2 (0.2)	0.49 (0.18–1.34)	0.164	2 (1.1)	0.60 (0.22–1.63)	0.311
SGA (<3rd percentile)	42 (2.4)	30 (2.3)	7 (2.2)	4.90 (3.46–6.95)	<0.001	5 (6.4)	5.25 (3.66–7.54)	<0.001
Preterm (<37th gestational week)	208 (4.6)	149 (4.6)	41 (4.1)	25.21 (19.63–32.38)	<0.001	18 (6.3)	24.94 (19.09–32.58)	<0.001

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



Color version available online

Fig. 1. Antenatal and postnatal mortality in different age groups.

Table 4. Multivariate logistic regression analysis of perinatal mortality

	Age-adjusted OR	95% CI
Age (years)		
25–34	1	reference
35–39	1.03	0.77–1.39
≥40	1.66	1.03–2.66
Maternal obesity	1.83	1.27–2.62
Immigrant status	1.72	1.29–2.30
Mode of delivery		
Vaginal delivery	1	reference
Cesarean section	1.3	1.01–1.68
SGA (weight below 3rd percentile)	5.57	3.97–7.79

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).

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. Zanconato 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.

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

Study	Design and period of study	Study population n/n[a]; area; PNM/SB rate	I/E criteria	PNM or SB; definition	MA, years	Risk for PNM/SB		Comments
						OR	95% CI	
Jolly et al. [30], 2000	population-based cohort study 1988–1997	1,893/385,120 North West Thames Region, UK SB 4.9/1,000	I: consecutive singleton pregnancies in women ≥18 years; includes fetal malformations	SB; not defined	 18–34 35–40 >40	 1 1.41 1.83	99% CI RG 1.17–1.70 1.29–2.61	AOR
Nybo Andersen et al. [31], 2000	population based 1978–1992	2,230/519,050 Denmark SB 4.3/1,000	I: all women with reproductive outcome	SB; ≥28 GW	25–29 30–34 35–39 ≥40	1 1.09 1.28 1.65	RG 1.00–1.20 1.11–1.48 1.14–2.31	COR
Froen et al. [32], 2001	hospital-based case control study 1986–1995	582 controls 76 cases Oslo, Norway	I: sudden intrauterine unexplained fetal death in singleton pregnancies	SB; ≥500 g or ≥22 GW	<25 ≥35	1 5.09	RG 1.32–19.57	AOR
Ziadeh and Yahaya [5], 2001	hospital-based case control 1997–1999	1,404 controls 468 cases Amman, Jordan PNM 4.3/1,000	not mentioned	PNM; not defined	 20–29 >40	PNM 0.6 0.2	 n.s.	
Astolfi et al. [33], 2002	population based 1993–1994	2,046/497,664 Italy SB 4.1/1,000	I: only legitimate singleton deliveries from whole of Italy (1994) and additionally Sardinia (1993)	SB; ≥26 GW	<35 ≥35	1.0 1.44	RG 1.35–1.53	COR
Seoud et al. [34], 2002	hospital-based case control study 1992–1996	326 controls 319 cases Beirut, Lebanon	I: singleton pregnancies	SB; >20 GW	20–30 ≥40	1 4.53	RG 1.45–18.68	COR
Tough et al. [35], 2002	population based 1990–1996	1,913/283,956 Alberta, USA SB 6.7/1,000	I: all deliveries including multiple births	SB; not defined	<35 ≥35	1 1.43	RG 1.26–1.63	COR
Jacobsson et al. [36], 2004	population-based cohort study 1987–2001	5,032/909,228 Sweden PNM 5.5/1,000	I: all deliveries in the respective age groups	PNM; ≥28 GW up to 6 days of life	20–29 40–44 ≥45	1 1.67 2.45	RG 1.48–1.88 1.51–3.98	AOR
Canterino et al. [37], 2004	population-based cohort study 1995–2000	23,238/7,910,679 USA SB 2.9/1,000	I: singleton pregnancies	SB; ≥24 GW	20–24 35–39 40–44 45–49	1 1.21 1.62 2.40	RG 1.17–1.30 1.68–1.46 1.77–3.27	AOR
Astolfi et al. [38], 2005	population based 1990–1996	15,872/3,616,622 Italy 4.3/1,000	I: singleton births, maternal age >20; excluded large for gestational age	SB; ≥26 GW	20–29 ≥35	1.0 1.59	RG 1.51–1.68	AOR
Cleary-Goldman et al. [20], 2005	hospital based 1999–2002	156/36,056 USA PNM 4.3/1,000	I: patients enrolled for the first trimester scan; AOR for pre-existing medical condition	PNM; intrauterine death ≥24 GW and NND up to 28 days	<35 35–39 ≥40	1.0 1.1 2.2	RG 0.6–1.9 1.1–4.5	AOR
Joseph et al. [26], 2005	population based 1988–2002	319/51,084 Nova Scotia, Canada PNM 6.2/1,000	E: fetal malformations and multiple pregnancies	PNM; SB; ≥500 g and ≥20 GW and neonatal death	20–24 35–39 ≥40	1.0 1.46 1.95	RG 1.11–1.92 1.13–3.35	AOR
Bateman and Simpson [39], 2006	hospital based 1995–2002	n.p./5,874,203 USA n.p.	I: deliveries including multiple births; 20% stratified sample of hospital discharges in USA	SB; not defined	20–34 35–39 ≥40	1.0 1.28 1.72	RG 1.24–1.32 1.63–1.81	COR
Reddy et al. [29], 2006	population based 2001–2002	25,003/5,438,735 36 states of USA SB 6.5/1,000	E: fetal malformations and multiple pregnancies	SB; ≥20 GW	<35 35–39 ≥40	1.0 1.32 1.88	RG 1.22–1.43 1.68–2.16	

Table 5. (continued)

Study	Design and period of study	Study population n/n[a]; area; PNM/SB rate	I/E criteria	PNM or SB; definition	MA, years	Risk for PNM/SB		Comments
						OR	95% CI	
Delbaere et al. [9], 2007	population-based cohort study 2002–2003	143/26,891 Belgium PNM 5.3/1,000	I: primiparous women delivering singleton child ≥500 g	PNM; not defined	25–29 ≥35	1.0 1.68	RG 1.06–2.65	AOR
Getahun et al. [40], 2007	population-based cohort study 1989–1997	1,550/370,752 Missouri, USA 4.2/1,000	I: singleton pregnancies	SB; 20–43 GW	25–29 30–34 ≥35	1.0 1.15 1.76	RG 1.03–1.29 1.54–2.00	COR
Hoffman et al. [41], 2007	hospital based 1989–2004	2,402/126,402 Miami, USA SB 19/1,000	E: lethal fetal anomalies	SB; ≥20 GW	 <35 35–39 ≥40	SB 1.0 1.45 1.83	$p < 0.005$	AOR
Bahtiyar et al. [11], 2008	population based 1995–1997	2,067/2,213,721 USA SB 0.9/1,000	I: singleton, term pregnancies 37–42 weeks; E: maternal diseases and fetal malformations	SB; not defined	25–29 30–34 35–39 40–44	1 1.24 1.45 3.04	RG 1.13–1.36 1.21–1.74 1.56–5.86	
Chan and Lao [6], 2008	hospital-based cohort study 1998–2001	77/15,727 Hong Kong, China PNM 4.9/1,000	I: singleton pregnancies without significant fetal anomalies >24 weeks of gestation	PNM; not defined	 <40 ≥40	PNM 0.5 0.3	n.s.	
Salihu et al. [10], 2008	population-based cohort study 1978–1997	5,405/1,235,307 Missouri, USA SB 4.4/1,000	I: singleton deliveries; E: congenital anomalies	SB; in utero fetal death between 20 and 44 GW	<20–24 25–29 30–34 35–39 ≥40	1.0 1.1 1.4 2.0 3.4	RG 1.0–1.1 1.3–1.5 1.7–2.4 2.8–4.2	adjusted hazard ratio
Balayla et al. [12], 2011	population-based cohort study 1995–2004	130,353/37,504,230[b] USA SB 3.5/1,000	E: of deliveries <24 weeks and congenital anomalies; I: multifetal pregnancies	SB; >24 weeks	25–29 30–34 35–39 40–45 >45	1 1.02 1.25 1.60 2.25	RG 0.99–1.04 1.21–1.28 1.53–1.67 2.91–2.53	

The study of Ananth et al. [17] was not included, as it did not provide data for calculation of the above parameters. PNM = Perinatal mortality; SB = stillbirth; I = patient inclusion; E = patient exclusion; MA = maternal age; RG = reference group; AOR = adjusted OR; COR = crude OR; n.s. = not significant; GW = gestational weeks; n.p. = not provided. [a] Number of SB/NNM/number of patients in all study groups. [b] Figure includes age from <15 to >45 years.

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 amendable 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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