



The Trend in Delayed Childbearing Age and Its Potential Impact on Adverse Maternal-Perinatal Outcomes in Developed and Developing Countries: A Narrative Review

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(Received 08 Jul 2024; accepted 10 Sep 2024)

Abstract

Due to the significant advancement of modern societies, higher education, career growth, and economic independence, more young girls are likely to delay childbearing beyond 30 years of age. The trend of delayed childbearing is more pronounced in industrialized countries but is also becoming common in emerging countries. Delayed childbearing has been linked with several adverse maternal-perinatal outcomes, including hypertensive disorders of pregnancy, abnormal placentation, gestational diabetes mellitus, pre-term births, low birthweight, perinatal mortality, congenital birth defects, and chromosomal abnormalities. In this review, we have highlighted the trend of delayed childbearing age, the role of education and employment in delayed childbearing age, and its potential impact on adverse maternal-perinatal outcomes in developed and developing countries.

Keywords: Delayed childbearing age; Fertility rate; Education; Occupation; Pregnancy outcomes

Introduction

Modern civilizations have significantly progressed in higher education, professional development, and economic independence. As a result, more young girls are likely to delay childbearing until they are at least 30 years old (1, 2). Advanced maternal age (AMA), defined as a mother of 35 years or older at the time of delivery, is increasing significantly in many developed and developing countries (3). For example, in the United States, birth rates among women with AMA have increased in three decades (1970-2000) from 5% to approximately 13% of all live births (4), and dur-

ing 2013-2014, the birth rate was increased by 3% in women with AMA (5). Between 2000 and 2014, the percentage of births to women with AMA increased by 23% from 7.4% to 9.1% (6). In a recently published study, women of very AMA increased by 194% from 1989 to 2018 in the United States (7). In Spain, around 38.7% of live births were born among women over 35 years of age and 8.4% over 40 years of age in 2016 (8). In another report, births to women aged 40 or older increased from 6.7% in 2013 to 7.4% in 2017 in Spain, and such increasing trends



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were also observed in Australia, Chile, Japan, and the United Kingdom (9).

In South Korea, the proportion of women with AMA has increased by 116.8% from 15.4% to 33.4% during one decade (2009-2019) (10). In Israel, during a decade (1998-2008), the first birth rate of women with AMA rose by more than 230% (11). In Western Australia, the birth rates for women with AMA have increased from 2.05 % in 1980 to 5.06% in 2003, with a 70% increase in first delivery (12). In Canada, the proportion of first births in women older than 34 years has increased from 6% to 25% during three decades (1975-2005) (13). In Japan, birth rates for women with AMA significantly increased from 8.6% in 1990 to 25.9% in 2012 (14). In China, a national study reported the percentage of AMA rose from 2.96% to 8.56% from 1996 to 2007. In the urban region, the proportion of AMA rose from 2.95% to 7.69%, whereas, in rural areas, the proportion of AMA increased from 2.99% to 10.35%. The increasing trend in delayed childbearing could be attributed to availing higher education, career development, and economic independence, widespread use of contraceptives and assisted reproductive technology (ART), and lack of support for parental social incentives (5, 15-17). Delayed childbearing is associated with several adverse maternal-neonatal outcomes (7, 18).

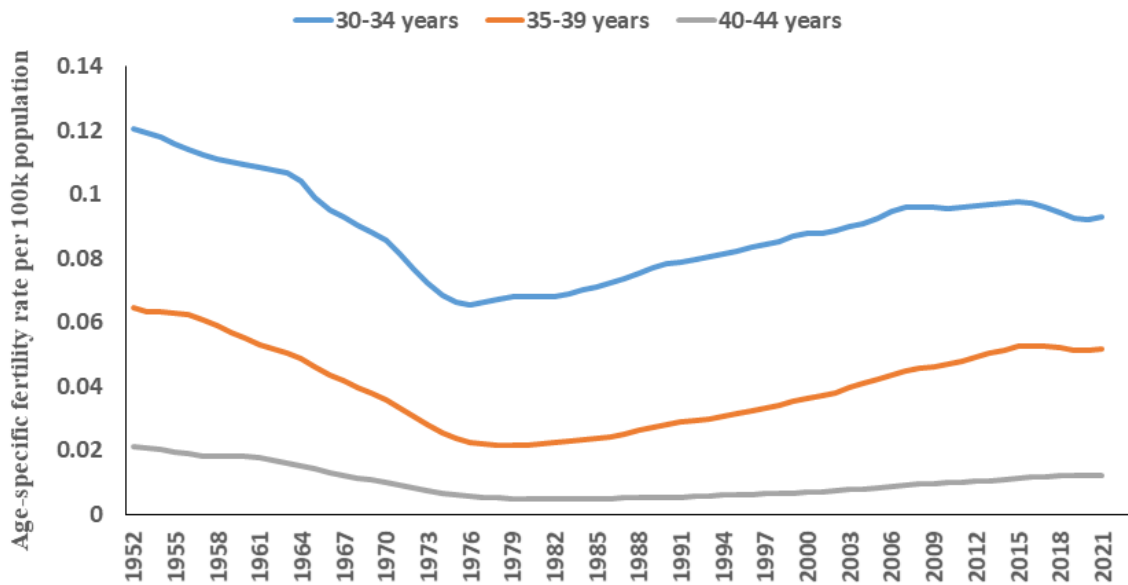
The trend in delayed childbearing age and fertility rate in developed and developing countries

Delayed childbearing is defined as women giving birth to babies in their old age. Maternal age at the time of first neonatal birth has dramatically increased in several countries. For example, in the United States, childbearing has risen from the early 20s in 1970 to the late 20s in 2006. Similarly, in Switzerland, women had their first child in nearly 30 years of age, five years older than Swiss

women in 1970. In 2009, the mean maternal age at their first delivery ranged from 21.3 years in Mexico to 30.5 years in New Zealand. Similarly, the average age when women have their first baby increased from 24 years to 28 years in almost four decades (1970-2008) (OECD, 2010) (19). In Italy, the mean maternal age at delivery has risen from 25.2 years to 31.7 years during three and half decades (1981-2015) (20), and in Australia, the average maternal age at first birth increased from 25.4 years to 29.3 years during 1971-2013 (21).

The mean maternal age at first birth rose from 27.3 years to 31.2 years in France, from 26.8 years to 31.3 years in Austria, and from 26.5 years to 31.1 years in the United Kingdom during 1970-2016 (22). From 1950 to 2015, the mean age of women at first birth increased from 24.1 years to 29.4 years in Sweden, from 26.7 years to 29.3 years in the Netherlands, from 25.1 years to 30.7 years in Spain (1975-2015), from 23.9 years to 28.0 years in Czechia, from 25.1 years to 31.1 years in South Korea (1980-2015), and from 24.8 years to 29.1 years in Japan (23). Many emerging countries, such as Turkey, Iran, and China, have also seen a trend in delayed childbearing (19). In 2013, the mean maternal age at first birth was 22.9 years, continuously increasing in Turkey (24). In the Iranian population, the average maternal age rose from 17.6 to 23.8 years between 1990 and 2006 (25). In China, the childbearing age has increased from 24.3 years to 26.24 years during one decade (2000-2010) (19). Moreover, the fertility rate among women of older ages has been declined in developed (i.e. high socio-demographic index (SDI) countries) and developing countries (low-middle SDI countries) over the last seven decades (1952-2021) (GBD 2021, <http://ghdx.healthdata.org/gbd-results-tool>) (26) as shown in Fig. 1.

(High SDI countries)



(Low-middle SDI countries)

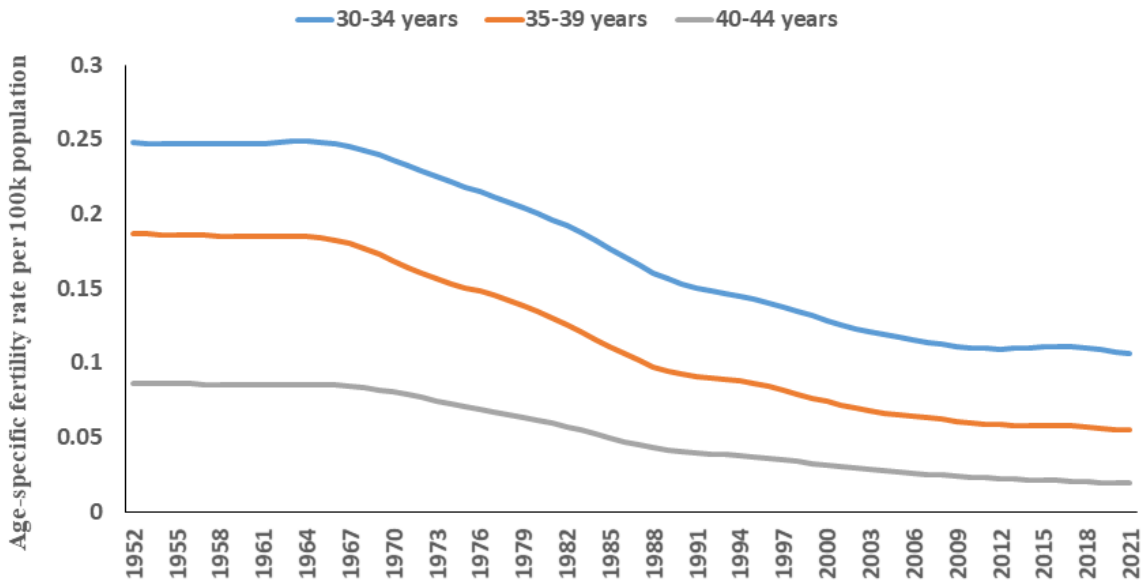


Fig. 1: Trend in age-specific fertility rate per 100,000 populations among women aged 30-44 years in high socio-demographic index (SDI) and low-middle SDI countries between 1952 and 2021

The main factors contributing to delayed childbearing

Several factors, including the rising trend of higher education and higher participation of women in employment, are attributed to delayed childbearing in women as shown in Fig. 2 (23).

Education, employment and delayed childbearing

The rising level of education in women is associated with delayed childbearing (27, 28). The association of maternal education with the rising

trend in delayed childbearing has been shown in Egypt, Mali, Uganda, Mozambique, and Burkina Faso. In Nepal and Bangladesh, improvement in maternal education was also accompanied by an increase in maternal age at first birth (29). In developed countries, women with higher education start childbearing at later ages compared to women with lower education levels. The attainment of an additional one-year education can delay childbearing age of around one year (30). In the USA population, Martin et al. (28) reported that compared to women with lower education levels, in women with a 4-year college degree, the rate of first and second births increased after age 30 during 1970-1990. The delayed childbearing in higher educated women is attributed to several reasons, such as balancing student life and motherhood life (31) pursuing their careers, which may postpone childbearing until they are well established on their career path. Education helps women acquire knowledge related to contraceptive products, thereby reducing unwanted pregnancy and early pregnancy. Preventing unwanted pregnancy increases the average maternal age at birth and results in delayed childbearing (19). These factors could predict delayed childbearing in women with higher educational levels (27). Women with higher education levels should be educated about the consequences of delayed childbearing, such as adverse maternal-neonatal outcomes.

Due to the rising trends in employment participation, women have faced significant and difficult trade-offs between employment and family. Tough et al. (32) determined factors influencing delayed childbearing in the Canadian population. They observed that in addition to partner suitability

to parents, financial security (85.8%) impacts the time of childbearing (32, 33). In the USA, part-time employment declined the likelihood of pregnancy in women and increased delayed childbearing (34). One year of delayed childbearing increases women's earnings by 9%, wage rate by 3%, and work experience by 6% in the USA (35). Employment increases the risk of getting a divorce because women with professional jobs are less likely to take care of their children and spend less time doing domestic work. Divorce of professional women at younger ages delayed childbirth as younger women seek a new husband. In previous studies, the economists found that delayed childbearing substantially increases earnings in women of professional occupations. All these factors associated with professional jobs tend to delay childbearing in professional women (35-37). Women of professional occupations get benefits to delay childbearing, such as personal development, higher education levels, increased income, career development, and relationship stability. However, delayed childbearing is associated with both maternal pregnancy complications and adverse neonatal outcomes. Therefore, it is highly essential to inform women of professional occupation that delayed childbearing could potentially affect conception, pregnancy, and perinatal outcomes.

Delayed childbearing and its potential consequences

Women with delayed childbearing are associated with a declined fertility rate and increased adverse maternal-neonatal outcomes as shown in Fig. 2 (19).

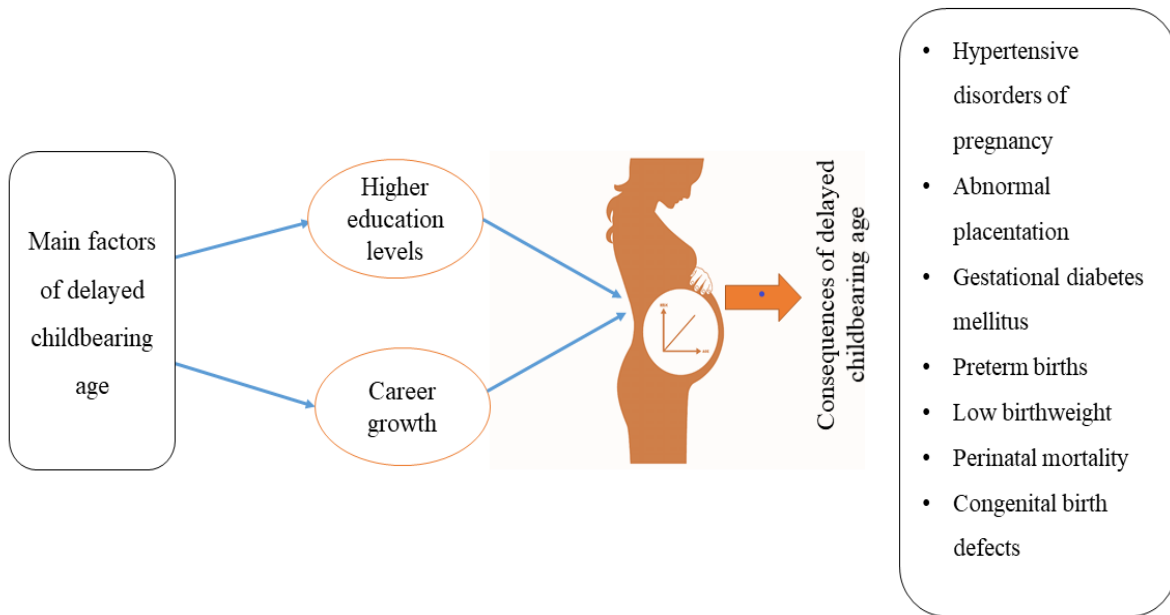


Fig. 2: Factors of delayed childbearing age and its potential consequences on adverse maternal-perinatal outcomes

Delayed childbearing and preterm births

Increasing maternal age at birth is associated with increasing risk of preterm births. Delayed childbearing, or AMA, has long been associated with preterm births. Many studies have found the association of AMA with the increased risk of preterm births (38). For example, Fuchs et al. (39) observed that the risk of preterm births followed a U-shaped distribution with maternal age. Women aged 20-24 years had 6.8%, 25-29 years had 6.0%, 30-34 years had 5.7%, 35-39 years had 6.3%, and 40 years or older had 7.8% preterm births. Compared with women aged (30-34 years), women aged 40 years or older had higher odds of extremely preterm births (aOR 1.33), spontaneous preterm births (aOR 1.20), and iatrogenic preterm births (aOR 1.31).

Waldenstrom et al. (2) examined the impact of AMA on the risk of preterm births in a population-based register study. Compared with women aged 20-24 years, women aged 40 years or older had a higher incidence of very preterm births (0.7% vs. 1.2%) and moderately preterm births (4.7% vs. 5.2%)—moreover, the risk of preterm births elevated with increasing maternal age regardless of parity. The adjusted ORs for preterm births in first, second, and third births ranged

from 1.18 to 1.28 in women aged 30-34 years, from 1.59 to 1.70 in women aged 35-39 years, and from 1.97 to 2.40 at ≥ 40 years. Women aged 35 years and older should be considered as a risk group for preterm births. The placental and myometrial vascular lesion could explain the increased risk of preterm birth in women with AMA. The association between indicated preterm births and PE and SGA mediate AMA, and these conditions are associated with hypo-perfusion of placental blood. Moreover, increasing maternal age is associated with declined progesterone levels, which is essential for pregnancy maintenance. Progesterone deficiency and emotional stress could be potential pathways between AMA and increased risk of preterm births (2).

Delayed childbearing and low birth weight (LBW)

It is well-established that maternal age at the time of childbirth is associated with the neonatal's birth weight. It has been found that women of older ages (≥ 35 years) tend to have a higher rate of LBW compared with women aged less than 35 years (40, 41). The incidence of LBW with maternal age is increasing in a parallel direction. Women aged 20-24 years had 8.4% LBW, 25-29

years, 30-34 years, 35-39 years, and ≥ 40 years had 9.1%, 10.4%, 12.8% and 14.7% LBW, respectively (42).

Khoshnood et al. (43) investigated the risk of LBW associated with AMA among four ethnic groups in the United States population of pregnant women. Delayed childbearing or AMA was associated with increased odds of LBW among four ethnic groups, and the effect of maternal age on LBW was reasonably similar among the four groups. Overall, women with AMA were at 82% higher odds of LBW (OR 1.82) and 55% increased odds of moderate LBW (OR 1.55) compared with women aged 20-34 years. The risk of LBW was higher among African American women (5.3-fold), followed by Puerto Ricans (4.3-fold), Mexicans (3.7-fold), and non-Hispanic whites (2.6-fold). These results suggest that delayed childbearing is associated with an increased risk of LBW regardless of ethnicity.

In a population-based cross-cohort comparison study, the association of maternal age with neonatal birth has been investigated and reported that after adjusting for socioeconomic position, women with AMA had higher odds of LBW 1.66 [95% CI 1.36, 2.02] compared with those aged 25-29 years (44). LBW is a significant public health problem worldwide, associated with short-term and long-term complications. Therefore, it is essential to identify and prevent modifiable factors such as delayed childbearing that contribute to increased LBW rates.

Delayed childbearing and perinatal mortality

Perinatal mortality is defined as the combination of late fetal mortality (stillbirths) and early neonatal mortality (0-6 days of life) (45). Among several risk factors, delayed childbearing is one of the common factors associated with the increased risk of perinatal mortality. Women aged 35 or 40 years have long been associated with increased rates of perinatal mortality (46, 47). Women aged ≥ 40 years had higher rates of perinatal deaths (1.1% vs. 0.5%), antenatal deaths (0.8% vs. 0.3%), and neonatal deaths (0.3% vs 0.2%) compared with women's age group (25-34 years). Women aged ≥ 40 years had increased odds of

perinatal mortality by 1.66 (95% CI: 1.03, 2.66) compared with the reference age group (25-34 years). Women aged ≥ 40 years carry a higher risk for perinatal motility (48). Higher neonatal mortality was associated with women aged >35 years (49).

After adjusting for confounding factors, women aged 30 years and older were associated with higher odds of stillbirth (50). Still, the risk of neonatal death was no longer associated with advancing maternal age. Women aged ≥ 35 years were not significantly associated with perinatal mortality (51). The variation in these findings could be explained by the study design (hospital-based vs. community-based), the definition of perinatal mortality, different confounding factors, the proportion of women with old age, and cut-off values for maternal age. The underlying biological mechanism associated with increased risk of perinatal mortality is unknown (52). However, myometrial underperfusion and aging endothelium of older women are considered to be associated with perinatal complications and mortality (53).

Delayed childbearing, congenital birth defects, and chromosomal abnormalities

Delayed childbearing is a well-established risk factor for congenital defects and chromosomal abnormalities. Compared with women aged <20 years, women aged ≥ 40 years had higher odds of cardiac defects, including esophageal atresia (2.9-fold), hypospadias (2.0-fold), and craniosynostosis (1.6-fold) (54). Hollier et al. (55) also determined the association between maternal age and non-chromosomal abnormalities. Compared with a reference age group (20-24 years), women aged 35-39 years (3.5% vs. 4.4%) and ≥ 40 years (3.5% vs. 5.0%) had a higher incidence of congenital defects. The ORs for cardiac defect in women aged ≥ 40 years was 3.95 (95% CI, 1.70, 9.17) compared with young mothers (20-24 years).

It is well-known that older maternal age is significantly associated with chromosomal congenital defects, including trisomies 13, 18, and 21 (56). Down's syndrome is one of the common chromosomal abnormalities and is associated with

chromosome 21 disjunction. A strong correlation exists between AMA and chromosome 21 disjunction (57). Chromosomal birth defects are more common in older women compared with non-chromosomal birth defects (58). Regardless of age, women who are aware of information on all risk factors and optimize their health condition before conception through prenatal care visits and supplementation with vitamin D and folic acid can reduce their risk for congenital defects.

Delayed childbearing and hypertensive disorders of pregnancy (HDP)

HDP is the most common and dangerous pregnancy complication. The two common HDPs are gestational hypertension (GH) and preeclampsia (PE). The trend in HDP is consistently increasing, and the increase in HDP is due to the number of women who delayed childbearing, which has significantly increased over the last few decades (59-61). HDP increases with maternal age. Women aged 18-28 years had 2.22%, 29-39 years had 2.51%, and >40 years had 5.41% HDP (18). Chronic GH is associated with AMA. Women aged 35-39 years (1.22 times) and 40-44.9 years (1.6 times) had higher odds of GH compared with women aged 25-29 years (62). Other findings suggest that in women aged ≥ 32 years, the risk of PE increases by 4% each year (63).

In the Chinese population, women aged 35-39 years and ≥ 40 years had a 1.84-fold and 2.39-fold higher risk of HDP, respectively, compared with women aged 25-29 years (64). In another study, women aged ≥ 35 years had a 60% higher prevalence of PIH compared with women aged 20-34 years (65). In a case-control study, compared with young mothers, women with AMA had higher rates of PE (10.7% versus 1.8%) (66). In the French population, the risk of HDP increased with increasing maternal age regardless of parity (67). In Australia, compared with women aged 30-34 years, women with AMA had a 1.45-fold increased risk of PIH (68). In the USA population, Sheen et al. (69) investigated PE's temporal trend and maternal age's impact on PE. They found that women with AMA had a higher risk of PE. The Latin American, Caribbean, and Tai-

wanese women aged ≥ 35 years showed 1.6 and 1.8-fold increased risk of PE compared with young women (20-34 years) (70, 71). The association between AMA and increased risk of HDP is not clear enough. However, low nitric oxide levels and high oxidative stress are signs of aging, which could adversely affect the relaxation of the endothelium. This may cause the development of pregnancy-induced hypertension (PIH) in women with AMA because pregnancy increases cardiac output.

Delayed childbearing and abnormal placentation

Placenta previa and placental abruption are the two most common forms of abnormal placentation. Delayed childbearing is one of the well-recognized risk factors associated with increased risk of placenta previa and placental abruption. Women aged ≥ 34 years had three folds higher risk of placenta previa compared with teenage mothers (<20 years) (72). Women aged 20-24, 25-29, 30-34, 35-39, and ≥ 40 years had a 1.61-fold, 2.82-fold, 4.71-fold, 7.30-fold and 10.41-fold increased risk of placenta previa, respectively (73). AMA increased the risk of placenta previa by 6.3-fold (aOR 6.3, 95%CI: 3.20, 12.51) (74). Similarly, Tuzovic and Ilijic observed that AMA 6-fold increases the risk of placenta previa (75). The prevalence of placenta previa rises with maternal age (76). In the Australian population, women aged 35-39 years and ≥ 40 years were associated with increased risk (2.8-fold and 3.6-fold, respectively) of placenta previa (77).

The increased risk of placenta previa among older women could be attributed to atherosclerotic changes in the uterine blood vessels that cause compromised uteroplacental blood flow. This has been observed in microscopic placenta studies from older women, which show hypo-uteroplacental blood flow and large placental infarcts. An increased surface area is required for placental attachment to maintain optimal blood flow, which may result in placental encroachment on the lower uterine segment (78). Moreover, women with AMA are mostly multiparous, and multiparity could also increase the risk of placenta

previa in older women. In a previous meta-analysis, multiparity was associated with an increased risk of placenta previa (73).

Delayed childbearing and gestational diabetes mellitus (GDM)

GDM is a common pregnancy complication in which hyperglycemia develops spontaneously during pregnancy without prior diagnosed diabetes. Delayed childbearing is the leading risk factor for GDM (79). The incidence of GDM increases with maternal age. Women aged 18-28, 29-39, and >40 years had 2.54%, 4.28%, and 6.44% GDM, respectively (18). Women aged >35 years had higher odds of GDM [OR 1.57 (95% CI, 1.24, 1.98)] compared with under 35 years of women (80).

In the Chinese population, Pregnancy obesity increased the risk of GDM by 3.6-fold in women with AMA compared with women aged 20-35 years (2.7-fold) (81). Similarly, excessive weight gain was also associated with increased odds of GDM in women with AMA (4.17-fold) compared with women aged 20-35 years (2.65-fold). It suggests that higher pre-pregnancy BMI and excessive weight gain independently increase the risk of GDM in women with AMA. Obstetricians should educate women with AMA about the potential consequences of excessive weight during pregnancy and provide more guidance and interventional strategies to reduce excessive weight during the first trimester of pregnancy.

In the Italian population, Londero et al. (18) investigated the effect of maternal age on the risk of adverse pregnancy outcomes. They showed that the incidence of GDM increased with maternal age. Women aged >40 years had elevated odds of GDM [OR 1.71(95% CI, 1.37, 2.12)] compared with women aged 18-28 years. The association between AMA and GDM development could be explained by the progressive vascular endothelial damage in women of older ages (82). Moreover, increasing maternal age is associated with reduced insulin sensitivity, impaired glucose tolerance (83), and deterioration of pancreatic β -cell function (84), exacerbating the risk of GDM in delayed childbearing.

Conclusion

Delayed childbearing age is a significant public health issue in developed and developing countries. More women are planning to become pregnant after 30 years of age, and the proportion of neonatal births to women aged >30 years is significantly increasing across the globe. The rising trend of higher education levels and higher participation of women in employment is attributed to delayed childbearing age. Delayed childbearing age is associated with an increased risk of several adverse maternal-perinatal outcomes. Therefore, it is highly essential to educate and inform women with higher education levels and professional occupations that delayed childbearing could potentially affect conception, pregnancy, and perinatal outcomes.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors

Acknowledgements

We are sincerely thankful to the Taixing People's Hospital, Taizhou, China for their generous financial support that made the publication of this work possible.

Conflict of interest

The authors have no conflict of interest regarding this review.

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