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A Product Binomial Modelling of Advanced Maternal Age on Pregnancy Outcome

Emmanuel Segun Oguntade1, Habib Kayode Nasiru2 Damilare Matthew Oladimeji3

1. Department of Statistics, Faculty of Science, University of Abuja

2. Department of Statistics, Faculty of Science, University of Abuja

3.Department of Statistics, Faculty of Science, University of Abuja

1. oguntadeemmanuel2015@gmail.com

2. nasiru.habib2015@uniabuja.edu.ng

3. oladimejidamilare@yahooo.com

Abstract

The maternal age is an important component in determining the pregnancy outcome. The age of the mother at time of delivery influences the chance of having adverse pregnancy outcomes. Such outcomes constitute public health issues due to increased risks of still birth, preterm birth, low birth weight, jaundice, macrosomia, Down syndrome, perinatal mortalities and an increased risk of caesarean delivery. Therefore, this study examined the relationship between advanced maternal age and pregnancy outcome using a product Binomial model. A retrospective study of pregnant women was done to ascertain the effect of advance maternal age on pregnancy outcomes across the six Area Council of Federal Capital Territory (FCT) Abuja, Nigeria. Delivered pregnant women who were medically and obstetrically free before pregnancy were sampled across six area council of FCT, and data on maternal age, sex of the baby and pregnancy outcomes were collected and analyzed using a product binomial sampling scheme and location as strata. Therefore, 6x2x2 contingency table were formed and a Product binomial distribution was adopted to model the relative effect of advance maternal age on pregnancy outcomes using Cochran's and Mantel Haenszel statistic (CMH) and Breslow-Day(BD) statistics to test for conditional independent and homogeneity of odd ratio respectively. The preliminary analysis revealed variations in maternal age across the area councils. The results further revealed that Gwagwalada has the highest number of a normal delivery among maternal age (>=35) 19 (63.3%) while the highest frequency for an adverse delivery in the same category was observed in Kwali27 (65.8%). The analysis based on the CMH statistic confirmed that pregnancy outcome was conditional dependent on maternal age. This suggests that maternal age is a strong determinant of a healthy pregnancy outcome. Likewise, results from BD shown that the odd ratio across the six Area Council of FCT was not homogenous. This study reveals the significant influences of maternal age on pregnancy outcomes. Therefore, it could be used to formulate policies on controlling adverse pregnancy outcomes and to create public awareness on the effect of maternal age on pregnancy

outcomes within the study area.

Keywords: Abuja, Maternal Age, Pregnancy Outcome

1. Introduction

Maternal age is an integral component of a child delivery system that influences results of the pregnancy outcome. Advance and more advanced maternal ages have been attributed to the frequent range of pregnancy complications recorded in recent time on the global scene. These pregnancy issues recorded in recent time include but not limited to fatal growth restriction, preeclampsia, placental abruption, pre-term, stillbirth, preterm birth and caesarean delivery. Globally, there has been an increase in risk of healthy pregnancy outcomes and this constitute a huge public health issues especially in the developing nations where there are poor socio-economic conditions and the availability of good health care facilities is still a mirage. Nutritional imbalance, prenatal care, child spacing, maternal age below 15 and above 35 years, overweight, obesity, consumption of alcohol, smoking and drug used are some of the reproductive health problems (Eni-olorunda *et al.*, 2015).There are about 515,000 women worldwide that lost their lives yearly due to causes related to pregnancy and child birth every year, and their demise leaved over one million children motherless (USAID, 2002; Eni-olorunda *et al.*, 2015). This huge statistics recorded is in the developing nations in which over 99% of these deaths occur (Eni-olorunda *et al.*, 2015).

While there are a number of studies on pregnancy outcomes of the advanced maternal age (AMA) in the developed world (Hoque, 2012; Lamminpää, 2015), there remains paucity of current data regarding the causation of stillbirth in advanced and more advanced pregnancy ages and literature on the subject matter especially in Sub-Saharan Africa (SSA) and particularly Nigeria has received less attention in recent times.Reducing the maternal mortality and new-born mortality rate is of paramount important especially now that the Sustainable Development Goals (SDGs) vision 2030 is of global interest. Normal healthy delivery with an AMA is a big challenge due to many factors.Issues ranging from gestational diabetes during pregnancy or likelihood of pre-existing diabetes in older women, high blood pressure, pregnancy loss, preeclampsia, comorbidity effects, premature birth and low birth weight amongst others in older women influence the pregnancy outcome in different ways (Bayrampour *et al.*, 2012). In recent years, reports on influence of maternal age on pregnancy outcomes particular in developing world like Nigeria are fairly limited. Hence, this study seeks to explore product binomial to model the relationship between AMA and pregnancy outcome based on the data collected from the major primary health care across the six Area Council of Abuja, Nigeria.

2. Literature Review

Over the years, there has been an increase in number of women with delayed in childbearing (Cooke et al, 2012). This delay has been attributed to many reasons like education, socio-economic related factors and choice of lifestyle adopted by an individual woman (Bayrampour *et al.*, 2012). An AMA is mainly an instance of a woman being of an older age at a stage of reproduction. A Pregnancy at age of 35 years and above is usually experience certain issues with the pregnancy outcomes. Such a high risk pregnancy comes with health problems such as still birth, complication in labour, preterm birth, chromosomal defects and sometimes a caesarean section(Eni-olorunda *et al.*, 2015).

Several studies have been reported in literature on an AMA and pregnancy outcome. Some of these methodologies explored were mainly usage of descriptive and preliminary analyses (Bayrampour *et al.*, 2012) while other explored chi-squared, correlation analysis and generalized linear models (Hoque, 2012; Lamminpää, 2015; Williamson *et al.,* 2014). This current study approached the subject matter using a Cochran–Mantel–Haenszel test for repeated tests of independence with a product binomial sampling scheme. The popular sampling scheme in literature is the hypergeometric which is a binomial experiment without replacement from a fixed number of trials (Adejumo and Adetunji, 2013). The Fisher's exact test apply the distribution of 2 × 2 tables with fixed margins is hypergeometric which various scholars have considered irrespective of sampling scheme. Most of the authors fixed row and column totals of partial tables arbitrarily and assumed a hypergeometric distribution to compute the various probabilities from the contingency tables so formed. For instance, Adejumo and Adetunji (2013) used hypergeometric distribution to model the Cochran mantel Haenszel with application to student performance.

3. Methodology

3.1 *Research Design*

This study is a retrospective study done on pregnant women and pregnancy outcome across the six Area Council of the federal capital territory (FCT), Abuja. Delivered pregnant women who were medically and obstetrical free before pregnancy were sampled across the six Area Councils in Abuja. Data on the maternal age, sex of the baby and pregnancy outcomes were collected. The sampling frame used was the delivery register of pregnant women who delivered in a particular health care centre. Also, during the sampling process, random sampling technique was applied in order to select a facility (health care) used for the study.

3.2 *Data Collection*

The data for this study were collected from major health care centres across the six Area Council of FCT, Abuja, Nigeria. The area councils considered include: Abaji, Bwari, Kwali, Gwagwalada, Abuja Municipal Area Council (AMAC) and Kuje. Samples from these councils were selected using stratified sampling. A total of 200 subjects were chosen from each of the selected health care units. These selections were done in line with requirement of the product binomial sampling scheme.

3.3 *Variable Coding and Classification*

The various variables used for this study were coded and classified to ease the computation complexity. These variables include maternal age, sex of the baby, pregnancy outcome and location of the healthcare unit. Tables 1 displays model variables and their descriptions

Table 1. Model Variables and Description in Related Studies

Variable	Type of variable	Group	Description	Source
Maternal Age	Independent	<35	Normal maternal age or control	Kahveci *et al.* (2018)

		>=35	Advanced maternal age	
Sex of the Baby	Covariate	Male	Male baby given birth to by maternal woman	Krefis *et al.* (2010)
		Female	Female baby given birth to by maternal woman. Classification was based on related literature.	
Pregnancy Outcome	Dependent	Normal	a pregnancy outcome with no complications	Xiaoli *et al.*(2014)
		Adverse	A case of death or any complications during pregnancy is defined as adverse	
Location	Control	Abaji Kwali Kuje Gwagwalada Bwari AMAC	This was done in line with other related studies documented in literature	Krefis *et al.* (2010) and Dev *et al.*(2016)

AMAC: Abuja Municipal Area Council

3.4. *A Product Binomial Model Sampling Scheme*

Let n_{k11} follows a binomial distribution with parameters n_{k1+} , π_{k11}. Similarly, let n_{k21} follows the binomial distribution with parameters n_{k2+} ,π_{k21} respectively, then,

$n_{k11} \sim b(n_{k1+}, \pi_{k11})$ $n_{k21} \sim b(n_{k2+}, \pi_{k21})$ as displaced in Tables 2 and 3, Since these are independent samples, it follows that the vector n = ($n_{k11}, n_{k12}, n_{k21}, n_{k22}$) follows a product binomial probability model in (1)

$$P(n|\ M_1\pi) = \binom{n_{k1\ +}}{n_{k11}} \pi_{k11}^{\ n_{k11}} \pi_{k12}^{\ n_{k12}} \binom{n_{k2\ +}}{n_{k21}} \pi_{k21}^{\ n_{k21}} \pi_{k22}^{\ n_{k22}} \quad (1)$$

With constraint $\sum_j n_{kij} = n_{ki+}$ and $\sum_j \pi_{kij}$ =1 for i, j=1,2 k= 1,2 …

Table 2: Contingency Table for Observed Scores

AMA	Pregnancy outcome		Total
	Adverse	normal	
>=35 years	n_{k11}	N_{k12}	N_{k1+}
<35 years	n_{k21}	N_{k22}	N_{k2+}
Total	N_{k+1}	N_{k+2}	N

AMA: Advanced maternal age

Table 3: Probability Table

AMA	Pregnancy outcome		Total
	Cases	control	
>=35 years	π_{k11}	π_{k12}	π_{k1+}
<35 years	π_{k21}	π_{k22}	π_{k2+}
Total	π_{k+1}	π_{k+2}	

AMA: Advanced Maternal Age

3.5 *Assumption of a Product Binomial*

1. Prospective studies, the marginal totals n_{ki+} is often fixed
2. Retrospective studies, the marginal totals n_{k+j} is often fixed
3. Cross sectional studies, the sample size N is assumed fixed

Therefore, based on these assumptions, this current study fixed the pregnancy outcomes across the six area councils in FCT

3.6 *Homogeneity Hypothesis*

In the above framework, the usual hypothesis of interest involves testing for the equality of the "cases" rates π_{k11} and π_{k21} for the two independent samples or sub- populations (>35 years and ≤35 years) across the six area council of FCT (strata). That is,

$H_{0:}: \pi_{k11} = \pi_{k21}$

Under H_0, let the common parameter for the two populations be π_α and its compliment π_β

$$\pi_\alpha + \pi_\beta = 1 \qquad (2)$$

Thus, under H_0 the probability model in the product binomial model $p(n|m_1, \pi)$ in (3).

$$P(n_{+1}|\, m_{1}, \pi_\alpha, H_0) = \binom{n_{k1+}}{n_{k11}} \pi_\alpha^{n_{k11}} \pi_\beta^{n_{k12}} \binom{n_{k2+}}{n_{k21}} \pi_\alpha^{n_{k21}} \pi_\beta^{n_{k22}} \qquad (3)$$

Chasing the algebra from (3) above gives:

$$P(n_{+1}|\, m_{1}, \pi_\alpha, H_0) = \binom{N}{n_{k+1}} \pi_\alpha^{n_{k+1}} \pi_\beta^{n_{k+2}}$$

Where $\sum_j n_{kij} = n_{k+j}$ is the column totals for j=1,2.

3.7 *Maximum Likelihood Estimates of* π_α

From the above expression, the likelihood equation is

$$L(\pi, n, H_0) = \binom{N}{n_{k1+}} \pi_\alpha^{n_{k+1}} \pi_\beta^{n_{k+2}}$$

$$e = \log N! - \sum\sum \log (n_{kij}) + n_{k+1} \log(\pi_\alpha) + n_{k+2} \log(\pi_\beta) \qquad (4)$$

Where e is the log-likelihood, let $G = n_{k+1} \log(\pi_\alpha) + n_{k+2} \log(\pi_\beta)$, the kernel of the log-likelihood; then, since the first two terms on the right hand side of (4) do not involve the πs, we will therefore maximize G subject to the constraints in (4). Using the Lagrange multipliers, we can write G^* as:

$$G^* = n_{k+1} \log(\pi_\alpha) + n_{k+2} \log(\pi_\beta) - \lambda(\pi_\alpha + \pi_\beta - 1)$$

Then

$$\frac{\partial G^*}{\partial \pi_\alpha} = \frac{n_{k+1}}{\pi_\alpha} - \lambda \quad (5)$$

$$\frac{\partial G^*}{\partial \pi_\beta} = \frac{n_{k+2}}{\pi_\beta} - \lambda \quad (6)$$

$$\frac{\partial G^*}{\partial \lambda} = -(\pi_\alpha + \pi_\beta - 1) \quad (7)$$

Setting the equations in (6) through (7) to zero, we have

$\pi_\alpha \lambda = n_{k+1}$

$\pi_\beta \lambda = n_{k+2}$

Adding these, and noting that from equation (7) we have $\lambda = N$,

Consequently,

$$\pi_\alpha = \frac{n_{k+1}}{N} \text{ and} \quad (8)$$

$$\pi_\beta = \frac{n_{k+2}}{N} \quad (9)$$

The corresponding expected frequencies under H_0 becomes

$$m_{ijk} = n_{ki+}\pi_\alpha \text{ if } i = 1,2 \text{ and } j=1 \quad (10)$$

$$m_{kij} = n_{ki+}\pi_\beta \text{ if } i = 1,2 \text{ and } j=1 \quad (11)$$

3.8 *Parameter Estimates and Cochran- Mantel-Haenszel (CMH) Test Statistic*

If we let the estimates of the success (or cases) rates for the response or outcome variable be given by

$P_{k11} = \frac{n_{k11}}{n_{k+1}}$, and $p_{k21} = \frac{n_{k21}}{n_{k2+}}$

And if we further let

$$d = p_{k11} - p_{k21} = \frac{n_{k11}}{n_{k+1}} - \frac{n_{k21}}{n_{k2+}} = \frac{(n_{k11}n_{k22} - n_{k12}n_{k21})}{n_{k1+}n_{k2+}} \quad (12)$$

Be the estimate of the observed difference of the success rates in the two subpopulations, then

$$E(d) = \pi_{k11} - \pi_{k21} \quad (13)$$

So that under H_0,

$E(d) = 0$

And $\quad var(d) = var(p_{k11} - p_{k21}) = \frac{\pi_{k11}\pi_{k12}}{n_{k1+}} + \frac{\pi_{k21}\pi_{k22}}{n_{k2+}}$

So that $\quad var(d|H_0) = \frac{\pi_\alpha\pi_\beta}{n_{k1+}} + \frac{\pi_\alpha\pi_\beta}{n_{k2+}} = \pi_\alpha\pi_\beta\left(\frac{1}{n_{k1+}} + \frac{1}{n_{k2+}}\right)$

$$= \frac{N\pi_\alpha\pi_\beta}{n_{k1+}n_{k2+}} = \frac{N\pi_\alpha(1-\pi_\alpha)}{n_{k1+}n_{k2+}} \quad (14)$$

Thus, the variance of d under, the null hypothesis depends on the nuisance parameter π_α.

$$m_{k11} = n_{k1+}\pi_\alpha = \frac{n_{k1.} * n_{k.1}}{N} = \frac{n_{k1.} * n_{k.1}}{N} \quad (15)$$

$$Var(n_{k11}) = var(n_{k1+}\pi_\alpha) = \frac{n_{k.1}n_{k1.}n_{k.2}n_{k2.}}{N^2} \quad (16)$$

$$CMH = \frac{(\sum_k |n_{k11} - m_{k11}|))^2}{\sum_k Var(n_{k11})}$$

3.9 *Common Odds Ratio*

An estimator of Mantel-Haenszel estimate of the common odd ratio in case-control studies is given in (17).

$$\theta_{BD} = \frac{\sum_{k=1}^{K}\left(\frac{n_{k11} * n_{k22}}{N}\right)}{\sum_{k=1}^{K}\left(\frac{n_{k12} * n_{k21}}{N}\right)} \quad (17)$$

3.10 *Breslow-Day Test for Homogeneity of the Odds Ratios*

The estimation of the common odds ratio assumes that the strength of association as measured by the odds ratios in each sub-table is the same. This assumption is tested by the test of homogeneity of the odds ratio. To test this hypothesis, the Breslow-Day test is often employed. This statistic is compared to a standard χ^2 distribution with $(K - 1)$ degrees of freedom. The null hypothesis of homogeneity of odds ratio across the sub - tables is rejected if P-value is, $< \alpha$

The Breslow-day statistic is computed as:

$$\theta_{BD} = \frac{\sum_{h=1}^{H} (n_{h11} - E(n_{h11} | \theta_{MH}))^2}{var(n_{h11} || \theta_{MH})} \quad (18)$$

4. Results and Discussion

4.1 *Preliminary Analysis and Results*

Table 4 displays the distribution of maternal age by area council in FCT. The results revealed that Kuje has 86.5% of the maternal women included in this research are less than 35years of age while 13.5% were greater or equal to 35years of age. Also, in Kwali, 79.5% of the maternal women considered for this study were<35years of age and 20.5% were >=35 years. In AMAC, 77% were <35 while 23% were >=35, In Abaji, 84% were <35 and 16% were >=35 years. In Gwagwalada, 85% were <35 and 15% were >=35 years, and in Bwari83% were <35years of age while 17% were>=35 years (Figure 1).

Table 4: Distribution of Maternal age by Area Councils

Location	Maternal Age	Frequency (%)
Kuje	<35	173(86.5)
	>=35	27(13.5)
Kwali	<35	159(79.5)
	>=35	41(20.5)
AMAC	<35	154(77)
	>=35	46(23)
Abaji	<35	168(84)
	>=35	32(16)
Gwagwalada	<35	170(85)
	>=35	30(15)
Bwari	<35	166(83)
	>=35	34(17)

AMAC: Abuja Municipal Area Council

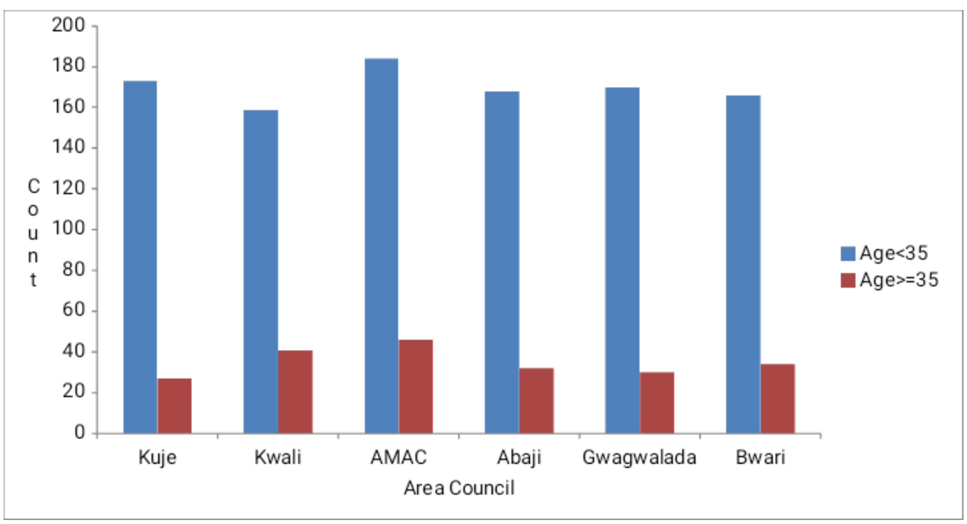

Figure 1. Maternal Age Distribution across the Six Area Councils in Abuja

The distribution of pregnancy outcome by area councils in FCT revealed that 79% of the women included in this research experienced a normal pregnancy outcome while 21%

experienced an adverse pregnancy outcome (Table 5).

Table 5: Distribution of Pregnancy Outcome by Area Council

Location	Pregnancy Outcome	Frequency(%)
Kuje	Normal	158(79)
	Adverse	42(21)
Kwali	Normal	158(79)
	Adverse	42(21)
AMAC	Normal	158(79)
	Adverse	42(21)
Abaji	Normal	158(79)
	Adverse	42(21)
Gwagwalada	Normal	158(79)
	Adverse	42(10)
Bwari	Normal	158(79)
	Adverse	42(21)

AMAC: Abuja Municipal Area Council

Table 6 displays the distribution of the sex of newborn babies across the six area council in FCT. The distribution revealed that Kuje area council has the highest number of male (115 (57.5%)) while the highest number of females were recorded in Bwari with a total number of 112 (56%).

Table 6: Distribution of Sex by Area Council

Location	Sex of The Baby	Frequency(%)
Kuje	Male	115(57.5)
	Female	85(42.5)
Kwali	Male	95(47.5)
	Female	105(52.5)
AMAC	Male	106(53)
	Female	94(47)
Abaji	Male	99(49.5)
	Female	101(50.5)

Gwagwalada	Male	107(53.5)
	Female	93(46.5)
Bwari	Male	88(44)
	Female	112(56)

AMAC: Abuja Municipal Area Council

Table 7 depicts the association between AMA and pregnancy outcome controlling for Area council. In Kuje Area council, 15 out of 27 AMA women experienced adverse pregnancy outcome while 27 out of 41 AMA women experienced adverse pregnancy outcome in Kwali. Likewise, out of 46 AMA women in AMAC, only 19 experienced adverse pregnancy outcomes while out of 32 AMA women 12 experienced adverse pregnancy outcome in Abaji. The null hypothesis that maternal age is independent of the pregnancy outcome for each area council were rejected in all the area councils as p-value<0.05. This Chi-squared result implied that maternal age was associated with pregnancy outcome in all the area councils.

Table 7. Association between the Maternal Age and Pregnancy Outcome

Location			**Pregnancy Outcome**			
Adverse				Normal	Total	p-value
Kuje	Maternal Age	>=35	15	12	27	
		<35	27	146	173	0.001
	Total		42	158	200	
Kwali	Maternal Age	>=35	27	14	41	
		<35	15	144	159	0.001
	Total		42	158	200	
AMAC	Maternal Age	>=35	19	27	46	

		<35	23	131	154	
	Total		42	158	200	0.001
Abaji	Maternal Age	>=35	12	20	32	
		<35	30	138	168	0.001
	Total		42	158	200	
Gwagwalada	Maternal Age	>=35	11	19	30	
		<35	31	139	170	0.001
	Total		42	158	200	
Bwari	Maternal Age	>=35	21	13	34	
		<35	21	145	166	0.001
	Total		42	158	200	

AMAC: Abuja Municipal Area Council

The odd of maternal age >=35 experiencing an adverse pregnancy outcome was 18.51 more likely than<35 in Kwali. This area council has the highest odd ratio across the six area councils considered in FCT. On the contrary, Abaji has the least odd ratio of 4.0. This result implied that those pregnant women who were exactly or above 35 years old were 4 times more likely to experience adverse pregnancy outcome than other women who were not up to 35 years old (Table 8).

Table 8: Partial Conditional Odd Ratio

		95% Confidence Interval	
Location	**Odds Ratio**	**Lower**	**Upper**
Kuje	6.76	2.85	16.02
Kwali	18.51	8.02	42.73
AMAC	4	1.92	8.36
Abaji	3.78	1.63	8.76
Gwagwalada	10.36	3.81	28.18

Bwari	10.57	4.64	24.11

AMAC: Abuja Municipal Area Council

Table 9 reveals the result independent test of maternal age on the pregnancy outcome across the six area councils. The results showed pregnancy outcome was conditionally dependent on maternal age (p-<0.05).

Table 9: Test of Conditional Independence for the Maternal Age

	Chi-squared	Df	p-value
Cochran's	162.65	1	P<0.001
Mantel-haenszel	159.36	1	P<0.001

df: degree of freedom

Table 10 shows the results of homogeneity of the odds ratio across the six area councils using Breslow-day. The null hypothesis which assumed that the odds ratio for maternal age by pregnancy outcome was equal for all the area councils was rejected, indicating that the odds ratios were not homogenous

Table 10: Tests of Homogeneity of the Odds Ratio for Maternal Age

	Chi-squared	df	p-value
Breslow-Day	16.06	5	0.03

df: degree of freedom

4.2 *Discussion*

In this study, conditional effect of AMA on pregnancy outcome was fitted through a product binomial sampling scheme which later resulted into CHM statistic. Pregnancy outcome was fixed across six area council of FCT while cell observations and AMA were treated as random variables. The distribution of pregnancy outcome by Area Council in FCT revealed that 79% of the women included in this research experienced a normal pregnancy outcome while 21% experienced an adverse pregnancy outcome. The reason for this could be due to the presence of good health facilities within and around Abuja metropolis. The presence of teaching hospital and other good health care delivery systems in the study area could be responsible for this particular study outcome. This result is in agreement with related study documented in literature (Pina *el al.* 2015).

This study showed that the maternal age is a strong determinant of pregnancy outcome and that sex of the baby at delivery has no significant effect on the pregnancy outcome. Based on the fact that AMA has both direct and indirect effect on pregnancy outcome by conditioning on location support redefined Health Action Process (HAP) (Wallston and Armstrong, 2002). The authors posited that action are not only a function of intentions and cognitive control but also are influenced by perceived and actual environment.

Additionally, variation in environment (location) showed a significant influence. This could be explained based on an intuitive ground and also on a concept of spatial variability in which objects within close geographical ranges experiences a similar pattern while there are always variations on distance objects. Hence, the distance apart between these area councils could be the main reason for this particular result. This is consistent with related study on spatial heterogeneity (Shi *et al*, 2018).

There was no common odd ratio as indicated in Breslow-day results. This agrees with previous study documented in literature (Palomba *et al.*, 2016). Also, the results revealed that most women with AMA experienced adverse pregnancy outcome. Therefore, from this present study, it shows that AMA is a very risky age for all child bearing women because of its tendency to predispose to complications which may put the life of the mother or the life of the foetus in danger. This result is consistent with the related study in literature (Bakir *et al.*, 2018).

5. Conclusion

Based on the research findings of this study, a product binomial sampling scheme is flexible and has justifiable assumptions to deal with real life data or phenomenon that presents itself in real life scenarios. Spatial effects through Bayesian analysis should be employed to ascertain the actual location effect on the results. It can also be concluded that advanced maternal age women had a higher prevalence of adverse pregnancies outcome than younger women.

Conflict of interest

The authors declared no conflict of interest.

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