

IVF results in patient with very low AMH are affected by chronological age

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Abstract

Background: The aim of present study was to assess what is the probability of pregnancy of women with very low AMH concentration undergoing IVF and which factors other than AMH might affect the possibility of conception in these women. **Aims and Objective:** 1. To assess the probability of pregnancy in very low AMH patients 2. To find out factors other than AMH affect the possibility of conception in these women. **Materials And Methods:** All patients undergoing IVF at Shembekar Hospital private limited between January 2019 to January 2020 were retrospectively studied. All women were below 40 years of age, because this was the age limit to be admitted to IVF program at our institution. Overall, 100 women underwent AMH measurement have serum AMH value of <1.1ng/ml were enrolled in the study. This study was carried out in Shembekar Hospital, Nagpur. The study was done on 100 patients with low AMH levels, admitted at Shembekar hospital, Nagpur for IVF. Detailed history and examination were done. Routine blood investigations, serum AMH levels was done in all patients. **Conclusions:** Woman with very low AMH levels undergoing IVF still have reasonable chances of achieving a pregnancy, but their prognosis is significantly affected by chronological age. Very low AMH levels are associated with a relevant risk of cycle cancellation but should not be considered a reason to exclude a couple from IVF.

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INTRODUCTION

Ovarian aging is the result of the continuous decline in the extent and quality of follicular ovarian reserve, which may vary substantially among woman of the same age. AMH is established marker of Ovarian Reserve and is considered the most reliable predictor of ovarian responsiveness to controlled ovarian stimulation. In spite of clear correlation between serum AMH concentration and ovarian response to COS, the role of AMH as a tool to predict IVF outcome

in clinical settings is a matter of current debate. These somehow conflicting results make it difficult to consider AMH as the sole discriminant between woman who should be offered IVF treatment and those who should be discouraged.

The aim of present study was to assess what is the probability of pregnancy of women with very low AMH concentration undergoing IVF and which factors other than AMH might affect the possibility of conception in these women.

AIMS AND OBJECTIVE:

To assess the probability of pregnancy in very low AMH patients

To find out factors other than AMH affect the possibility of conception in these women.

MATERIALS AND METHODS

All patients undergoing IVF at Shembekar Hospital private limited between January 2019 to January 2020 were retrospectively studied. All women were below 40 years of

age, because this was the age limit to be admitted to IVF program at our institution. Overall 100 women underwent AMH measurement have serum AMH value of <1.1ng/ml were enrolled in the study.

IVF PROCEDURE

COS PROTOCOL

Short protocol was decided

A GnRh antagonist was given subcutaneously from stimulation day 7 or when follicle reach size of 14 mm at a daily dose of 0.25mg.

Recombinant FSH or HMG was administered to stimulate the ovary. A starting daily dose of gonadotropins was 300 IU, as established by our guidelines for woman with very low AMH, but it was adjusted according to the individual response from stimulation day 6 to 7, reaching maximum of 600 IU. The ovarian response to COS was monitored by TVS and serum estradiol (E2) measurement every second day from stimulation day 6 to 7. Ovulation was triggered by injection of ovitrille + leupride 2 mg, when the leading follicle reached 18-20mm diameter and estradiol concentration were appropriate. Oocyte pickup was performed by transvaginal USG guided aspiration approximately 36 hours after hcg injection. Under short GA mature, metaphase II oocyte were retrieved from the cumulus oocyte complexes and later inseminated using IVF or ICSI, according to clinical indication. After 48 hours of vitro culture, 2 or 3 embryos were transferred in utero using a soft catheter under US guidance. A single embryo transfer was performed when only one embryo was available. Intravaginal progesterone was used to support the luteal phase, starting from the day of embryo transfer and keep in for 15 days. Pregnancy was assessed by serum Hcg measurement 12 day after ET and was confirmed when gestational sac was visualized at TVS after 2 weeks. Besides AMH, the variables were registered for each patient at every IVF cycle includes age, antral follicle count, type of COS protocol, type and total dose administered gonadotropins, number of retrieved COCs, number of MII oocyte, number of fertilized oocytes, number of embryos available for transfer/freezing, embryo morphological score according to Holte *et al.*(16), and proportion of top-quality embryos

OBSERVATIONS AND RESULTS

1. AGEWISE DISTRIBUTION

Table 1:

AGE	FREQUENCY
26 – 30	35
31 – 35	32
36 – 40	33

Out of 100 women
35 patients were in age group of 26-30 years.

32 patients were in age group of 31-35 years
33 patients were in age group of 36-40 years.

2.DISTRIBUTION OF PREGNANT PATIENT ACCORDING TO AGE GROUPS

58 patients were pregnant
26 were in age group of 26-30 year
17 were in age group of 31-35 year
15 were in age group of 36-40 year

Table 2:

AGE	TOTAL PREGNANT	PERCENTAGE
26 – 30	26	45 %
31 – 35	17	29 %
36 – 40	15	26 %

3.AGE WISE DISTRIBUTION OF NON-PREGNANT PATIENTS.

27 patients were non-pregnant
5 were in age group of 26-30 year
10 were in age group of 31-35 year
12 were in age group of 36-40 year.

Table 3:

AGE	NON-PREGNANT PATIENTS	PERCENTAGE
26 – 30	5	19
31 – 35	10	37
36 – 40	12	44

4.AGEWISE DISTRIBUTION OF CANCELLED CYCLE

15 patients cycle was cancelled
4 were in age group of 26-30 year
5 were in age group of 31-35 year
6 were in age group of 36-40 year

Table 4:

AGE	CANCELLED CYCLE	PERCENTAGE
26 – 30	4	27
31 – 35	5	33
36 – 40	6	40

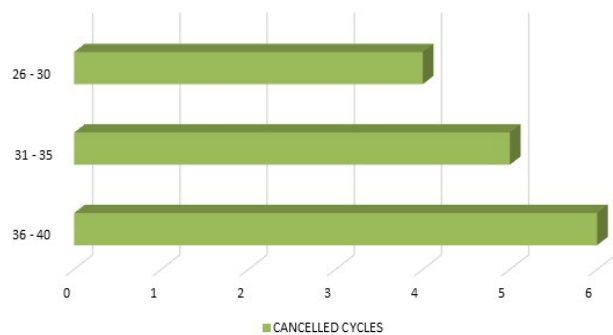


Figure 1: Cancelled cycles

5. AGE WISE DISTRIBUTION OF TAKE HOME BABIES

Out of 58 pregnant patient 35 patient had take home baby. 20 were in age group of 26-30 year. 10 were in age group of 31-35 year. 5 were in age group of 36-40 year.

Table 5:

AGE	TAKE HOME BABIES	PERCENTAGE
26 – 30	20	57
31 – 35	10	29
36 – 40	5	14



Figure 2: Take home Babies

6. AGEWISE DISTRIBUTION OF ABORTIONS

Out of 53 patient 23 had abortion. 6 patients were in age group of 26-30 year. 7 patients were in age group of 31-35 year. 10 patients were in age group of 36-40 year.

Table 6:

AGE	ABORTIONS	PERCENTAGE
26 – 30	6	26
31 – 35	7	30
36 – 40	10	44

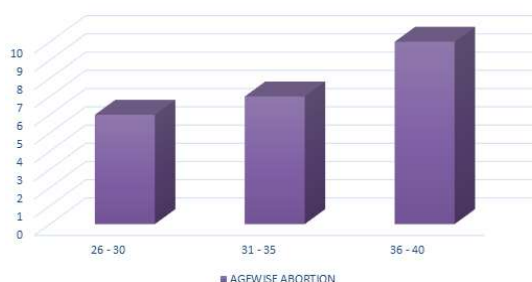


Figure 3: Age wise Abortion

7. COMPARATIVE DISTRIBUTION OF TOTAL SUCCESSFUL OUTCOMES

Table 7:

Age	Total patient	Pregnant	Take home babies
26 – 30	35	26	20
31 – 35	32	17	10
36 – 40	33	15	5

Out of total 35 patients of age group 26-30 year-26 were pregnant. Out of total 32 patients of age group 31-36 year-17 were pregnant. Out of total 33 patients of age group 36-40 year-15 were pregnant.

DISCUSSION

A number of variables, either alone or in combination, have been used to develop prediction models of IVF outcome, so far with limited success. AMH is an established marker of OR, and previous work showed its value in predicting the ovarian response to COS. More recently, the accuracy of AMH in predicting live birth was tested by independent groups, some data showed that AMH could be used as a prognostic factor, but its predictive value at low or very low concentrations was not clearly clarified. In fact, some authors reported acceptable results in terms of clinical pregnancies even in patient with very low AMH levels whereas others suggested their exclusion from IVF treatment due to a very poor prognosis. Herein, we studied 100 IVF patients with circulating AMH in the very low range (<1.1ng/ml) with the aim of assessing their probability of obtaining a clinical pregnancy and which variables could significantly affect IVF outcome. We observed that out of 100 patient 58 patient were pregnant, 26 were in the age group of 26-30 year, 17 were in the age group of 31-36 year and 15 were in the age of 36-40 year. The p value of the age group distribution was 0.0093 which is clinically significant. Out of 100 patient 27 patient were non pregnant, 5 was in the age group of 26-30 year, 10 were in the age group of 31-35 year, 12 were in the age group of 36-40 year. The p value of non-pregnant patient was 0.235 which is clinically not significant. Out of 100 patients 15 patient were undergone cycle cancellation, 4 patients in the age group of 26-30 year, 5 were in the age group of 31-35 year, 6 were in the age of 36-40 year, with a p value of 0.08187 which is clinically not significant. We observed the result suggest that a successful IVF is not very unlikely despite very low levels of serum AMH. Indeed, moderate but still reasonable pregnancy and live birth rate were reported in a series of 100 patient with AMH level < 1.1ng/ml. In our study appreciable cumulative pregnancy rate were higher in woman with low AMH concentration had age between 26-30 year. AMH could be simply a quantitative index of ovarian responsiveness, but not a reliable marker of oocyte competence to pregnancy. Comparing patients who conceived to those who did not, the first were significantly younger and had a significantly higher AFC than those who did not. When data of woman who underwent OPU were stratified according to chronological age, patients below 35 years displayed a significantly higher oocyte

yield and a remarkable CPR/OPU despite their low AMH levels, conversely, the oldest patients of the age group 36-40, show significantly lower CPR/OPU. Multivariable logistic regression analysis confirmed that the likelihood of becoming pregnant was significantly affected by chronological age, patients age 36-40 year were significantly less likely to get pregnant than patients below 35 year, whereas AMH and AFC did not significantly affect the probability to conceive. The take home babies were 20 in the age group of 26-30 as compared to the age group of 36-40 as of 5 babies. The p value of comparative take home babies was 0.0068 which was clinically significant. In our study, age and AFC were the only clinical parameters that were significantly different between the group of patients who conceived and those who did not. However, in the logistic regression analysis, AFC lost significance, leaving age as the only variable significantly related to IVF success. Indeed, woman younger than 35 obtained a remarkable CPR and a significant trend towards a decreased success rate with increasing age was observed, despite all patients had similar, very low AMH levels. The study of age group study with low AMH value for IVF has a p value of 0.04756 which is clinically significant. So, taken together, these observations suggest that the patients of relatively young age with deeply reduced ovarian reserve may still have favorable IVF outcome due to a well-preserved oocyte competence. This view is further supported by a recent meta-analysis found that female age is the most important predictor of pregnancy in IVF in almost all analyzed studies. The interaction between age, AMH and IVF success, however is still a matter of debate. Some studies, in fact, showed a correlation between AMH and live birth rate after IVF, depending solely on oocyte yield, whereas a recent study suggested that AMH is an independent marker of pregnancy and live birth after adjustment for female age and oocyte yield. These somehow conflicting evidences could depend on the complexity of the interaction between age and AMH. Age could affect mainly the proportion of follicles switching from the primordial to the recruitable pool, whereas AMH per se could mainly reflect the number of FSH- sensitive, recruitable follicle. It was recently suggested that the intraovarian inhibiting effect of AMH on follicle recruitment could be modulated according to the patient's age. In this complex picture, the positive association between IVF success and ovarian reserve as measured by serum AMH could have variable strength according to the patient's chronological age. From a clinical standpoint, the most important finding of the present study is that young patients with very low AMH levels still have reasonable chances of achieving a pregnancy with IVF and they should be reassured about their reproduction prognosis.

Furthermore, similar to others, we could not identify a threshold AMH value below in which no pregnancy is likely to occur, and IVF should be discouraged. Although with a significantly lower rate, we obtained clinical and ongoing pregnancies even in older patients with very low AMH levels. Overall, our results suggest that the clinical rationale for measuring AMH prior to IVF should be limited to the prediction of ovarian response to COS and of the risk of cycle cancellation, particularly in woman of more advanced reproductive age. In view of our findings, pre-IVF AMH assessment cannot be used to exclude a couple from IVF.

SUMMARY

This study was carried out in Shembekar Hospital, Nagpur. The study was done on 100 patients with low AMH levels, admitted at Shembekar hospital, Nagpur for IVF. Detailed history and examination were done. Routine blood investigations, serum AMH levels was done in all patients. Following are the salient features of the present study

- Pregnancy was more common among the age group of 26 – 30 years.
- Non-pregnancy and abortions were both more common among the older age group of 36-40 years.
- Take home babies were more among the younger age group of 26 – 30 years.
- Younger age group have a lesser chance of non-pregnancy, cycle cancellation and abortions.

CONCLUSIONS

Woman with very low AMH levels undergoing IVF still have reasonable chances of achieving a pregnancy, but their prognosis is significantly affected by chronological age. Very low AMH levels are associated with a relevant risk of cycle cancellation but should not be considered a reason to exclude a couple from IVF.

REFERENCES

1. Broekmans FJ, Knauff EA, te Velde ER, Macklon NS, Fauser BC. Female reproductive ageing: current knowledge and future trends. *Trends Endocrinol Metab.* 2007;18:58–65.
2. Steiner AZ. Clinical implications of ovarian reserve testing. *Obstet Gynecol Surv.* 2009;64:120–8.
3. Broekmans FJ, Kwee J, Hendriks DJ, Mol BW, Lambalk CB. A systematic review of tests predicting ovarian reserve and IVF out- come. *Hum Reprod Update.* 2006;12:685–718.
4. Dewailly D, Andersen CY, Balen A, Broekmans F, Dilaver N, Fanchin R, *et al.* The physiology and clinical utility of anti- mullerian hormone in women. *Hum Reprod Update.* 2014;20:370–85.
5. Marinakis G, Nikolaou D. What is the role of assisted reproduction technology in the management of age-related infertility? *Hum Fertil (Camb).* 2011;14:8–15.

6. La Marca A, Sunkara SK. Individualization of controlled ovarian stimulation in IVF using ovarian reserve markers: from theory to practice. *Hum Reprod Update.* 2014;20:124–40.
7. Nardo LG, Gelbaya TA, Wilkinson H, Roberts SA, Yates A, Pemberton P, *et al.* Circulating basal anti-müllerian hormone level as predictor of ovarian response in women undergoing ovarian stimulation for in vitro fertilization. *Fertil Steril.* 2009;92:1586–93.
8. Gleicher N, Weghofer A, Barad DH. Anti-müllerian hormone (AMH) defines, independent of age, low versus good live-birth chances in women with severely diminished ovarian reserve. *Fertil Steril.* 2010;94:2824–7.
9. Iliodromiti S, Kelsey TW, Wu O, Anderson RA, Nelson SM. The predictive accuracy of anti-müllerian hormone for live birth after assisted conception: a systematic review and meta-analysis of the literature. *Hum Reprod Update.* 2014;20:560–70.
10. Tocci A, Ferrero S, Iacobelli M, Greco E. Negligible serum anti-mullerian hormone: pregnancy and birth after a 1-month course of an oral contraceptive, ovarian hyperstimulation, and intracytoplasmic sperm injection. *Fertil Steril.* 2009;92:395 e399–
11. Weghofer A, Dietrich W, Barad DH, Gleicher N. Live birth chances in women with extremely low-serum anti-mullerian hormone levels. *Hum Reprod.* 2011;26:1905–9.
12. van Loendersloot LL, van Wely M, Limpens J, Bossuyt PM, Repping S, van der Veen F. Predictive factors in in vitro fertilization (IVF): a systematic review and meta-analysis. *Hum Reprod Update.* 2010;16:577–89.

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