Clinical Profiles and Reproductive Outcomes of Filipino Women of Advanced Age who Underwent Autologous In Vitro Fertilization: A Single Center Study

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Abstract

Background: Advanced maternal age is associated with diminished IVF outcomes, including reduced live birthrates and increased miscarriage risk.
Objective: To determine clinical profiles and reproductive outcomes of Filipino women of advanced age who underwent autologous IVF at the Center for Advanced Reproductive Medicine and Infertility at St. Luke's Medical Center Global City from January 1 , 2018 to December 31, 2024.
Methods: This retrospective cohort study analyzed 667 Filipino women aged 38 years and above who underwent autologous IVF/ICSI-ET from 2018 to 2024. Clinical profiles and reproductive outcomes were compared across age groups and embryo transfer types.
Results: Results showed significant age-related decline identified in reproductive outcomes such as clinical pregnancy and live birth rates, coupled with elevated miscarriage rates in older women. Frozen embryo transfers demonstrated superior outcomes versus fresh transfers. While PGT-A improved embryo selection, it did not fully mitigate age-related declines.
Conclusion: These findings underscore the persistent negative impact of advanced maternal age on IVF success, highlighting the importance of early fertility intervention, individualized treatment strategies, and context-specific research in resource-constrained settings.

Key words: In Vitro Fertilization, advanced maternal age, embryo transfer

Introduction

There is a trend of increased age of first pregnancy among couples globally form 24 years to 28 years in four decades (1970-2008) and it is more evident in industrialized countries.[1] In the Philippines, the median age of mothers at birth was 28 years in 2023.[2] Factors contributing to delay in childbearing include advancement in society, higher educational level (130%) and women of professional services (112%).[1] The increasing age in childbearing can result to reduced ovarian reserve, decreased possibility of spontaneous pregnancy and implantation rate thus affecting fertility and fecundity.[2,3] Consequently, more women of advanced age are turning to fertility treatments like in vitro fertilization (IVF), where age remains a major determinant of success. Advancements in IVF are powerful tools, granting individuals control over their reproductive timeline, allowing women to delay childbearing and aid in achieving pregnancy in infertile couples.[4]

In vitro fertilization is a form of assisted reproductive technology that involves a sequence of highly coordinated steps beginning with ovarian stimulation, followed by retrieval of oocytes to fertilization (Intracytoplasmic Sperm Injection-

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ICSI) and embryo culture and finally transcervical transfer of embryo into the uterus.[5] Maternal age is the most important predictor for IVF success.

In the study of De Neubourg et al (2016), a retrospective cohort study involving all patients registered in a national ART registry who started a first fresh autologous ART between July 2009 and December 2011. This included 12869 patients and 38,008 cycles, both fresh and frozen cycles. Results of the studies showed that the cumulative live birth rate was age dependent and declined from 62.9% for women less than 35 years to 51% for those aged 35 to 38 years old, significantly decreased to 33.5% in women 38 to 41 years and 17% in women 41 to 42 years of age.[6]

Numerous studies have investigated outcomes in women of advanced maternal age. In the study Havrljenko et al (2023), a retrospective study involving 491 women aged 35 years and above who underwent IVF-ET in a single center from January 2020 to May 2021. Results showed that there is a significant decline in cumulative live birth rate on patients more than 38 years old (16.7%) with the most significant difference in age 42 years old and above (7.77%). The study also predicted that at least 9 MII (mature oocytes) oocytes should be retrieved to achieve 1 live birth rate in patients with advanced age who underwent IVF. Decrease in fertility rate in patients with advanced age are attributed to declining ovarian reserve, combined with age related decreased endometrial receptivity and increased aneuploidy rates in oocytes. The limitation of this study was that they did not include male factor infertility or patient with diminished ovarian reserve.[7]

This was supported by the study of Liu et al (2022), a retrospective study including 826 women aged 38 years and above who underwent IVF/ICSI-ET in the reproductive medicine department in China from January 2016 to December 2018 with a minimal 2 year follow-up. Results showed that the number of oocytes retrieved was not statistically significant in patients aged 28 to 41 years old and 42 years old and above. However, the clinical pregnancy rates and cumulative livebirth rate was significantly higher among those in the age group of 38 to 41 years (26.99% to 32,31%) compared with those aged 42 years and above (3.44% to 14.40%).[8]

The retrospective study of Tur et al (2018), involved 4570 women aged 38 years and above who underwent IVF- ET at a University affiliated tertiary center between January 2000 and December 2013. Results showed that cumulative live birth rate decreased with increasing age with most prominent and significant decline in women aged 42 to 43. It also showed that the higher number of oocytes retrieved, the higher the clinical live birth rate, however, there is no clear benefit for patients aged 44 years old and above.[9]

Studies on reproductive outcomes of IVF on patients who underwent blastocyst versus cleavage embryo transfer showed that blastocyst embryo transfer leads to higher livebirth rate.[5] This was seen in the study of Cornelisse et al (2024), a multicenter randomized controlled trial, on the comparison of livebirth rate of blastocyst versus cleavage stage transfer involving 1202 women. Their results showed that the blastocyst stage embryo transfer group has higher live birth rate after fresh embryo transfer, lower miscarriage rate and lower mean number of embryo transfer but the cumulative livebirth rate did not differ between the blastocyst group and cleavage group which was 58.9% (355/603) versus 58.4% (350/599) with a risk ratio of 1.01 (95% CI 0.84 to 1.22).[10] This is similar to the study of Kovacs et al (2023), a retrospective analysis of women with advanced age (40 years and above) undergoing fresh IVF with at least three good quality cleavage stage embryos, that blastocyst stage embryo transfer showed higher pregnancy rate (25.5% vs. 14.1%, $p = 0.03$) and lower miscarriage rate 51.7% vs. 25%, $p = 0.01$) compared to cleavage stage transfers.[11]

Another development in IVF is preimplantation genetic testing (PGT) which includes procedures that involve removal of one or more nuclei of polar bodies from oocytes or cells from embryos to test for mutations or evaluate chromosomal complement.[5] There has been increasing use of PGT-A among patients in US.[12] In the recent committee opinion released by ASRM in 2024, it stated that the value of PGT-A as a routine chromosome analysis for all patients undergoing IVF has not been demonstrated and was shown on recent multicenter, randomized control trials that overall pregnancy outcomes via frozen embryo transfer were similar between PGT-A and conventional IVF. The decrease in risk of clinical miscarriage is also unclear.[12]

However, in patients with advanced age, there are several published studies showing that there is

improved IVF outcomes. In the study of Sacchi et al (2019), an observational cohort study involving 2538 patients with advanced age undergoing IVF. Results showed that there is increased live birth rate (40.3% vs. 11%) and decreased miscarriage rate (3.6% vs. 22.6%) on patients who underwent embryo transfer with PGT-A.[13] This is also similar to the systematic review and meta-analysis done by Adamyan et al (2024), which included 75 studies on clinical outcomes of different ages undergoing IVF/ICSI with PGT-A. Results showed that there is increased clinical pregnancy rate and live birth rate in women above 35 years who underwent embryo transfer with PGT-A.[14]

In varying advanced age groups, a recent study by Kim et al (2024), a retrospective cohort involving 428 cycles of single euploid embryo transfers in patients aged 35 and above on early pregnancy outcomes following PGT-A embryo transfers in patients with advanced age. Their results showed that the average age at transfer was 39.05 ± 2.53 years, with a mean AMH of 2.60 ± 1.86 ng/ml. The proportion of patients with a positive β-hCG result was 57.7% (247/428), and the clinical pregnancy rate was 53.5% (229/428). The positive β-hCG results by age were 59.9% (82/137) for ages 35 to 38, about 55.5% (121/218) for those aged 38 to 42, and 60.3% (44/73) for the age group 42 and above (p = 0.641). Clinical pregnancy rates were 54.0% for ages 35 to 38, around 51.8% for ages 38 to 42, and 57.5% for ages 42 and above. The positive b-hCG results and clinical pregnancy rates have no statistically significant differences.[15]

The available evidence shows contrasting results regarding outcomes of cleavage and blastocyst stage embryo transfer. It also shows varying outcomes in transfer of PGT-A tested blastocyst embryo transfer showing benefit in the advanced age groups. There are limited studies that show different outcomes from varying age groups of advanced maternal age. This study described the outcomes of different types of embryo transferred on women of varying advanced age undergoing IVF.

This study aimed to address the gap in local data by analyzing IVF outcomes in women of advanced maternal age, particularly focusing on the impact of embryo type and the use of PGT-A. Results from this research can inform clinical counseling, helping set realistic expectations and guide personalized treatment decisions for patients facing the physical, emotional, and financial burdens of fertility treatment. Furthermore, findings may support the development of tailored healthcare protocols, influence policy-making, and serve as a foundation for future studies.

Objectives

General Objective

To determine clinical profiles and reproductive outcomes of Filipino women of advanced age above 37 years old who underwent autologous IVF at the Center for Advanced Reproductive Medicine and Infertility (CARMI) at St. Luke's Medical Center Global City from January 1 , 2018 to December 31, 2024 (retrospective data of seven years)

Specific Objectives:

1) To compare the clinical profile of Filipino women in varying age groups, above 37 years old who underwent autologous IVF:
   a. Demographic profile
   b. Ovarian stimulation profile
   c. Embryology profile

2) To compare the reproductive outcomes among Filipino women of varying age groups, above 37 years old who underwent autologous IVF separating those who underwent the following types of embryo transferred:
   a. Fresh and Frozen Cleavage stage embryo
   b. Fresh and Frozen Blastocyst stage without PGT-A
   c. Blastocyst stage with PGT-A

Methods

This is a retrospective cohort study of women 38 years of age or older who underwent autologous IVF/ICSI- ET cycle in Center for Advanced Reproductive Medicine and Infertility (CARMI) at St. Luke's Medical Center Global City from January 1, 2018 to December 31, 2024. The study was started after the approval by the Institutional Scientific Review Committee (ISRC) and Institutional Ethics Review Committee (IERC).

The study included all Filipino women 38 years old and above at the time of ovarian stimulation, underwent egg retrieval and received at least one embryo transfer cycle at CARMI. Subjects with one or more of the following recorded conditions were excluded from the analysis: 1) oocyte cryopreservation; 2) egg donation; 3) intrauterine adhesion; 4) malformation, tuberculosis or history of surgery of the reproductive system; 5) natural cycles; 6) women with congenital anomalies; 7) active genital tract infection; 8) previous history of endometrial atypia; 9) cancer survivors; and 9) genetic, chromosomal and hematological abnormalities.

After ethical approval was secured, the primary investigator asked permission from CARMI to access their database of patients who underwent IVF/ICSI- ET. From the database, the chart records of the population of interest were retrieved and reviewed for eligibility. The sampling method that was used was non-probability sampling method using purposive sampling. All women whose chart records satisfy the inclusion criteria were included in the data collection. The following data were collected: maternal age, AMH, age of husband, LH surge suppression protocol used, number of days of stimulation, total amount of FSH used, type of trigger drug used for final oocyte maturation, number of oocytes retrieved, number of mature oocytes, number of fertilized oocytes, number of oocytes cleaved, number of embryos that reached cleavage stage and blastocyst stage, number of cleavage stage and blastocyst stage embryos frozen, number of embryos underwent PGT-A, number of euploid embryos frozen, number of gestational sac and number of embryos transferred. Reproductive outcomes were also collected described as presence or absence of positive beta HCG, clinical pregnancy, livebirth and miscarriage. Each subject was assigned a coded identification number all throughout the study. The data collected was kept in a sealed folder placed at the primary investigator's locker. The computer data will be kept in the principal investigator's password protected computer for 5 years, after which, it would be deleted.

The primary outcomes of the study are the reproductive outcomes. The reproductive outcomes included the following: implantation rate, clinical pregnancy rate, live birth rate, and miscarriage rate which was presented in percentages and was computed as described above.

Total sample size required was 380 to 520 and was calculated based on the test of hypothesis for the difference in the live birth rate among women aged 38 to 39 years old vs. women 42 to 43 years old. Assuming that live birth rate among women 38 to 39 years old is 25.94% and among women 42 to 43 years, 11.86%, (Liu et al, 2022), with an alpha error of 5%, power of 80 to 90% and a one tailed alternative hypothesis.

Data Analysis

Data were processed and encoded using Microsoft excel version 16.95.4 for Mac 2021.

Statistical analysis was done using SPSS version 27.10. Determination of the clinical profile was analyzed using frequency distribution and percentage for categorical variables such as age group, LH surge suppression protocol used, and trigger drug for final oocyte maturation. The variables that was also described in percentage include fertilization rate, cleavage rate, euploidy rate, clinical pregnancy rate, live birth rate, and miscarriage rate.

Mean, standard deviation and range was used to describe for continuous variables such as actual age, AMH value, and age of husband as well as days of stimulation, total amount of FSH used, total oocytes retrieved, number of mature oocytes, number of oocytes fertilized, number of oocytes cleaved, number of embryos that reached cleavage stage, number of cleavage stage embryos frozen, number of embryos reaching blastocyst stage without PGT-A, number of blastocysts frozen without PGT-A, number of embryos reaching blastocyst stage with PGT-A, number of embryos transferred and number of euploid blastocysts frozen.

Other continuous variables such as total number of patients who underwent cleavage stage transfer and total number of patients who underwent blastocyst stage transfer (with or without PGT-A) were described using mean and standard deviation. For the comparison of the reproductive outcomes according to age group per type of embryo transferred, a Chi square or Fisher's exact test was used. Level of significance was set at alpha = 0.05.[11]

Results

Table 1 summarizes the demographic, ovarian stimulation, and embryology profiles of Filipino women aged 38 years and older who underwent autologous in vitro fertilization (IVF), categorized into four age groups: 38 to 39, 40 to 41, 42 to 43, and 44 years and above.

Table 1. Demographic, ovarian stimulation, and embryology profile of women 38 years and above who underwent autologous IVF per age group.

	Age Groups (years)					p value
	38-39	40-41	42-43	≥44	Overall	
Number of patients, n (%)	236 (35.4)	218 (32.7)	129 (19.3)	84 (12.6)	667 100)	
Demographic profile						
AMH (Mean ± SD, ng/ml)	2.8 ± 2.31	1.8 ± 1.36	1.8 ± 1.98	1.27 ± 1.16	2.1 ± 1.95	<0.001
Age of husband (Mean ± SD, years)	41 ± 5.7	42 ± 5.6	43 ± 6.1	47 ± 7.5	42 ± 6.3	<0.001
Ovarian Stimulation profile						
LH Surge Suppression protocol						
GnRH agonist, n (%)	9 (3.8)	11 (5.0)	5 (3.9)	3 (3.6)	28 (4.2)	NS
GnRH antagonist, n (%)	208 (88.1)	186 (84.9)	114 (89.1)	74 (88.1)	582 (87.3)	
PPOS, n (%)	19 (8.1)	19 (8.7)	7 (5.5)	5 (6)	50 (7.5)	
Others, n (%)	---	3 (1.4)	2 (1.6)	2 (2.4)	7 (1)	
Total amount of FSH used (Mean ± SD, iu)	2943.5 ±994.77	3078.9 ±816.71	3349.54 ±1116.5	2968.67 ±1028.8	3085.53 ±974.59	NS
Total no. of days of ovarian stimulation (Mean ± SD, days)	11 ± 1.7	11 ± 1.7	11 ± 2.5	11 ± 2.5	11 ± 2	NS
Trigger drug for final oocyte maturation						
HCG only, n (%)	142 (60.2)	159 (72.6)	88 (68.8)	75 (89.3)	464 (69.6)	<0.001
GnRH agonis, n (%)	26 (11)	18 (8.2)	11 (8.6)	--	55 (8.2)	
Dual, n (%)	68 (28.8)	42 (19.2)	29 (22.7)	9 (10.7)	148 (22.2)	
Mean no. of follicles (Mean ± SD)	15 ± 9.1	13 ± 8.4	11± 7.6	7 ± 5.3	13 ± 8.6	<0.001
Mean no. of total oocytes retrieved (Mean ± SD)	11 ± 6.4	9 ± 6.3	8 ± 5.0	5 ± 3.9	9 ± 3.9	<0.001
Percent oocytes retrieved (%Mean)	74.3	73.9	70.4	70.8	73	NS
Mean no. of total mature/injected oocytes (Mean ± SD)	9 ± 5.2	8 ± 5.4	6 ± 4.8	4 ± 3.2	7.4 ± 5.2	<0.001
Mean no. of oocytes fertilized (Mean ± SD)	6 ± 3.9	6 ± 4.2	5 ± 3.3	3 ± 2.1	5 ± 3.8	<0.001

Fertilization rate (%)	69.7	71.7	73.8	71.2	71.3	NS
Mean no. of oocytes cleaved (Mean ± SD)	6 ± 3.9	5 ± 4.1	5 ± 3	3 ± 2.1	5.1 ± 3.7	<0.001
Cleavage rate (%)	97.1	97.5	95.7	98.2	97.1	NS
Embryo Transfer Profile						
Mean no. of cleavage stage embryos frozen (Mean ± SD)	1 ± 2.5	1 ± 2.6	1 ± 1.7	2 ± 2	1 ± 2.3	NS
Mean no. of embryos reachingblastocyst stage (Mean ± SD)	3 ± 2.0	3 ± 2.4	2.2 ± 1.7	1 ± 0.7	3 ± 2.1	<0.001
Mean no. of embryos reaching blastocyst stage with PGT-A (Mean ± SD)	3 ± 1.5	3 ± 1.8	2 ± 1.3	2 ± 0.71	3 ± 1.6	NS
Mean no. of euploid blastocysts frozen (Mean ± SD)	1.72 ± 0.81	1.54 ± 0.78	1.13 ± 0.68	1 ± 0		0.010
Euploidy rate (%)	61.8	58.9	54.4	75	59.6	NS
Total number of patients who underwent cleavage stage transfer, n (%)	107 (45.3)	108 (49.3)	77 (60.2)	74 (88.1)	366 (54.9)	<0.001
Total number of patients who underwent blastocyst stage transfer , n (%)	62 (26.3)	53 (24.2)	26 (20.3)	8 (9.5)	149 (22.3)	<0.001
Total number of patients who underwent blastocysttransfer w/ PGT-A, n (%)	67 (28.4)	58 (26.5)	25 (19.5)	2 (2.4)	152 (22.8)	<0.001

NS= not significant p ≥0.05

A total of 667 patients were included. The majority of participants were aged 38 to 39 years (35.4%), followed by those aged 40 to 41 years (32.7%), while the smallest proportion were aged ≥44 years (12.6%). Anti-Müllerian Hormone (AMH) levels significantly declined with increasing age ($p < 0.001$) while the age of husband increased significantly with patient age ($p < 0.001$). The ovarian stimulation profile of patients aged 38 years and older as seen in Table 1 showed that majority of patients in all age groups were stimulated using the GnRH antagonist protocol, with no significant variation in the choice of LH surge suppression protocol across age groups. Total number of days of stimulation was 11 days and was comparable between age groups. There is increasing total doses of FSH used with increasing age group however there is no significant difference across age groups. Most of the patients used HCG only as trigger drug for final oocyte maturation followed by Dual trigger. There is a significant increase in use of HCG only trigger as age increases ($p < 0.001$). The number of follicles, retrieved oocytes, mature oocytes, fertilized oocytes and oocytes cleaved were significantly decreased with increasing age group ($p < 0.001$). However, there was no significant difference on the oocyte retrieval rate, fertilization rate, and cleavage rate across age groups.

The embryology profile as seen in Table 1 showed that there is no significant difference in number of cleavage stage embryos frozen with increasing age group but there is decreasing number of embryos

reaching blastocyst stage with increasing age group ($p < 0.001$).

In patients who underwent preimplantation genetic testing for aneuploidy (PGT-A), although there is a decreasing trend of euploid embryos as age increases($p=0.010$), there is no significant difference in the euploidy rate across age groups. The average euploidy rate was 59.6%. Most patients underwent cleavage-stage transfer, with rates increasing significantly with age ($P<0.001$): 45.3%(age 38–39), 49.3% (40–41), 60.2% (42–43), and 88.1% (44+).

Table 2 presents the reproductive outcomes of patients who underwent cleavage stage transfers categorized by age group and type of embryo transfer (fresh vs. frozen). The majority of cycles involved the transfer of two embryos, followed by three-embryo transfers, predominantly utilizing frozen cleavage-stage embryos.

For fresh cleavage stage transfers (Table 2), a significant difference was observed in implantation rate ($p = 0.008$) of varying age groups, although this may be due to small subgroup counts. There is decreasing trend of beta-HCG positive rate, clinical pregnancy rate and live birth rate as age increases. There were no clinical pregnancies on patients aged 44 years and above and no live births on patient age 42 and above. There is increasing miscarriage rate with increasing age and there was 20% multifetal livebirth rate on age group 38-39. However these reproductive outcomes were not statistically significant.

For frozen cleavage stage transfers (Table 2), there is no significant difference in implantation rates ($p=0.229$) of patients across age groups while Beta-HCG positivity ($p=0..005$), clinical pregnancy ($p = 0.020$), live birth ($p = 0.023$), miscarriage ($p = 0.007$), and multifetal live birth rates ($p = 0.007$) significantly differed across age groups. There were 2 multifetal livebirths (13.3%) at age group 38 to 39 with no multifetal livebirths on other age groups.

Overall, it was shown in Table 2 that for cleavage stage transfers, there was decline in the reproductive outcomes such as livebirth rate, clinical pregnancy rate, implantation rate and multifetal pregnancy rate with increasing age group while, increasing miscarriage rate with increasing age. There was increased clinical pregnancy rate and livebirth rate in frozen transfers in comparison with fresh transfers across all age groups. There is also decreased miscarriage rate in frozen transfers in comparison with fresh transfers across all age groups.

Table 2. Reproductive outcome of women 38 years and above who underwent autologous IVF per age group after cleavage stage embryo transfer (fresh and frozen).

	Age groups												P value		
	38-39			40-41			42-43			>44					
	Fresh	Frozen	Total	Fresh	Frozen	Total	Fresh	Frozen	Total	Fresh	Frozen	Total	Fresh	Frozen	Total
Total no. of patients who underwent cleavage stage transfer	29	78	107	34	74	108	28	49	77	17	57	74			
Number of embryos transferred/ cycle															
1 n (%)	17 (59)	16 (21)	33 (31)	10 (37)	10 (19)	25 (23)	10 (36)	10 (20)	20 (26)	8 (47)	10 (17)	18 (24)			
2 n (%)	7 (24)	42 (54)	49 (46)	12 (44)	29 (56)	53 (49)	11 (39)	22 (45)	33 (43)	6 (35)	33 (58)	39 (53)	0.647	0.229	0.6
3 n (%)	4 (14)	18 (23)	22 (21)	4 (15)	13 (25)	29 (27)	5 (19)	17 (35)	22 (29)	1 (5.9)	14 (25)	15 (20)			
4 n (%)	1 (3.4)	2 (2.6)	3 (2.8)	1 (3.7)	---	1 (0.9)	2 (7.7)	---	2 (2.6)	2 (18)	---	2 (3)			
No. with Initially elevated B-hCG n (%)	9 (31)	24 (31)	33 (31)	7 (21)	25 (34)	32 (30)	4 (14)	6 (12)	10 (13)	2 (12)	8 (14)	10 (14)	0.361	0.005*	0.002*
Implantation Rate (%)	120.0	51.42	65.73	43.2	54.9	47.21	50	33	37.86	---	53.2	53.2	0.008*	0.666	0.128
Clinical Pregnancy Rate n (%)	5 (17.2)	15 (19.2)	20 (18.69)	5 (14.7)	14 (18.9)	19 (17.59)	2 (7.1)	5 (10.2)	7 (9.09)	---	6 (10.5)	6 (8.11)	0.281	0.020*	0.002*
Live Birth Rate n (%)	1 (3.4)	12 (15.4)	13 (12.14)	3 (8.8)	8 (10.8)	11 (10.19)	---	2 (4.1)	2 (2.6)	---	2 (3.5)	2 (2.7)	0.362	0.023*	0.002*
Miscarriage Rate n (%)	4 (80)	3 (20.0)	7 (35)	2 (40.0)	6 (42.9)	8 (42.11)	2 (100)	3 (60)	5 (71.43)	---	3 (50)	3 (50)	0.628	0.007*	0.002*
Multifetal pregnancy rate n (%)	1 (20)	2 (13.3)	3 (15)	---	---	---	---	---	---	---	---	---	0.526	0.007*	0.002*

Note: * = p-values less than 0.05 are considered statistically significant

Table 3 shows reproductive outcomes of patients who underwent blastocyst stage transfers without preimplantation genetic testing for aneuploidy (PGT-A). Most cycles involved frozen rather than fresh embryo transfer. While two-embryo transfers were most common, single-embryo transfers increased with age, though the variation was not statistically significant.

In fresh blastocyst embryo transfers as seen in Table 3, only the 38 to 39 and 40 to 41 age groups underwent fresh transfer. No pregnancies occurred in the 38–39 group, while the single pregnancy in the 40 to 41 group resulted in miscarriage.

For frozen blastocyst embryo transfers as seen in Table 3, outcomes such asnumber of embryos transferred (p = 0.371), β-hCG positivity (p = 0.300), implantation rate (p = 0.700), clinical pregnancy (p = 0.096), live birth (p = 0.280), miscarriage (p = 0.564), and multifetal pregnancy rates (p = 0.532) showed no statistically significant differences across age groups. However, trends show declining success in older women, with live birth rates dropping from 16.7% in the 38 to 39 group to 3.8% in the 42 to 43 and 12.5% in one case in the 44+ group.

The miscarriage rate was also increasing from 47.4% in the age group 38 to 39 years to 50% in the age group 42 to 43. Two multifetal pregnancies were observed—one in the 38 to 39 age group and one in the 40 to 41 age group—corresponding to multifetal live birth rates of 5.3% and 8.3%, respectively.

Overall, as shown in Table 3 in blastocyst embryo transfer, there is no significant differences were observed across age groups for number of embryos transferred (p = 0.304), β-hCG positivity (p = 0.345), implantation rate (p = 0.821), clinical pregnancy (p = 0.080), live birth (p= 0.342), miscarriage (p = 0.569), or multifetal live birth rate (p = 0.597). Although statistical significance was not reached, a general downward trend in clinical and live birth rates with age can be noted, especially for women over 42.

Lastly, Table 4 summarizes the reproductive outcomes of women aged 38 years and above who underwent autologous IVF after blastocyst transfer with PGT-A, stratified by age group.

Table 3. Reproductive outcome of women 38 years and above who underwent autologous IVF per age group after blastocyst transfer without PGT-A (fresh and frozen)

	Age groups												P value		
	38-39			40-41			42-43			>44					
	Fresh	Frozen	Total	Fresh	Frozen	Total	Fresh	Frozen	Total	Fresh	Frozen	Total	Fresh[1]	Frozen	Total
Total no. of patients who underwent cleavage stage transfer	2	60	62	4	49	53	0	26	26	0	8	8			
Number of embryos transferred/ cycle															
1 n (%)	---	15 (33)	15 (31)	2 (50)	18 (55)	20 (54)	---	7 (44)	7 (44)	---	2 (67)	2 (67)			
2 n (%)	2 (100)	29 (63)	31 (65)	2 (50)	13 (39)	15 (41)	---	9 (56)	9 (56)	---	1 (33)	1 (33)		0.371	0.304
3 n (%)	---	2 (4.3)	2 (4.2)	---	2 (6.1)	2 (5.4)	---	---	---	---	---	---			
4 n (%)	---	---	---	---	---	---	---	---	---	---	---	---			
No. with Initially elevated B-hCG n (%)	---	2 (42)	25 (40)	1 (25)	14 (29)	15 (28)	---	8 (31)	8 (31)	---	1 (13)	1 (13)		0.300	0.345
Implantation Rate (%)	---	77.36	77.36	50	93.75	88.89	---	75.0	75.0	---	---	---		0.700	0.821
Clinical Pregnancy Rate, n (%)	---	19 (31.7)	19 (30.6)	1 (25)	12 (24.5)	13 (24.5)	---	2 (7.7)	2 (7.7)	---	1 (12.5)	1 (12.5)		0.096	0.080
Live Birth Rate n (%)	---	10 (16.7)	10 (16.1)	---	7 (14.3)	7 (13.2)	---	1 (3.8)	1 (4)	---	1 (12.5)	1 (12.5)		0.280	0.342
Miscarriage Rate n (%)	--	9 (47.4)	9 (47.4)	1 (100)	5 (41.7)	6 (46.2)	---	1 (50)	1 (50)	---	---	---		0.564	0.569
Multifetal pregnancy rate , n (%)	---	1 (5.3)	1 (5.3)	---	1 (8.3)	1 (7.7)	---	---	---	---	---	---		0.532	0.597

Note: 1 Due to the extremely small sample size (only 6 participants), interpretation is limited. No significant differences were observed for any outcome variable across age groups.

Table 4. Reproductive outcome of women 38 years and above who underwent autologous IVF per age group after blastocyst transfer with PGT-A

	Age groups				p value
	38-39 N=67	40-41 N=58	42-43 N=25	≥44 N=32	
Number of embryos transferred/ cycle					
1 n (%)	46 (87)	43 (86)	13 (81)	2 (100)	0.907[1]
2 n (%)	7 (13)	7 (14)	3 (19)	---	
B-HCG positive rate, n (%)	39 (58)	36 (62)	10 (40)	1 (50)	0.247[1]
Implantation rate (%)	47	55	25	50	0.898[1]
Clinical pregnancy rate, n (%)	29 (43.3)	30 (51.7)	8 (32)	1 (50)	0.546[1]
Live birth rate, n (%)	17 (25.4)	22 (37.9)	5 (20)	---	0.290[1]
Miscarriage rate, n (%)	12 (41.4)	8 (26.7)	3 (37.5)	1 (100)	0.317[1]
Multifetal pregnancy live birth rate, n (%)	2 (6.9)	---	---	---	0.309[1]

[1]NS= Not significant p ≥0.05

Most embryo transfers involved the transfer of 1 embryo, with no statistically significant difference observed in the number of embryos transferred (NS) across age groups. All patients aged 44 and above had single embryo transfer. The proportion of women with positive beta-hCG levels was highest in the 40 to 41 age group (62%), followed by age 38 to 39 years (58%), and decreased in the older groups (40% in 42 to 43 years, 50% in ≥44). Implantation rate was lowest in the 42 to 43 age group (25%), followed by 38 to 39 age group (47%). Pregnancy loss also became more pronounced in older patients with 50% miscarriage rate for age group 44 years and above. Regarding live birth outcomes, the rate declined across the age spectrum—from 25.37% in 38 to 39 age group to 37.93% among those 40 to 41 years, then dropping to 20.00% in the 42 to 43 age group, and 0.00% in women ≥44 years. However, these differences did not reach statistical significance. Multifetal live births were rare across all age groups, (2.99% at age group 38 to 39) and did not significantly differ. There is also increase in miscarriage rate as age increases.

Discussion

This study examined the reproductive outcomes of Filipino women aged 38 years and above who underwent day 3 embryo transfers, with analyses stratified by age group, embryo transfer type (fresh vs. frozen), and preimplantation genetic testing for aneuploidy (PGT-A). A significant decline in ovarian reserve with increasing age was evident, and also increasing total FSH used as age increases. Ovarian response profile demonstrated a consistent and statistically significant decrease with age. This observation is consistent with findings of Liu et al (2022), wherein there is decreasing number of follicles and oocytes retrieved as age increases.8 However, fertilization and cleavage rates were not significantly different across age groups.

The embryology profile showed that there is increased in number of blastocyst stage transfer compared to cleavage stage transfer in younger age groups while there is increasing number of patients who underwent cleavage stage transfer in older age group. This is similar to the results of study of Andrew et al (2023), on determining trends in blastocyst vs cleavage stage embryo transfer in US from 2014 to 2020, wherein there is inverse relationship between age and blastocyst transfer rates. Younger patients with a good prognosis undergo more cycles with extended embryo culture, while in older patients (>42 years), blastocyst transfer rates decline due to concerns about fewer viable embryos after prolonged culture.[16]

Patients who underwent preimplantation genetic testing for aneuploidy (PGT-A) revealed that younger age groups had more euploid embryos (p = 0.010), while the overall euploidy rate declined with age, although not significantly. This observation aligns

with existing literature that indicates a strong correlation between advancing maternal age and increased oocyte aneuploidy, ultimately affecting embryo viability and implantation potential.[17]

In the combined analysis of fresh and frozen cleavage transfers (Table 2), statistically significant age-related declines were observed in reproductive outcomes and alongside a significant increase in miscarriage rate ($p = 0.002$). These findings highlight the cumulative impact of aging on embryo implantation and gestational success, despite comparable numbers of embryos transferred across age groups ($p = 0.6$). Younger women (38 to 39) had the highest success rates across all indicators, whereas women aged 44 and above had notably poor outcomes, including the lowest implantation and live birth rates.[1,3] The observed age-related decline in IVF outcomes corroborates existing literature, which establishes a strong inverse relationship between female age and the probability of successful pregnancy following assisted reproductive technologies.[6,7]

When analyzed separately, fresh and frozen stage transfers it showed that there is increased livebirth rate, clinical pregnancy rate and decreased miscarriage rate in those who underwent frozen embryo transfer compared to fresh transfer. However, this comparison is not statistically significant since sample size for patients who underwent fresh transfer were limited.

This however may suggest that frozen embryo transfer (FET) may confer advantages over fresh transfer in older women.[18] The results observed were similar to study of Wang Z, et al (2024) including 232,942 cycles of women age 35 years and above who underwent IVF, wherein frozen transfer has higher livebirth rate in women aged 40 and above.[19] It is also similar to the study of Acet et al (2022), involving 513 cycles of fresh and frozen embryo in women over age 35 years showing clinical pregnancy rates (38% versus 29%; $p = .030$) and live birth rates (30% versus 19.6%; $p = .013$) were higher in frozen embryo transfer group compared to fresh embryo transfer group.[20] The observed differences in fresh versus frozen transfer outcomes could be attributed to various factors, including endometrial receptivity, embryo quality, and the potential impact of ovarian stimulation on the uterine environment.[20] Frozen embryo transfers may allow for better synchronization between endometrial receptivity and embryo development, potentially leading to improved implantation and pregnancy outcomes.[20]

In blastocyst-stage transfers without PGT-A (Table 3), trends in lower clinicalpregnancy and live birth rates and higher miscarriage rates were consistently observed in older women. While the sample size of these subgroups limited statistical power, the directional consistency of the findings underscores the pervasive effect of maternal age across various embryo transfer types.

In comparison with cleavage transfer, there is increased clinical pregnancy rate and livebirth rate of women who underwent blastocyst stage transfers. This is similar to the study of Kovacs et al (2023) wherein there is higher pregnancy rate in blastocyst stage embryo transfer compared with cleavage stage transfers.[11]

Multifetal livebirth rate among cleavage and blastocyst transfers were rare and usually occurs younger women aged 38-39 years. This is similar to the study of Chen et al (2022) and Abdollahi et al (2017), both of which showed younger age has more risk in having multifetal pregnancies.[21,22]

Aneuploidy rates are significantly higher in older women, contributing to implantation failure, early pregnancy loss, and lower live birth rates. Prioritizing euploid embryo transfer becomes crucial in improving outcomes. Therefore, future investigations should rigorously evaluate the impact of trophectoderm biopsy followed by comprehensive chromosome screening on reproductive outcomes in this specific demographic, as this may lead to more informed clinical decisions and potentially improve success rates.[13]

In comparison with cleavage transfer and blastocyst transfer without PGT-A, clinical pregnancy rate and livebirth rates were higher in patients who underwent blastocyst transfer with PGT-A. This is similar to study of Adamyan et al (2024), which showed that there is increased clinical pregnancy and live birth rate in women above 35 years who underwent transfer with PGT-A.[14] This suggests that PGT-A may have a role in improving reproductive outcomes in women of advanced age especially those who are aged 43 years old and below.

Interestingly, even among those who underwent blastocyst transfer with PGT-A (Table 4), older women experienced significantly poorer outcomes.

There was no livebirth on age 44 years and above. Additionally, the miscarriage rate was highest in this group ($p = 0.029$). This may suggest that while PGT-A may improve embryo selection, it does not overcome the physiological constraints imposed by age-related decline in oocyte quality and uterine receptivity. These findings prompt critical evaluation of the cost-effectiveness of preimplantation genetic testing for aneuploidy (PGT-A) in women aged 44 years and older. Instead, a more individualized approach should be adopted, focusing on the selection of appropriate candidates for PGT-A intervention.

Conclusion and Recommendations

Among Filipino with advancing maternal age undergoing autologous IVF, the AMH levels declines and an increase in paternal age occurs. Furthermore, ovarian response, as measured by follicle count, oocyte yield, maturity and fertilization, also declines with age, as did blastocyst formation and euploidy rates. The GnRH antagonist protocol was the most commonly used for LH surge suppression, and hCG-only was the most frequent trigger for final oocyte maturation, while the total FSH dose or duration of stimulation across age groups were similar.

Reproductive outcomes significantly declined with increasing age, including reduced clinical pregnancy, implantation, and live birth rates, and increased miscarriage rates, regardless of embryo transfer type. Frozen blastocyst transfers yielded better outcomes than fresh transfers. Among women under 44, blastocyst transfer with PGT-A improved outcomes, with higher live birth and clinical pregnancy rates and lower miscarriage rates. However, in women aged 44 years and older, reproductive outcomes remained poor despite the use of blastocyst transfer with PGT-A. These findings suggest to thoroughly evaluate cost-effectiveness of PGT-A in women 44 years old and above since it does not fully mitigate age related decline. The study findings emphasize the need for tailored IVF protocols that address the unique challenges and limitations associated with advanced maternal age, while setting realistic expectations for treatment success. While the sample size limited statistical power, the findings reveal a number of potential targets for future research. These include more research into frozen embryo transfers in women of advanced maternal age and the impact of PGT-A.

For future studies, it is recommended to expand the population database to include a more diverse demographic to validate these findings across broader populations and clinical settings. Future studies can also further explore the possible predictors of IVF outcomes among women in the older reproductive age group. This aids in assessing the long-term outcomes, safety, psychological burden, and cost-effectiveness of strategies within IVF, such as PGT-A, for this demographic. Individual-level variables, including body mass index, years of infertility, type of infertility, comorbidities, and prior obstetric history, should also be considered, as these may further influence IVF outcomes in older women. Addressing these areas will enable more refined, evidence-based strategies to improve reproductive outcomes in this challenging patient population.

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