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ORIGINAL ARTICLE

MOTHER Study: A Multicenter Observational, Retrospective Study to Determine Coorelation Between Physical CHaracteristics and Ovarian REserve Markers in Sub-feRtile Women

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Abstract

Background The physical characteristics which are known to affect the ovarian reserve are age, body mass index (BMI), occupational exposures, age at menarche and menstrual cycle length. A correlation between different physical characteristics and the ovarian reserve will help to identify areas which need to be tackled to increase the chances of fertility of women in India.

Methods In this retrospective, observational study, namely the MOTHER Study, data of women between 18 and 45 years of age, attending the selected fertility centers across different states in India were taken for evaluation. Demographic information along with information on factors potentially related to fertility like age of menarche, menstrual cycle length and occupational factors were collected by review of medical records at screening visit. Most recent AMH assay and antral follicle count (AFC) where the subject has not taken any contraceptives 12 months prior to the test were collected.

Results Age of woman, years of marriage, years of infertility and smoking have shown effect on ovarian reserve testing like AMH and AFC. The other physical characteristics which were evaluated and considered to affect the ovarian reserve like body mass index BMI, occupational exposures, age at menarche and menstrual cycle length have not shown statistically significant correlation.

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Conclusion Age of woman and years of infertility are inversely proportional to ovarian reserve markers, namely AMH and AFC. Addictions like smoking and alcohol affect ovarian reserve.

Keywords Age of woman · AFC · AMH · Ovarian reserve · Infertility

Introduction

Infertility is a medical problem that affects 15–20% of couples in reproductive age group [1]. In the recent times infertility has emerged as a serious health problem in India [2].

The primary function of the female ovary is to produce mature and viable oocytes for fertilization. At birth, the ovary contains about two million oocytes. This available reserve of oocytes is termed "the ovarian reserve (OR)." OR refers to the number and quality of oocytes which, at any given age, are available to produce a dominant follicle during the late follicular phase of the menstrual cycle. It has a significant effect on the fertility of the couple because as the ovary ages, the ovarian reserve declines. The determination of OR is important in the assessment and treatment of infertility [1].

The goal of OR testing is to add more prognostic information to the counseling and planning process so as to help couples choose the best available treatment option. [3] It may also help to assess the likely success of the assisted reproductive technique (ART) such as in vitro fertilization (IVF). There are many serum and ultrasound markers which can reflect the ovarian reserve. Of these, there are two markers which have been studied to better reflect ovarian reserve; they are anti-mullerian hormone assessment (AMH) and AFC [4].

Majority of AMH is secreted by the primary and preantral follicles. The levels are gonadotropin independent and therefore a more consistent measure of ovarian reserve than FSH. Low AMH has been associated with natural aging and infertility [4–6].

AFC is an ultrasound marker of ovarian aging. Transvaginal ultrasound on day 2–3 of menstrual cycle gives better idea of antral follicle count and thus the ovarian reserve.

The physical characteristics which are known to affect the ovarian reserve are age, body mass index (BMI), occupational exposures, age at menarche and menstrual cycle length [7–9] .

A correlation between different physical characteristics and the ovarian reserve will help to identify areas which need to be tackled to increase the chances of fertility of women in India. India is a poor resource country and all the patients attending the fertility centers cannot afford costly treatments to optimize their fertility. Any factor which can increase their fertility can reduce their financial and emotional burden.

Methods

It is a multicenter, observational and retrospective study of sub fertile women attending the selected fertility centers distributed across India, meeting the following study eligibility criteria. The MOTHER Study has been conducted in nine centers in different zones of India with the support of the Federation of Obstetric and Gynecological Societies of India (FOGSI) and ethics committee approval has been obtained from the Royal Pune Independent Ethics Committee, India with CTRI number CTRI/2018/12/016,772 and was registered on 21/12/2018.

Inclusion Criteria

1. Women between 18 and 45 years of age;
2. Not attained menopause;
3. Unable to conceive in last 12 months (at time of study consent);
4. Regular menstrual cycles with length of 25–35 days with ≤ 4 days difference between cycles;
5. Presence of both ovaries;
6. Willing and able to sign the study informed consent form.

Exclusion Criteria

1. Presence of gynecological disorders such as menorrhagia or dysfunctional uterine bleeding;
2. History of ovarian surgery;
3. Irregular menstruation (interval: less than 21 days or more than 45 days);
4. History of hypertension (controlled or uncontrolled);
5. History of taking injectable hormonal contraception in the preceding year or hormonal therapy/herbal product in last 12 months prior to most recent AMH or AFC test;
6. Malignancy or exposure to cytotoxic drugs and pelvic radiotherapy, endocrinological disorders, including abnormal prolactin, TSH or diabetes.

Total nine study centers with 422 subjects had participated in the study. The centers were from New Delhi, Mumbai, Guwahati, Chennai, Indore, Trichy, Islampur, Bhopal and Tumkur.

On screening visit (day 0) consent was obtained from each enrolled woman. Data was recorded from medical records of the patient available at the study site. Any study

specific information missing in the medical records, was collected in pending data collection visit (within 7 days of screening visit).

This second visit was also performed over the telephone and the conversation was recorded on subject medical record.

The medical records were reviewed for a cutoff period of one year prior to the date of informed consent and study specific data were collected as given below:

1. Height, weight and BMI value.
2. AMH test result
3. AFC result.

If most recent data were not available, these measurements were done at screening visit.

4. Demographic information along with information like age of menarche, menstrual cycle length and occupational factors, etc. was collected and recorded on the case report form.

The study data was analyzed using recommended version of SPSS software. The database created was subjected to linear regression models to examine the association of the ovarian reserve markers AMH and AFC with the physical characteristics like age, BMI, occupational exposures, age at menarche and menstrual cycle length.

Results

In the demographic history most of the women were of 20–45 age. The urban (51.07%) as well as rural (32.35%) population was covered with 16% of semi-urban women. 16% study population was having professional background while almost 51.42% women were home makers. More than 65% women were graduates and had non-vegetarian diet pattern (Table 1).

When the behavioral pattern was studied almost 99% women had never smoked (Table 2) nor consumed alcohol, though significant reduction of ovarian reserve was observed in small population of smokers (Table 10).

Primary infertility was the most common complaint and in that ovarian causes, male factor and tubal factor were on the rise after the unexplained variety, together contributing to almost 90.76% causes of infertility. (Table 3) Mean body mass index of study population was 25.75. The obstetric history and menstrual pattern is shown in Tables 4 and 5, respectively (Table 6).

The AFC calculated on day 2 or 3 of menstrual cycle was normal in 92.64% cases (390 women). It was poor in 31 cases i.e., 07.31% of study population. Almost similar findings were found in case of AMH estimations which showed

Table 1 Demographic history

Parameters	Frequency (%)
Age in years * (n = 422)	30.81 ± 4.84 20–45 years
Locality	
Local	355 (84.12)
Immigrant	67 (15.88)
Type of Locality[#]	
Urban	191 (51.07)
Rural	121 (32.35)
Semi urban	62 (16.58)
Occupation	
Professional	70 (16.59)
Semi professional	39 (9.24)
Semi	23 (5.45)
Semi skilled	19 (4.50)
Unskilled	2 (0.47)
Unemployed	48 (11.37)
Farmer	3 (0.71)
Laborer	1 (0.24)
Home maker	217 (51.42)
Education	
Post graduate	83 (19.67)
Graduate	203 (48.10)
Higher secondary school	82 (19.43)
School 5–10 Y	41 (9.72)
School < 5 Y	10 (2.37)
Illiterate	3 (0.71)
Diet[$]	
Vegetarian	126 (33.78)
Non Vegetarian	247 (66.22)

*Mean ± SD with Range; [#]Data is missing for 48 cases, [$]Data is missing for 49 cases

Table 2 Behavioral history

Parameters	Frequency (%)
History of smoking	
Current	3 (0.71)
Never	419 (99.29)
Years of smoking	
10-Years	2
5- Years	1
History of alcohol[^]	
Current	2 (0.48)
Never	419 (99.52)

^Data is missing for one case

Table 3 Infertility history

Parameters	Frequency (%)
Years of Marriage* (*N* = 373)	5.81 ± 3.92 1–28 Years
Years of Infertility* (*N* = 418)	4.66 ± 3.60 0.5–19 Years
Duration of sexual activity without contraception (Months)* (*N* = 422)	51.77 ± 44.50 1.5–228 Months
Type of infertility	
Primary	314 (74.41)
Secondary	108 (25.59)
Cause of infertility	
Combined factor	14 (3.32)
Male	70 (16.59)
Not known	3 (0.71)
Ovarian	86 (20.38)
Sexual dysfunction	6 (1.42)
Tubal	52 (12.32)
Unexplained	175 (41.47)
Uterine	16 (3.79)
Treatment for infertility	
Yes	263 (62.32)
No	159 (37.68)
Contraceptive usage in 1Year	
Yes	2 (0.47)
No	420 (99.53)

*Mean ± SD with range

normal results in 91.71% cases. Values showing poor ovarian reserve (low AMH) were noted in 8.29% (Tables 7 and 8).

Univariate logistic regression was done. The outcome variable was AFC group (Normal/Poor reserve). Here age was the only factor which was associated with the outcome variable. (Table 9) If there was a one unit increase in age then the odds of being in the poor reserve group increased by 1.12 units with the 95% CI (1.04–1.208) which does not include 1 in the CI. Also the *P* value is statistically significant ($P = 0.002$) ($P < 0.05$). All other independent factors don't have any association with the outcome variable. When the behavioral pattern was studied almost 99% women had never smoked. As depicted below in Table 10, current smokers were compared with never smokers. The odds of being in the poor reserve group (based on the AF count) is 26.82 times more for the smokers as compared to non-smokers with 95% CI and the *P* value is 0.008 ($P < 0.05$), which is statistically significant. Thus, smoking is one of the determinants of reducing ovarian reserve.

The variables such as years of marriage and years of infertility were associated with the outcome variable. If the marriage year has increased by one unit then the odds of being in the poor reserve group increased by 1.104 units with *P* value = 0.018 ($P < 0.05$) and it is statistically significant.

Table 4 Menstrual and obstetric history

Parameters	Frequency (%)
Age at Menarche (*N* = 422)*	12.91 ± 1.16 10–19 y
Menstrual cycle@	
Regular	324 (87.10)
Irregular	48 (12.90)
Gravida	
0	372 (88.15)
1	36 (8.53)
2	9 (2.13)
3	4 (0.95)
6	1 (0.24)
Para	
0	382 (90.52)
1	35 (8.29)
2	5 (1.18)
Living	
0	391 (92.65)
1	30 (7.11)
2	1 (0.24)
Abortion	
0	346 (81.99)
1	54 (12.80)
2	15 (3.55)
3	4 (0.95)
4	1 (0.24)
5	1 (0.24)
6	1 (0.24)

Table 5 Body measurements

Parameters	N	Mean(SD)	Range
Height (cm)	422	155.48(7.73)	120–174
Weight (kg)	422	61.3(11.41)	36–107.6
Body Mass Index(BMI)	422	25.75(5.12)	12.55–59.5

Table 6 AFC categories

AFC	Frequency (%)
Normal reserve	390(92.64)
Poor reserve	31(7.36)
Total	421(100)

Table 7 AMH categories

AMH	Frequency (%)
Normal Reserve	387(91.71)
Poor Reserve	35(8.29)
Total	422(100)

Table 8 AFC group as an outcome variable with demographic details

Parameters	Frequency (%)	Odds Ratio	P value	95% CI
Age in years	421	1.12	0.002 (S)	1.04–1.208
Locality				
Local*	355 (84.12)	1		0.376–2.75
Immigrant	67 (15.88)	1.017	0.973	
Type of Locality				
Urban*	191 (51.07)	1		
Rural	121 (32.35)	0.9375	0.883	0.396–2.214
Semi Urban	62 (16.58)	0.388	0.218	0.086–1.75
Occupation				
Professional*	70 (16.59)	1		
Semi professional	39 (9.24)	1.207	0.840	0.192–7.55
Skilled	23 (5.45)	2.12	0.425	0.332–13.59
Semi skilled	19 (4.50)	4.1875	0.097	0.77–22.71
Unskilled	2 (0.47)	NA	NA	NA
Unemployed	48 (11.37)	2.59	0.207	0.59–11.42
Farmer	3 (0.71)	11.16	0.076	0.77–160.37
Laborer	1 (0.24)	NA	NA	NA
Home maker	217 (51.42)	1.66	0.431	0.468–5.93
Education				
Post graduate*	83 (19.67)	1		
Graduate	203 (48.10)	0.882	0.807	0.323–2.406
Higher secondary school	82 (19.43)	0.833	0.771	0.244–2.845
School 5–10 Years	41 (9.72)	1.78	0.365	0.51–6.22
School < 5 Years	10 (2.37)	1.425	0.755	0.153–13.21
Illiterate	3 (0.71)	6.41	0.151	0.505–81.37
Diet				
Vegetarian*	126 (33.78)	1		
Non Vegetarian	247 (66.22)	0.75	0.504	0.328–1.72

*Reference category, *S* Significant

In the above table, univariate logistic regression was done. The outcome variable is AFC group (Normal / Poor reserved). Here the age is the only factor which is associated with the outcome variable. If there is a one unit increase in age then the odds of being in the poor reserved group increases by 1.12 units with the 95% CI (1.04–1.208) which does not include 1 in the CI. Also the P value is statistically significant. $P = 0.002 < 0.05$. All the other independent factors do not have any association with the outcome variable

Table 9 AFC group as an outcome variable with behavioral history

Parameters	Frequency (%)	Odds Ratio	P value	95% CI
History of smoking				
Current	3 (0.71)	26.82	0.008 (S)	2.36–304.708
Never*	419 (99.29)	1		
History of alcohol				
Current	2 (0.48)	NA		
Never	419 (99.52)			

*Reference category; *NA* variable is omitted because of few numbers *S* Significant

In the above table current smokers were compared with never smokers. The odds of being in the poor reserved group (based on the AF count) is 26.82 times more for the smokers as compared to non-smokers with 95% CI and the *P* value is $0.008 < 0.05$, which is statistically significant

Table 10 AFC group as an outcome variable with infertility history

Parameters	Frequency (%)	Odds Ratio	P value	95% CI
Years of marriage	373	1.104	0.018 (S)	1.016–1.199
Years of infertility	418	1.097	0.039 (S)	1.004–1.19
Duration of sexual activity without contraception (Months)	422	1.005	0.119	0.998–1.013
Type of infertility				
Primary *	314 (74.41)	1		
Secondary	108 (25.59)	1.202	0.655	0.535–2.698
Cause of infertility				
Combined factor *	14 (3.32)	1		
Male	70 (16.59)	0.582	0.650	0.056–6.04
Not known	3 (0.71)	NA	NA	NA
Ovarian	86 (20.38)	1.71	0.623	0.20–14.51
Sexual dysfunction	6 (1.42)	6.50	0.166	0.459–91.92
Tubal	52 (12.32)	1.083	0.945	0.11–10.54
Unexplained	175 (41.47)	0.79	0.831	0.094–6.68
Uterine	16 (3.79)	0.866	0.922	0.049–15.27
Treatment for infertility				
Yes *	263 (62.32)	1		
No	159 (37.68)	0.556	0.166	0.242–1.27
Contraceptive usage in 1Year				
Yes	2 (0.47)			
No	420 (99.53)	NA		

*Reference category, *NA* variable is omitted because of few numbers, *S* Significant

In the above table, the variables such as years of marriage and years of infertility were associated with the outcome variable. If the marriage year has been increased by one unit then the odds of being in the poor reserved group increases by 1.104 units with P value $0.018 < 0.05$ and it is statistically significant. Similarly if the year of infertility has increased by one unit then the odds of being in the poor reserved group increases by 1.097 units with the significant P value $0.039 < 0.05$ and all the other variables were not associated with the outcome variable

Similarly, if the year of infertility has increased by one unit then the odds of being in the poor reserve group increases by 1.097 units with the significant P value = 0.039 ($P < 0.05$). All the other variables were not associated with the outcome variable. (Table 11) The other factors like causes of infertility, whether couple had received treatment for infertility have not shown statistical significance when its relation was studied with AFC.

The other factors which were studied have shown no statistical significant impact on antral follicle count and hence the ovarian reserve.

In our study there was mixed population ranging from those trying to conceive for first time to multigravidas and cases of multiple abortions who were cases of secondary infertility. In Tables 12, 13, none of the obstetric parameters were associated with the outcome variables of antral follicle count and hence ovarian reserve or vice versa.

Age at menarche was also the factor of importance from ovarian reserve point of view but in our study both age at menarche and pattern of menstrual cycle were not associated with the outcome variable.

It is believed that body mass index affects ovarian reserve but from Table 14 it is clear that in our study height, weight (independently) and BMI were not associated with the outcome variable. An cases of ovarian surgery (including drilling) and irregular menstrual cycles were excluded many classic cases of polycystic ovary syndrome were not included so BMI is not found to correlate with antral follicle count of non-metabolic cases of infertility (Table 15).

After univariate logistic regression with the outcome variable-AMH (Normal/Poor reserve), the age of woman and the participants' locality were the only factors which were associated with the outcome variable. If there is a one unit increase in age then the odds of being in the poor reserve group increases by 1.18 units with the 95% CI (1.104–1.278) which does not include 1 in the CI. Also the P value is statistically significant. $P = 0.0001$ ($P < 0.05$). As compared to local residents the odds of being in the poor reserve group is 2.709 times more for the immigrant residents. All the other independent factors do not have any association with the outcome variable.

Table 11 AFC group as an outcome variable with obstetric history

Parameters	Frequency (%)	Odds Ratio	*P* value	95% CI
Gravida				
0*	372 (88.15)	1		
1	36 (8.53)	0.78	0.743	0.177–3.43
2	9 (2.13)	3.79	0.107	0.749–19.18
3	4 (0.95)	4.42	0.205	0.44–44.02
6	1 (0.24)	NA		
Para				
0*	382 (90.52)	1		
1	35 (8.29)	1.76	0.319	0.577–5.37
2	5 (1.18)	3.413	0.280	0.36–31.65
Living				
0	391 (92.65)	NA		
1	30 (7.11)			
2	1 (0.24)			
Abortion				
0*	346 (81.99)	1		
1	54 (12.80)	1.75	0.247	0.67–4.51
2	15 (3.55)	1	0.99	0.12–7.94
3	4 (0.95)	4.66	0.190	0.46–46.65
4	1 (0.24)	NA		
5	1 (0.24)	NA		
6	1 (0.24)	NA		

*Reference category; *NA* variable is omitted because of few numbers

In the above table, none of the obstetric parameters were associated with the outcome variable

Table 12 AFC group as an outcome variable with menstrual history

Parameters	Frequency (%)	Odds Ratio	P value	95% CI
Age at menarche	422	0.804	0.208	0.57–1.12
Menstrual cycle				
Regular*	324 (87.10)	1		
Irregular	48 (12.90)	1.42	0.494	0.517–3.92

*Reference category

In the above table, none of the parameters related with menstrual history were associated with the outcome variable

Table 13 AFC group as an outcome variable with body measurements

Parameters	N	Odds ratio	*P* value	95% CI
Height	422	0.99	0.682	0.946–1.03
Weight	422	0.99	0.950	0.967–1.03
Body Mass Index(BMI)	422	1.004	0.911	0.935–1.07

In the above table, none of the body measurement parameters were associated with the outcome variable

In Table 16, none of the parameters related with the behavioral history were associated with the outcome variable.

In table, the variables such as years of infertility and duration of sexual activity without contraception were associated with the outcome variable. If the year of infertility increases by one unit then the odds of being in the poor reserve group increases by 1.114 units with the significant '*P*' value of 0.009 (<0.05). If the duration of sexual activity without contraception increases by 1 unit then the odds of reserve increase by 1.012 units with *P* value 0.0001 ($P<0.05$). All the other variables were not associated with the outcome variable (Table 17).

In Tables 18 and 19 none of the parameters were associated with the outcome variable.

Discussion

Various factors of infertility have been discussed and are predicted to affect the ovarian reserve.

Age of menarche, age at marriage and body mass index are the most frequently studied parameters.

Table 14 AMH group as an outcome variable with demographic details

Parameters	Frequency (%)	Odds ratio	*P* value	95% CI
Age in years	422	1.18	0.0001 (S)	1.104–1.278
Locality				
Local*	355 (84.12)	1		
Immigrant	67 (15.88)	2.709	0.011 (S)	1.257–5.83
Type of locality				
Urban *	191 (51.07)	1		
Rural	121 (32.35)	1.636	0.267	0.686–3.9
Semi Urban	62 (16.58)	0.832	0.783	0.224–3.083
Occupation				
Professional*	70 (16.59)			
Semi professional	39 (9.24)			
Skilled	23 (5.45)			
Semi-skilled	19 (4.50)	NA	NA	
Unskilled	2 (0.47)			NA
Unemployed	48 (11.37)			
Farmer	3 (0.71)			
Laborer	1 (0.24)			
Home maker	217 (51.42)			
Education				
Post graduate*	83 (19.67)	1		
Graduate	203 (48.10)	1.056	0.906	0.423–2.63
Higher secondary school	82 (19.43)	0.55	0.366	0.156–1.979
School 5–10 Years	41 (9.72)	1.17	0.808	0.323–4.26
School < 5 Years	10 (2.37)	1.206	0.868	0.132–10.95
Illiterate	3 (0.71)	5.42	0.189	0.435–67.61
Diet				
Vegetarian *	126 (33.78)	1		
Non Vegetarian	247 (66.22)	0.696	0.400	0.300–1.616

*Reference category, *NA* variable is omitted because of few numbers, *S* Significant

In the above table, univariate logistic regression was done. The outcome variable is AMH group (Normal/Poor reserved). Here the age and the participants' locality are the only factors which were associated with the outcome variable. If there is a one unit increase in age then the odds of being in the poor reserved group increases by 1.18 units with the 95% CI (1.104–1.278) which does not include 1 in the CI. Also the *P* value is statistically significant. $P = 0.0001 < 0.05$. As compared to local residents the odds of being in the poor resident group is 2.709 times more for the immigrant residents. All the other independent factors do not have any association with the outcome variable

Table 15 AMH group as an outcome variable with behavioral history

Parameters	Frequency (%)	Odds Ratio	*P* value	95% CI
History of Smoking				
Current	3 (0.71)	5.66	0.161	0.5–64.05
Never *	419 (99.29)	1		
History of Alcohol				
Current	2 (0.48)			
Never	419 (99.52)	NA		

*Reference category; *NA* variable is omitted because of few numbers, *S* Significant

In the above table, none of the parameters related with the behavioral history were associated with the outcome variable

Table 16 AMH group as an outcome variable with infertility history

Parameters	Frequency (%)	Odds Ratio	*P* value	95% CI
Years of marriage	373	1.038	0.426	0.945–1.141
Years of infertility	418	1.114	0.009 (S)	1.0269–1.208
Duration of sexual activity without contraception (Months)	422	1.012	0.0001 (S)	1.005–1.019
Type of infertility				
Primary*	314 (74.41)	1		
Secondary	108 (25.59)	1.006	0.986	0.456–2.222
Cause of infertility				
Combined Factor*	14 (3.32)	1		
Male	70 (16.59)	0.176	0.098	0.022–1.37
Not Known	3 (0.71)	NA	NA	NA
Ovarian	86 (20.38)	0.701	0.673	0.134–3.646
Sexual Dysfunction	6 (1.42)	6	0.109	0.67–53.68
Tubal	52 (12.32)	0.782	0.780	0.139–4.378
Unexplained	175 (41.47)	0.441	0.319	0.0885–2.204
Uterine	16 (3.79)	0.4	0.476	0.0322–4.959
Treatment for infertility				
Yes *	263 (62.32)	1		
No	159 (37.68)	0.316	0.012 (S)	0.128–0.780
Contraceptive usage in 1Year				
Yes	2 (0.47)			
No	420 (99.53)	NA		

*Reference category, *NA* variable is omitted because of few numbers, *S* Significant

In the above table, the variables such as years of infertility and duration of sexual activity without contraception were associated with the outcome variable. If the year of infertility has increased by one unit then the odds of being in the poor reserved group increases by 1.114 units with the significant *P* value $0.009 < 0.05$. Also the duration of sexual activity without contraception increases by 1 unit then the odds of reservation increase by 1.012 units with P value $0.0001 < 0.05$ and all the other variables were not associated with the outcome variable

The MOTHER study demonstrates that age of the woman and years of infertility have inverse relationship with ovarian reserve tests like anti-mullerian hormone (AMH) and antral follicle count (AFC). In the study by Erica et al. [10] the age of the female correlates with levels of AMH. The comparative study by Hvidman et al. in 2016 on ovarian reserve testing of women with infertility below age 40 with women of the same age with no history of infertility shows no difference in the results of both AMH and AFC. This study concludes that women of the same age group have similar ovarian reserve irrespective of fertility status. [11] The MOTHER study has shown that increasing age in infertile women is associated with reduced ovarian reserve markers $P = 0.002$ ($P < 0.05$).

In our study, years of marriage and years of infertility are associated with a poor reserve *P* value = 0.018 ($p < 0.05$). This, when studied in depth again correlates with age of women.

The other factors like cause of infertility and couple receiving treatment for infertility do not show statistical significance in relation to AFC and AMH. The exclusion criteria have also affected these observations as most of the classic cases of PCOS on treatment and those approaching POF have been excluded.

Table 17 AMH group as an outcome variable with obstetric history

Parameters	Frequency (%)	Odds Ratio	P value	95% CI
Gravida				
0*	372 (88.15)	1		
1	36 (8.53)	2.55	0.055	0.978–6.674
2	9 (2.13)	1.59	0.664	0.1925–13.24
3	4 (0.95)	4.25	0.216	0.428–42.34
6	1 (0.24)	NA		
Para				
0*	382 (90.52)	1	0.968	0.297–3.53
1	35 (8.29)	1.025		
2	5 (1.18)	NA		
Living				
0	391 (92.65)	1		
1	30 (7.11)	1.246	0.729	0.358–4.33
2	1 (0.24)	NA		
Abortion				
0*	346 (81.99)	1		
1	54 (12.80)	1.75	0.211	0.725–4.26
2	15 (3.55)	0.843	0.872	0.106–6.66
3	4 (0.95)	NA		
4	1 (0.24)	NA		
5	1 (0.24)	NA		
6	1 (0.24)	NA		

*Reference category *NA* variable is omitted because of few numbers

In the above table, none of the obstetric parameters were associated with the outcome variable

Table 18 AMH group as an outcome variable with menstrual history

Parameters	Frequency (%)	Odds ratio	*P* value	95% CI
Age at menarche	422	0.979	0.892	0.725–1.322
Menstrual cycle				
Regular*	324 (87.10)	1		
Irregular	48 (12.90)	1.57	0.347	0.612–4.029

*Reference category

In the above table, none of the parameters related with menstrual history were associated with the outcome variable

Table 19 AMH group as an outcome variable with body measurements

Parameters	N	Odds ratio	*P* value	95% CI
Height	422	0.99	0.892	0.953–1.041
Weight	422	0.985	0.366	0.954–1.017
Body mass index	422	0.964	0.339	0.895–1.038

In the above table, none of the body measurement parameters were associated with the outcome variable

The next parameter analyzed is the effect of body mass index [BMI] on the ovarian reserve tests. In our study height, weight and BMI are not affecting ovarian reserve tests. This is in contrast to various studies which show significant association between body size and ovarian reserve tests. [10] In the study by Bernardi et al. [12] excessive obesity is associated with a compromised ovarian reserve. The study by H. Irene Su shows that AMH is lower in obese women in comparison to women with normal weight but AFC is not affected by body size [13] . Our study excludes women with PCOS and hence ovulatory infertility due to obesity is excluded. In the study by Rich Edwards, ovulatory infertility is related to overweight women and a sedentary lifestyle [14].

The effect of occupational exposures like moving or lifting heavy objects, level of physical exertion and work shifts on ovarian reserve tests are studied in this study. They do not show any effect on the ovarian reserve tests.

The baseline reproductive characteristics of the study population like age at menarche and menstrual cycle patterns are analyzed in this study. They show no effect on the ovarian reserve tests in our study. In the study by Gizzo et al. the menstrual cycle diary is more predictive than chronological age for determining ovarian reserve and age. In women who are older than 35 years, lengthening of menstrual cycle is considered as a marker of ovarian aging. Chronological age is more accurate for predicting pregnancy [15]. In the study by Erica et al. [10] menstrual cycle

length of more than 35 days is associated with increased AMH .The study by Zhu.R et al. shows that AMH and AFC positively correlate with menstrual cycle length (MCL). A longer MCL (more than 35 days and between 25–34 days) shows an association with increased AMH in this study. A shorter MCL is associated with decreased AMH. MCL is associated with age factor also but is not associated with lifestyle factors [16].

Age at menarche does not show any association with ovarian reserve tests in the MOTHER Study. In the study by Ramona et al. age at menarche is associated with a poor ovarian reserve in later ages. In this study by Ramona et al. [17] occurrence of menarche is related to follicular size and speed of follicular recruitment which in turn predicts poor ovarian reserve in later life.

In our study, the behavior of women like smoking and alcohol usage and their effects on ovarian reserve tests were studied. 99% of women are non-smokers and have never consumed alcohol. In this small population of smokers there is a significant reduction in ovarian reserve mainly affecting AMH and to some effect AFC.

MOTHER study has various limitations like not being a comparative study between a fertile and an infertile population of women with respect to ovarian reserve tests. The sample size is not equal from all zones in the country. This was an attempt to find out the fertility potential and factors affecting it in various population zones of India.

Conclusion

Age of woman and years of infertility are inversely proportional to ovarian reserve markers, namely AMH and AFC. Addictions like smoking and alcohol affect ovarian reserve. Further comparative and prospective studies are needed. But MOTHER study has given a clear message to Indian women to avoid late marriages, late conceptions and all addictions.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval Royal Pune Independent Ethics Committee, India with CTRI number CTRI/2018/12/016772 and was registered on 21/12/2018.

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