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Risk factors and pregnancy outcome in women aged over 40 years at Korle-Bu Teaching Hospital in Accra, Ghana

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Abstract

Objective: To examine the risk factors and pregnancy outcomes in women aged 40 years and older at the Korle-Bu Teaching Hospital, Accra, Ghana.

Methods: A descriptive case–control study comparing women aged 40 years and older at the time of delivery with those between 20 and 34 who delivered at the Korle-Bu Teaching Hospital between April 1, 2014 and March 31, 2015. Data were collected using interviewer-administered questionnaires and supplemented with information from patients' medical records. A multivariate logistic regression was used to estimate the odds ratio and the 95% confidence interval of various risk factors and complications associated with delivery in women aged 40 years or older. Statistical significance was set at $P<0.05$.

Results: There were 339 women in the study of which 113 were aged 40 years or older and 226 were aged between 20 and 34 years. Delivery at age 40 years or older was associated with grand multiparity, and unplanned and undesirable pregnancy. There was a higher incidence of gestational diabetes (7.1% vs 2.2%, $P=0.036$), cesarean delivery (70.1% vs 57.1%, $P=0.018$), and venous thromboembolism (VTE) (7.1% vs 1.3%, $P=0.008$) among women older than 40 years. VTE risk was increased sixfold in the women older than 40 years compared with the younger ones.

Conclusion: Women delivering after age 40 years had a higher incidence of gestational diabetes, cesarean delivery, and VTE compared with younger women. VTE risk increased sixfold in the older women.

KEYWORDS

Advanced maternal age; Cesarean delivery; Gestational diabetes; Preterm birth; Stillbirth; Unplanned pregnancy

1 | INTRODUCTION

Pregnancy at advanced maternal age (AMA), defined as giving birth at age 35 years or older,[1] is associated with several adverse outcomes including preterm birth, low birth weight, stillbirth, chromosomal defects, labor complications, and cesarean delivery.[2–6] There are reports of increasing incidence of deliveries at AMA all around the world with many more women delaying childbirth well into their forties. In Canada, a recent report showed that the number of live births in women aged over 35 years increased from 59 755 in 2005 to 78 615 in 2014, and the number of births in women aged over 40 years tripled from 2005 to 2014.[7]

Pregnancy and delivery at AMA are also considered a high risk because of the high incidence of non-communicable diseases such as hypertension, diabetes mellitus, and venous thromboembolism (VTE) at these ages.[5,6,8] Other studies have associated AMA with chromosomal abnormalities and subfertility and even maternal death.[9,10]

The reasons behind delayed childbearing may vary from one socioeconomic setting to another. In high-income countries, AMA has been associated with higher academic and career pursuit, delayed marriage, delayed conception due to infertility, primiparity, and longer life expectancy.[11–13] In contrast, AMA in low- and middle-income countries has been associated with ineffective contraceptive usage, cultural disposition to large family size, and grand multiparity.[11] In addition, Obed et al.[10] suggested that ignorance and male-dominant marriage are associated with pregnancy among older women in Ghana.

A departmental morbidity and mortality audit at the Korle-Bu Teaching Hospital revealed the proportion of pregnant women giving birth after age 35 years rose from 1.2% in 2008 to 5% in 2012. Although the proportion of women in AMA was relatively small in this audit, there was a 500% increased risk for mortality among those aged 40 years and over (age-specific maternal mortality of 6.4%) compared with those younger than 34 years (unpublished data).

The present study seeks to identify the factors associated with pregnancy and delivery among women aged 40 years and over at the Korle-Bu Teaching Hospital and their pregnancy outcome.

2 | MATERIALS AND METHODS

This descriptive case–control study compared women aged 40 years and over at the time of delivery with those aged between 20 and 34 years; all the women delivered at the Korle-Bu Teaching Hospital, Accra, between April 1, 2014 and March 31, 2015. Ethical approval was obtained from the Ethical and Protocol Review Committee of the College of Health Sciences, University of Ghana.

The study was conducted at the maternity unit of the Korle-Bu Teaching Hospital, which is the largest tertiary referral high-risk obstetric unit in Ghana with about 11 000 deliveries during the study period. We calculated the minimum sample size required for this study to be 339, using a 5% difference in complication rate between women aged more than 40 years and those in the younger age group, at a case–control ratio of 1:2. This gives an 80% power for the study and a type I error probability associated with the null hypothesis of 0.05.

All women with a singleton pregnancy at age 40 years and over who delivered at the study site during the study period were eligible for participation and were identified as *cases*, and were approached for informed consent and enrollment. For each case selected, two other women aged 20–34 years who delivered just before and after her were enrolled as *controls* following informed consent. Women less than 20 years of age or between 35 and 39 years were excluded, as were women who delivered before arrival at the hospital, and those who refused to give consent or were unable to give consent. Participants were interviewed with a structured questionnaire to obtain sociodemographic information, preparedness for the pregnancy, contraceptive practices, method of conception including fertility treatment, medical and obstetric information as well as any complication in the index pregnancy and its outcome. The case notes of the participants were reviewed for pregnancy history, medical complications, and pregnancy outcome.

TABLE 1 Demographic and baseline obstetric characteristics of mothers with and without advanced maternal age.

Variable	>40 y (n=113)	20–34 y (n=226)	*P* value
Age at delivery (y)	41.55 ± 1.74	28.78 ± 3.78	<0.001
Marriage age, n (%)			
≤30 y	11 (9.7)	18 (8.0)	<0.001
>30 y	43 (38.1)	117 (51.8)	
Married, n (%)	105 (92.9)	171 (75.7)	<0.001
	8 (7.1)	55 (24.3)	
Post-basic education, n (%)	47 (41.6)	113 (50.0)	0.076
Formal employment, n (%)	86 (76.1)	142 (62.8)	0.111
Primipara, n (%)	13 (11.5)	88 (38.9)	<0.001
Grand multipara P5+, n (%)	24 (21.2)	4 (1.8)	<0.001
Previous cesarean delivery, n (%)	38 (33.6)	53 (23.4)	>0.990
Previous stillbirth, n (%)	8 (7.1)	10 (4.4)	0.810
Chronic hypertension, n (%)	8 (7.1)	5 (2.2)	0.159
Previous APH, n (%)	1 (0.9)	1 (0.4)	>0.990
Previous preterm birth, n (%)	1 (0.9)	4 (1.8)	0.641
Pre-gestational diabetes, n (%)	0 (0.0)	2 (0.9)	0.554
Booked, n (%)	109 (96.5)	216 (95.6)	0.781
Booking Hb, mean (±SD)	10.9 (±1.56)	10.83 (±1.50)	0.634

Abbreviations: APH, antepartum hemorrhage; Hb, hemoglobin levels; P, parity; SD, standard deviation.

The following terminology was used in our data collection and case definition:

Hypertensive disorder of pregnancy was considered to have occurred when any blood pressure was elevated (≥140 mm Hg in systolic and ≥ 90 mm Hg diastolic) on at least two occasions recorded at least 4 hours apart anytime during the pregnancy and up to 6 weeks after delivery.

Pre-eclampsia was defined as systolic blood pressure of 140 mm Hg or diastolic blood pressure of 90 mm Hg or higher on any two occasions, 4 hours apart, first recorded after 20 weeks of pregnancy in the presence of proteinuria of 1+ or more on urine dipstick testing.

Gestational diabetes was defined as new-onset diabetes first diagnosed in the current pregnancy in a patient who was not previously known to have any form of diabetes.

Venous thromboembolism refers to formation of blood clots originating in a vein and comprises deep vein thrombosis and pulmonary embolism.

The data were entered using Excel spreadsheet (Microsoft Company, USA) and cleaned before transferring to SPSS version 22

(Armonk, NY; IBM Corp) for analysis. Descriptive statistics on marital status, education, contraceptive usage, and pregnancy outcome were performed. Continuous variables were compared using the student's *t* test for normal distribution variables and Wilcoxon sum rank test or Mann-Whitney *U* test for non-normal distribution variables. Proportions were compared using the χ^2 test. Bivariate regression was employed to compare predictor variable and outcome variables between the two groups. Subsequently, variables that were statistically significant in the bivariate analysis were introduced in a stepwise multivariate logistic regression model and the adjusted odds ratios and their 95% confidence intervals were estimated. A *P* value of less than 0.05 was considered statistically significant.

3 | RESULTS

There were 339 women who participated in the study, made up of 113 cases and 226 controls. The ages (mean ± SD) of cases and controls were significantly different (41.55 ± 1.74 vs 28.78 ± 3.78, *P*<0.001). There were significantly more married women among the cases than controls (*P*<0.001). The proportion of participants who had post-basic education or were engaged in formal employment were not significantly different between cases and controls. There was a significantly higher proportion of grand multiparity (parity ≥ 5) among the women aged 40 years and over than among those aged between 20 and 34 years (*P*<0.001). Similarly, there were significantly more women having their first delivery in the 20–34 years age group than in the over 40 years age group (*P*<0.001) (Table 1). Essential hypertension was significantly more common among cases than controls (3.5% [4/113] vs 0.0% [0/226], *P*=0.012). Previous histories of hypertension or pre-gestational diabetes, previous preterm birth, previous stillbirth, or previous cesarean deliveries were not significantly different between the two groups (Table 1). Booking status and hemoglobin at booking were similar between the two groups (Table 1).

There was no statistical difference in contraceptive usage between the two groups prior to the index pregnancy (*P*=0.622). The difference in proportions of pregnancies resulting from contraceptive failure or pregnancies resulting from infertility treatment were not significant (*P*=0.539 and *P*=0.056, respectively) (Table 2). Nearly two-thirds (64.6%) of the women aged over 40 years said their pregnancies were unplanned compared with less than half (47.3%) in the younger age group (*P*=0.003); and about two-fifths (38.9%) of cases indicated the pregnancies were actually undesirable compared with a quarter (25.2%) of controls (*P*=0.012). During the pregnancy, significantly more of the older women always regretted getting pregnant (*P*=0.004). Four women in the older age group had assisted conception (three in vitro fertilization cases and one intrauterine insemination) whilst only one in the younger age group had in vitro fertilization (*P*=0.004) (Table 2).

Major complications such as gestational diabetes (*P*=0.036) and VTE (*P*=0.008) occurred more frequently among pregnant women who were 40 years and older compared with the younger counterparts.

TABLE 2 Reproductive and family planning characteristics of pregnant women with and without advanced maternal age.

Variable	>40 (n=113)	20–34 years (n=226)	*P* value
Ever used modern contraception			
Yes	34 (30.1)	75 (33.2)	0.622
Contraception 6 mo prior to pregnancy			
Yes	11 (9.7)	28 (12.4)	0.671
Pregnancy due to contraceptive failure?			
Yes	5 (4.4)	8 (3.5)	0.539
Infertility treatment prior to this pregnancy	6 (5.3)	8 (3.5)	0.056
Was the pregnancy planned?			
Yes	40 (35.4)	119 (52.7)	0.003
No	73 (64.6)	107 (47.3)	
Was the pregnancy desirable?			
Yes	69 (61.1)	169 (74.8)	0.012
No	44 (38.9)	57 (25.2)	
Do you wish at any time in the course of your pregnancy that you never got pregnant?			
Always	8 (7.1)	5 (2.2)	0.004
Sometimes	25 (22.1)	28 (12.4)	
Never	80 (70.8)	193 (85.4)	
Was the pregnancy conceived following assisted conception?			
Yes	4 (3.5)	1 (0.4)	0.044

However, there was no significant difference in the occurrence of hypertensive disorders of pregnancy among cases and controls (*P*=0.201) (Table 3). The rate of induction of labor was similar between cases and controls (*P*=0.862) but there was a statistically higher rate of cesarean delivery among the cases than the controls (*P*=0.018) (Table 3). Perinatal outcomes such as birth weight, neonatal intensive care unit (NICU) admission, and stillbirth rates were similar between cases and controls. There was, however, a marginally increased rate of gross congenital anomalies at birth among cases compared with controls (*P*=0.044) (Table 3).

In a multiple logistic regression analysis to determine the odds of complication associated with AMA, there was a sixfold increase in the venous thromboembolic events among women delivering at age 40 years and over compared with their younger counterparts. Gestational diabetes, cesarean delivery, preterm birth, and postpartum hemorrhage did not increase among women with AMA (Table 4).

4 | DISCUSSION

In this case–control study, AMA was associated with grand multiparity, hypertension, unplanned pregnancy, and use of assisted conception compared with maternal age between 20 and 34 years old. Similarly, pregnant women with AMA were more likely to develop gestational

TABLE 3 Maternal and perinatal outcome of pregnancy in women with and without advanced maternal age.

Variable	Maternal age ≥40 y (n=113)	Maternal age 20–35 y (n=226)	*P* value
Preterm birth, n (%)	13 (11.5)	29 (12.8)	0.801
Gestational diabetes, n (%)	8 (7.1)	5 (2.2)	0.036
Hypertensive disorder, n (%)	21 (18.6)	30 (13.3)	0.201
Thromboembolic event, n (%)	8 (7.1)	3 (1.3)	0.008
Placenta previa, n (%)	3 (2.7)	5 (2.2)	>0.990
Placenta abruption (%)	2 (1.8)	4 (1.8)	>0.990
PPROM, n (%)	49 (43.3)	79 (35.1)	0.155
Anemia, n (%)	8 (7.1)	8 (3.5)	0.176
Gestational age at delivery, wk	38.3 ± 2.2	38.3 ± 2.7	0.998
Induction of labor, n (%)	13 (11.5)	28 (12.4)	0.862
Cesarean delivery, n (%)	80 (70.8)	129 (57.1)	0.018
Was maternal age primary indication for cesarean delivery?			
Yes, n (%)	17 (21.3)	0 (0.0)	<0.001
PPH, n (%)	6 (5.3)	4 (1.8)	0.090
Blood transfused, n (%)	10 (8.8)	15 (6.6)	0.510
Stillbirth, n (%)	3 (2.7)	13 (5.8)	0.281
Antepartum stillbirth, n (%)	2 (66.7)	8 (61.5)	1.000
Intrapartum stillbirth, n (%)	1 (33.3)	5 (38.5)	
NICU admission, n (%)	23 (20.4)	50 (22.1)	0.780
Infant with congenital anomaly, n (%)	4 (3.5)	1 (0.4)	0.044
Birth weight (kg)	2.94 ± 0.54	2.92 ± 0.62	0.722

Abbreviations: NICU, neonatal intensive care unit; PPH, postpartum hemorrhage; PPROM, preterm premature rupture of membranes.

TABLE 4 Multivariate logistic regression for pregnancy complications associated with advanced maternal age.

Variable	Adjusted odds ratio	95% confidence interval	*P* value
Gestational diabetes	2.00	0.44–8.81	0.371
Cesarean delivery	1.61	0.94–2.74	0.082
VTE	6.32	1.60–24.95	0.009
Preterm birth	0.88	0.43–1.79	0.719
PPH	4.00	0.87–18.36	0.075

Abbreviations: PPH, postpartum hemorrhage; VTE, venous thromboembolism.

diabetes and VTE and to be delivered by cesarean. AMA was associated with a sixfold increase in the risk of VTE compared with younger maternal age. In spite of this higher risk of antepartum and intrapartum complications, perinatal complications such as preterm birth, NICU admission, and stillbirth rates were not increased in women with AMA.

There appears to be very little change regarding the reproductive characteristics and behavior of women with AMA at Korle-Bu Teaching Hospital over the past 25 years. The incidence of unwanted pregnancy remains high with very low usage of contraception just as it was reported by Obed et al. in 1995.[10] A large proportion of AMA women actually responded that their pregnancies were unplanned, undesirable, and 7.1% actually regretted getting pregnant throughout their pregnancy, even though they had no family planning and did not opt for termination of pregnancy. This proportion reflects an unmet need for family planning, considering that these same women also had an increased risk for adverse maternal outcomes such as gestational diabetes, pre-eclampsia, and cesarean delivery.[13]

In two recent studies that, like ours, defined AMA as being over 40 years, AMA was associated with gestational diabetes and cesarean delivery but the rate of preterm birth and stillbirth were not increased, as in our study.[14,15] In another large multi-country survey by Laopaiboon et al.,[16] involving over 350 health facilities in 29 countries across the world, AMA was associated with composite adverse maternal and perinatal outcome. In the present study, however, AMA was not associated with increased adverse perinatal outcomes such as preterm birth, stillbirth, or NICU admission.

Studies that compare pregnancy outcome in women with AMA and various age categories may conceal the real impact of progressive age change on pregnancy outcomes along the spectrum. A large population-based data review from Taiwan showed a significant jump in the risk of preterm birth, congenital anomaly, and stillbirth in women older than 40 years compared with women of younger age in a linear regression model with 27 years as the reference point.[17] It appears that the relationship between AMA and adverse perinatal outcome is not consistent. In the present study at a tertiary obstetric unit in Accra, though chronic hypertension, gestational diabetes, and cesarean delivery were more common in women with AMA, this did not adversely affect perinatal outcomes, contrary to findings reported in some other studies.[18] As in our study, several other studies from Africa and elsewhere have confirmed that AMA was not associated with preterm birth, stillbirth, and NICU admission.[14,19,20] However, in a large population-based cohort study in the UK, AMA greater than 40 years was also associated with increased perinatal outcome such as stillbirth, preterm birth, very preterm birth, and fetal macrosomia, even after controlling for known confounders such as body mass index, ethnicity, and parity.[21]

While pregnancy-associated VTE is well characterized, few studies have identified maternal age as a risk factor for VTE in pregnancy.[22–24] In the present study AMA was associated with a sixfold increased risk of VTE. The mechanism for this is not well understood but we speculate that the combined effect of pregnancy-induced hypercoagulability and age-associated endothelial damage may play a role in this observation.

We recognize that the present study may have several limitations. Firstly, this was a cross-sectional study with only a limited period of observation. The outcomes reported are those limited to the immediate postpartum period. Secondly, this was a single-site study in a tertiary health facility in an urban setting. The socio-demographic factors associated with AMA in our study may therefore be different from those pertaining to other rural areas in the country. Despite these limitations the present study makes important observations, especially the strong association between AMA and VTE, considering the latter can have serious consequences if not detected and treated early. In addition, the data collection spanned a whole year and therefore catered for any seasonal variations in pregnancy outcome.

In conclusion, in this single-center case–control study, women with AMA were more likely to be multiparous, have unplanned and undesirable pregnancy, and regretted their pregnancy. These women had a higher incidence of gestational diabetes, venous-thromboembolic events, and cesarean delivery compared with their younger counterparts aged 20–34 years. In spite of these higher antepartum and intrapartum events, their perinatal complications such as preterm birth, NICU admission, and stillbirth rates were not increased. Women with AMA who deliver in our facility still have an unmet need for family planning that must be incorporated into their care through intensive antepartum and postpartum contraceptive counseling. Special attention should be paid to thromboprophylaxis in women aged 40 years and over who deliver in order to reduce the risk of VTE in this population.

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AUTHOR CONTRIBUTIONS

SAO conceived the idea; SAO and MT developed the proposal and submitted it for ethical approval; MT performed the data collection; SAO, MT, and TB performed data analysis, wrote and reviewed the draft as well as approved the final manuscript for submission.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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