

Ministry of Higher Education and Scientific Research
Diyala University _ College of Medicine
Department of Obstetrics & Gynecology
2022-2023



Advanced maternal age and obstetric outcome

This Study was submitted in partial fulfilment of the requirement for the M. B. Ch. B

Done By:

Ghada Hussein Mohammed Salih

Supervised By:

Asst. Prof. Dr. Enas Jaleel Al-Obaidy

Contents

Subject	Page
Abstract	3
Chapter 1	
Introduction	6
Aims of study	7
Chapter 2	
Methodology	9
Statistical Analysis	10
Chapter 3	
Results	12
Discussion	15
Conclusions	17
References	19

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

{فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَى إِلَيْكَ
وَحْيُهُ وَقُلْ رَبِّ زِدْنِي عِلْمًا}

سورة طه / آية ١١٤

الى نور يضى عمتي عندما تطفئني الأيام والظروف
الى غيمة تظلي وتسقيني دون رغبة بردي لجميلها
الى الايدي التي تمد لي العون عندما اتعثر
الى عائلتي...

الى جميع أطباء وطبيبات محافظة ديالى وبالأخص مشرفتي في كتابة هذا البحث
الدكتورة ايناس جليل العبيدي
الى روح الدكتور الشهيد احمد طلال المدفعي رحمه الله...

Abstract

Background: Advanced maternal age defined as age 35 years or more at estimated date of delivery is considered to have higher incidence of obstetric complications and adverse pregnancy outcome than younger women.

Patient and method: A prospective comparative study conducted at Al-Batool teaching hospital in the department of obstetrics and gynecology over the period of three months from 25th September to 30th December 2022.

Included 106 pregnant women, divided into two age groups 50% ≥ 35 years, while the remaining 50% < 35 years old, The control group taken were women aged 20-34 years.

Aim of this study was to compare the obstetric and perinatal outcome of pregnancies in women with advanced maternal age ≥ 35 years with that of younger women < 35 years.

Result:

- Maternal age ≥ 35 years was significantly associated with parity, Pre-eclampsia, chronic HT, GDM, DM (type 1 or 2), antenatal hemorrhage and delivery by caesarean section as compared to women younger than 35 years.
- Maternal age < 35 years had was not significantly associated with adverse obstetric outcome.
- Preterm delivery was significantly associated with maternal age ≥ 35 years.
- While in perinatal outcome, there were no difference in neonatal death, admission to NCU, low birth weight and APGAR score at 5 minutes of life in two groups.

Conclusion: advanced age women had higher incidence of maternal medical disease, were more likely to deliver by caesarean section and increased incidence of preterm delivery.

Key words: Advanced maternal age pregnancy, adverse perinatal outcomes, adverse obstetrical outcomes, pregnancy



Chapter 1



Introduction

Advanced maternal age (AMA) is defined as maternal age ≥ 35 years at the time of delivery, this has been increasing all over the world in recent decades [1, 2] and to become more specific conception at the age of ≥ 40 years is known as very advanced maternal age (VAMA) and extremely advanced maternal age (EAMA) is that of ≥ 45 years [3]

Worldwide, there has been a trend toward later motherhood, there are many reasons why couples may postpone conceiving. In fact, it is considered multifactorial and became popular as some couples may wait until they are more financially stable, while others may choose to wait for social and lifestyle factors, women's careers, or a desire for better preparation [4]

In addition, ART plays an essential part, as the application of assisted reproductive techniques (ART) became widespread the maternal age became increasing to that of >35 and mid-forties as it. [5]

Understanding the various complications of AMA and pre-existing co-morbidities before the management of pregnant women in such an age group is very crucial. [6]

Advanced maternal age is also associated with a higher risk of pregnancy-related complications, such as preeclampsia (PE), Gestational diabetes (GDM), intrauterine growth restriction (IUGR), preterm delivery, and placental complications compared with women younger than age 35 [7] On the other hand, identifying the outcomes of AMA pregnancy will be very useful for building up specific programs for parents to allow them to understand and deal with the implications of pregnancies during advanced maternal age and that's for neonatal outcomes including low birth weight, birth asphyxia, low ABGAR score, increase admission to neonatal care unit (NCU), congenital anomalies and even fetal death. [8]

Advanced maternal age (AMA) is a leading cause of a decrease in fertility, therefore increasing the need for assisted reproductive technology (ART) which has allowed a larger proportion of advanced-age women to become pregnant. However, we must never forget the risks that ART can bring as it increases fetal loss before 28 weeks of gestation because of the genetic disorders and the impaction on chromosomes. [9, 10]

Finally, obstetric outcomes in women of advanced age have been improved with the progression of advanced technologies in perinatology. [11]

Despite the increased risks, many women of advanced maternal age have healthy pregnancies and deliver healthy babies. It is important for women who are planning to conceive at an advanced maternal age to discuss their pregnancy risks and options with their healthcare provider. Prenatal care and appropriate management of any complications that arise can help improve pregnancy outcomes. [12, 13]

Thus the aim of this study was to compare the maternal complications, risks, and obstetrics outcome of pregnancy in women with advanced maternal age against those of younger age group.



Chapter 2



Patient and methods

This is a prospective comparative study conducted at Al-Batool teaching hospital in the department of obstetrics and gynecology over the period of three months from 25th September to 30th December 2022 to assess the association of advanced maternal age pregnancy with adverse obstetrical and perinatal outcomes.

Ethics approval was obtained from the hospital in this study, as well as consent was obtained from all women involved in this study.

The study included 106 pregnant women who delivered at the time of clinical research, divided into two age groups 50% of them were ≥ 35 years, while the remaining 50% were < 35 years old

The inclusion criteria's were;

1. Patients over 35 years of age and patients under 35 years of age.
2. Patients with spontaneous pregnancy or after ovulation induction.
3. Patients with past medical history.
4. Patients with singleton and twin pregnancy.

The exclusion criteria were;

1. Major fetal defects
2. Intrauterine fetal demise
3. Pregnancy loss before 28 weeks of gestation

The control group taken were women aged 20-34 years, the demographic data of these women, gestational age at the time of delivery and complication during pregnancy were noted. They were followed till discharge perinatal outcome and any intrapartum and postpartum complications were also recorded in a specially designed research proforma.

Maternal characteristics were collected: previous maternal conditions (chronic hypertension, diabetes mellitus type I or II, thrombophilia,

heart disease, renal disease, neurological disease, asthma and psychiatric disorders), pre-pregnancy body mass index (BMI) categories (underweight, normal, overweight or obese), drug/alcohol/tobacco use (yes or no), Previous obstetric history: parity, previous cesarean section, and previous pregnancy related complications was also asked.

Neonatal characteristics were also collected: gender, weight, gestational age at the time of delivery, admission to NCU and fifth minute ABGAR score.

Statistical Analysis

The statistical analysis procedure performed according to chi-square test for independence, according to P value (whereas < 0.050 is significant), the collected data was checked for its completeness, entered, edited, cleaned and analyzed by the available computer software facility of Microsoft office Excel.



Chapter 3



Results

Table-1: shows the maternal characteristics according to maternal age groups.

Antepartum complications of women with advanced maternal age were compared with that of younger women.

The median age of the study group (≥ 35 years old) was found to be 36.9 years whereas the mean age of the control group (< 35 years old) was 24.8 years. Parity was significantly associated with maternal age ($p < 0.05$) as 12.3% of women with advanced maternal age were nulliparous as compared to 3.8% of adult women.

As well as among the antenatal complications was significantly associated with maternal age ≥ 35 years ($p < 0.05$).

Table-1: Maternal baseline information and antenatal complications

Maternal baseline information	Study group n=53 (advanced maternal age)	Control group n=53 (adult women)	p value
Mean age	36.9 years	24.8 years	
Parity			0.017
Nulliparous	13 (12.3%)	4 (3.8%)	
Multiparous	40 (37.7%)	49 (46.2%)	
Antenatal complications			0.022
Preeclampsia	15 (14.5%)	8 (7.5%)	
Chronic hypertension	2 (1.9%)	1 (0.9%)	
Gestational DM	5 (4.7%)	0 (0.0%)	
DM (Type 1 or 2)	1 (0.9%)	0 (0.0%)	
Antepartum hemorrhage	9 (8.5%)	7 (6.6%)	

Table-2 compares the mood of delivery of women with advanced age with that of younger women.

Vaginal delivery was higher in women with AMA than those of younger age group (8.5% vs 2.8%) and the rate of caesarean section due to previous scars, tubal ligation, emergency conditions and following IVF pregnancy was found to be significantly higher in advanced age women (31% vs 18.9%), while the rate of caesarean section due to malpresentation, failure to progress, CPD was higher in younger age (26.4% vs 10.3% in AMA).

Preterm delivery was significantly associated with maternal age ($p < 0.05$) as 14.2% of women with advanced maternal age had preterm delivery as compared to 5.7% of adult women.

There was no significance regarding twin pregnancy in both groups ($p > 0.05$).

Table-2: Maternal age and mode of delivery

Type of delivery	Study group n=53 (advanced maternal age)	Control group n=53 (adult women)	P value
Normal delivery	9 (8.5%)	3 (2.8%)	0.010
CS due to previous scars	28 (26.4%)	18 (17.0%)	
CS due to malpresentation	3 (2.8%)	9 (3.5%)	
CS for tubal ligation	1 (0.9%)	0 (0.0%)	
CS due to failure to progress	7 (6.6%)	9 (8.5%)	
CS due to CPD	1 (0.9%)	10 (9.4%)	
CS due to emergency condition	3 (2.8%)	2 (1.9%)	
CS IVF pregnancy	0 (0.0%)	1 (0.9%)	
Preterm delivery	15 (14.2%)	6 (5.7%)	0.028
Twin delivery	1 (0.9%)	1 (0.9%)	1.000(NS)

Table-3: Maternal age and perinatal outcome.

In perinatal outcome, there were no difference regarding gender, neonatal death, admission to NCU, low birth weight and APGAR score at 5 minutes of life in two groups.

Table-3: Maternal age and perinatal outcome

Variables	Study group n=53 (advanced maternal age)	Control group n=53 (adult women)	P value
Gender			0.697(NS)
Male	26 (24.5%)	24 (22.6%)	
Female	27 (25.5%)	29 (27.4%)	
Gestational age			0.104(NS)
37-42	36 (34.0%)	45 (42.5%)	
<37	16 (15.1%)	7 (6.6%)	
>42	1 (0.9%)	1 (0.9%)	
Birth weight			0.089(NS)
≥2500g	45 (43.4%)	46 (42.5%)	
2000-2400g	4 (3.8%)	7 (6.6%)	
<2000g	4 (3.8%)	0 (0.0%)	
Neonatal death	2 (1.9%)	1 (0.9%)	0.558(NS)
Admission to NCU	18 (17.0%)	19 (17.9%)	0.839(NS)
Apgar score < 7 at 5mins of life	8 (7.5%)	6 (5.7%)	0.566(NS)

Discussion

Delayed childbearing has become very popular over the past decades. [14]

This study has demonstrated the relationship between adverse obstetrical and perinatal outcomes in advanced-age women against younger age, whereas it become obvious after this study that advanced maternal age is an important risk factor for many obstetrical and perinatal outcomes complications.

AMA is significantly associated with Parity (as 12.3% were nulliparous), antenatal complications as hypertensive disorders of pregnancy, GDM, and antepartum hemorrhage.

This results resembles Bekir Kahveci et al. in a case-control study conducted in Turkey with 957 women divided into three age groups which found an association between maternal age and hypertensive disorders during pregnancy, and concluded that the risk of pregnancy-induced hypertension and pre-eclampsia was significantly lower in women younger than 35 years [15]. Nevertheless, in a retrospective paired cohort, Favilli et al. compared women ≥ 40 years with women between < 30 years old and found that hypertensive disorders of pregnancy were similar in both groups [16].

As well as cesarean delivery due to previous scars or emergency condition, found to be significantly associates with AMA (but not due to malpresentation, failure to progress, or CPD).

This study demonstrated that advanced maternal age was an important risk factor for iatrogenic preterm delivery (14.2%) on the contrary,

according to Schummers et al. [17], there was no association between the risk of iatrogenic preterm delivery with maternal age.

Women with maternal age ≥ 35 years are frequently labeled as 'higher risk' (even if they had no other risk factors) and such a generalization lowers the antenatal care and follow-up in these pregnant women, leading to increased rates of CS for non-medical reasons [18,19,20,21]

In women at AMA, there has been a significantly increased use of ART, as fertility proportionally decreases with advanced age [22, 23, 24]. It is known that ART carries its own increased risks of adverse pregnancy outcomes [25, 26].

This study shows a significant relationship between AMA and CS after IVF pregnancy.

Placenta Privia was also found to be significantly related to AMA as 9(8.5%) of cases were found to develop it, leading to increasing the rate of iatrogenic preterm delivery and CS.

The development of those pregnancy complications in advanced age women, is mainly attributed to placental insufficiency, as demonstrated by lower placental weight-to-birth weight ratios, decreased uteroplacental spiral vasculature volume and abnormal placental-derived hormones and biomarkers [27].

In the current study, the most common reason for women to become pregnant at an advanced age was a desire for a male child, however, only 24.5% of them gave birth to a male child so the ratio was not significant.

And regarding the neonatal outcome, this study also showed that maternal age was a leading cause for low birth weight $<2000\text{g}$ (but this difference did not reach statistical significance), and this resembles studies conducted in Brazil ($p < 0.001$), Alongside this, a huge study at many countries was done (including 29 middle and low income countries) also found that advanced maternal age was a risk factor for low birth weight [28].

AMA was also found to be a major risk factor for small gestational age at birth as 16 (15.1%) of advanced age women give birth to neonates who are < 37 weeks (but this difference also did not reach statistical significance).

This study shows no relation between AMA and low APGAR score at 5 minutes (< 7), this result was supported by studies done at Jordan and Malaysian where they shows no association between low fifth minute Apgar score and advanced maternal age pregnancy [29, 30], On the contrary, with the studies done in Turkey, India, and Brazil [31, 32, 33]. Where they shows a liner relationship in low 5 min. APGAR score with AMA pregnancies, this could be due to a difference in sample size. The rate of neonatal death, admission to NCU were not significant.

Conclusion

From this study, it can be concluded that advanced age women had higher incidence of hypertensive disorder of pregnancies and Gestational DM, were more likely to deliver by caesarean section and had increased incidence of preterm delivery.

In terms of neonatal outcomes, advanced maternal age was associated with increased rate of low birth weight and small gestational age neonates but not for male child, low APGAR score at 5 min. and NCU admission.

Future investigation should be addressed to develop medical interventions and additional pregnancy surveillance, especially preventive strategies that could improve pregnancy outcomes in patients with advanced maternal age.

Abbreviations

AMA: Advanced maternal age; VAMA: Very advanced maternal age; EAMA: Extremely advanced maternal age; ART: Assisted reproductive techniques; GD: Gestational diabetes; PE: Preeclampsia; NCU: Neonatal care unit;

Recommendation

In the future we need a larger study to assess these obstetrical and perinatal adverse outcomes

Since these outcomes influenced by AMA as a part of decrease fertility and increasing the need for ART we need a fertility and IVF center in Diyala government to assess the more liable women for pregnancy in AMA and follow up in more accurate manner.

Acknowledgement

I would like to thank the esteemed gynecology specialist at Diyala University College of medicine Dr. Enas Jaleel Al-Obaidy who gave me the support and opportunity to work on this project.

References

1. Jackson S, Hong C, Wang ET, Alexander C, Gregory KD, Pisarska MD. Pregnancy outcomes in very advanced maternal age pregnancies: the impact of assisted reproductive technology. *Fertil Steril*. 2015;103:76–80.
2. Le RC, Scherier S, Anselem O, Marszalek A, Tsatsaris V, Cabrol D, et al. Association between oocyte donation and maternal and perinatal outcomes in women aged 43 years or older. *Hum Reprod*. 2012;27:896–901.
3. Lean SC, Derricott H, Jones RL, Heazell AEP. 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>.
4. Heras Pérez, B.; Gobernado Tejedor, J.; Mora Cepeda, P.; Almaraz Gómez, A. La edad materna como factor de riesgo obstétrico. Resultados perinatales en gestantes de edad avanzada. *Prog. Obs. Ginecol*. 2011, 54, 575–580. [CrossRef]
5. (Gill et al. 2015; Schimmel MS, Bromiker R, Hammerman C, Chertman L, Ioscovich A, Granovsky-Grisaru S, Samueloff A, Elstein D. 2015. The effects of maternal age and parity on maternal and neonatal outcome. *Archives of Gynecology and Obstetrics* 291:793–798.12; Schimmel et al. 2015).
6. Wang Y, Tanbo T, Abyholm T, Henriksen T. The impact of advanced maternal age and parity on obstetric and perinatal outcomes in singleton gestations. *Arch Gynecol Obstet* 2011; 284: 31-
7. Naheed F, Tufail A, Kammeruddin K, Madiha S. Obstetrical risks with increased maternal age > 35 years. *Pakistan J Surg* 2009; 25: 240-3.
8. Moya Toneut, C.; Garaboto García, M.E.; Moré Vega, A.; Borges Fernández, R.; Moya Arechavaleta, N.; Moya Arechavaleta, A. Resultados maternos y perinatales en gestantes con avanzada edad materna. *Rev. Cubana Obstet. Ginecol*. 2017, 43, 1–13.
9. Balasch J, Gratacos E. 2012. Delayed childbearing. *Current Opinion in Obstetrics and Gynecology* 24:187–193.
10. Wennberg AL, Opdahl S, Bergh C, Aaris Henningsen AK, Gissler M, Romundstad LB, et al. Effect of maternal age on maternal and neonatal

- outcomes after assisted reproductive technology. *Fertil Steril*. 2016;106: 1142–1149.e1114.
11. Alshami HA, Kadasne AR, Khalfan M, Iqbal SZ, Mirghani HM. Pregnancy outcome in late maternal age in a high-income developing country. *Arch Gynecol Obstet*. 2011;284:1113–6.
 12. Paulson RJ, Boostanfar R, Saadat P, Mor E, Tourgeman DE, Slater CC, et al. Pregnancy in the sixth decade of life: obstetric outcomes in women of advanced reproductive age. *JAMA*. 2002;288:2320–3.
 13. Kort DH, Gosselin J, Choi JM, Thornton MH, Cleary-Goldman J, Sauer MV. Pregnancy after age 50: defining risks for mother and child. *Am J Perinatol*. 2012;29:245–50.
 14. Carolan M. Maternal age ≥ 45 years and maternal and perinatal outcomes: a review of the evidence. *Midwifery*. 2013; 29(5): 479–489, doi: 10.1016/j.midw.2012.04.001, indexed in Pubmed: 23159159.
 15. Kahveci, B.; Melekoglu, R.; Evruke, I.C.; Cetin, C. The effect of advanced maternal age on perinatal outcomes in nulliparous singleton pregnancies. *BMC Pregnancy Childbirth* 2018, 18, 343. [CrossRef]
 16. Favilli, A.; Pericoli, S.; Acanfora, M.M.; Bini, V.; Di Renzo, G.C.; Gerli, S. Pregnancy outcome in women aged 40 years or more. *J. Matern. Fetal Neonatal Med*. 2012, 25, 1260–1263. [CrossRef]
 17. Schummers L, Hutcheon JA, Hacker MR, et al. Absolute risks of obstetric outcomes by maternal age at first birth: a population-based cohort. *Epidemiology*. 2018; 29(3): 379–387, doi: 10.1097/EDE.0000000000000818, indexed in Pubmed: 29517506.
 18. Cohen W. Does maternal age affect pregnancy outcome? *BJOG*. 2014;121:252-4.
 19. Wang Y, Tanbo T, Abyholm T, Henriksen T. The impact of advanced maternal age and parity on obstetric and perinatal outcomes in singleton gestations. *Arch Gynecol Obstet*. 2011;284:31-7
 20. Usta IM, Nassar AH. Advanced maternal age. Part I: obstetric complications. *Am J Perinatol*. 2008;25:521-34.
 21. Li Y, Townend J, Rowe R, Knight M, Brocklehurst P, Hollowell J. The effect of maternal age and planned place of birth on intrapartum outcomes in healthy women with straightforward pregnancies secondary analysis of the Birthplace national prospective cohort study. *BMJ Open*. 2014;4:e004026.

22. Jackson S, Hong C, Wang ET, Alexander C, Gregory KD, Pisarska MD. Pregnancy outcomes in very advanced maternal age pregnancies: the impact of assisted reproductive technology. *Fertil Steril.* 2015;103:76–80
23. Sauer MV. Reproduction at an advanced maternal age and maternal health. *Fertil Steril.* 2015;103:1136–43.
24. Kort DH, Gosselin J, Choi JM, Thornton MH, Cleary-Goldman J, Sauer MV. Pregnancy after age 50: defining risks for mother and child. *Am J Perinatol.* 2012;29:245–50.
25. Wennberg AL, Opdahl S, Bergh C, Aaris Henningsen AK, Gissler M, Romundstad LB, et al. Effect of maternal age on maternal and neonatal outcomes after assisted reproductive technology. *Fertil Steril.* 2016;106:1142–1149.e1114.
26. Liu K.E., Case A. No. 346-Advanced Reproductive Age and Fertility. *Obstet Gynaecol Can* 2017;39(8):685-695.\
27. Cooke CLM, Davidge ST. Advanced maternal age and the impact on maternal and offspring cardiovascular health. *Am J Physiol Heart Circ Physiol.* 2019; 317(2): H387–H394, doi: 10.1152/ajpheart.00045.2019, indexed in Pubmed: 31199185.
28. Laopaiboon M, Lumbiganon P, et al. Advanced maternal age and pregnancy outcomes: a multi country assessment. *BJOG* 2014 Mar; 121 Suppl 1:49–56.
29. Rashed HEM, Maria Awaluddin S, Ahmad NA, et al. Advanced maternal age and adverse pregnancy outcomes in Muar, Johor. *Malays Sains Malaysiana.* 2016;45(10):1537–42
30. Vera Amarín. Effect of maternal age on pregnancy outcome: a hospital based study. *J Med Med Res* 2013 December; vol. 1(4): 28–31.
31. Yilmaz E, Tosun ÖA, Tarhan N, et al. Perinatal outcomes in advanced age pregnancies. *J Clin Exp Investig.* 2016;7(2):157–62.
32. Kamlesh Nagarwal, Chandrakanta, Kusum Gaur, et al. Pregnancy Outcome Comparison in Elderly and Non Elderly Primigravida attending at Mahila Chikitsalay. Jaipur (Rajasthan) India International Multispecialty J Health. 2015 March; Vol-1: Issue-1
33. Almeida NK, Almeida RM, Pedreira CE. Adverse perinatal outcomes for advanced maternal age: a cross-sectional study of Brazilian births. *J Pediatr (Rio J).* 2015;91(5):493–8.