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Original Research Article

Awareness of PCOS (polycystic ovarian syndrome) in adolescent and young girls

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is an endocrine disorder which affects the adolescent girls It affects 5% to 10% of women in their reproductive age. Awareness and accurate diagnosis is the first step in managing PCOS as it improves quality of life of the patient. The study was conducted to assess the knowledge on PCOS among the medical students.

Methods: Survey of 200 girls was done to assess the knowledge on the polycystic ovarian syndrome among the medical students of different colleges studying in 1st, 2nd, and 3rd year. The data was collected from the students by using structured questionnaire.

Results: In present study, 51% girls had normal BMI, 19.5% were overweight, 16.5% were obese while 13% were underweight. 33.5% females had acne, 16% had irregularity of menses, 5% had hirsutism while 2% had infertility. In present study, 33% adolescent and young girls had information about PCOS from teacher, 19% got information from friend, 11.5% got information from a doctor, 3.5% got information from newspaper while 5% got information from internet. 28% adolescent and young girls were unaware of PCOS.

Conclusions: Thorough knowledge of the disorder and counseling for adolescents should be included in the curriculum which will provide awareness towards the disorder and lifestyle modification. Accurate diagnosis at a younger age may be a key.

Keywords: Adolescent girls, BMI, PCOS, Young girls

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a condition in which woman has an imbalance of female sex hormones.[1] This may lead to changes in the menstrual cycle, cyst in the ovary, failure to conceive and other health problems.[1] It is a common health problem among teenagers and young women.[1] It affects 5% to 10% of women in their reproductive years. These problems cause infertility.[1] Research has suggested that PCOS may be related to increased insulin production. PCOS seems to run in families, too, so if someone in the family has it, they might be more likely to develop it.[1]

Although there is no cure for PCOS, there are several ways to treat and manage the condition.[1] If a girl is overweight, Weight loss can be very effective in lessening many of the health conditions associated with PCOS.[1]

Sometimes weight loss alone can restore hormone level to normal, causes many of the symptoms to disappear or become less severe. Healthy food habits and exercise helps to combat the weight gain.[1] India has witnessed about 30% rise in PCOS cases in the last couple of years. Lack of knowledge and lifestyle changes are considered to be the major factor leading to this phenomenon.[1] There

is a need to increase awareness among women so as to avoid major cases of fertility problems in the future.[1]

The prevalence has been increasing in the adolescent population.[2] In more than 40% of cases, PCOS is associated with obesity, as well as impaired glucose tolerance, type 2 diabetes, and the metabolic syndrome.[3]

While the pathophysiology of PCOS remains unclear, insulin resistance has been implicated as a major causative factor.[4] Accurate diagnosis of PCOS is of critical importance to public health, given the chronic nature of the disorder and its association with multiple health consequences.[3]

PCOS is being under evaluated and possibly underdiagnosed in the adolescent population.[3] Awareness of PCOS and its diagnosis must be increased among physicians caring for adolescent girls.[3] Given the high prevalence of PCOS, its short- and long-term effects on physical and mental health, and its costs to the health care system, one might wonder why there is such a lack of awareness about PCOS.[4]

There is an increasing awareness of PCOS among the adolescent population along with an increase in diagnosis and an increased incidence of established co-morbidities such as obesity and type 2 diabetes. The Poly Cystic Ovaries Syndrome is considered to be most prevalent of all endocrine disorders which women face.[5]

The diverse manifestations of PCOS start at an early age when a girl is maturing into a young woman.[6] it is important to make an early diagnosis in order to prevent early and late sequel of the syndrome.[6] PCOS may occur at a younger age in girls who develop early pubarche and thelarche. Therefore, the diagnosis and workup should be considered in young girls with risk factors suggestive of PCOS.[7] Increased awareness of PCOS in young females is needed.[7]

The study was conducted to assess the knowledge on the polycystic ovarian syndrome (PCOS) among the medical students of 1st, 2nd and 3rd year; to find the source of information; to find the prevalence and to educate them about polycystic ovarian syndrome.

METHODS

The survey was conducted on 200 medical students of 1st, 2nd and 3rd year of different colleges by using simple random sampling technique.

The data was collected by using structured knowledge questionnaire on PCOS.

The investigator obtained permission from the students, prior to the data collection and assured confidentiality to the subject to get their cooperation and explained the purpose of the study. The results were analyzed.

Data collection was as follows:

- Age
- Weight in kg and height in cm to calculate BMI
- Type of diet- Vegetarian or mixed diet
- Irregularity of menses
- Signs of hyperandrogenism-Hirsutism or acne
- Source of information-Teacher, doctor, friend, paper or internet
- Type of consultation-Dermatologist or gynaecologist or any other
- No. of diagnosed cases

Operational definitions

- Adolescent girls- 10-19 years (for present study 18-19 years).
- Young girls- 20-24 years.
- Body mass index-
  Normal: BMI =18-22.9 kg/m^2,
  Underweight: BMI <17.9 kg/m^2,
  Overweight: BMI >23 kg/m^2,
  Obese: BMI >25 kg/m^2 for girls above 18 years

RESULTS

In present study, 62.5% girls were young girls in the age group of 20-24 years while 37.5% girls were adolescent girls in the group of 18-19 years.

Table 1: Age group.

18-19 years	75	37.5
20-24 years	125	62.5

Adolescent girls were from 1st or 2nd year. Young girls were from 2nd or 3rd year. A few were from 4th year when they learn PCOS in syllabus.

Table 2: BMI (Body mass index).

<17.9 kg/m^2 underweight	26	13
18-22.9 kg/m^2 normal	102	51
>23 kg/m^2 overweigh	39	19.5
>25 kg/m^2 obese	33	16.5

In present study, 51% girls had normal BMI, 19.5% were overweight, 16.5% were obese while 13% were underweight. Overweight and obese girls are more prone for PCOS. Counselling was given and weight reduction was advised. Also, hormonal profile for thyroid, hyperandrogenism was suggested.

In present study, 51% girls were consuming pure vegetarian diet while 49% girls were consuming mixed (vegetarian and non-vegetarian) food. Advice regarding healthy food was given.

Table 3: Type of diet.

Type of diet	No. of girls	Percent
Mixed (veg and non-veg)	98	49
Vegetarian	102	51

Table 4: Problems in adolescent and young girls.

Problems	No. of patients	Percent
Irregularity of menses	32	16
Hirsutism	10	5
Acne	67	33.5

In present study, 33.5% girls had acne, 16% had irregularity of menses, 5% had hirsutism. Hormonal profile for hyperandrogenism was suggested.eg. Serum Testosterone, Serum DHEAS. If these levels were high, the girls were referred to endocrinologist for further management.

Table 5: Source of information about PCOS.

Source of information about PCOS	No. of patients	Percent
Teacher	66	33
Friend	38	19
Doctor	23	11.5
Paper	7	3.5
Internet	10	5
No information	56	28

In present study, 33% adolescent and young girls had information about PCOS from teacher, 19% got information from friend, 11.5% got information from a doctor, 3.5% got information from newspaper while 5% got information from internet. 28% adolescent and young girls were unaware of PCOS.

Being medical students, main source of information was teacher. Still 28% of girls were unaware about PCOS when they are in first or second year. So, 72% girls were aware of PCOS while 28% were unaware of PCOS.

Table 6: Type of doctor attended.

Type of doctor attended	No. of girls	Percent
Dermatologist	19	9.5
Gynaecologist	9	4.5
Ayurvedic	2	1
Homeopathic	2	1

In this study, 9.5% girls consulted dermatologist for either hirsutism or acne, 4.5% consulted gynaecologist for irregularity of menses, 1% girls sought ayurvedic treatment while 1% opted for homeopathy. Amongst 16% girls who consulted a doctor, 9% girls did ultrasonography and blood investigations. Amongst them, 6% girls were diagnosed as having PCOS. So, prevalence of PCOS in present study is 6%.

Table 7: Prevalence of PCOS.

	No. of girls	Percent
Consultation with doctor	32	16
Investigations done	18	9
Proved PCOS	12	6

DISCUSSION

Age distribution

The present study was conducted on 200 medical students by using simple random sampling technique. In current study, 62.5% girls were young girls in the age group of 20-24 years while 37.5% girls were adolescent girls in the group of 15-19 years. Sunanda B et al revealed that 85% of the samples were in the age group of 21-25 years, 75% of the samples were Christians, 82% of the samples were consuming mixed diet, and 92% samples had regular menstrual cycle.[1] Sills S et al found that from 657 participants, the majority (63%) were between 26-34 years.[2] Moghul S found that the increasing trend of PCOS is predominantly seen in the age group 15 to 30 years.[8]

BMI (Body mass index)

In present study, 51% girls had normal BMI, 19.5% were overweight, 16.5% were obese while 13% were underweight. Sanchez N et al found that 32% were obese.[4]

Type of diet

In present study, 51% girls were consuming pure vegetarian diet while 49% girls were consuming mixed (vegetarian and non-vegetarian) food.

Problems in girls

In present study, 33.5% females had acne, 16% had irregularity of menses,5% had hirsutism. Sanchez N et al found that 32% were obese, 21% had acne, and 7% were hirsute (all associated with elevated testosterone levels and PCO appearance on ultrasound.[4] Joshi et al found that history of oligomenorrhea had a positive predictive value of 93.3% and negative predictive value of 86.7% to detect a possible case of PCOS.[6]

Source of information

In present study, 33% adolescent and young girls had information about PCOS from teacher, 19% got information from friend, 11.5% got information from a doctor, 3.5% got information from newspaper while 5% got information from internet. 28% adolescent and young girls were unaware of PCOS. 72% girls were aware of PCOS while 28% were unaware of PCOS. Sunanda B et al found that 76% of the samples were with average knowledge and 10.7% with good knowledge regarding

polycystic ovarian syndrome.[1] Sills ES et al found that more than 97% (n =638) of the respondents were familiar with PCOS, while 1.9% had not been told about PCOS, and <1% were uncertain.[2]

Sills ES et al found that those subjects between age 26-34 were significantly more aware of PCOS than any other age group.[2] Gul S et al found that only 20 out of 177 women had any knowledge about this syndrome. Out of these 20 women 11 were those who had degrees in Medical Sciences.[6] Gul S. et al found that 10% of women knew about this disorder.[5]

Consultation for complaints

In this study, 9.5% girls consulted dermatologist for either hirsutism or acne, 4.5% consulted gynaecologist for irregularity of menses, 1% girls sought ayurvedic treatment while 1% opted for homeopathy. Sills ES et al found that Physicians were the most common provider of PCOS information for all study participants, irrespective of age.[2]

Prevalence of PCOS

In current study amongst 16% girls who consulted a doctor, 9% girls did ultrasonography and blood investigations. Amongst them, 6% girls were diagnosed as having PCOS. So, prevalence of PCOS in present study is 6%. Sanchez N et al found that the prevalence of PCOS in adult women aged 18-45 years in the US is estimated to be 6.6%.[4]

Joshi B et al found that globally, prevalence estimates of PCOS are highly variable, ranging from 2.2% to as high as 26%.[6] Joshi B et al found that the prevalence of PCOS was 22.5% by Rotterdam and 10.7% by Androgen Excess Society criteria.[6] Joshi B et al demonstrated that PCOS is an emerging disorder during adolescence and screening could provide opportunity to target the group for promoting healthy lifestyles and early interventions to prevent future morbidities.[6]

Shetty D found that around 10% of Indian women are affected with Polycystic Ovary Syndrome, commonly known as PCOS.[9] Choudhary N et al found that prevalence of PCOS in Indian adolescents is 9.13%.[10] Vaidya R et al found that according to World Health Organization, there are PCOS affected 116 million women worldwide in 2012 (3.4% of women).[11] Lakshmi KS et al found that the prevalence of PCOS at a tertiary care hospital was 32%.[12]

Radha P et al found that the rates of polycystic ovarian syndrome are high among Indian women compared to their Caucasian counterparts, with an estimated prevalence of 9.13% in Indian adolescents.[13] Radha P et al found that 20% of participants were diagnosed with PCOS. The proportion of PCOS was higher in urban population in comparison to rural counter parts.[13]

CONCLUSION

From this study, it is concluded that 72% of girls were aware of PCOS while 28% of girls were unaware of PCOS. Prevalence of PCOS in present study is 6%. Most common source of information about PCOS was teacher as the girls were medical students.

Girls who were having BMI more than 23 should be educated about its hazards and should be advised weight loss. Girls who had irregularity of menses and signs of hyperandrogenism should be investigated and must be managed accordingly.

Early diagnosis of PCOS and its prompt treatment will help the girls to improve quality of life and prevent further health hazards.

Recommendations

- Counseling for adolescents should be included in the curriculum which will provide an awareness towards the disorder and lifestyle modification.
- There is a need for intensified efforts in early detection.
- Accurate diagnosis at a younger age may be a key to preventing many of the long-term health consequences associated with this syndrome.

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Original Research Article

Anti-Mullerian hormone (AMH) as predictor of ovarian reserve

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ABSTRACT

Background: Anti-Müllerian hormone (AMH) is produced by the granulosa cells of preantral and small antral follicles and its levels can be assessed in serum. Since the number of ovarian follicles declines with increasing age, AMH levels might be used as a marker for ovarian ageing. Therefore, we studied the relationship between AMH levels and ovarian response during ovarian stimulation for In vitro fertilization.
Methods: A total of 100 patients who have undergone their ICSI treatment cycle using a GnRH antagonist protocol were retrospectively included. Co-relation between AMH and antral follicular count (AFC) was assessed.
Results: In present study, 36% patients had normal AMH, 18% patients were in low normal range, 5% patients had low values and 2% patients had very low values. 41% of patients had values in high range suggestive of PCOS. Amongst this, 21% had values between 4 to 8 ng/ml where we got good AFC count and good result in terms of pregnancy. 80% were good responders while 20% were poor responders. When we evaluated the relationship of retrieved oocyte counts with the parameters included, we found that only basal AMH levels and the number of antral follicles were statistically correlated.
Conclusions: High AMH levels correlated with low cancellation rates, retrieval of more eggs, higher live birth rates and a high chance for freezing of embryos. Low AMH levels (alone) do not predict low success rates in women under 35 years of age.

Keywords: Anti-mullerian hormone, Antral follicular count, Oocytes

INTRODUCTION

Ovarian reserve is defined as the functional potential of the ovary, and reflects the number and quality of the oocytes in the ovary at any given time.[1]

With the understanding that chronological age alone is an inadequate predictor of the ovarian reserve, multiple tests have been developed to assess ovarian function (i.e., "ovarian reserve" tests). Some of these tests include basal FSH, basal inhibin B, the clomiphene citrate (CC) challenge test, basal E_2, the GnRH challenge test, the ovarian antral follicle count (AFC) as assessed by transvaginal ultrasound examination, and serum levels of anti-Müllerian hormone (AMH). Although such tests are frequently labeled ovarian reserve tests, they are more accurately ovarian response tests.[2]

Anti-Müllerian hormone (AMH) is produced by the granulosa cells of preantral and small antral follicles and its levels can be assessed in serum. Since the number of ovarian follicles declines with increasing age, AMH levels might be used as a marker for ovarian ageing.[3]

Human female serum contains measurable amounts of AMH during the reproductive life span.[3] Since AMH is

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CERTIFICATE

To whom so ever it may concern

This is to certify that Dr. Chaitanya Ashok Shembekar MD (Obs & Gynae) has worked under me from 01/07/ 2001 to 30 June 2002 for the purpose of learning Ultrasound

I have no hesitation in saying that he carries excellent skills in performing obstetrical and gynaecological sonographies and has sound understanding of the subject .

DR. R. R. KHANDELWAL , MD (RADIOLOGICAL), FCD

Dr. R. R. KHANDELWAL
MD, FCD (Fellow in colour Dop
Thomas Jefferson University
Consultant Radiolo
Reg. No. MMC 655

KAILAS TOWERS BESIDES TARUN BHARA

solely produced in the growing ovarian follicles, serum levels may be used as a marker for ovarian reserve, representing the quantity and quality of the ovarian follicle pool.[3] The ovarian reserve, constituted by the size of the ovarian follicle pool and the quality of the oocytes therein, declines with increasing age, resulting in the decrease of a woman's reproductive function.[3]

Anti-Müllerian hormone seems to be the best endocrine marker for assessing the age-related decline of the ovarian pool in healthy women; thus, it has a potential ability to predict future reproductive lifespan. The most established role for AMH measurements is before in vitro fertilization is initiated, because AMH can be predictive of the ovarian response, namely poor and hyper-responses.[4]

Plasma AMH assessments are superior to FSH in identifying women with reduced ovarian reserve.[4] Anti-müllerian hormone assessment should be considered as a useful adjunct to FSH/oestradiol levels and antral follicle count when estimating ovarian reserve.[5]

It is widely accepted that the reduction of AMH levels in serum is the first indication of a decline in the follicular reserve of the ovaries.[6] AMH concentration remains stable throughout the menstrual cycle.[6] In conditions with high LH and normal or low FSH levels, as in PCOS, AMH concentrations are positively correlated with LH concentrations, while they are not negatively correlated with FSH.[6]

In a normal ovary, AMH works to slow and prevent the premature development of the follicles before they are mature – keeping the ovary from developing eggs prematurely.[7]

Present study was undertaken to determine the predictive value of antimüllerian hormone (AMH) as a marker for ovarian reserve.

METHODS

It was a retrospective analysis carried out at in vitro fertilization (IVF) clinic. A total of 100 patients who have undergone their ICSI treatment cycle using a GnRH antagonist protocol were retrospectively included.

All patients recruited for ICSI, irrespective of indications, were included in the study. On day 2 of a spontaneous cycle, patients underwent a transvaginal ultrasound examination to assess the number of antral follicles, measuring 2–5 mm and endometrial thickness. Patients with thin endometrium were recruited. On the same day a venous blood sample was obtained for the measurement of AMH, FSH, estradiol (E2) and inhibin B

Ovulation induction was initiated with recombinant FSH, 150–300 IU/day, depending on AMH, age and AFC. After more than three follicles larger than 18 mm were observed, 250 microgram of recombinant hCG was administered subcutaneously and 35 hours later oocyte retrieval was done under general anesthesia.

The study group was divided into two subgroups according to the number of oocytes retrieved. Patients with an oocyte count of five or more were considered good responders, and patients with less than five oocytes as poor responders. ICSI (intracytoplasmic sperm injection) was done in all patients.

The transfer of the embryos was performed 48 hours after the procedure. Four cell grade 1 embryos were transferred. A maximum of three embryos were transferred. On the 12th to 14th days of the transfer, a serum β-hCG test was performed to confirm pregnancy. To support the luteal phase, micronized progesterone was given.

The main outcome measures of the study were the number of oocytes retrieved i.e. ovarian response to stimulation. As described previously, poor response was defined as fewer than 4 oocytes obtained.

RESULTS

Maximum patients i.e. 42% patients were between 31-35 years. 29% patients were between 26-30 years, 16% patients were between 36-40 years, 12% patients were between 21-25 years while only 1% of patients were above 40 years of age.

Table 1: Age group.

21-25 years	12	12
26-30 years	29	29
31-35 years	42	42
36-40 years	16	16
>40 years	1	1

Table 2: Type of infertility.

Primary	74	74
Secondary	26	26

In present study, 74% of patients had primary infertility while 26% of patients had secondary infertility.

Table 3: Indication for ICSI.

Tubal factor	22	22
Male factor	20	20
PCOS	17	17
Endometriosis	5	5
Unexplained infertility	18	18
More than 1 factor	18	18

In present study, 22% of patients had tubal factor, 20% of patients had male factor, 17% of patients had polycystic ovarian syndrome (PCOS) while 5% patients had endometriosis. 18% of patients had unexplained infertility.

Table 4: Number of ICSI cycle.

No. of ICSI cycle	No. of patients	%
First	93	93
Second	3	3
Third	2	2
Fourth	2	2

In present study, 93% of patients had their first cycle of ICSI, 3% of patients had their second cycle of ICSI, 2% of patients had third cycle of ICSI and 2% of patients had their fourth cycle of ICSI.

Table 5: AMH levels.

	AMH levels	No. of patients	%
High	Over 4.0ng/ml	41	41
Normal	1.5 - 4.0ng/ml	36	36
Low normal range	1.0 - 1.5ng/ml	18	18
Low	0.5 - 1.0ng/ml	5	5
Very low	Less than 0.5ng/ml	2	2

In present study, 36% patients had normal AMH, 18% patients were in low normal range, 5% patients had low values and 2% patients had very low values. 41% of patients had values in high range suggestive of PCOS. Amongst this, 21% had values between 4 to 8 ng/ml where we got good AFC count and good result in terms of pregnancy.

Table 6: Ovarian response.

Ovarian response	No. of patients	%
Good responders	80	80
Poor responders	20	20

The study group was divided into two subgroups according to the number of oocytes retrieved. Patients with an oocyte count of five or more were considered good responders, and patients with less than five as poor responders. In present study, 80% were good responders while 20% were poor responders.

Table 7: Pregnancy outcome.

Pregnancy outcome	No. of patients	%
Total no. of pregnancies	54	54
Triplets	3	3
Twins	7	7
Abortion	10	10
Biochemical pregnancies	8	8

In present study, fifty four patients conceived. Three patients had triplets, seven of them continued as twin pregnancies, and forty four patients as singleton pregnancy. Ten pregnancies ended up in abortion and eight were biochemical pregnancies.

When we evaluated the relationship of retrieved oocyte counts with the parameters included, we found that only basal AMH levels and the number of antral follicles correlated well.

DISCUSSION

Maximum patients i.e. 42% patients were between 31-35 years. 29% patients were between 26-30 years, 16% patients were between 36-40 years,12% patients were between 21-25 years while only 1% of patients were above 40 years of age. Patients with low and very low values of AMH were above 35 years of age.

K. Hansen et al found that even after correcting for chronological age, two of the tests, the ovarian AFC and serum levels of AMH, were still significantly correlated with the ovarian primordial follicle number. In addition, approximately 74% of the variation in ovarian primordial follicle count could be explained with only two of the parameters, chronological age and the ovarian AFC.2 Kelton P et al found that plasma AMH levels remained relatively static (20–25 pmol/L) from 18 to 29 years of age. By 30 years of age, plasma AMH levels start to drop rapidly, reaching only10 pmol/L by 37 years.[5]

In present study, 74% of patients had primary infertility while 26% of patients had secondary infertility. 93% of patients had their first cycle of ICSI, 3% of patients had their second cycle of ICSI, 2% of patients had third cycle of ICSI and 2% of patients had their fourth cycle of ICSI.

In present study, 36% patients had normal AMH, 18% patients were in low normal range, 5% patients had low values and 2% patients had very low values. 41% of patients had values in high range suggestive of PCOS. Amongst this, 21% had values between 4 to 8 ng/ml where we got good AFC count and good result in terms of pregnancy.

The study group was divided into two subgroups according to the number of oocytes retrieved. Patients with an oocyte count of five or more were considered good responders, and patients with less than five as poor responders. In present study, 80% were good responders while 20% were poor responders. When we evaluated the relationship of retrieved oocyte counts with the parameters included, we found that only basal AMH levels and the number of antral follicles were statistically correlated.

Kelton P et al found that using a cut off value of 8.1 pmol/L, plasma AMH assessment could predict poor ovarian reserve on a subsequent IVF cycle with a

sensitivity of 80% and a specificity of 85%.[5] Kelton P et al found that plasma AMH assessments are superior to FSH in identifying women with reduced ovarian reserve. Anti-müllerian hormone assessment should be considered as a useful adjunct to FSH/oestradiol levels and antral follicle count when estimating ovarian reserve.[5]

Fiçicioğlu C et al found that patients with fewer than five retrieved oocytes had lower day 3 AMH levels, fewer antral follicles, and lower hCG day E2 levels. Thus, basal antral follicle count and basal AMH levels are good tools for use in counseling patients.[8] C Fiçicioğlu et al found that levels of AMH would predict the number of oocytes with a positive predictive rate of 96%, although it had little value for predicting pregnancy.8 C Fiçicioğlu et al revealed that the most sensitive and specific indicator of ovarian reserve is the level of AMH, it does not indicate pregnancy success as well when 0.25 pg/mL is taken as a cut-off value.[8] Fiçicioğlu C et al demonstrated an association between early follicular phase serum AMH and number of retrieved oocytes despite clinically similar day.[8] Fiçicioğlu C et al measured serum FSH and E2 levels in patients of all age groups. Baseline FSH, LH, and E2 levels are good predictors of ovarian reserve.[8] C Fiçicioğlu et al found that basal antral follicle count is correlated but weakly with the number of retrieved oocytes during assisted reproduction cycles.[8] Fiçicioğlu C et al found that AMH was the best indicator of ovarian reserve with a high sensitivity and specificity.[8]

Better AMH than FSH specificity has been previously demonstrated and is also supported by Fiçicioğlu C et al. AMH <1.05 ng/mL, however, does not define DOR. It only defines DOR with significantly decreased live-birth chances. It also does not warrant withholding of treatment because even DOR patients with very low to undetectable AMH still achieve rather surprising live-birth rates.[8]

Van Rooij et al found that serum AMH levels were highly correlated with the number of antral follicles ($r = 0.77$; $P < 0.01$) and the number of oocytes retrieved ($r = 0.57$, $P < 0.01$).[9] Van Rooij et al combined antral follicle count with AMH and inhibin B to provide for better prediction.[9,12] Dillon K et al found that participants with a pre-treatment AMH level >2 ng/mL recovered at a rate of 11.9% per month after chemotherapy, whereas participants with pre-treatment AMH levels ≤2 ng/mL recovered at a rate of 2.6% per month after therapy.[10]

Akira Ivase et al found that the median AMH level was 2.98 ng/mL and 3.92 ng/mL before operation and was significantly reduced to a median level of 2.24 ng/mL and 3.29 ng/mL at 1 month after operation in the endometrioma group (n = 29) and the non-endometrioma group (n = 21), respectively.[11] Kelton T found that Serum AMH is a sensitive marker of age-related decline in ovarian reserve status. A serum AMH result >36 pmol L−1, or above the 75th percentile for age, is highly suggestive of a diagnosis of PCOS. A serum AMH result below the 10th percentile for age suggests accelerated loss of ovarian reserve, while an AMH result exceeding 20 pmol L−1 suggests an increased risk of OHSS during IVF treatment.[12] Brodin T et al found that all ORTs correlated significantly with each other, with the strongest correlation between AFC and AMH ($r = 0.71$, $p < 0.0001$). Univariately, AMH and age equivalently predicted live birth (c-statistic 0.61), and together they provided a significantly better model (c-statistic 0.64). For prediction of poor and excessive response the best model included AMH, AFC and age (c-statistic 0.89).[13]

Lauren Z et al found that among 97 women who underwent AMH testing, 32 (33.0%) had elevated AMH levels. Hyperandrogenism was reported by 8 (25.0%) women with elevated AMH and none with AMH concentrations lower than 4.7 ng/mL ($P < 0.001$). Irregular menstrual cycles before hormonal contraceptive use were reported by 16 (24.6%) of 65 women with AMH concentrations lower than 4.7 ng/mL and 11 (34.4%) with elevated AMH ($P = 0.34$). Of the 20 women with elevated AMH who returned for further evaluation, 16 (80.0%) had polycystic ovaries and 13 (65.0%) were diagnosed with PCOS (Rotterdam criteria).[14]

CONCLUSION

When basal AMH levels and the number of antral follicles were correlated, high AMH levels correlate with low cancellation rates, retrieval of more eggs, higher live birth rates and a high chance for freezing of embryos. Low AMH levels (alone) do not predict low success rates in women less than 35 years of age. Couples should not be excluded from attempting assisted reproductive cycles due to low AMH values alone because live birth success rates were reasonable in these cases.

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Original Research Article

Antenatal screening for aneuploidy

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ABSTRACT

Background: It is uncertain how best to screen pregnant women for the presence of fetal Down's syndrome and other aneuploides, whether to perform first-trimester screening or to perform second-trimester screening or both.
Methods: Women with singleton and multiple pregnancies underwent first-trimester combined screening (measurement of nuchal translucency, pregnancy-associated plasma protein A [PAPP-A], and the free beta subunit of human chorionic gonadotropin at 10 weeks 3 days through 13 weeks 6 days of gestation). Also, second-trimester quadruple screening (measurement of alpha-fetoprotein, total human chorionic gonadotropin, unconjugated estriol, and inhibin A) and triple marker test was done from 15 to 18 weeks of gestation.
Results: 12 (5%) patients had positive screening test for combined screening in first trimester, 6 (10.9%) patients had positive screening for quadruple test while 1 (2.85%) patients had positive screening for triple test. Out of 19 positive screening, 16 (84.21%) had their amniocentesis done for confirmation of diagnosis. In all 16 patients, chromosomal analysis was normal. Not a single patient turned out to have a baby with Down syndrome or any other aneuploidy. False positive rate for combined screening in first trimester was 5%, false positive rate for quadruple test in second trimester was 10.9%, false positive rate for triple marker test in second trimester was 2.85%.
Conclusions: First-trimester combined screening is better than second-trimester quadruple test or triple marker test for syndrome or any other aneuploidy.

Keywords: Combined screening, Down syndrome, Quadruple screening

INTRODUCTION

The natural frequency of chromosomal abnormalities at birth, in the absence of any prenatal diagnosis, has been at 6 per 1,000 births. The aneuploides are the most frequent, with trisomy 21 (Down syndrome) the most common, with an often-quoted birth prevalence of 1 in 800.[1] The other common autosomal trisomies including trisomy 18 (Edward syndrome) and trisomy 13 (Patau syndrome) occur with 1 in 6,500 and 1 in 12,500, respectively.[1]

Presently, invasive procedures remain the definitive test for fetal aneuploidies. However, these procedures themselves carry a potential fetal loss rate, though small may be unacceptable to certain women. Therefore, prenatal screening programs provide information by which couples can make appropriate informed choices

about reproductive decisions, rather than focusing on disabilities and their eradication.[1]

As both amniocentesis and CVS are associated with a risk of miscarriage, these procedures are currently applied only to small group of women who are in a higher risk of having an offspring with a chromosomal defect in comparison to the general population. The aim of the currently available screening tests is to identify, with the highest sensitivity and specificity, those women who should be offered the invasive procedure. The risk for many of the chromosomal defects increases with maternal age. Additionally, because fetuses with chromosomal defects are more likely to die in utero than normal fetuses though the risk decreases with gestational age.[2]

Non-invasive screening based on biochemical analysis of maternal serum or urine, or fetal ultrasound measurements, allows estimates of the risk of a pregnancy being affected. It also provides information to make decisions about definitive testing. Before screening tests, parents need to be fully informed about the risks, benefits and possible consequences of such a test. This includes subsequent choices for further tests and the implications of both false positive and false negative screening tests (i.e. invasive diagnostic testing, and the possibility that a miscarried fetus may be chromosomally normal).[3]

According to the American College of Obstetricians and Gynecologists, it has become routine in prenatal care to offer screening tests for neural tube defects and genetic abnormalities. There have been some changes in the method of prenatal screening. Measurement of AFP alone can detect the vast majority of neural tube defects and a small portion of trisomy 21 in patients of all ages. Adding hcG and unconjugated estriol to this screen increases the rate of detection of trisomies 21 and 18. Counseling patients about the risks and benefits of such screening is important.[4]

Down syndrome is the commonest congenital cause of mental retardation. Noninvasive screening based on biochemical analysis of maternal serum or urine, or fetal ultrasound measurements, allows estimates of the risk of a pregnancy being affected. It also provides information to guide decisions about definitive testing.[5]

First-trimester screening for Down's syndrome that includes ultrasound to assess nuchal translucency has become widespread since its introduction by Nicolaides and colleagues in the early 1990s.[6]

Second-trimester screening remains the most common method to assess the risk of Down's syndrome in the United States.[7]

Biochemical screening at 16-18 weeks of pregnancy can detect about 60% of pregnancies with Down's syndrome, about 90% of pregnancies with open spina bifida, and virtually all cases of anencephaly.[8]

With any type of testing, there is a possibility of false-positive results and false-negative results too. A screening test result that shows there is a problem when it does not exist is called a false-positive result. A screening test result that shows there is not a problem when it exists, is called a false-negative result. Your doctor can give you information about the rates of false-positive and false-negative results for each test.[8]

Expected Detection Rates for Down Syndrome at a 5% False Positive Rate Using a Variety of Combinations of Second Trimester Biochemical Markers (Cuckle).[9]

Nuchal scanning alone detects 62% of all Down syndrome with a false positive rate of 5.0%; combined with blood testing gives corresponding values of 73% and 4.7%.[10]

Objectives of present study are to assess the effectiveness of combined ultrasound and biochemical (CUB) screening in first trimester and quadruple and triple screening in second trimester for Down syndrome and other chromosomal abnormalities in singleton pregnancies in a routine antenatal clinic and laboratory setting

METHODS

This retrospective study was conducted at Patne hospital and Maternity home, Aurangabad from January 2015 to January 2016 in 330 antenatal patients.

In recent years, antenatal screening has become one of the most routine procedure of pregnancy-follow up and the subject of hot debate in bioethics circles.

330 women whose pregnancies fell within the gestational age range of 11 to 14 weeks by ultrasound assessment were offered combined screening on the basis of measurement of nuchal translucency (NT), maternal serum free beta-human chorionic gonadotropin (Beta chg) and pregnancy-associated plasma protein A (PAPP-A). NT measurements were obtained using a standardized method. Each screening marker measurement was converted to a multiple of the appropriate gestational median and a risk was derived for each marker in chromosomally abnormal and unaffected pregnancies. A combined risk of Down syndrome and of trisomy 18/13, incorporating the maternal age risk, was calculated for all women.

Patients whose screening test came as positive were offered integrated screening test. This combines the results of the first-trimester tests with those of second-trimester screening (triple or quadruple screening). These patients were also given the option of chorionic villus biopsy directly for confirmation of diagnosis if they wish.

If quadruple test turned out to be positive, these patients were advised amniocentesis for confirmation of diagnosis.

RESULTS

In present study, out of total 330 patients, 290 (87.8%) patients were of less than 35 years while 40 (12.1%) patients were above 35 years with the median age of 27 years.

Table 1: Age group.

Age	No. of patients	Percentage
<35 years	290	87.8
>35 years	40	12.1

Table 2: Period of screening.

Period of screening	No. of patients	Percentage
First trimester	240	72.72
Second trimester	90	27.27

In present study, out 330 patients, 240 (72.72%) patients came in first trimester in which combined screening was done while 90 (27.27%) patients came in second trimester where triple marker test or quadruple test was done.

Table 3: Type of screening.

Type of screening	No. of patients	Percentage
Combined screening (First trimester)	240	72.72
Triple test (Second trimester)	35	10.60
Quadruple test (Second trimester)	55	16.66

In present study, in 240 (72.72%) patients who came for check up in first trimester, combined screening was done, in 55 (16.66%) patients who reported in second trimester, quadruple test was done while in 35 (10.60%) patients who reported in second trimester, triple test was done.

Table 4: Nuchal translucency.

MoM	No. of patients	Percentage
0.5-0.9	52	21.66
1-1.5	138	57.5
1.6-2	32	13.33
2-2.5	18	7.5

Out of 240 patients in first trimester, 52 patients (21.66%) had nuchal translucency between 0.5-0.9, 138 patients (57.5%) had nuchal translucency between 1-1.5, 32 patients (13.33%) had nuchal translucency between 1.6-2 and 6 patients (7.5%) had nuchal translucency between 2-2.5. These are multiple of median (MoM) values. Not a single patient had abnormal value for normal translucency.

Table 5: Positive screening.

Screening	No. of patients	Percentage
Combined screening (First trimester)	12	5
Triple test (Second trimester)	1	2.85
Quadruple test (Second trimester)	6	10.9

In present study, 12 (5%) patients had positive screening test for combined screening in first trimester, 6 (10.9%) patients had positive screening for quadruple test while 1 (2.85%) patients had positive screening for triple test.

Table 6: Confirmation by amniocentesis or chorionic villus biopsy.

Confirmation by amniocentesis/Chorionic villus biopsy	No. of patients	Percentage	Aneuploidy	Percentage
Amniocentesis	16	84.21	0	0
Chorionic villus biopsy	0	0	0	0
Lost to follow up	3	15.78	-	-

In present study, out of 19 positive screening, 16 (84.21%) had their amniocentesis done for confirmation of diagnosis, 3 (15.78%) patients lost to follow up while not a single patient opted for chorionic villus biopsy. In all 16 patients, chromosomal analysis was normal. Not a single patient turned out to have a baby with Down syndrome or any other aneuploidy. False positive rate for combined screening in first trimester was 5%, false positive rate for quadruple test in second trimester was 10.9%, false positive rate for triple marker test in second trimester was 2.85%.

DISCUSSION

In present study, out of total 330 patients, 290 (87.8%) patients were of less than 35 years while 40 (12.1%) patients were above 35 years. Zournatzi V et al reported that 69 women (12%) were 35 years old or more.[2]

In present study, out 330 patients, 240 (72.72%) patients came in first trimester in which combined screening was done while 90 (27.27%) patients came in second trimester out of which in 55 (16.66%) patients quadruple test was done while in 35 (10.60%) patients triple test was done.

In present study, not a single patient had abnormal value for normal translucency.

In present study, 12 (5%) patients had positive screening test for combined screening in first trimester, 6 (10.9%) patients had positive screening for quadruple test while 1 (2.85%) patients had positive screening for triple test.

In present study, out of 19 positive screening, 16 (84.21%) had their amniocentesis done for confirmation of diagnosis, 3 (15.78%) patients lost to follow up while not a single patient opted for chorionic villus biopsy.

In all 16 patients, chromosomal analysis was normal. Not a single patient turned out to have a baby with Down syndrome or any other aneuploidy.

False positive rate for combined screening in first trimester was 5%, false positive rate for quadruple test in second trimester was 10.9%, false positive rate for triple marker test in second trimester was 2.85%.

Alldred SK et al reported that both direct and indirect comparisons, the combined NT, PAPP-A, free ß hcG and maternal age test strategy showed superior diagnostic accuracy to an NT and maternal age test strategy ($P < 0.0001$).

Based on the indirect comparison of all available studies for the two tests, the sensitivity (95% confidence interval) estimated at a 5% FPR for the combined NT, PAPP-A, free hcG and maternal age test strategy (69 studies; 1,173,853 fetuses including 6010 with Down's syndrome) was 87% (86 to 89) and for the NT and maternal age test strategy (50 studies; 530,874 fetuses including 2701 Down's syndrome pregnancies) was 71% (66 to 75).5 They detect about nine out of 10 Down's affected pregnancies for a fixed 5% FPR. Although the absence of nasal bone appeared to have a high diagnostic accuracy, only five out of 10 affected Down's pregnancies were detected at a 1% FPR.[3]

First-trimester screening was performed by Fergal D et al in 38,167 patients; 117 had a fetus with Down's syndrome. At a 5 percent false positive rate, the rates of detection of Down's syndrome were as follows: with first-trimester combined screening, 87 percent, 85 percent, and 82 percent for measurements performed at 11, 12, and 13 weeks, respectively; with second-trimester quadruple screening, 81 percent; with stepwise sequential screening, 95 percent; with serum integrated screening, 88 percent; and with fully integrated screening with first-trimester measurements performed at 11 weeks, 96 percent.[6]

Wapner R. et al found that the largest U.S. study of first-trimester screening to date, involving 8514 pregnancies, reported a 79 percent detection rate at a 5 percent false positive rate.[11]

Alldred SK et al found that tests involving two markers in combination with maternal age, specifically PAPP-A, free hcG and maternal age are significantly better than those involving single markers with and without age. They detect seven out of 10 Down's affected pregnancies for a fixed 5% FPR. The addition of further markers (triple tests) has not been shown to be statistically superior.[12]

Alldred SK et al reported that tests involving second trimester ß-core fragment and estriol with maternal age are significantly more sensitive than the single marker second trimester ß-core fragment and maternal age, however, there were few studies. There is a paucity of evidence available to support the use of urine testing for Down's syndrome screening in clinical practice where alternatives are available.[13]

Alldred SK et al reported that meta-analysis of the six most frequently evaluated test combinations showed that a test strategy involving maternal age and a combination of first trimester NT and PAPP-A, and second trimester total hcG, uE3, AFP and Inhibin A significantly outperformed other test combinations that involved only one serum marker or NT in the first trimester, detecting about nine out of every 10 Down's syndrome pregnancies at a 5% false positive rate.[14]

Alldred SK et al reported that meta-analysis of 12 best performing or frequently evaluated test combinations showed double and triple tests (involving AFP, uE3, total hcG, free hcG) significantly outperform individual markers, detecting six to seven out of every 10 Down's syndrome pregnancies at a 5% false positive rate.

Tests additionally involving inhibin performed best (eight out of every 10 Down's syndrome pregnancies) but were not shown to be significantly better than standard triple tests in direct comparisons. Lower sensitivity occurred in women above 35 years of age.[15]

When the amniocentesis results of the patients were reviewed by Danisman N et al as numerically normal or abnormal; 40 (2.7%) of 1456 amniocentesis procedures performed for advanced maternal age, 5 (0.9%) of 531 procedures performed for an increased double-test risk and 14 (1.3%) of 1095 procedures performed for an increased triple test risk were found to have chromosomal aneuploidy.[16]

Stenhouse EJ found that the detection rate for Down syndrome was 93% (14/15) at a false-positive rate of 5.9% and for all chromosome abnormalities it was 96% (25/26) at an overall false-positive rate of 6.3%.[17]

CONCLUSION

Present study confirms that by first trimester screening, the number of women who have indication for invasive prenatal diagnostic procedure is significantly reduced. As a result the cost for prenatal diagnosis of the population and also the risk of iatrogenic missed miscarriages is also reduced. Finally, this screening method gives the advantage of early diagnosis.

False positive rate for combined screening in first trimester was 5%, false positive rate for quadruple test in second trimester was 10.9%, false positive rate for triple marker test in second trimester was 2.85%.

To conclude, first-trimester combined screening is better than second-trimester quadruple or triple screening.

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Original Research Article

Preventive gynaecology: awareness, attitude and practices of gynecologists

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ABSTRACT

Background: Gynecologists are aware of screening tests of all gynecological malignancies. However, attitude and practices do not match with this. Present study was conducted in 214 gynecologists to evaluate awareness, attitude and practices of preventive gynecology.
Methods: A survey was conducted among 214 gynecologists of Nagpur, using a questionnaire. This evaluated implementation of screening and preventive measures used by them for self-protection as well as for the women seeking their services. Their attitude regarding HPV vaccine as a preventive measure was also noted.
Results: In present study, 160 (74.76%) gynecologists routinely advice pap smear to the patients, 54 (25.23%) gynecologists advice pap smear to the patients only if it is indicated. 102 (47.66%) gynecologists and spouses have got their own pap smear done. 192 (89.71%) were doing their self breast examination regularly and 66 (30.84%) had done their mammography. 168 (78.50%) had their ultrasound done and 98 (45.79%) had their P/V done. 132 (61.68%) are advising HPV vaccination to the patients routinely and 48 (22.42%) gynecologists had given HPV vaccination to their daughters.
Conclusions: Proper and effective utilization of available facilities would depend on creating better understanding and change in their outlook. Stepping up and strengthening of preventive health care services is essential.

Keywords: Cervical cancer, HPV vaccine, Mammography, Pap smear

INTRODUCTION

In the last decades, papilloma and herpes viruses got more importance in the development of epithelial dysplasia, neoplasia and cervical cancer. Cervical cancer has the second place in mortality from gynecology diseases. It occurs with the incidence of 350,000 new cases diagnosed each year.[1] Diagnosis is made by general, gynecologic, family history, clinical examination including general, gynecological speculum examination, bimanual and rectal examination, by taking the smear by Papanicolaou method and histological examination after biopsy. Papanicolaou test is the standard test for cervical cancer screening.

Results of several studies have shown that this cytological test reduces the incidence of cervical cancer.[1]

Primary prevention involves regular gynecological examinations and screening.[1]

Primary prevention includes introduction of the primary and secondary measures for disease prevention; early detection of the diseases and its treatment. This reduces the numbers of cases in the advanced stages; significant improvement of gynecological health and reduction of costs of the treatment of advanced stages of disease.[2]

Gynecological cancer screening incorporates inspection, palpation, education, screening tests, and evaluation. It encompasses assessment of the vulva, vagina, cervix, uterus, ovaries, and recto-vaginal area.[2]

Reducing the incidence of gynecological cancer not only requires improving treatment, but also incorporating cancer prevention and detection strategies into clinical practice. By reviewing cancers of vulva, cervix, endometrial and ovary, their associated risk factors, means of prevention and early detection, and signs and symptoms, it helps patients to understand the potential risks and the detection methods.[3]

These prevention and early detection efforts succeed best when patients are well informed and have a relationship with their doctors who follow screening and detection recommendations appropriate in their own lives.[3]

Carcinoma breast and carcinoma cervix are leading causes for cancer deaths in India. However, these get detected only in late stages. Preventive measures and early detection of disease will decrease the burden of these cancers.[4]

HPV vaccination was introduced for primary prevention of carcinoma cervix after the attribution of High risk HPV as the causative agent. Screening for premalignant lesions using Pap smear and HPV DNA are now recommended as methods for secondary prevention of carcinoma cervix.[4]

Vaccinating girls between 9 and 12 years may offer an option to decrease this burden. The use of HPV Vaccine has been approved by the Drug Controller of India.[4]

Breast and cervical cancer are the most common causes of cancer mortality among women all over world, but actually they are largely preventable diseases. Doctors in developing countries regularly see women with advanced, incurable cancers. Health of a rural Indian women and her access to health facility is compromised because of socio-cultural, economical, and environmental factors.[5]

The World Health Organization (WHO) recommends routine screening for cervical cancer. WHO Global Monitoring Framework suggests that every nation monitors cervical cancer screening.[6]

Barrier and spermicidal contraceptives decrease the risk of cervical cancer by 50%. Combined oral contraceptives prevent both endometrial and epithelial ovarian cancers. The risk of endometrial cancer in former oral contraceptive users is reduced by about 50% and that of ovarian cancer by about 30% to 60%. Weight control gives strong protection against endometrial cancer. Breast-feeding and tubal sterilization also appear to protect against ovarian cancer.[7]

Objectives of present study was to evaluate awareness, attitude and practices of preventive gynecology in gynaecologists.

METHODS

A survey was conducted among 214 gynecologists of various cities attending MSR conference in Nagpur in November 2017, using a questionnaire.

This was a cross sectional study conducted. Selection of gynecologists and their spouses was done randomly.

Inclusion criteria

Gynecologists and their spouses above 30 years of age were included.

Exclusion criteria

Gynecologists and their spouses below 30 years of age were excluded as very young gynecologists don't think of investigating themselves.

This evaluated implementation of screening and preventive measures used by them for self-protection as well as for the women seeking their services. This was regarding cancer cervix, ovarian cancer and breast cancer. Their attitude regarding HPV vaccine as a preventive measure was also noted. Their practice about HPV vaccination was judged by asking whether the gynecologists have given HPV vaccination to their daughters between 9-13 years or not. Data was collected and analyzed. Statistics was done in percentages.

Questionnaire

1. Name
2. Age
3. Advice for pap smear to the patients was given routinely or only if it was indicated
   - Own pap smear got done or not
   - Own Ultrasound got done or not
   - Own P/V got done or not
   - Own mammography got done or not
4. Self breast examination doing regularly or not
5. Advice HPV vaccination to the patients
6. HPV vaccination given to daughter or not
7. Reasons for not giving HPV vaccination like-