ORIGINAL RESEARCH ARTICLE

Maternal age and miscarriage: A unique association curve in Sudan

DOI: 10.29063/ajrh2022/v26i7.2

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Abstract

This study's aim was to estimate the prevalence and maternal age and other risk factors of miscarriage among Sudanese women. A cross-sectional study was conducted at the Saad Abuelela Tertiary Hospital in Khartoum, Sudan, from February to December 2019. Sociodemographic, obstetric and clinical data were collected. A multivariate logistic regression analysis was performed. Four hundred thirteen (20.5%) women reported experiencing a miscarriage. Risk factors included older age, high parity, histories of caesarean delivery, and obesity. Logistic regression showed that the lowest risk for women aged less than 20 years (adjusted odds ratio [AOR], 0.33) or 20 to 24 years (AOR, 0.57), primiparas (AOR, 0.42) and women educated below the secondary level (AOR, 0.78). Unlike the global age-associated risk of miscarriage, the risk of miscarriage among Sudanese women follows a unique curve in relation to maternal age. Interestingly, the curve showed a lower risk for women less than 20 years and at 40 years. *(Afr J Reprod Health 2022; 26 [7]: 15-21).*

Keywords: Maternal age, miscarriage, spontaneous abortion, parity, Sudan

Résumé

L'objectif de cette étude était d'estimer la prévalence et l'âge maternel et d'autres facteurs de risque de fausse couche chez les femmes soudanaises. Une étude transversale a été menée à l'hôpital tertiaire Saad Abuelela de Khartoum, au Soudan, de février à décembre 2019. Des données sociodémographiques, obstétricales et cliniques ont été recueillies. Une analyse de régression logistique multivariée a été réalisée. Quatre cent treize (20,5 %) femmes ont déclaré avoir fait une fausse couche. Les facteurs de risque comprenaient l'âge avancé, une parité élevée et des antécédents d'accouchement par césarienne et d'obésité. Une régression logistique a montré que le risque le plus faible concernait les femmes âgées de moins de 20 ans (odds ratio ajusté [AOR], 0,33) ou de 20 à 24 ans (AOR, 0,57), les primipares (AOR, 0,42) et les femmes ayant un niveau d'éducation inférieur au secondaire (AOR, 0,78). Contrairement au risque global de fausse couche lié à l'âge, le risque de fausse couche chez les femmes soudanaises suit une courbe unique en fonction de l'âge maternel. Fait intéressant, la courbe a montré un risque plus faible pour les femmes de moins de 20 ans et à 40 ans. *(Afr J Reprod Health 2022; 26[7]: 15-21).*

Mots-clés: Âge maternel, fausse couche, avortement spontané, parité, Soudan

Introduction

The definition of miscarriage (spontaneous abortion) differs between countries, and the literature shows a wide variation in the differentiation between miscarriage and stillbirth[1]. In the United Kingdom, a foetal loss is one considered a miscarriage if it occurs before 24 weeks gestation[2]. In some African countries, abortion is any foetal loss before 28 weeks of gestation[3]. This variation in the definitions can be explained by the fact that searches combine miscarriages (spontaneous abortion) with induced abortion. Survival of the expelled foetus due to the sophisticated neonatal care also affects the definition of miscarriage at 28 weeks. The overall incidence of miscarriage is between 10% and 20%[4,5]. Neighbouring countries reported a prevalence of 18.9% in Kenya[6] and 8.4% in Uganda[6].

In most cases, miscarriage is of unknown cause (more than 50%); however, recognised risk factors include parental age, genetic factors, hormonal factors, and immunological and environmental factors[7]. Moreover, infections, such as malaria, brucellosis, cytomegalovirus and human

immunodeficiency virus, dengue fever, influenza virus, and bacterial vaginosis are associated with an increased risk of miscarriage[8,9]. Advanced maternal age (more than 35 years)[10] is a significant risk factor for miscarriage[11]. Moreover, advanced maternal age is associated with maternal gestational diabetes, foetal growth restriction and stillbirth[10].

The association between miscarriage and maternal age is not yet fully investigated, and additional research is needed in various populations. There are very few published studies addressing the relationship between maternal age and miscarriage in Africa. To our knowledge, there is no published data on maternal age and miscarriage in Sudan. This cross-sectional study was conducted at Saad Abuelela Tertiary Hospital (SATH) in Khartoum, Sudan. We aimed to estimate the prevalence of miscarriage and its association with maternal age and other factors in Sudan.

Methods

Study design and settings

This cross-sectional study was conducted at SATH in Khartoum, Sudan, from February to December 2019.

Sample size

The sample size was calculated using sample size for a descriptive study. The required sample size was found to be 2010 when the prevalence of miscarriage was 15.0%, as recently reported[4], and when the fraction of women aged 35 years or more was between 13.0% and 20.0%. With this sample size, the probability of a type I error would not exceed 5%, and power would be 80% ($\beta = 0.2$) if 10% of the participants were excluded due to non-response or incomplete data.

Study population

Inclusion criteria: The women included all who have previous histories of pregnancy that ended in delivery or miscarriage, and who were able to communicate with the research team and provided informed consent.

Exclusion criteria: Women who have never been pregnant.

Data collection

Trained medical officers gathered sociodemographic and obstetrical information (age, parity, education, occupation, early pregnancy [< 14 weeks], body mass index [BMI] and caesarean section). Definitions and measurement: Gestation of 24 weeks was used as the cut-off for defining miscarriage. It was calculated using the woman's last menstrual period[2]. Early pregnancy weight and height were used to calculate BMI in kg/m^2, and this was used to classify the women as being underweight (< 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (30.0–34.9 kg/m^2) based on guidelines provided by the World Health Organization[12]. A woman was considered young if she was under 20 years old, middle age if she was between 20 and 35 years of age, and advanced maternal age if she was more than 35 years old.

Statistics

Data analysis was performed using SPSS for Windows. The normality of the continuous variables was verified using the Shapiro-Wilk test. Participant characteristics were described using means (standard deviations), medians (interquartile ranges), frequencies, or percentages. In logistic regression, miscarriage was the dependent variable while sociodemographic factors, education, occupation, and BMI were the independent variables.

A logistic regression model was formed for the obstetric risk factors of miscarriage (age, parity, occupation, education, history of caesarean delivery, and interpregnancy interval). Maternal age was grouped into less than 20 years, 20 to 24 years, 25 to 29 years, 30 to 34 years, 35 to 40 years, and greater than 40 years. Variables with p-values less than 0.20 were included in the multivariable logistic regression model using the backward stepwise method (likelihood ratio). The crude odds ratio (COR), AOR, and their 95% confidence intervals (CIs) were computed to describe the strength of association. A two-sided p-value of < 0.05 was considered statistically significant.

Results

The general characteristics across the cohort of 2010 women are shown in Table 1. Of the 2010 recruited participants, 413 (20.5%) miscarried one, two, or more than three pregnancies (n = 116 [28.1%], n = 128 [31.0%], and n = 169 [(40.9%], respectively).

Table 1: General characteristics of the 2010 enrolled women in Saad Abuelela tertiary hospital, Khartoum, Sudan, from February to December 2019

Variables	Frequency	Percent
Age group, years		
< 20 years	541	26.9
20-24years	184	9.2
25-29-year	493	24.5
30-34-year	447	22.2
35 - 40 year	292	14.5
> 40 years.	53	2.6
Parity		
Primipara	842	41.9
Parous (2-4)	734	36.5
Multiparty (≥ 5)	434	21.6
Education		
≥ secondary level	1063	52.9
< secondary level	947	47.1
Occupation		
Housewives	1770	88.1
Employed	240	11.9
History of cesarean delivery		
Yes	1655	82.3
No	355	17.7
Body mass index		
underweight	708	35.2
normal	31	1.5
Overweight	959	47.7
Obese	312	15.5

Compared to those without histories of miscarriage, those who miscarried were of greater median age, parity, and BMI (30.0 [26–34] years vs. 26 [22.0–31.0] years, 3 [2–5] vs. 2 [1–4], and 26.2 [24.2–28.3] kg/m^2 vs. 26.2 [23.4–27.5] kg/m^2, respectively). In all cases, p < 0. 001. They also were older, of higher parity, had histories of caesarean delivery, and were obese. Differences in education level and occupation were not significant (Table 2).

As shown in Figure 1, logistic regression showed that, compared to those aged 25 to 29 years, risk of miscarriage was lower in those aged less than 20 years (ARO, 0.33; 95% CI, 0.16–0.67; p = 0.022) or 20 to 24 years (AOR, 0.57; 95% CI, 0.40–0.81; p = 0.022).

As shown in Table 3, primiparas had a lower risk compared to those of any other parity (AOR, 0.42; 95% CI, 0.32–0.57; p < 0.001), and those with less than a secondary level of education had a lower risk than those of any other education level (AOR, 0.78; 95%CI, 0.61–0.99; p = 0.044)

Discussion

The prevalence of miscarriage in this study sample (20.5%) is approximately the same as reported in Kenya (18.9%)[6], but is greater than in Uganda (8.4%)[3]. Differences in the social and demographic factors could explain the disparity. It is worth mentioning that our study was hospital-based and might not reflect the community. In a community-based study of a small eastern Sudanese community, the incidence of miscarriage was reportedly(1.4%)[13]. In contrast to the global age-related trend in miscarriages[1], we showed that younger age (less than 24 years) was associated with a lower risk of miscarriage.

Others have shown that the risk of miscarriage increases at ages exceeding 30 years, reaching 53% when the woman's age is 45 years or more[1]. In Ethiopia, the reported prevalence is greatest among those aged 15 to 19 years and 30 to 49 years[14]. The data are similar in Uganda: the risk was greatest among those aged less than 20 years and those aged 45 to 49 years[3]. Advanced maternal age is an important risk factor for miscarriage: rates were reportedly 50% among women aged more than 42 years and 75% among those aged more than 45 years[2].

In this study, the greatest prevalence was among those aged 30 to 34 years (29.8%) and those aged 25 to 29 years (28.8%). The lowest prevalence was found among those aged less than 20 years (2.4%) and 40 years (4.8%). This partly agrees with another report which shows that the prevalence among Sudanese women is 6% among those aged 41 to 45 years[15].

Several theories about the effect of age on pregnancy have been tested. A mitochondrial theory states that, in aging ovaries, the oocyte undergoes abnormal chromosome division and mutations in the mitochondrial DNA, resulting in oxidative stress and low antioxidant levels[16]. When both maternal and paternal ages are advanced, these mitochondrial abnormalities could result in an increased risk of spontaneous pregnancy loss, thus explaining the greater rate of miscarriage after in vitro fertilization[17,18]. On the other hand, miscarriage at an early age could be due to immature physiologic maternal changes[19].

The common U-shaped pattern of age-related miscarriage shows greater miscarriage rates at both extremes of maternal age[3,14,20], but we found a unique age-related curve among Sudanese women. Since this hospital-based study cannot represent the entire community, it might have overlooked many miscarriages, particularly those

Table 2: Comparing risk factors of miscarriage between women with history of miscarriage and women without miscarriage history in a tertiary hospital, Khartoum, Sudan, from February to December 2019

Variables	Women with history of miscarriage n(%) =413(20.5)	Women without history of miscarriage n(%) =1597(79.5)	P value
Age group, years			<0.001
< 20 years	10(2.4)	174(10.9)	
20-24years	60(14.5)	433(27.1)	
25-29-year	119(28.8)	422(26.4)	
30-34-year	123(29.8)	324(20.3)	
35,40 year	81(19.6)	211(13.2)	
> 40 years.	20(4.8)	33(2.1)	
Parity			
Primipara	73(17.7)	661(41.1)	<0.001
Parous (2-4)	207(50.1)	635(39.8)	
Multiparty (≥ 5)	133(32.2)	301(18.8)	
Education			
≥ secondary level	234(56.7)	829(51.9)	0.087
< secondary level	179(43.3)	768(48.1)	
Occupation			
Housewives	353(85.5)	1417(88.7)	0.074
Employed	60(14.5)	180(11.3)	
History of cesarean delivery			
Yes	98(23.7)	257(16.1)	<0.001
No	315(76.3)	1340(83.9)	
Body mass index			
underweight	6(1.5)	25(1.6)	0.008
normal	119(28.8)	589(36.9)	
Overweight	208(50.4)	751(47.0)	
Obese	80(19.4)	232(14.5)	

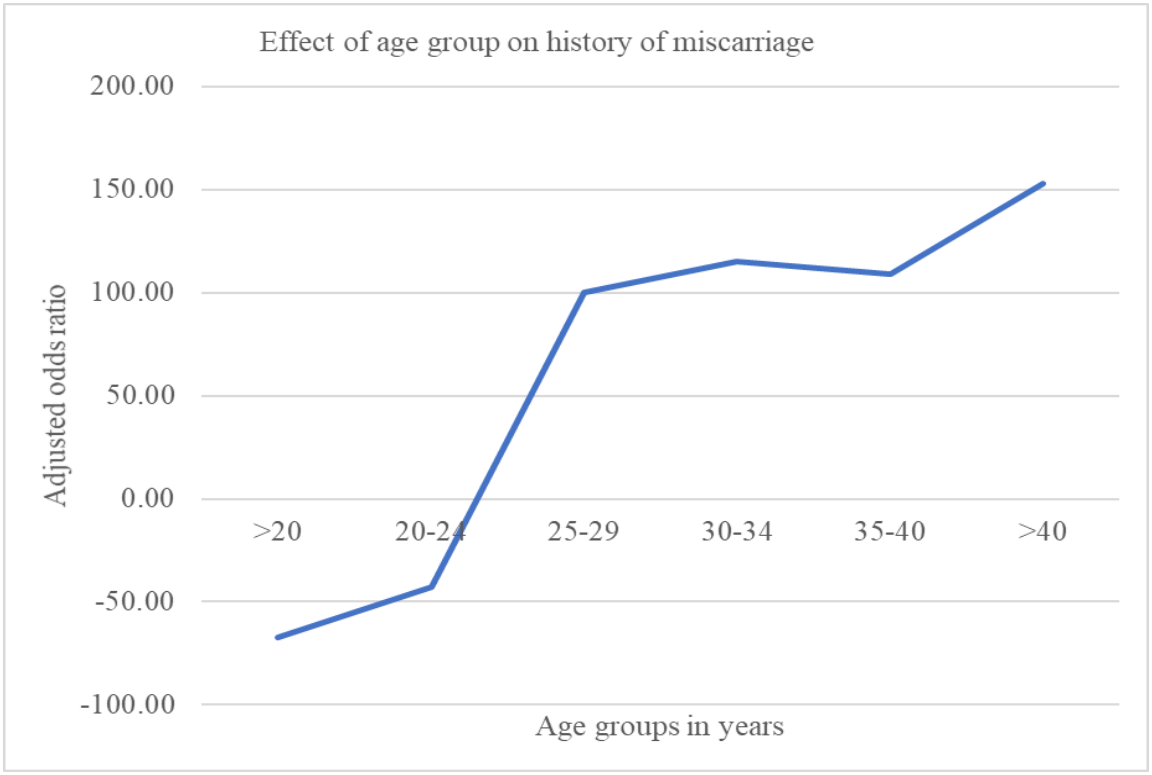

Figure 1: The effect of maternal age group on history of miscarriage in a tertiary hospital, Khartoum, Sudan, from February to December 2019

Table 3: Logistic regression model for associated risk factors of miscarriage among 2010 women in a tertiary hospital, Khartoum, Sudan, from February to December 2019

	Non adjusted			Adjusted		
Variables	OR	95% CI	P	OR	95% CI	P value
Age group, years						
< 20 years	0.31	0.91–1.07	0.065	0.33	0.16–0.67	0.022
20-24years	0.62	0.41–0.95	0.029	0.57	0.40–0.81	0.022
25-29-year	Reference					
30-34-year	1.11	0.78–1.57	0.546	1.15	0.85–1.55	0.353
35–40 year	0.93	0.62–1.93	0.739	1.09	0.77–1.55	0.610
>40 years	1.48	0.78–2.81	0.223	1.53	0.83–2.84	0.171
Parity						
Primipara	3.96	1.70–9.20	0.001	0.42	0.32–0.57	<0.001
Parous (2-4)	Reference			Reference		
Multiparty (≥ 5)	1.39	1.02–1.88	0.032	1.21	0.91–1.62	0.176
Education						
≥ secondary level	Reference			Reference		
< secondary level	0.73	0.55–0.96	0.027	0.78	0.61–0.99	0.044
Occupation				–	–	–
Housewives	Reference			–	–	–
Employed	1.02	0.67–1.55	0.920	–	–	–
History of cesarean delivery						
Yes	1.05	0.78–1.41	0.730	–	–	–
No	Reference					
Body mass index						
underweight	1.73	0.62–4.82	1.73			
normal	Reference					
Overweight	1.21	0.90–1.64	0.201	–	–	–
Obese	1.18	0.80–1.74	0.392	–	–	–
IPI	1.00	0.99–1.010	0.950	–	–	–

that occurred in early gestation. Early gestation miscarriage can be misinterpreted as being part of the menstrual cycle.

Another possible explanation is that Sudanese women reach high parity at a relatively young age. Alsamani et. al observed that Sudanese women reached grand multiparity (more than five deliveries) before 35 years of age[21]. We showed that primiparas had a 58% risk of miscarriage (AOR, 0.42). A similar finding was reported in Nigeria, where high parity increased the odds of miscarriage (AOR, 5.02)[22]. Interestingly, we found that less-educated women had a significantly lower risk for miscarriage (AOR, 0.78). This supports a study in Ghana showing that educated women were more likely to miscarry (AOR, 2.29)[23]. Similar findings were recently found in Iran[11].

In Sudan, women of higher education usually marry and begin their reproductive lives late. This explains the higher rate of miscarriage among those of greater age and with higher education. This study showed greater rates of miscarriage among women who delivered by caesarean section. A recent study based on a Norwegian registry showed a similar finding[1]. The indications for caesarean section might be the same as the causes of miscarriage in the same cohort of women.

The current study noted that obesity was significantly higher in those with histories of miscarriage. A Danish study reported the same[24], finding that obesity is one of the potentially preventable risk factors. This study's limitations include the fact that it was conducted in one hospital which might not represent the entire community. Moreover, some risk factors, such as pregnancy spacing, were not studied due to incomplete data.

Conclusion

The association between maternal age and risk of miscarriage was different in this study compared to the curve that describes the global trend, where a greater miscarriage rate is seen in the two extremes of maternal age. Younger women and those above 40 years old showed the lowest risks of miscarriage; the highest rate was found for those who were middle-aged. This is the first study in Sudan which

evaluates the risk of miscarriage based on maternal age. Community-based studies are recommended in this field in order to detect the risk factors for miscarriages. Detection of these risk factors and health education about pregnancy timing and spacing will help to modify the preventable risk factors of miscarriage.

Funding

None

Conflict of interest

None

References

1. Magnus MC, Wilcox AJ, Morken NH, Weinberg CR and Håberg SE. Role of maternal age and pregnancy history in risk of miscarriage: prospective register based study. *BMJ*. 2019;364:l869. Published 2019 Mar 20. doi:10.1136/bmj.l869.
2. The Johns Hopkins Manual of Gynecology and Obstetrics (Lippincott Manual Series): 9781605474335: Medicine & Health Science Books @ Amazon.com. https://www.amazon.com/Hopkins-Manual-Gynecology-Obstetrics-Lippincott/dp/1605474339. Accessed 12 Jul 2020.
3. Asiki G, Baisley K, Newton R, Marions L, Seeley J, Kamali K and Smedman L. Adverse pregnancy outcomes in rural Uganda (1996-2013): trends and associated factors from serial cross sectional surveys. *BMC Pregnancy Childbirth*. 2015;15:279. Published 2015 Oct 29. doi:10.1186/s12884-015-0708-8.
4. Cohain JS, Buxbaum RE and Mankuta D. Spontaneous first trimester miscarriage rates per woman among parous women with 1 or more pregnancies of 24 weeks or more. *BMC Pregnancy Childbirth*. 2017;17(1):437. Published 2017 Dec 22. doi:10.1186/s12884-017-1620-1.
5. Regan L and Rai R. Epidemiology and the medical causes of miscarriage. *Baillieres Best Pract Res Clin Obstet Gynaecol*. 2000;14(5):839-854. doi:10.1053/beog.2000.0123.
6. Dellicour S, Aol G, Ouma P, Yan N, Bigogo G, Hamel MJ, Burton DC, Oneko M, Breiman RF, Slutsker L, Feikin D, Kariuki S, Odhiambo F, Calip G, Stergachis A, Laserson KF, ter Kuile FO and Desai M. Weekly miscarriage rates in a community-based prospective cohort study in rural western Kenya. *BMJ open*, 2016,*6*(4), e011088. https://doi.org/10.1136/bmjopen-2016-011088.
7. Garrido-Gimenez, C and Alijotas-Reig J. Recurrent miscarriage: causes, evaluation and management. *Postgraduate medical journal*, *2015*, *91*(1073), 151–162. https://doi.org/10.1136/postgradmedj-2014-132672.
8. Giakoumelou S, Wheelhouse N, Cuschieri K, Entrican G, Howie SE and Horne AW. The role of infection in miscarriage. *Human reproduction update*,2016, *22*(1), 116–133. https://doi.org/10.1093/humupd/dmv041.
9. Baudin M, Jumaa AM, Jomma H, Karsany MS, Bucht G, Näslund J, Ahlm C, Evander M and Mohamed N. Association of Rift Valley fever virus infection with miscarriage in Sudanese women: a cross-sectional study. *The Lancet. Global health*, 2016,*4*(11), e864–e871. https://doi.org/10.1016/S2214-109X(16)30176-0.
10. Lean SC, Derricott H, Jones RL and Heazell A. Advanced maternal age and adverse pregnancy outcomes: A systematic review and meta-analysis. *PloS one*, 2017,*12*(10), e0186287. https://doi.org/10.1371/journal.pone.0186287.
11. Moradinazar M, Najafi F, Nazar ZM, Hamzeh B, Pasdar Y and Shakiba E. Lifetime Prevalence of Abortion and Risk Factors in Women: Evidence from a Cohort Study. *J Pregnancy*. 2020;2020:4871494. Published 2020 Apr 27. doi:10.1155/2020/4871494.
12. Ota E, Haruna M, Suzuki M, Anh DD, Tho l, Tam NT, Thiem VD, Anh NT, Isozaki M, Shibuya K, Ariyoshi K, Murashima S, Moriuchi H and Yanai H. Maternal body mass index and gestational weight gain and their association with perinatal outcomes in Viet Nam. *Bulletin of the World Health Organization*,2011, *89*(2), 127–136. https://doi.org/10.2471/BLT.10.077982.
13. Elghazali G, Adam I, Hamad A and El-Bashir MI. Plasmodium falciparum infection during pregnancy in an unstable transmission area in eastern Sudan. *East Mediterr Health J*. 2003;9(4):570-580.
14. Assefa N, Berhane Y and Worku A. Pregnancy rates and pregnancy loss in Eastern Ethiopia. *Acta Obstet Gynecol Scand*. 2013;92(6):642-647. doi:10.1111/aogs.12097.
15. Esmeal MEA, Khalid NHM, Ilkheir RH and Fathelrahman SA. Evaluation of First Trimester Miscarriage among Sudanese Woman in Khartoum State Using Ultrasonography. *International Journal of Innovative Research in Medical Science*,2019, *4*(12), 647- 651. https://doi.org/10.23958/ijirms/vol04-i12/784.
16. Wilding M. Potential long-term risks associated with maternal aging (the role of the mitochondria). *Fertil Steril*. 2015;103(6):1397-1401. doi:10.1016/j.fertnstert.2015.03.034.
17. Shirasuna K and Iwata H. Effect of aging on the female reproductive function. *Contracept Reprod Med*. 2017;2:23. Published 2017 Oct 3. doi:10.1186/s40834-017-0050-9.
18. Belloc S, Cohen-Bacrie P, Benkhalifa M, Cohen-Bacrie M, De Mouzon J, Hazout A and Ménézo Y. Effect of maternal and paternal age on pregnancy and miscarriage rates after intrauterine insemination. *Reproductive biomedicine online*,2008, *17*(3), 392–397. https://doi.org/10.1016/s1472-6483(10)60223-4.

19. Kirchengast S. Maternal age and pregnancy outcome--an anthropological approach. *Anthropol Anz*. 2007;65(2):181-191.
20. Ciancimino L, Laganà AS, Chiofalo B, Granese R, Grasso R and Triolo O. Would it be too late? A retrospective case-control analysis to evaluate maternal-fetal outcomes in advanced maternal age. *Arch Gynecol Obstet*. 2014;290(6):1109-1114. doi:10.1007/s00404-014-3367-5.
21. Alsammani MA, Jafer AM, Khieri SA, Ali AO and Shaaeldin MA. Effect of Grand Multiparity on Pregnancy Outcomes in Women Under 35 Years of Age: a Comparative Study. *Med Arch*. 2019;73(2):92-96. doi:10.5455/medarh.2019.73.92-96.
22. Sadiq AA, Poggensee G, Nguku P, Sabitu K, Abubakar A and Puone T. Factors associated with adverse pregnancy outcomes and perceptions of risk factors among reproductive age women in Soba LGA, Kaduna State 2013. *Pan Afr Med J*. 2016;25:111. Published 2016 Oct 25. doi:10.11604/pamj.2016.25.111.8739.
23. Adjei G, Enuameh Y, Asante KP, Baiden FA, Nettey OE, Abubakari S, Mahama E, Gyaase S and Owusu-Agyei S. Predictors of abortions in Rural Ghana: a cross-sectional study. *BMC public health*, 2015;15:202. Published 2015 Feb 28. doi:10.1186/s12889-015-1572-1.

Feodor Nilsson S, Andersen PK, Strandberg-Larsen K and Nybo Andersen AM. Risk factors for miscarriage from a prevention perspective: a nationwide follow-up study. *BJOG*. 2014;121(11):1375-1384. doi:10.1111/1471-0528.12694.