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# The association of advanced maternal age with maternal and neonatal outcomes of pregnancy in Filipino patients in a tertiary medical center: An analytical cross-sectional study

**Leolina Remeceta M Gamboa-Chua[1], Agnes L. Soriano-Estrella[1,2]**

*[1]Department of Obstetrics and Gynecology, St. Luke's Medical Center-Global City, Taguig City, Philippines, [2]Department of Obstetrics and Gynecology, Philippine General Hospital, University of the Philippines-Manila*

**Address for correspondence:**
Leolina Remeceta Medenilla Gamboa-Chua, MD, Obstetrics and Gynecology, St. Luke's Medical Center-Global City, Taguig, Philippines. E-mail: yim_jel@yahoo.com

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**Abstract:**

**BACKGROUND:** For the past decade, advanced maternal age (AMA) became more common in developed and developing countries due to the postponement of pregnancy because of career goals, widespread use of family planning, and advances in assisted reproductive techniques. This increase bears an impact on maternal and perinatal outcomes. The link between AMA and adverse maternal, perinatal, and neonatal outcome showed contradicting results. This study was conducted to investigate the association between AMA and adverse outcomes among nulliparous, Filipino with singleton pregnancies who gave birth in a private tertiary hospital.

**METHODOLOGY:** Medical records of patients admitted for delivery between January 2015 and December 2019 were reviewed retrospectively. The control (20–34 years), AMA 35–39 years, very AMA 40–44 years, and extremely advanced maternal age (EAMA) 45 years and above groups included 206, 111, 18, and 2, respectively.

**RESULTS:** Five-year total deliveries at a private tertiary hospital were 8495 with a prevalence of 38.9% (95% confidence interval CI: 33.6%–44.3%) for elderly Filipino primigravids. AMA is a risk factor for diabetes mellitus and small for gestational age newborn in all 3 advanced age groups. Pregnancy induced hypertension, having cesarean section, admission of newborn to neonatal intensive care unit, and administration of antibiotics were more common to AMA but same risk for EAMA. AMA predisposes to having oligohydramnios, placenta previa and preterm delivery but pregnancy at EAMA predisposes more complications in maternal and neonatal outcomes such as having polyhydramnios, abruptio placenta, postpartum hemorrhage, maternal and neonatal death, low Appearance Pulse Grimace Activity and Respiration score, and stillbirth. There is no noted association between AMA and large for gestational age newborn, having meconium staining and delivering by classical cesarean section.

**CONCLUSION:** AMA in Filipino gravida patients is markedly linked with adverse obstetrical, perinatal, and neonatal outcomes. This study confirms the current trend among women over 45 years that leads to more significant obstetric complications and neonatal morbidities.

**Keywords:**

Advanced maternal age, pregnancy outcomes.



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## Introduction

The fertility rate of women follows a characteristic pattern; after menarche, rate starts at low level then peaks at ages

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20–29 years, and will gradually decline until complete cessation after menopause. Both ends of the reproductive spectrum shows a higher risk of adverse pregnancy outcome.[1] It has been shown that at age ≥35 years, women are more likely to experience gestational diabetes mellitus (GDM), placenta previa, malpresentation, and operative vaginal delivery than younger women aged 20–29 years. Other observed complications that are prevalent to advanced maternal age (AMA) are preeclampsia, gestational hypertension (GH), cesarean delivery (CS), abruptio placenta, preterm delivery, low birth weight, and stillbirth.[2] Furthermore, the prevalence of chronic medical conditions (e.g., diabetes mellitus, hypertension) and other diseases with a possible influence on a course of pregnancy such as cancer, are higher among older patients. Multiple studies suggests that the incidence rate of perinatal complications only begins to increase after the age of 35 years, but the most significant growth can be observed after the age of 40 years.[3]

Worldwide statistics show significant increase in average age of first birth with the greatest increase seen among the age 35–39 years. Although the birth rate of these women continues to grow, overall number remains small.[4] In the Philippines, median age at first birth for all women age 25–49 years is 23.5.[5] The trend of AMA is contributed to changing sociodemographics, these women of AMA are more likely to be well educated, higher socioeconomic status, and low parity compared to older mothers from the past.[4] Furthermore, recent changes in work and society have been reflected in women's desire to develop their careers, obtain financial security and build stable relationship with their partner before becoming mothers. Higher education of these women leads to a better knowledge and awareness of different types of contraception and greater access to birth control methods.[3] In addition, the most significant reason for delayed child bearing is the progress in assisted reproductive technology (ART) (e.g., *in vitro* fertilization [IVF], oocyte donation, intrauterine insemination [IUI]) which contributed to the rise of number of pregnancies in women in their 40–50s.[2,4]

This study is started with the intent that appropriate interventions may be given to further improve pregnancy outcomes among women from the older end of the reproductive age spectrum.

## Definition of terms

1. AMA – Childbearing ≥35 years of age[6]
2. Very AMA (VAMA) – Childbearing ≥40 years of age[7]
3. Extremely AMA (EAMA) – Childbearing ≥45 years of age[7]
4. Operative delivery
   a. Operative vaginal delivery - Delivery vaginally assisted with vacuum/forceps device[6]
   b. Cesarean delivery – Delivery laparotomy and then hysterotomy[6]
5. Hypertension in pregnancy
   a. GH – blood pressure (BP) of ≥140 mmHg systolic or ≥90 mmHg diastolic, or both, on two separate occasions at least 4hours apart after 20 weeks of gestation in a woman with previously known normal BP. It occurs in women with hypertension without proteinuria or no severe features develop and BP level returns to normal in postpartum period[8]
   b. Preeclampsia – first time-onset hypertension with new onset proteinuria, or symptoms such as headache, right upper quadrant pain, blurring of vision, with or without proteinuria, occurring after 20 weeks age of gestation and frequently near term. GH with the absence of proteinuria but with associated thrombocytopenia, impaired liver function and severe persistent right upper quadrant or epigastric pain, renal insufficiencies, pulmonary edema or new onset headache not responsive to acetaminophen is also classified as preeclampsia[8]
6. GDM – condition consists of carbohydrate or glucose intolerance with first recognition during pregnancy[9]
7. Placenta previa – presence of placental tissues which extends over the internal cervical os during pregnancy[10]
8. Abruptio placenta – early placental separation from the uterine lining prior delivery[11]
9. Gestational age – time elapsed between the first day of the last normal menstrual period (LMP) and the day of delivery. If a patient is unsure, the gestational age is based on the earliest sonographic aging until 13 6/7 weeks[12] age of gestation will be based on the 1st day of LMP or first trimester ultrasound while pediatric aging will be based on the Ballard score[13]
10. Preterm labor and birth – birth <37 completed weeks or <259 days since the 1st day of the LMP[14]
11. Preterm prelabor rupture of membranes (PPROM) – rupture of fetal membranes prior labor and <37 weeks' gestational age[15]
12. Stillbirth – Fetal death; delivery of dead fetus at ≥20 weeks, or weight ≥500 g and exhibiting no signs of life such as breathing, heartbeats, umbilical cord pulsations or definite voluntary muscle movements[16]
13. Early neonatal death – death of a liveborn infant regardless of gestational age at birth, within the first 28 completed days of life[17]
14. Appearance Pulse Grimace Activity and Respiration (APGAR) score – scoring for rapid assessment of a newborn's clinical status at 1 and 5 min after birth, including need and response from resuscitation; consists of 5components, namely, heart rate, respiratory effort, muscle tone, reflex irritability,

and color. Each component is assigned a score of 0, 1, or 2. Poor APGAR score is a score of <7 at 5 min period[18]

15. Small for gestational age (SGA) – birthweight <10th percentile for gestational age[18]
16. Large for gestational age – birthweight >90th percentile for gestational age[18]
17. Intrauterine growth restriction (IUGR) – sonographic fetal weight <10th percentile of expected weight for gestational age (Hadlock formula), linked with the increased pulsatility index of umbilical artery ≥2 standard deviations, and a postpartum verification with a birthweight <10th percentile.[19]

## Objectives

This study was initiated to determine the association between AMA and adverse maternal and perinatal outcomes among nulliparous, Filipino patients with singleton pregnancy compared to women aged 20–34 years. The percentage of women who were at AMA at the time of delivery and its adverse maternal outcome (i.e. maternal death, operative delivery); pregnancy-related complications (i.e. prelabor rupture of membranes, abnormal placentation, postpartum hemorrhage); and adverse neonatal outcomes (i.e. stillbirth, early neonatal death, preterm birth, poor APGAR score, large or SGA, and neonatal intensive care or intermediate medical care unit admission (NICU/IMCU) were obtained.

## Methodology

This study was a retrospective cross-sectional study of Filipino women of at least 20 years who delivered singleton from January 2015 to December 2019 at the Department of Obstetrics and Gynecology of the St. Luke's Medical Center-Global City. The study was approved by the Research Ethics Committee of the said institution. Patients who met the following criteria were enrolled: (1) nulliparous, (2) singleton, (3) gestational age ≥20 weeks, and (4) birthweight ≥500 g. The exclusion criteria were: (1) multiple gestation, (2) any concomitant chronic diseases diagnosed prior to pregnancy, (3) history of uterine surgery, (4) any Mullerian abnormality, (5) presence of uterine or adnexal mass, and (6) smoking, alcohol or illicit drug use since the said conditions were associated with increased risk for poor pregnancy outcomes regardless of age.

The medical records of eligible patients were retrieved and assessed and all identifying information were removed. The patients' name was coded during input. Only the data pertinent to the objectives of the study were extracted from the medical records and recorded on the patient data extraction from [Table 1]. Data included were the following:

**Table 1: Data collection form**

| | | |
|---|---|---|
| **DEMOGRAPHIC DATA** | | |
| Age | | Nationality |
| **CLINICAL DATA** | | |
| BMI | | Gravidity/ Parity |
| **ADMITTING DIAGNOSIS** | | |
| Pregnancy<br>Spontaneous<br>Assisted (IVF/IUI) | | Infertility<br>Yes<br>No |
| Medical Condition<br>Chronic HPN<br>GHPN/ Preeclampsia<br>Gestational DM<br>Thyroid disease<br>Bronchial Asthma<br>Heart disease<br>Others | | Internal examination upon admission Cervical dilatation<br>cm<br>Membranes<br>Intact<br>Ruptured<br>Presentation<br>Cephalic<br>Breech<br>Transverse |
| Amniotic fluid<br>Normal<br>Oligohydramnios<br>Hydramnios | Placental location<br>Normal<br>Previa<br>Accreta | Perinatal complication<br>PROM<br>Others |
| Mode of delivery<br>NSD<br>Degree of tear<br>OFE<br>Degree of tear<br>Vacuum<br>Degree of tear<br>Abdominal | If abdominal<br>LTCS<br>Classical | If CS, indication<br>Dystocia<br>Malpresentation<br>NRFHR<br>Placenta previa<br>Deteriorating maternal status<br>Others |
| Birth weight<br>grams<br>(_)SGA (_)AGA (_)LGA | Livebirth<br>Yes<br>No | Meconium staining<br>Yes<br>No |
| Pediatric aging<br>Weeks<br>(_) Preterm<br>(_) Term<br>(_) Post term | 5minute APGAR score<br>0-3 Low<br>4-6 intermediate<br>7-10 Normal | Disposition<br>Room in<br>IMCU<br>NICU<br>Antibiotics: (_)Y (_)N<br>Surfactant: (_)Y (_)N |

1. Maternal demographic data: age, body mass index (BMI), spontaneous or assisted pregnancy (IVF or IUI), gestational age upon delivery, presence of medical conditions, abnormal placentation, and PPROM
2. Pregnancy outcome: route of delivery, indication for operative delivery, maternal morbidity or mortality
3. Neonatal outcomes: occurrence of stillbirth or neonatal death, pediatric aging, APGAR score, birthweight, and NICU/IMCU admission.

Charts collected and data collection forms retrieved were only handled by the authorized investigators.

### Statistical analysis

Demographic data, maternal and clinical outcomes of patients were gathered and encoded into Microsoft Excel Spreadsheet. Descriptive statistics such as mean, median, standard deviation were used to summarize the characteristics of the participants. Frequency and proportion were used for categorical variables while mean and standard deviation for numerical variables. Fisher's Exact or Chi-square test was used to determine the difference frequency profile between groups. Group means were compared using *t*-test or Mann–Whitney *U*-test. Odds and risk ratios were reported to measure the degree of association. All statistical analysis was performed at 5% level of significance.

## Results

Five-year total deliveries were 8495 with the prevalence of 38.9% (95% confidence interval [CI]: 33.6%–44.3%) of AMA obtained and demographic analysis showed that the mean age of the study group was 38 ± 2.01 years (range 35–47).

A total of 337 samples were collected through randomization comprising of 206 (61%) for control, 111 (33%) for AMA of 35–35 years age, 18 (5%) for VAMA of 40–44 years age and 2 (1%) for EAMA of >45 years of age [Table 2].

**Table 2: Sample data collected and frequency**

| Age group (years) | Frequency (%) |
|---|---|
| 20-34 | 206 (61.1) |
| 35-39 | 111 (32.9) |
| 40-44 | 18 (5.3) |
| ≥45 | 2 (0.6) |
| Total | 337 |

Clinical characteristics of four maternal groups and pregnancy complications are shown in Table 3. For the control and AMA, majority has BMI of overweight while VAMA and EAMA were mostly Obese I. All groups had spontaneous pregnancy and no infertility. Based on the performed Chi-square test, there is a significant association between AMA and assisted pregnancy ($\chi^2 = 36.5$, $P < 0.001$) and maternal age and infertility ($\chi^2 = 115.7$, $P < 0.0001$).

The likelihood of patients being admitted for labor induction [Table 4] is 2.5 times for AMA ($z = 3.57$, $P = 0.0002$) and 6.60 times for VAMA ($z = 2.90$, $P = 0.0019$). For patients being admitted, no association whether they came in active labor (internal examination of ≥4 cm) or ruptured bag of water in all three groups. There is likelihood that patients having malpresentation is 4.2 times in VAMA and 13.28 times in EAMA compared to younger age group.

The likelihood of patients having pregnancy-induced hypertension (PIH) [Table 5] is 2.7 times for AMA ($z = 2.46$, $P = 0.0070$) and 6.9 times for VAMA ($z = 3.281$, $P = 0.0005$). The likelihood of patients having GDM is 3.1 times for AMA ($z = 3.68$, $P = 0.0001$) and 4 times for VAMA ($z = 2.64$, $P = 0.0042$). The calculated odds ratio for EAMA compared to younger age group is 1.562, however, there is no sufficient evidence to say that this association is statistically significant ($z = 0.285$, $P = 0.3879$). There is association with oligohydramnios in AMA ($z = 2.41$, $P = 0.081$) about 2.8 times more likely to be observed in younger age group but no significant association in VAMA ($z = 0.521$, $P = 0.3013$) and EAMA ($z = 0.835$, $P = 0.2019$). For polyhydramnios, there is no link with maternal age for both AMA and VAMA groups but 82.6 times likelihood to EAMA ($z = 2.102$, $P = 0.0177$). For the occurrence of abnormal placentation, placenta previa is 3.6 times more likely to occur in AMA ($z = 1.89$, $P = 0.0291$). But for

**Table 3: Descriptive data of Filipino advanced maternal age with singleton births**

| Characteristics | Age group (years) | | | | *P* ($\chi^2$) |
|---|---|---|---|---|---|
| | 20-34 (%) | 35-39 (%) | 40-44 (%) | ≥45 (%) | |
| BMI (kg/m$^2$) | | | | | |
| Underweight <18.5 | 3 (1.5) | 1 (0.9) | 0 | 0 | <0.0001 (51.1) |
| Normal 18.5-24.9 | 80 (38.8) | 16 (14.4) | 0 | 0 | |
| Overweight 25.0-29.9 | 92 (44.7) | 50 (45.0) | 6 (33.3) | 1 (50.0) | |
| Obese Class I 30.0-34.9 | 28 (13.6) | 40 (36.0) | 11 (61.1) | 1 (50.0) | |
| Obese Class II 35.0-39.9 | 3 (1.5) | 4 (3.6) | 1 (5.6) | 0 | |
| Obese Class III ≥40.0 | 0 | 0 | 0 | 0 | |
| Pregnancy | | | | | |
| Spontaneous | 203 (98.5) | 93 (83.8) | 13 (72.2) | 1 (50.0) | <0.001 (36.5) |
| Assisted (IVF/IUI) | 3 (1.5) | 18 (16.2) | 5 (27.8) | 1 (50.0) | |
| N/A | | | | | |
| Infertility | 6 (2.9) | 47 (42.3) | 14 (77.8) | 2 (100.0) | <0.0001 (115.7) |
| Not infertility | 200 (97.1) | 64 (57.7) | 4 (22.2) | 0 (0.0) | |

IVF: *In vitro* fertilization, IUI: Intrauterine insemination, BMI: Body mass index

**Table 4: Comparison of all the women aged 35-39 and ≥40 with the control group (20-34) on maternal characteristics upon admission**

| Characteristics | Age group (years) | | | | | |
|---|---|---|---|---|---|---|
| | AMA 35-39 years old | | VAMA 40-44 years old | | EAMA ≥45 years old | |
| | *Z* score (*P* $\chi^2$) | OR (95% CI) | *Z* score (*P* $\chi^2$) | OR (95% CI) | *Z* score (*P* $\chi^2$) | OR (95% CI) |
| Not in labor | 3.573 (0.0002) | 2.446 (1.498-3.996) | 2.724 (0.0032) | 6.600 (1.698-25.659) | 1.035 (0.1504) | 5.000 (0.237-105.431) |
| Internal examination of ≥4 cm | −4.621 (1.0000) | 0.277 (0.161-0.478) | −2.670 (0.9962) | 0.100 (0.018-0.542) | −0.935 (0.8251) | 0.234 (0.011-4.924) |
| Ruptured amniotic fluid membrane | 1.636 (0.0509) | 1.729 (0.897-3.331) | 0.304 (0.3806) | 1.242 (0.306-5.040) | 0.316 (0.3760) | 1.640 (0.076-35.251) |
| Nonvertex fetal presentation | 0.749 (0.2268) | 1.373 (0.599-3.149) | 2.342 (0.0096) | 4.120 (1.260-13.472) | 2.180 (0.0146) | 13.276 (1.298-135.809) |

AMA: Advanced maternal age, VAMA: Very advanced maternal age, EAMA: Extremely maternal age, OR: Odds ratio, CI: Confidence interval

**Table 5: Comparison of all the women aged 35-39 and ≥40 with the control group (20-34) on pregnancy complications and mode of delivery**

| Characteristics | Age group (years) | | | | | |
|---|---|---|---|---|---|---|
| | AMA 35-39 | | VAMA 40-44 | | EAMA ≥45 | |
| | *Z* score (*P* $\chi^2$) | OR (95% CI) | Z score (*P* $\chi^2$) | OR (95% CI) | Z score (*P* $\chi^2$) | OR (95% CI) |
| Pregnancy complications | | | | | | |
| Pregnancy induced hypertension | 2.458 (0.0070) | 2.731 (1.226-6.082) | 3.281 (0.0005) | 6.926 (2.180-22.009) | 0.775 (0.2191) | 3.400 (0.154-75.030) |
| Gestational diabetes mellitus | 3.679 (0.0001) | 3.056 (1.685-5.540) | 2.639 (0.0042) | 4.060 (1.434-11.494) | 0.285 (0.3879) | 1.562 (0.073-33.529) |
| Oligohydramnios | 2.416 (0.0079) | 2.783 (1.213-6.386) | 0.521 (0.3013) | 1.604 (0.271-9.506) | 0.835 (0.2019) | 3.743 (0.169-83.020) |
| Polyhdramnios | 0.308 (0.3792) | 1.852 (0.036-93.976) | 1.197 (0.1156) | 11.162 (0.215-578.989) | 2.103 (0.0177) | 82.600 (1.350-5052.317) |
| Placenta previa | 1.894 (0.0291) | 3.582 (0.956-13.418) | 1.595 (0.0554) | 4.984 (0.692-35.883) | 1.496 (0.0674) | 11.629 (0.467-289.594) |
| Abruptio placenta | 0.308 (0.3792) | 1.852 (0.036-93.976) | 1.197 (0.1156) | 11.162 (0.215-578.989) | 2.103 (0.0177) | 82.600 (1.350-5052.317) |
| Prelabor rupture of membrane | −0.388 (0.6511) | 0.858 (0.395-1.861) | 0.153 (0.4392) | 1.145 (0.202-6.488) | -0.454 (0.6751) | 0.491 (0.023-10.611) |
| Postpartum hemorrhage | 0.308 (0.3792) | 1.852 (0.036-93.976) | 1.197 (0.1156) | 11.162 (0.215-578.989) | 2.103 (0.0177) | 82.600 (1.350-5052.317) |
| Death | 0.308 (0.3792) | 1.852 (0.036-93.976) | 1.197 (0.1156) | 11.162 (0.215-578.989) | 2.103 (0.0177) | 82.600 (1.350-5052.317) |
| Mode of delivery | | | | | | |
| Cesarean section | 7.010 (0.0001) | 9.579 (5.092-18.018) | 2.894 (0.0019) | 5.814 (1.765-19.151) | 1.210 (0.1132) | 6.564 (0.311-138.446) |
| Classical CS | 0.407 (0.3421) | 1.528 (0.198-11.811) | 0.389 (0.3488) | 1.903 (0.074-48.881) | 1.407 (0.0797) | 11.800 (0.379-367.510) |
| Assisted vaginal | 0.604 (0.2728) | 1.768 (0.279-11.223) | 2.911 (0.0018) | 24.556 (2.846-211.895) | 1.322 (0.0931) | 14.733 (0.273-795.738) |

AMA: Advanced maternal age, VAMA: Very advanced maternal age, EAMA: Extremely maternal age, OR: Odds ratio, CI: Confidence interval, CS: Cesarean delivery

**Table 6: Comparison of all the women aged 35-39 and ≥40 with the control group (20-34) on neonatal complications**

| Characteristics | Age group (years) | | | | | |
|---|---|---|---|---|---|---|
| | AMA 35-39 years old | | VAMA 40-44 years old | | EAMA ≥45 years old | |
| | Z score (P $\chi^2$) | OR (95% CI) | Z score (P $\chi^2$) | OR (95% CI) | Z score (P $\chi^2$) | OR (95% CI) |
| Perinatal outcome | | | | | | |
| Preterm | 2.441 (0.0073) | 4.171 (1.325-13.126) | 1.384 (0.0831) | 3.857 (0.570-26.083) | 1.356 (0.0876) | 9.000 (0.375-215.744) |
| Postterm | 0.340 (0.3670) | 1.976 (0.039-100.290) | 1.215 (0.1122) | 11.571 (0.223-601.148) | 2.094 (0.0181) | 81.000 (1.324-4954.672) |
| Birth weight: SGA | 1.849 (0.0322) | 5.804 (0.900-37.421) | 2.030 (0.0212) | 11.000 (1.086-111.432) | 1.852 (0.0320) | 25.667 (0.827-796.663) |
| LGA | 0.434 (0.3322) | 1.218 (0.499-2.971) | –0.614 (0.7305) | 0.407 (0.023-7.148) | 0.666 (0.2528) | 2.852 (0.130-62.435) |
| Low APGAR score | 0.308 (0.3792) | 1.852 (0.036-93.976) | 1.197 (0.1156) | 11.162 (0.215-578.989) | 2.103 (0.0177) | 82.600 (1.350-5052.317) |
| With meconium staining | 1.131 (0.1290) | 1.900 (0.625-5.781) | 1.035 (0.1504) | 2.644 (0.419-16.671) | 1.137 (0.1277) | 6.169 (0.268-141.863) |
| NICU/IMCU admission | 4.275 (<0.0001) | 3.650 (2.016-6.610) | 4.871 (<0.0001) | 12.573 (4.540-34.824) | 0.316 (0.3760) | 1.640 (0.076-35.251) |
| With antibiotics | 2.958 (0.0015) | 2.706 (1.399-5.232) | 3.079 (0.0010) | 5.298 (1.833-15.313) | 0.454 (0.3249) | 2.038 (0.094-44.064) |
| With surfactant | 1.053 (0.1462) | 5.606 (0.226-138.780) | 2.159 (0.0154) | 35.400 (1.390-901.774) | 2.103 (0.0177) | 82.600 (1.350-5052.317) |
| Stillbirth | 0.308 (0.3792) | 1.852 (0.036-93.976) | 1.197 (0.1156) | 11.162 (0.215-578.989) | 2.103 (0.0177) | 82.600 (1.350-5052.317) |
| Death | 0.308 (0.3792) | 1.852 (0.036-93.976) | 1.197 (0.1156) | 11.162 (0.215-578.989) | 2.103 (0.0177) | 82.600 (1.350-5052.317) |

AMA: Advanced maternal age, VAMA: Very advanced maternal age, EAMA: Extremely maternal age, OR: Odds ratio, CI: Confidence interval, SGA: Small for gestational age, LGA: Large for gestational age, APGAR: Appearance pulse grimace activity and respiration, NICU: Neonatal intensive care, IMCU: Intermediate medical care unit

abruptio placenta and post-partum hemorrhage, there was no association with both AMA and VAMA but is 82.6 times likelihood in EAMA group ($z = 2.102$, $P = 0.0177$).

Patients in AMA ($z = 7.010$, $P = 0.0001$) and VAMA ($z = 2.894$, $P = 0.0019$) are more likely to deliver by CS. For those who underwent abdominal delivery, there is no risk for delivering through classical CS for all groups while for those who underwent vaginal delivery, an increased likelihood of 24.6 times of having operative vaginal delivery for VAMA ($z = 2.911$, $P = 0.0018$).

For the maternal age in association to neonatal outcomes [Table 6], there was 4.2 times likelihood of having preterm delivery with AMA ($z = 2.44$, $P = 0.0073$). There was also no significant association between postterm delivery and AMA and VAMA but 81 × likely to occur in EAMA group ($z = 2.094$, $P = 0.0181$). The likelihood of patients giving birth to SGA is 5.8 times for AMA ($z = 1.85$, $P = 0.0322$), 11 times for VAMA ($z = 2.03$, $P = 0.0212$) and 25.7 times for EAMA ($z = 0.1.85$, $P = 0.0320$). However, there is no noted association for birthing large for gestational age to all three groups. Delivering a newborn with low APGAR is 82.6 times associated with EAMA ($z = 2.10$, $P = 0.0177$) but found of no risk for AMA and VAMA. There was no noted association of delivering newborn with meconium staining for all three groups.

The likelihood of NICU/IMCU admission is 3.65 times in AMA ($z = 4.28$, $P < 0.001$) and 12.57 times in VAMA ($z = 4.87$, $P < 0.001$) but none in EAMA ($z = 0.32$, $P = 0.3760$). At NICU/IMCU, the likelihood of administering antibiotics is 2.7 times in AMA ($z = 2.96$, $P = 0.0015$) and 5.3 times in VAMA ($z = 3.08$, $P = 0.0010$). The use of surfactant in newborn admitted at NICU is 35 times more likely in VAMA ($z = 2.16$, $P = 0.0154$) and EAMA ($z = 2.10$, $P = 0.0177$). The risk of having stillbirth and neonatal death is 82.6 times more likely in EAMA ($z = 2.102$, $P = 0.0177$), but the same risk for AMA and VAMA compared to younger groups.

## Discussion

AMA represents a substantial proportion of pregnancies in higher-income countries but only a few data on pregnancy outcome in lower-income countries.[20] The note of shift of childbearing age to 5th decade and beyond from third to fourth decade marks introduction of two new terminologies; namely, VAMA and EAMA, which is defined as childbearing at ≥40 and ≥45 years, respectively.[7]

PIH on this study is greatly associated with AMA and VAMA but not for EAMA. This could be due to contrasting course of aging on hemodynamic changes

in pregnancy making adaptation to pregnancy more difficult due to loss of myocardial compliance, decline in vascular responsiveness to endothelium-dependent vasodilators, gradual loss of compliance, and less aortic flow during diastole.[6,21] Confounding variables also include preexisting medical condition, use of ART, history of adverse pregnancy outcome, education, marital status, smoking, and BMI.[22]

AMA is more likely to develop some form of diabetes.[21] This study showed significant association of all three groups to GDM, which could be attributed to the changes in metabolism of carbohydrates secondary to the fall of pancreatic B-cell function and sensitivity associated with advancing age. Hence, studies shows that up to 16% of AMA in pregnancy have an abnormal oral glucose tolerance test.[6,21] GDM and its complications, which include macrosomia, polyhydramnios, and preterm labor, may also contribute to the increased prevalence of pre-eclampsia, placental abruption, and IUGR related with AMA.[21]

Placenta previa has an incidence of 0.3%–2%. In study conducted, placenta previa is 3.6 times more likely associated in AMA but none in VAMA and EAMA. Placental abruption results form a cascade of pathophysiological processes that complicates approximately 1% of births.[18] Placenta abruption is noted to be 82.6 times risk in EAMA. The impact of AMA on the risk of placental abnormalities may likely due to decreased uterine blood flow, uteroplacental hypoperfusion, and major placental infarctions leading to hemorrhagic disorders in older women.[11,18]

Preterm birth is one of the most important factors in determining neonatal morbidity and mortality.[23] In the study, it is noted to be linked to AMA but not with VAMA and EAMA. Proposed theories state that increased risk of preterm birth among AMA is contributed to early labor induction for indicated medical conditions. Other factors include hypertensive disorders, multiple gestations, and infections like urinary tract infection.[21]

The relationship between AMA and SGA is believed to be U-shaped; it can be observed in women <30 and >40 years of age. It is noted that AMA is proven as an independent risk factor for IUGR.[24] This is consistent with our findings that SGA is associated with all study group. While accurate association between AMA and SGA has not been clearly established, studies suggested that the poor exchange of oxygen demonstrated in AMA may be the underlying factor.[24]

AMA is frequently labeled as a higher risk even if there are no known risk factors. High CS rate may be due to the patient and attending doctor's preferences not to labor assuming that it would be the patient's last delivery.[7] This generalization results in increased rate of CS delivery for nonmedical reasons, consequently making AMA as a risk factor for operative abdominal birth and also hypothesizing a biological basis for the findings of (1) a poor progression and longer duration of labor with advancing age, (2) dystocia, and (3) impairment of myometrial contractility due to reduced sensitivity of myometrial oxytocin receptors as the most frequent reasons.[12,25]

A relevant increase in AMA and perinatal outcome is attributed to the increasing number of women postponing their age in having children. Reports show that AMA has a significantly increased risk of preterm birth, perinatal death, early neonatal mortality, low birth weight, APGAR score of <7 at 5 min, and chance of NICU/IMCU admission.[20] Based from the data gathered, all three groups of AMA were noted to be significantly associated with SGA, only AMA has been shown to have linkage to preterm delivery but high likelihood of AMA and VAMA to have newborn admitted at NICU/IMCU and administration with antibiotics and as high as 82.6 times likelihood of VAMA having low APGAR score at 5 min, surfactant administration to newborn and perinatal death. These results were consistent with study conducted by Odibo *et al.*,[24] wherein preexisting maternal diseases, reproductive-assisted conceptions, obesity, multifetal pregnancy, and parity variables were controlled, disclosed that nulliparous women of advanced age with no known previous chronic diseases, there is an increased odds of adverse neonatal and perinatal outcome, including GH or preeclampsia, GDM, CS and spontaneous late preterm delivery, but not spontaneous delivery before 34 weeks. Prolonged rupture of membranes, PPROM, abruptio placenta, placenta previa, large for gestational age and operative vaginal delivery were also observed.[24]

The rate of fetal death is lowest at age of <30 but it increases as age advances, with women age >40 having a fetal death rate of twice of women younger than 30.[12] Based on the gathered data on this study, EAMA predisposed 82.6 times likelihood of having stillbirth and neonatal death compared to younger group. Even after controlling common diseases associated with AMA and complications of pregnancy, AMA remains as independent risk factor.[12]

This study is limited by its monocentric character and retrospective study design aspect. In comparison with 1 local study in AMA done by Acda, *et al.*,[26] from a tertiary referral center with 6.91% prevalence of AMA (95% CI: 6.11%–7.81%), it was suggested that there were no noted difference in terms of maternal and neonatal outcomes between elderly primigravida, however, the studied

hospital is a tertiary private facility that has a center for ART, thus obtained samples may have included more patients using these techniques and may have included in the higher middle to high socioeconomical status wherein patients included were also on the higher age bracket with the prevalence of 38.9% (95% CI: 33.6%–44.3%).

## Conclusion

Advanced age in Filipino gravida patients are markedly linked with adverse outcomes. During the study period, there were 38.9% (95% CI: 33.6%–44.3%) AMA who delivered. This study confirms the current trend among this group of women >45 years of age to know that EAMA leads to more significant obstetric complication and neonatal morbidities. AMA is a risk factor for PIH, SGA newborn and antiphospholipid antibody syndrome in all 3 advanced age group. PIH, having CS, admission of newborn to NICU/IMCU is more common to AMA but same risk for EAMA and younger group. There is no noted association between AMA and large for gestational age newborn, having meconium staining and delivering by classical cesarean section. Therefore, as obstetrics and gynecologists, we should provide thorough counseling of all couples, who seek to have a child in their late ages, about the risks of AMA pregnancy.

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### Conflicts of interest
There are no conflicts of interest.

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