www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v6i9.53

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Role of Anti-Mullerian Hormone as a predictor of ovarian function in Assisted Reproductive Techniques

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Abstract
Predicting the ovarian reserve and success in ART cycles is necessary in planning the treatment schedules, preventing OHSS and advising the couple. The present study aims to validate the reliability of AMH estimation as predictor of fertility potential of the woman. This is a retrospective analysis of the success of the multiple IVF/ICSI cycles on one hundred women at an Infertility centre, all the protocols, procedures done by the same team. 20 women had high, 23 had low and 57 had normal AMH. All women with normal AMH had good ovarian response; in women with high AMH all woman except one had good ovarian response; all women with low AMH had poor ovarian response. 128 cycles of IVF/ICSI were performed on hundred women, 184 embryo transfers were done with fresh and cryopreserved embryos, with clinical pregnancy in 49 women. In 57women with normal AMH in 76 ART cycles, 123 embryo transfers, 39 clinical pregnancies occurred; in 20 women with high AMH in 28 ART cycles, 44 embryo transfers, 9 had clinical pregnancy; in 23 women with low AMH in 24 ART cycles, 17 embryo transfers, only one became pregnant.
Keywords: *AMH, ART, ovarian reserve, clinical pregnancy.*

Introduction

AMH is a dimeric glycoprotein. During reproductive age AMH is secreted by granulosa cells of preantral and small antral follicles in the ovary. It is expressed as early as 36 weeks of gestation.

According to the pattern of AMH secretion, serum level of AMH can show the age and storage of the ovary. Evaluation of ovarian storage is an essential step for treatment of infertility. There are several methods for evaluation of ovarian storage such as Antral follicle count which is done by transvaginal ultrasound on day 2 of cycle. Other methods are serum Oestrogens, Follicle stimulating hormone and Inhibin levels.

AMH has an important advantage over FSH as it can be reliably measured at any stage of the menstrual cycle unlike FSH which requires

venous sampling on the day 2 or day 3 of menses and baseline FSH levels fluctuate from cycle to cycle. Serum AMH is not affected by consumption of oral contraceptive pills unlike serum levels of FSH and other markers.

Normal level of AMH blood level is 1.5-4.0 ng/ml.

The Aim of the study is to determine the predictive value of AMH as a marker of ovarian reserve

Material and Methods

A total number of 100 patients of less than 40 years of age referred to an IVF Clinic who underwent IVF/ICSI using either GnRH agonist/ GnRH antagonist protocol during theperiod April 2016 to April 2018 were studied by retrospective analysis.

On day 2 of menstrual cycle blood sample was obtained for measuring serum AMH, FSH, Oestradiol and Transvaginal ultrasound examination to assess the number of antral follicles [2-5 mm] was done.

A standard down regulation long protocol using GnRH Agonist or Antagonist protocol was used.HCG was administered when more than 3 follicles more than 18 mm were reached. Oocyte retrieval was done after 34-36 hours.2 or 3 embryos were transferred on day of 3 of fertilization and rest of the embryos were freezed and transferred in subsequent cycles.

Results

Table 1: AMH Levels

AMH	Range	No. of patients	Percentage
High	>4ng/ml	20	20%
Normal	1.5-4.0 ng/ml	57	57%
Low	0.5-1.5 ng/ml	23	23%

The study group was divided into three subgroups according to AMH levels. Maximum patients i.e.57% had normal AMH, 20% had high AMH and 23% had low AMH.

Table 2: AMH and age group

Age group	High AMH	Normal AMH	Low AMH	No of patients	Percentage
21-25 years	3	8	-	11	11%
26-30 years	5	13	2	20	20%
31-35 years	12	32	7	51	51%
36-40 years	-	4	14	18	18%

In the present study of 100 patients, 11% were in the age group of 21-25 years, 20% were in the age group of 26-30 years, 51% were in the age group of 31-35 years and 18% were in the age group of 36-40 years.

Table 3: Ovarian response

Response	High AMH	Normal AMH	Low AMH	No. of patients	Percentage
Good response	19	56	-	76	76%
Poor response	1	-	23	24	24%

Patients with Oocyte count four or more were considered good responders and patients with less than four as poor responders. In present study 76% were good responders who had normal AMH and high AMH values whereas 24% were poor responders who had low AMH values.

Table 4: Outcome of first IVF/ICSI cycle in 100 women

AMH	No. of Patients	Oocytes retrieved	Embryos fertilised	First transfer	Second transfer	Clinical pregnancies
High	20	144	74	20	12	8
Normal	57	586	498	57	38	32
Low	23	70	28	16	-	1

In this study of 100 patients-- 57 patients had normal AMH, total no of oocytes retrieved were 586, 498 embryos were fertilised, all 57 patients had embryo transfer on day 3 after Oocyte retrieval in the same cycle. Freezing of the embryos were done in those patients who had more than three embryos and transfer was done in the second cycle. In this study 38 patients with normal AMH had second cycle of frozen embryo transfer. In 57 patients with normal AMH we observed 32 clinical pregnancies in 95 cycles of transfer.

144 Oocytes were retrieved in 20 patients with high AMH, embryos fertilised were 74. All the 20 patients with high AMH had first cycle of embryo transfer, second cycle of frozen embryo transfer was done in 12 patients. Total number of clinical pregnancies were 8.

In 23 patients with low AMH, 70 Oocytes were retrieved,28 embryos were fertilised. Embryo transfer was done in the same cycle in 16 patients. In 7 patients embryo transfer was not done because of poor response to stimulation and poor Oocyte quality.

Table 5 : Outcome of second ICSI/IVF cycle in 24 women

AMH	No of Patients	Oocytes retrieved	Embryos fertilised	First transfer	Second transfer	Clinical pregnancies
High	7	52	31	7	3	1
Normal	16	96	80	16	7	6
Low	1	2	1	1	-	-

Out of 24 patients 16 patients had normal AMH. Total number of Oocytes retrieved were 96, 80 embryos were fertilised, transfer of embryos were done in the same cycle in all the 16 patients, second cycle of embryo transfer was done in 7 patients. Total number of clinical pregnancies achieved were6.

In 7 high AMH patients, 52 Oocytes were retrieved and 31 embryos were fertilised, all the 7 patients had transfer in the same cycle, 3 patients had second cycle transfer also. Total number of clinical pregnancies were 1.

In 1 patient with low AMH, 2 Oocytes were retrieved and 1 was fertilised and transferred in the same cycle, there was no clinical pregnancy.

Table: 6 Outcome of third ICSI cycle in 4 women

AMH	No of Patients	Oocytes retrieved	Embryos fertilised	First transfer	second transfer	clinical pregnancies
High	1	8	4	1	1	-
Normal	3	22	16	3	2	1
Low	-	-	-	-	-	-

22 Oocytes were retrieved in 3 patients with normal AMH, 16 embryos were fertilised, embryo transfer was done in the same cycle in 3 patients, 2 patients had transfer in the second cycle also, 1 patient had clinical pregnancy.

In 1 patient with high AMH 8 Oocytes were retrieved, 4 embryos were fertilised, embryo transfer was done in 2 cycles and patient had clinical pregnancy.

Discussion

Maximum number of patients 51% were in the age group of 31-35 years. Normal AMH values were observed in the younger patients, High AMH values were seen in PCOS patients, low AMH values were seen with the advancing age above 35 years of age.

Ae van Rooj et al, 2005; Robertson et al, 2008 found that reduction in ovarian reserve is a physiological process occurring in the late reproductive period and consistently associated with a decrease in AMH levels and low antral follicle count.

In 20 PCOS patients it was observed that AMH levels were high >4ng/ml and increased follicular count which can be used for predicting hyper response and risk of OHSS so that Gonadotropins doses can be adjusted.

Four prospective studies which were performed [Kwee et al., 2007, Nelson et al., 2007, Lee et al 2008, Nardo et al.,2008] reported relevant value of AMH for the prediction of hyper response and OHSS.

Onofriescu et al 2014 found that measurement of serum AMH is a valuable marker for PCOS patients to confirm diagnosis and evaluate the extent of follicular dysfunction in relation with hyperandrogenism.

FSH>10U/L on day 2, AFC<3 from both ovaries and ovarian volume <3 cm3 have been found to be associated with reduced ovarian reserve.

La marca et al 2007, Nelsosm et al 2007 have shown a positive correlation with serum AMH levels and clinical pregnancy rates.

In this study of 100 patients, 128 cycles of ICSI were done in 3 cycles.

76 cycles of ICSI were done in 57 patients with normal AMH, 704 Oocytes were retrieved, 594 embryos were fertilised, 39 clinical pregnancies were observed.

28 cycles of ICSI were done in 20 patients with high AMH, 204 Oocytes were retrieved.109 embryos were fertilised, 9 clinical pregnancies were observed.

24 cycles of ICSI were done in 23 patients with low AMH, 72 Oocytes were retrieved, 29 embryos were fertilised, 1 pregnancy was observed.

Evaluation of AMH with retrieved oocyte count correlated well with High AMH and normal AMH values. High oocyte retrieval count was observed in High AMH and normal AMH patients.

Conclusion

Serum AMH is a potential reliable marker in predicting ovarian reserve and reproductive performance. Along with antral follicle count it is a better predictor than serum FSH.

In women with PCOS AMH can be used as a diagnostic and prognostic marker for ovarian response and hyperstimulation and alter the stimulation protocol to prevent OHSS. It is a good predictor of poor response to fertility treatment and to plan the treatment accordingly.

Conflict of interest: Nil

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