International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Godara J et al. Int J Reprod Contracept Obstet Gynecol. 2025 Apr;14(4):1016-1022
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20250836

Original Research Article

A comparative study of pregnancy complications and birth outcomes in very advanced maternal age women: a retrospective cohort analysis

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Received: 28 January 2025
Revised: 11 March 2025
Accepted: 13 March 2025

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ABSTRACT

Background: There has been a noted increment in the number of women having children at a very advanced maternal age (VAMA), in the recent decades. This changing trend raises concerns regarding the risks involved and the associated complications with pregnancy occurring in both the mother and the newborn. The associated complications include stillbirths, placental problems, higher risks of cesarean sections and gestational diabetes. Existing research on the correlative aspects of pregnancy outcomes and VAMA, however have shown contradicting results. Hence, the findings of the same remain debatable.
Methods: This was a hospital-based retrospective cohort study, conducted on 100 women delivering between the years 2018 and 2023. The participants were classified into two different groups: group I- low-risk women, including 50 pregnant females of age less than 35 years and group II- VAMA females, 50 pregnant females of age up to 45 years.
Results: Women falling in the category of VAMA reported an increased rate of complications; most of these were gestational diabetes and hypertensive disorders. With this evidence, pregnancy results for advanced-aged women ought to be enhanced using targeted care and greater alertness in antenatal checkups.
Conclusions: More attention should be paid to women exposed to VAMA during pregnancy. Better education and timely intervention are critical in preventing complications and contributing to healthier pregnancies in this group.

Keywords: Maternal risk, Neonatal risk, Pregnancy outcomes, Preterm deliveries, Reproductive age, VAMA

INTRODUCTION

Very advanced maternal age (VAMA) and the shift in maternal demographics advances in maternal age refer to pregnancies among women who are 35 years of age or older. Advanced maternal age is continuously on the rise over the last few decades.[1] A number of changes in the society including delayed marriages, increased workforce participation of females, extended educational pursuits and advancements in reproductive technologies can be among the few causes.[2] The trend worldwide is now strongly in the direction of postponing childbearing, especially in developed countries, where births to women age thirty-nine and older are increasingly common.[3]

However, VAMA is closely associated with varying degrees of complications, with both mother and fetus being at an increased risk of complications, even after having access to progressed healthcare facilities.[4] Biologically, VAMA is associated with a sharp decline in reproductive health, which is mainly attributed to a decreased ovarian reserve and a gradual deterioration in the quality of oocytes. Which in turn is associated with a higher incidence of infertility and chromosomal abnormalities.[5] Oocyte aneuploidy is a condition that sharply increases with increasing maternal age and refers to the abnormal number of chromosomes present in the egg. For example, Down syndrome, which represents an

excessively copied chromosome 21, is one of the main causes of chromosomal abnormalities.[6]

Another much more direct influence on uterine conditions is that old females tend to have decreased endometrial receptivity. This decrease impacts implantation rates and increases the chance of early pregnancy loss. VAMA is also associated with maternal complications, including hypertensive disorders and gestational diabetes mellitus (GDM). Lopian et al stated that the elderly mothers are significantly more likely to develop gestational hypertension, preeclampsia and GDM all of which adversely affect both maternal and neonatal health.[7] Preeclampsia is a hypertensive condition of placental origin characterized by new-onset hypertension during pregnancy, leading to organ damage and thereby making it a significant threat to both the mother and the fetus. It is also associated with preterm delivery and remains a major cause of maternal morbidity and mortality worldwide.[8] Such risks make it essential to have a close follow up and to have special management plans for VAMA pregnancies. For instance, studies like those of Jacobsson et al show the association of increased maternal age with worse maternal outcomes and emphasizes the need for individualized care approaches.[9]

Besides the increase in maternal complications in VAMA women, there is also greater risk of adverse perinatal outcomes such as preterm births, low birth weight and stillbirths in children. A review article by Huang et al published in the Canadian Medical Association Journal states that VAMA is a risk factor that may cause stillbirth, especially in the later weeks of pregnancy.[10] Age-related placental dysfunction has been hypothesized to be the major cause of morbidity because it inhibits the delivery of oxygen and nutrients to the developing fetus. Older women are at increased risk of placental dysfunction including abruptio placentae which includes both preterm delivery and fetal hypoxia.

A review by Preda et al stated that preterm deliveries related to both spontaneous onset and clinical interventions were found in older pregnant women due to medical conditions such as preeclampsia and GDM.[11] Preterm infants are at higher risk of developing various complications including respiratory distress, developmental delay and long term metabolic complications. These complications of VAMA are not limited only to women giving birth but also to children. A study has shown that children who are born to older mothers tend to develop several neuro-developmental and metabolic disorders.

While some changes are thought to be age-related, concern about the aging oocytes is on the rise too, that may change gene expression in their progeny leading to some chronic health disorders later in life. Ratiu et al reported that neonates to mothers of VAMA who carried their babies full term, are likely to experience low birth weight and difficulty in breathing at birth, all of which are detrimental to long term functional growth.[12]

These factors instigate the need for more advanced and modified healthcare systems, inculcated for both the mother and the child in order to combat any challenges during antenatal and postnatal care. This demographic change should mean greater attention being paid to maternal-fetal health, effective and timely preventative actions to be taken when required. In addressing these challenges, there is not only need for medical technologies but also structural changes in policies and care given to VAMA women when required.

METHODS

Retrospective cohort analysis was done, considering information from registries of births and hospital records. We obtained a representative and varied sample of pregnant women in the VAMA (high risk) and younger maternal age groups (low risk) by examining a sizable dataset. Examining historical data made it easier to spot patterns and correlations over time to support the retrospective design. The sample size was determined by the total number of pregnant women (45 years or older) for high risk and below 35 years for low risk between the years 2018 to 2023. Robust statistical techniques were employed in the study to compare the birth outcomes and pregnancy problems between the two groups while accounting for possible confounding variables.

Sample size

100 maternal participants were selected for the study comprising 50 low risk women and 50 VAMA women for comparison.

Sample size was considered using the incidence rates such as incidence of low birth weight (LBW), c-section and preterm deliveries.

Twins and higher-order gestations were excluded from the study.

Patients with critical illness or complications like type I diabetes, neuro related diseases, cancer were also avoided to not deviate from our objective.

Patients presenting to the department of obstetrics and gynecology with VAMA were considered in this study to evaluate the perinatal outcomes when compared with normal-aged women. This study addressed several critical gaps in the current literature on VAMA pregnancies. All patients with very advanced maternal age during the study period were selected by adhering to inclusion and exclusion criteria and a structured questionnaire was framed to collect the data. The collected data was subjected to statistical evaluation using SPSS 21.0 software.

RESULTS

Maternal characteristics

The mean age of participants in the VAMA group was 46.02 years (SD: 1.14), significantly higher than 28.5 years in the low-risk group. The mean gestational age was slightly lower in the VAMA group (37.0 weeks) compared to the low-risk group (38.0 weeks). The mean BMI was similar between both groups (30.74 versus 30.66, SD: 5.37) (Table 1).

Prevalence of medical conditions

The incidence of hypertension was markedly higher in the VAMA group (14%) compared to the low-risk group (2.8%). Similarly, diabetes was more prevalent in VAMA (30% versus 7.5%). The occurrence of gestational diabetes mellitus (GDM) was more than double in the VAMA group (25.0%) compared to the low-risk group (11.6%), indicating a higher metabolic risk in older pregnancies (Table 2).

Table 1: Age and BMI distribution.

Age (SD: 1.14 years)	Mean age	Mean gestational age	BMI (SD: 5.37)	Variables
45-49 years	46.02 years	37.0 weeks	30.74	VAMA
18-42 years	28.5 years	38.0 weeks	30.66	Low risk

Table 2: Prevalence of medical conditions.

Condition	VAMA	Low risk
Hypertension	14%	2.8%
Diabetes	30%	7.5%
Gestational diabetes mellitus	25.0%	11.6%

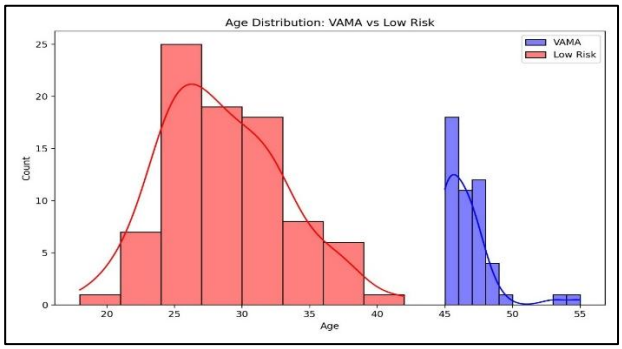

Figure 1: Age distribution.

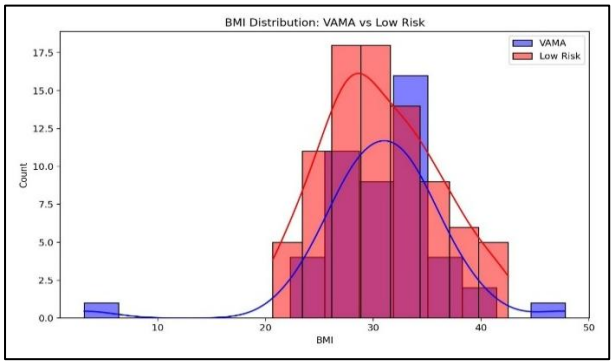

Figure 2: BMI distribution.

Delivery methods and anesthesia usage

A significantly higher proportion of VAMA participants underwent caesarean section or instrumental delivery (54%) compared to the low-risk group (22%). Conversely, vaginal deliveries were more frequent in the low-risk group (78% versus 46% in VAMA) (Table 3).

Table 3: Delivery methods and anesthesia usage.

Variables	VAMA group	Low risk
Caesarean sections and instrumental delivery	54%	22%
Vaginal delivery	46%	78%
ART usage	5%	None
Spinal anesthesia	47.9%	13%
General anesthesia	4.2%	7%
Epidural	39.9%	8.1%
No anesthesia	8%	72.1%

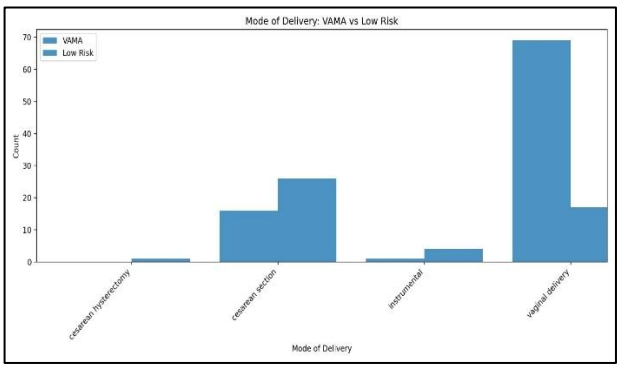

Figure 4: Mode of delivery.

Assisted reproductive technology (ART) was used in 5% of VAMA cases, whereas it was absent in the low-risk group. Spinal anesthesia was administered to 47.9% of VAMA patients, compared to only 13% in the low-risk group. Similarly, epidural anesthesia was more commonly used in the VAMA group (39.9% versus 8.1%). In contrast, a significantly higher proportion of low-risk women delivered without anesthesia (72.1% versus 8% in VAMA).

Neonatal outcomes

The mean birth weight was lower in the VAMA group (2895.7 gm, SD: 719.9 gm) compared to the low-risk group (3145.9 gm, SD: 525.8 gm). NICU admissions were higher in VAMA (34%) compared to the low-risk group (26.6%), suggesting an increased risk of neonatal complications in this group. However, the rates of induction of labor were similar between both groups (31.3% in VAMA versus 32.6% in low-risk) (Table 4).

Table 4: Comparison of neonatal outcomes.

Neonatal outcome	VAMA group	Low risk group
Mean birth weight	2895.7 gm	3145.9 gm
Standard deviation in birth weight	719.9 gm	525.8 gm
NICU admissions	34%	26.6%
Induction of labor	31.3%	32.6%

Maternal complications

The prevalence of maternal complications was significantly higher in the VAMA group across multiple parameters. Preeclampsia was observed in 12.5% of VAMA participants, compared to only 2.3% in the low-risk group. Gestational diabetes mellitus remained twice as prevalent in VAMA (25.0% versus 11.6%) (Table 5).

Table 5: Complications in VAMA and low risk groups.

Complications	VAMA	Low risk
Preeclampsia	12.5%	2.3%
Gestational diabetes mellitus	25.0%	11.6%
Placenta previa	8.3%	1.2%
Down's syndrome	2%	None
Intrauterine growth restriction	10.4%	3.5%

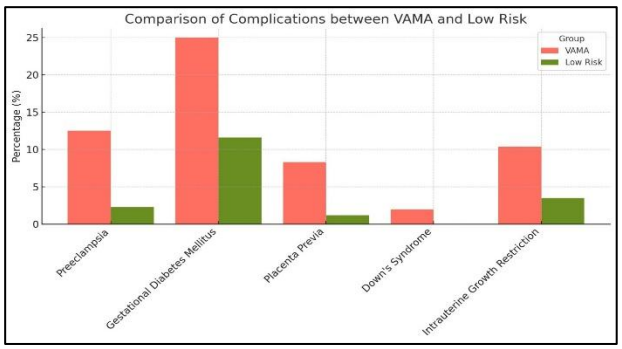

Figure 5: Comparison of complications between VAMA and low risk.

The occurrence of placenta previa was significantly higher in the VAMA group (8.3% versus 1.2%). Similarly, intrauterine growth restriction (IUGR) was noted in 10.4% of VAMA pregnancies, compared to 3.5% in low-risk pregnancies. Additionally, 2% of neonates in the VAMA group had Down's syndrome, whereas no cases were observed in the low-risk group.

DISCUSSION

In recent years, there has been a significant alteration in childbearing age, especially in high-income countries. An increasing trend towards delayed childbearing, whereby many women are postponing pregnancy until later in life which is aided by advancement in reproductive technology such as IVF and egg donation or freezing. However, with advancing maternal age, 45 years and above, especially in VAMA, there are numerous complications that may affect both the outcome of the mother and baby. Although tremendous advances have been made in pregnancy care, gestational complications, labor outcomes, and neonatal health always seem to be alarming for women classified under VAMA.[11]

Our study aims to examine this type of risk, by comparing pregnancy complications of VAMA women and those of younger childbearing women (low risk women) to contribute towards a better understanding of the risks involved among both the groups. Aging brings about many physiological changes, and most of these changes affect pregnancy outcomes. One critical factor that is indeed alarming is the decline in ovarian reserve and oocyte quality owing to menopause, thereby risking an increased level of chromosomal anomalies such as Down's syndrome.[3,4] Furthermore, aging has predisposed women to conditions such as gestational diabetes and hypertensive disorders due to the natural progression of the age related factors such as insulin resistance and cardiovascular rigidity.[12] Studies have demonstrated that the placenta of older mothers tends to function less effectively, which results in complications such as preeclampsia, intrauterine growth restriction, and preterm birth.[13] Additionally, the incidence of placenta previa in VAMA pregnancies was found to be higher, a condition often associated with complications like hemorrhage and preterm delivery.[14] The cumulative influence of long-standing comorbidities such as hypertension, obesity and metabolic syndrome contributes to increased pregnancy complications in VAMA women. These molecular and physiological changes form the background for the findings of our cohort study.

In our study a significantly higher incidence of gestational diabetes among VAMA women than younger women (42% versus 18%) was seen, a result well-supported by existing literature. Similar studies by Chakraborty, Li et al reflect the same results as they reported higher prevalence of gestational diabetes among older pregnant women mainly attributed to age-related decline in insulin sensitivity.[15,16] It then decreases in efficiency to compensate for the rising insulin resistance during pregnancy, and this is compounded by advancing age.

Moreover, the progressive increase in body mass index is well known and observed in aging women which further exacerbates these metabolic challenges to increase the risk of gestational diabetes. Notably, gestational diabetes itself poses threats to both the mother as well as the baby, risks such as a higher chance of preterm birth, cesarean section, and neonatal hypoglycemia, so that its management should take precedence in pregnancies complicated by VAMA. We also found hypertensive disorders of pregnancy, including gestational hypertension and preeclampsia, to be significantly more common in the VAMA group i.e. 36% compared to the younger group, which was 12%.

Also, advanced maternal age has been linked to a higher risk of placental abruption, which is further associated with maternal hemorrhage and fetal morbidity. These findings concur with the results of other studies Khedagi who found maternal age to be one of the major risk factors for hypertensive disorders of pregnancy.[17] Much of these conditions relate to vascular changes related to aging, such as arterial stiffness and reduced endothelial function. In older women, the cardiovascular system is compromised due to exposure to risk factors like hyperlipidemia or sedentary lifestyles, predisposing them to complications during pregnancy.

Moreover, the increased risk of preeclampsia in VAMA pregnancies might be exacerbated by placental dysfunction where older placentas have lesser efficiency with their nutrient transfer and gas exchange functions. However, what it brings to attention is close monitoring and early intervention during VAMA pregnancies because hypertensive disorders often result in grave outcomes, including preterm delivery, placental abruption, and even maternal mortality. One notable finding of our research was the significantly higher rate of cesarean sections amongst VAMA women 64% compared to younger women, which was only 26%. Advanced maternal age has been associated with higher rates of cesarean sections accounted for a synergistic combination of both medical indications and elective decision-making. Studies like those done by Ecker and Janoudi conclude that the risks of cesarean delivery underlie for older mothers with certain concerns regarding well-being of both mother and baby other than obstetric complications like labor dystocia and fetal malpresentation.[18,19] The patients and clinicians may prefer cesarean sections in VAMA pregnancies to avoid prolonged labor with risks of fetal distress, but this should not be forgotten that the cesarean delivery, in itself, is associated with increased risks of complications, like postpartum hemorrhage and infections, especially in the older mothers. There is evidence that advanced maternal age may lead to a higher likelihood of uterine atony, which can result in severe postpartum hemorrhage followed by related complications.[20]

Since our study revealed a high rate of cesarean sections, the effort must also include at other stages including the importance of proper counseling and preparation in prenatal care for all VAMA women regarding the risk-benefit differences between elective and emergency cesarean delivery. Chromosomal anomalies such as Down's syndrome (trisomy 21) frequently pose a greater hazard with advanced maternal age. Research indicates that women over 45 years face a greater chance of having chromosomal defects mainly from reduced oocyte quality as they age.[21] Along with chromosomal irregularities, growing maternal age is associated with a higher occurrence of spontaneous miscarriage and stillbirth caused by placental problems and existing maternal conditions.[22]

Beyond chromosomal problems, parental age exceeding 45 years links higher incidences of neurodevelopmental disorders like autism spectrum disorder (ASD) and ADHD in children.[23] The older a woman, the higher risk she carries while experiencing multiple births particularly in women using assisted reproductive methods (ART).[24] Having multiple offspring creates complications that can lead to premature births and lowered birth weights. However, contrary to these studies, other research findings indicated reduced differences in outcomes between VAMA and younger women. For example, Mnabwiru et al recently reported that although maternal age was associated with some increased risks, such as preeclampsia and cesarean delivery, the overall differences in neonatal outcomes were far less dramatic than expected.[25] This may have been due to differences in study populations, healthcare systems, or just the degree to which pre-existing conditions were controlled. Also, the fact that most of the pregnancies in VAMA are through assisted reproductive technologies confuses the analysis as ART itself predisposes to complications such as preeclampsia and preterm delivery regardless of the maternal age.[26]

GDM can cause complications to both the mother and the newborn like preterm births, an increase in the likelihood of c-section deliveries, and neonatal hypoglycemia. Recent research suggests that the metabolic changes in a pregnant woman may worsen these risks and affect maternal health along with the risk of morbidity in the newborn.[27] There is an overwhelming increase in the rate of cesarean deliveries in more complicated pregnancies which makes some level of integrated care in obstetrics necessary. Studies show that GDM is associated with maternal metabolic abnormalities and other comorbid conditions that strongly influence the outcomes of deliveries, thus highlighting the importance of appropriate clinical judgement.[28]

The strengths of our study are in comparing VAMA women with younger, low-risk women directly so that the specific challenges of older mothers are more clearly depicted. Most prior studies were based on broad age ranges or did not include control groups, so the risks and complications associated with VAMA pregnancies cannot be precisely analyzed through our cohort. Further, by including maternal and neonatal outcomes together, we can give a much more complete understanding of the effects of advanced maternal age on the whole process of

the pregnancy starting from conception through to delivery.

Nonetheless, the present study has several drawbacks. The sample size is relatively small in size, and hence generalizability may be poor; in addition, a single center design may not reflect differences in healthcare practice from region to region. Risk associated with VAMA pregnancies would require further clarification with larger, more diverse populations and much more detailed control for confounding variables.

CONCLUSION

Gestational diabetes and hypertensive disorders are considerable issues occurring in pregnancy with VAMA, also the caesarean section rates have increased by two folds for births with VAMA and pregnancies significantly appear to be at higher risk. Due to these concerns close monitoring and specifically targeted obstetric care in the older female who gets pregnant prove invaluable. It would be possible to give VAMA women better informed guidance to address pregnancy complications in a more productive way toward better maternal and neonatal outcomes with better knowledge of the molecular and physiological changes that occur as part of aging. Indeed, in light of increasing delayed childbearing, the research of this study highlights a continuous necessity for further research and public health initiatives in optimally providing care for this emerging population.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Review Board MBRU IRB-2024-371, Dubai Scientific Research Ethics Committee, DSREC-09/2024_32

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Cite this article as: Godara J, Vasanth U, Waheed S, Makhdoom T, Binashoor AK, AlSayari SY. A comparative study of pregnancy complications and birth outcomes in very advanced maternal age women: a retrospective cohort analysis. Int J Reprod Contracept Obstet Gynecol 2025;14:1016-22.