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Potential medications and treatment options for polycystic ovarian syndrome are found using text mining and data analysis

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ABSTRACT

PCOS is one of the most common endocrine and metabolic disorders in premenopausal women. PCOS is a heterogeneous condition that presents with a combination of signs and symptoms of both androgen excess and ovarian dysfunction, unless there are other specific diagnoses. A increasing amount of studies suggests that PCOS may be a complex multigenic disorder with important environmental and epigenetic factors, including dietary and lifestyle decisions, even if the actual origin of the condition is still mostly unknown. The various conditions linked to PCOS include irregular menstrual and ovarian cycles, infertility, hirsutism, metabolic disorders, and a host of other problems that significantly impair patients' quality of life and the nation's healthcare system. 1120 women with PCOS/PCOD participated in a polycentric, prospective, observational, cross-sectional study. The participants were divided into three age groups: 15–25 years, 26–35 years, and 36–45 years. Finding the relationships between several socioeconomic factors—such as age, marital status, infertility, medication history, and the existence and severity of obesity and other symptoms—was the main objective of the study. Period irregularities (34.19%), acne (22.23%), hirsutism (12.05%), diabetes (10.71%), and obesity (20.80%) were found to be statistically significant for different age groups.

KEYWORDS- Menstrual Irregularity, Hormonal imbalance, epigenetic influences, PCOS/PCOD.

INTRODUCTION :

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting individuals of reproductive age, primarily women. It is characterized by hormonal imbalance, menstrual irregularities, and the presence of multiple cysts on the ovaries. PCOS is one of the most common hormonal disorders among women, with prevalence rates ranging from 6% to 12% globally.

Adolescent girls and women who suffer from PCOS (polycystic ovarian syndrome) have problems with their hormone levels. It may result in issues with the menstrual cycle and make conception challenging. This condition gets its name from the many little cysts that grow in women's ovaries. Worldwide, PCOS is regarded as the primary cause of female infertility. PCOS is a complex illness with a range of etiologic variables that may be associated with the condition, exacerbate it, or cause adult-onset PCOS phenotypic features in women. The primary cause of infertility and the most prevalent endocrine problem in women is anovulation. It has an impact on women's lives from the moment of conception till death.

Additionally, there are a number of health risks associated with PCOS, which raise morbidity, lower quality of life, and raise the death rate (1). The prevalence of PCOS varies because different investigators employ different criteria to diagnose the condition, and different organizations recommend different norms for diagnosis. It is an endocrine syndrome characterized by polycystic ovaries in women, hyperandrogenism, and irregular menstruation . About 15-20% of people have PCOS, according to the European Society for Human Reproduction & Embryology/American Society for Reproductive Medicine's diagnostic criteria (2). Afterwards, a meta-analysis was carried out by incorporating Iranian studies that were published between 2006 and 2011 The incidence rate according to the National Institute of Child Health and Human Disease's standards of the US was 6.8%, 19.5% according to Rotterdam rules, and 4.4% according to ultrasonography standards (3). It is estimated that between 5 and 10% of Indian subcontinent women who are of reproductive age have PCOS.

The hallmarks of PCOS are polycystic ovaries, chronic anovulation, and hyperandrogenism. When combined with insulin resistance, hyperinsulinemia, hypertension, abdominal obesity, and dyslipidemia, these conditions can lead to severe long-term consequences like endometrial hyperplasia, type 2 diabetes mellitus, and coronary artery disease. Additionally, they stated that although a woman may be genetically predisposed to the development of PCOS, it is only the combination of environmental variables (obesity) and genetic factors that leads to the manifestation of PCOS (4).

Many women may have PCOS conditions and manage them without receiving a formal diagnosis. March et al. (5) highlighted the significance of PCOS diagnosis in the community and noted that around 68% of women with PCOS had never had a PCOS test. This demonstrated the gravity of PCOS diagnosis issues in the community. Additionally, the onset of PCOS may have an impact on the individuals' mental health, which may possibly be connected to the psychiatric issues these patients experience as a result of their inability to conceive. In PCOS participants, the prevalence

of anxiety and depression was 13.3% and 27.5%, respectively, compared to 2.0% and 3.0% in control subjects (6). Additionally, compensatory hyperinsulinemia and insulin resistance were seen in roughly 65–70% of women with PCOS (7). Furthermore, women with PCOS may have a hereditary ovarian abnormality that leaves the ovary susceptible to insulin-stimulated androgen production. On the other hand, scant information also implies that hyperinsulinemia may increase the ovaries' synthesis of testosterone (8). Later, Baptiste et al. delineated multiple stages leading up to the onset of PCOS: (a) a change in the gonadotropin-releasing hormone that promotes the secretion of luteal hormone; (b) an enzymatic default in the ovarian and/or adrenal steroidogenesis; or (c) modifications in the activities of insulin that result in insulin resistance with compensatory hyperinsulinemia. There are some women who do not exhibit insulin resistance despite having PCOS, which supports the theory that PCOS is a hereditary condition. The majority of PCOS-affected women, but not all of them, would demonstrate this by developing compensatory hyperinsulinemia and insulin resistance (9). Evidence suggests that environmental factors may be important in the declining state of reproductive health, and that some environmental factors—such as diet and nutrition, geography, socioeconomic level, and exposure to pollutants in the environment—are crucial in this decline (10). However, there is a lack of study or conflicting data regarding the relationship between these environmental factors and PCOS pathogenesis, necessitating more systematic studies.

Based on the evidence currently available, this review is provided regarding the contribution of lifestyle, environmental, and occupational factors to PCOS. The data was gathered by looking through a variety of websites, including Google, PubMed, Medline, Toxline, and other websites, as well as by examining relevant literature. This overview is divided into several sections, the first of which covers the knowledge now available on the acknowledged host and genetic variables linked to PCOS. The topics covered in the second and third parts are lifestyle choices that may be linked to PCOS as well as chemical and occupational exposures. Furthermore, the role of oxidative stress in the development of PCOS is also discussed. Reviews of PCOS that are now accessible focus more on the genetic and host variables than they do on the connection between PCOS and lifestyle factors and exposure to environmental and/or occupational Toxicants.

Insulin sensitizing agents have been recommended for a variety of purposes, including ovarian hyperstimulation syndrome prevention, weight loss, androgenic symptom counteraction, long-term pregnancy loss prevention, ovarian hyperstimulation syndrome prevention, and even improving the outcome of in vitro fertilization therapy. Research is continuously being done to improve therapy for women with PCOS.

in the world, 4–20% of women of reproductive age suffer from PCOS, one of the most prevalent female endocrine disorders. According to Physicians, 10% of Indian women suffer from PCOS. However, there is no accurate published statistical information on the prevalence of the condition in India. According to the studies, PCOS is more common than ever in the general population and affects between 5 and 10 percent of women of reproductive age. [11][12] Depression affects about 40% of PCOS patients, particularly young girls. The incidence was screened to be 9.13 % in Indian adolescents

One of the main reasons for female infertility is PCOS. Although the cysts are not hazardous, they can cause hormone abnormalities, irregular periods, and difficulty getting pregnant. A hormonal imbalance in women leads to PCOS, a medical disorder with increased levels of testosterone, androstenedione, prolactin, LH, and dehydroepiandrosterone sulfate (DHEA-S), combined with normal, high, or low estrogen levels. Although insulin resistance can develop in lean women with PCOS, Hyperinsulinemia, insulin resistance, and poor glucose tolerance are very common in women with PCOS. [13] According to the National Institutes of Health (NIH), anovulation and signs of hyperandrogenism should coexist as part of the PCOS diagnostic criteria.

Although the exact cause of PCOS is unknown or heterogeneous in nature, it is undoubtedly related to a number of etiological factors, such as genetics, an imbalance between male and female sex hormones, ovarian follicular defects, epigenetic changes, central obesity, sedentary lifestyles, diets, a lack of exercise, medications (like Valproic acid), stress, and other psychological factors. Menstrual cycle irregularities, alopecia, acne, hirsutism, Acanthosis Nigricans, obesity, and infertility are a few of the frequent PCOD indications and symptoms. PCOD is linked to numerous metabolic and mental health hazards in addition to physical disruptions and problems with reproduction.[14]

The number of follicles in an ovary belonging to a PCOS patient exceeds 10. Comparatively speaking, the polycystic ovary has more follicles and a dense core called the stroma where testosterone is produced. According to Rotterdam's criteria, PCOS, oligoanovulation, biochemical or clinical evidence of hyperandrogenism, and the presence of polycystic ovaries on ultrasound examination are all regarded to exist. The non-specific finding of polycystic ovaries is seen in women who do not have endocrine or metabolic disorders. Anovulation, infertility, and recurrent pregnancy loss affect 75% of women with PCOS in clinical settings. It is unclear, though, whether these problems result from uterine failure per se or from the disruption of communication between uterine cells and the growing embryo. The risk of developing endometrial cancer is higher in young women with PCOS-induced endometrial hyperplasia than in those without the condition. Uncertainty surrounds PCOS's exact origin and pathophysiology. Ultrasonography, magnetic resonance imaging (MRI), and computed tomography (CT) scanning are frequently used to detect PCOS. [15][16]

Medical management is focused on specific symptoms such as anovulation, infertility, hirsutism, and acne and only in conjunction with lifestyle changes because there is no medicine that reverses the hormonal abnormalities of PCOS and resolves all clinical aspects. Lifestyle changes, such as weight loss and dietary adjustments, are primarily effective in regulating periods. [17] Pharmacological treatments include oral contraceptives for treating irregular cycles, orlistat for

weight loss, Eflornithine cream for unwanted facial hair, retinoid for acne, and clomiphene, gonadotropins, and metformin for ovulation induction. Diabetes, obesity, and hyperandrogenism are some of the biochemical and clinical indicators of depressive disorders in PCOD. By treating the insulin resistance linked to PCOD, depression may be alleviated. Anti-androgen therapy helps ease depressed symptoms in PCOD, and if they continue after three months, you might want to add antidepressants. Depression and anxiety are frequent among women with PCOD, although they are frequently ignored and neglected. Obesity, body dissatisfaction, excessive body hair (hirsutism), changes in physical appearance, acne, and infertility are the main causes of psychological stress or issues in PCOD women.

MATERIALS AND METHODS

Study Site: Quantifying the Prevalence and Interdependent Relationship of PCOD, Depression, and Obesity – A Prospective Observational Polycentric Study was conducted in the departments of “Obstetrics and Gynecology & Psychiatry” of various Hospitals around Durg and Rajnandgaon district, Chhattisgarh.

Study duration: 4 month (February 2024 to May 2024) Study data collection was for 4 month and statistical analysis was done for 1 month.

Study Design: It was a Multi-Centered, Descriptive, and Prospective Observational non-Comparative Cross-Sectional study.

This was a non-comparative cross-sectional study conducted among 1120 women diagnosed with PCOS/PCOD at the Department of Obstetrics and Gynecology & Psychiatry of various Hospitals around Durg and Rajnandgaon district, Chhattisgarh. Information about menstrual cycle, clinical features was also collected from patient with the help of Mitani (meaning female friend in local dialect), a precursor of ASHA who play an indispensable role in early detection of health related problems and are helping in improving overall community health status in Chhattisgarh state.

All the patients gave voluntary written informed consent before participating in the study.

Study Criteria/Patient Enrollments: Subjects are enrolled in the study based on inclusion and exclusion criteria;

According to the following Inclusion Criteria, women were included in the current study:

(a) Females of reproductive age (15 – 45 years)

- (b) Infertility or recurring miscarriage history, and
- (c) Diagnosis of PCOS by the consulting Gynecologist/Physician based on the Rotterdam criteria; any two of the following three criteria must be met for PCOS diagnosis;
 - i) Ultrasound imaging reveals polycystic ovaries
 - ii) Clinical/biochemical hyperandrogenism;
 - iii) Oligomenorrhoea.

Patients who were willing to participate in our study, who could read and write in English, Hindi and Chhattisgarhi, who were willing to provide informed consent, and who agreed to comply with the study procedures were also required to meet the other inclusion criteria. From these patients, we obtained their acceptance of the Patient Informed Consent Form (PICF), from which the necessary information was gathered.

Exclusion Criteria: Subjects were barred from the study if they met either of the ensuing conditions.

- a) Age of less than 15 years and greater than 45 years.
- b) No PCOS opinion by the consulting gynecologist.

Women with other co-morbidities along with PCOD; like chromosomal abnormalities, severe natural anomalies, severe natural deformations, women born prematurely, cardiovascular, metabolic and renal conditions, neurological conditions, adrenal hyperplasia, thyroid dysfunction, hyperprolactinemia or having a concurrent significant medical illness, women with known psychiatric illness, women with substance abuse, who are diagnosed from other than Rotterdam criteria, cases with deficient information (no proper history details) and who didn't accept our Case Informed concurrence Form (PICF) were barred from the study.

Study Materials:

- ♣ Patient Informed Consent Form
- ♣ A unique Patient Data Collection Proforma

Study Method: The study began after receiving signed consent from the participants to ensure their secrecy and willingness to participate in the study. Patients are enrolled solely on the basis of

the study's inclusion and exclusion criteria. For patient selection in this investigation, convenience sampling was used. To collect information regarding socioeconomic status and clinical complaints, a semi-structured questionnaire was employed. Menstrual history (abnormal menstruation, absence of menstruation, heavy menstruation, irregular menstruation, short and light menstruation or spotting), reproductive history (infertility), BMI (obesity, overweight, or weight gain), dark patches of skin in folds and creases, depression, inappropriate male features, loss of scalp hair, oily skin, body hair, and acne were all evaluated. The subject's education, employment, marital status, medications, obstetric history, personal history of mental illness, prior counselling or treatments, family history of mental illness, and any other verbal communication data were recorded in the demographic questionnaire. In order to identify clinical symptoms and evaluate the depression, questionnaires were filled out by the individuals during their clinic visits as well as during an online survey using a semi-structured demographic questionnaire.

Subject's description: A highly prevalent disorder, (PCOS) affects 5–10% of women between the ages of 12 and 45 Years. A woman's hormones are out of balance, which is the problem. It may result in irregular menstrual cycles, difficulty getting pregnant and radiological results that cannot be explained by anything else. An endocrine disorder that causes marginal cysts on the ovaries' surface and larger ovaries as a result. Despite the fact that the precise cause of polycystic ovary syndrome is unknown, it is possible that both inherited and environmental factors are to blame. Obesity, acne, irregular menstruation, and excessive hair growth are a few of the signs. The available therapies include hormones to increase fertility, birth control tablets to manage periods, metformin to prevent diabetes, statins to decrease cholesterol, and hair removal procedures, to name a few.

A custom constructed Proforma was used to record all cases of PCOD/PCOS socio demographic data. Obesity is a common finding in PCOS patients, with 40 to 80 percent of these patients being overweight or obese. PCOS familial aggregation significantly suggests a genetic predisposition to the condition. It is difficult to determine how PCOS and obesity are related.

Result

A 4-month multi-centered, descriptive and prospective observational cross-sectional study was conducted among 1120 women diagnosed with PCOS at Departments of Obstetrics and Gynecology/Psychiatry in various hospitals and villages in the Durg and Rajnandgaon districts of Chhattisgarh.

For the purpose of this research, a total of 1120 PCOS/PCOD women who met the inclusion criteria were recruited. According to the following criteria, the data on PCOS/PCOD women were analyzed:

Age groups-wise distribution of study subjects
Based on Marital status distribution of study subjects in Age groups
Distribution of research participants based on clinical complications

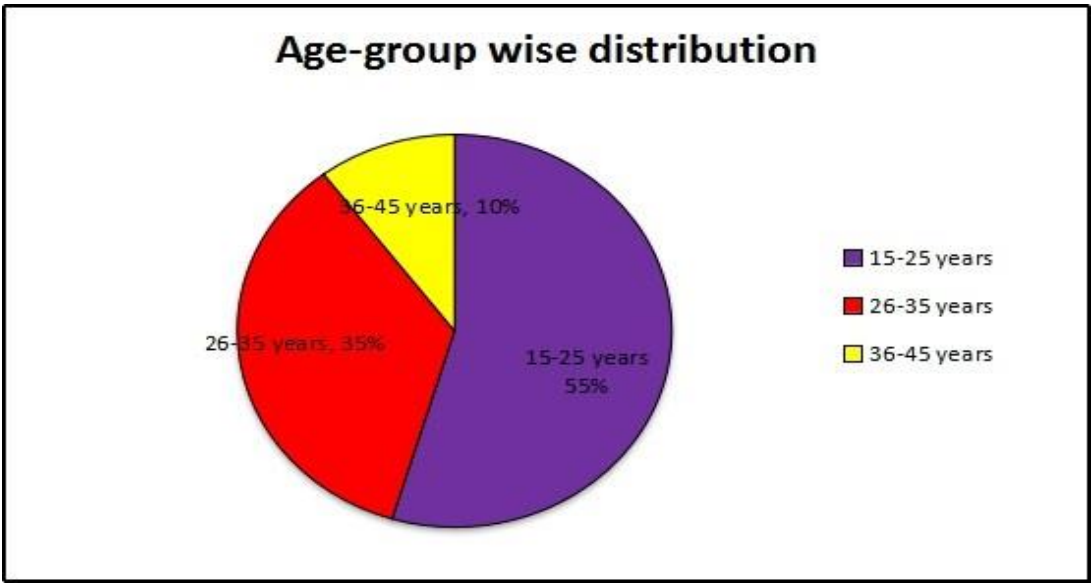
Age groups-wise distribution of study subjects:

A total of 1120 patients of the age group 15 – 45 years who were diagnosed with PCOD were enrolled in this study. Under the age group of 15-25 years, the study population percentage was found to be 54.64 %. Under the age group of 26 – 35 years, the study population percentage was found to be 35.06 %. Under the age group of 36 – 45 years, the study population percentage was found to be 10.29%.

Table 1: Age Groups Wise Distribution Of Study Subjects (N= 1120).

S.No.	Age Groups	Frequency	Percentage
1.	15-25 years	642	54.64%
2.	26-35 years	412	35.06%
3.	36-45 years	121	10.29%
Total		1175	100%

Fig. 1: Age Groups Wise Distribution Of Study Subjects



Clinical Complications:

Acne: Out of 1120 Subjects, 249 subjects (22.23%) were having acne and 871 subjects (77.76%) were not having acne.

Hirsutism: Out of 1120 Subjects, 135 subjects (12.05%) were having Hirsutism and 985 subjects (87.94%) were not having Hirsutism.

Irregular periods: Out of 1120 Subjects, 383 subjects (34.19%) were having irregular periods and 737 subjects (65.80%) were not having irregular periods.

Diabetes: Out of 1120 Subjects, 120 subjects (10.71%) were having diabetes and 1000 subjects (89.28%) were not having diabetes.

Obesity: Out of 1120 Subjects, 233 subjects (20.80%) were obese and subjects 887 (79.19%) were not having diabetes.

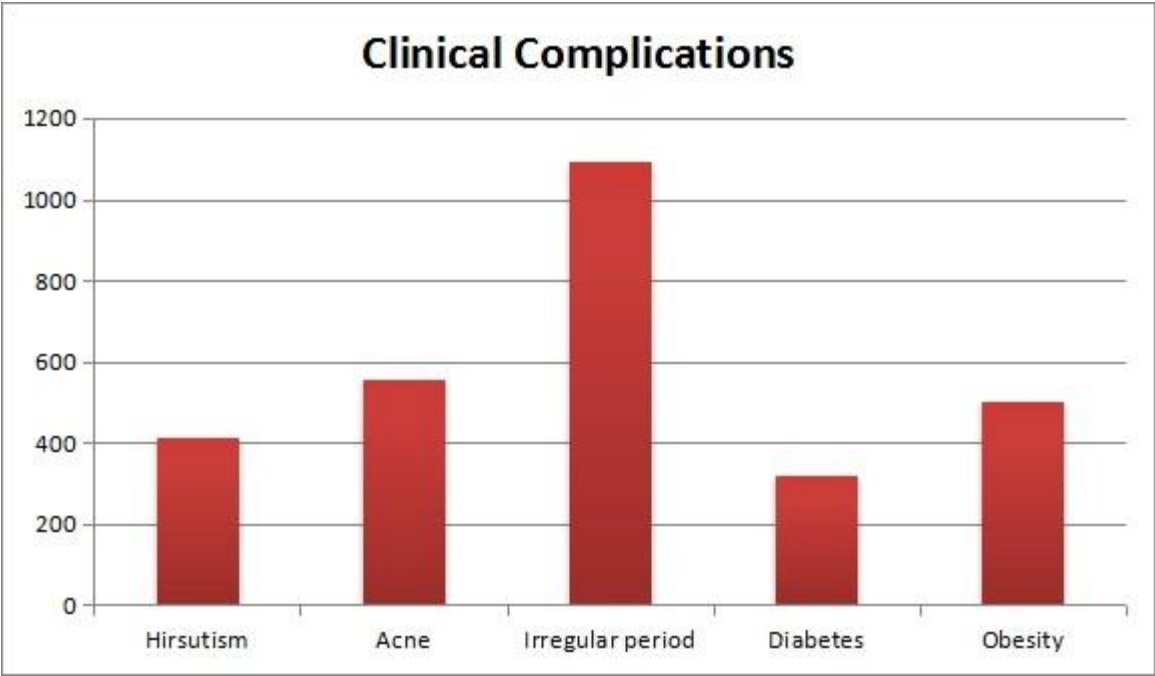


Fig. 3: Clinical Complications Of Study Subjects.

Based on Marital status distribution of study subjects in Age groups:

In a total of 1120 subjects enrolled for the study, 663 subjects (59.19%) were married and 475 subjects (40.80%) were unmarried.

The study subjects were distributed into 3 age groups as; under the age group of 15– 25 years, 527 subjects (47.05%) were there, of which 396 subjects (86.56%) were unmarried and 131 subjects (19.75%) were married.

Under the age group of 26–35 years, 466 subjects (41.60%) were there, of which 54 subjects (11.81%) were unmarried and 412 subjects (62.14%) were married.

Under the age group of 36–45 Years, 127 subjects (11.33%) subjects were present,of which only 7 subjects (1.53%) were unmarried and 120 subjects (18.09%) were married.

S.No.	Age Groups (years)	No. of subjects Unmarried (%)	No. of subjects Married (%)	Total No. of subjects (%)
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1.	15-25	396 (86.65%)	131 (19.75%)	527 (47.05%)
2.	26-35	54 (11.81%)	412 (62.14%)	466 (41.60%)
3.	36-45	7 (1.53%)	120 (18.09%)	127 (11.33%)
Total		457 (40.80%)	663 (59.19%)	1120 (100%)

Table 3: Age Group Wise Distribution Of Study Subjects Based On Marital Status (Married & Unmarried).

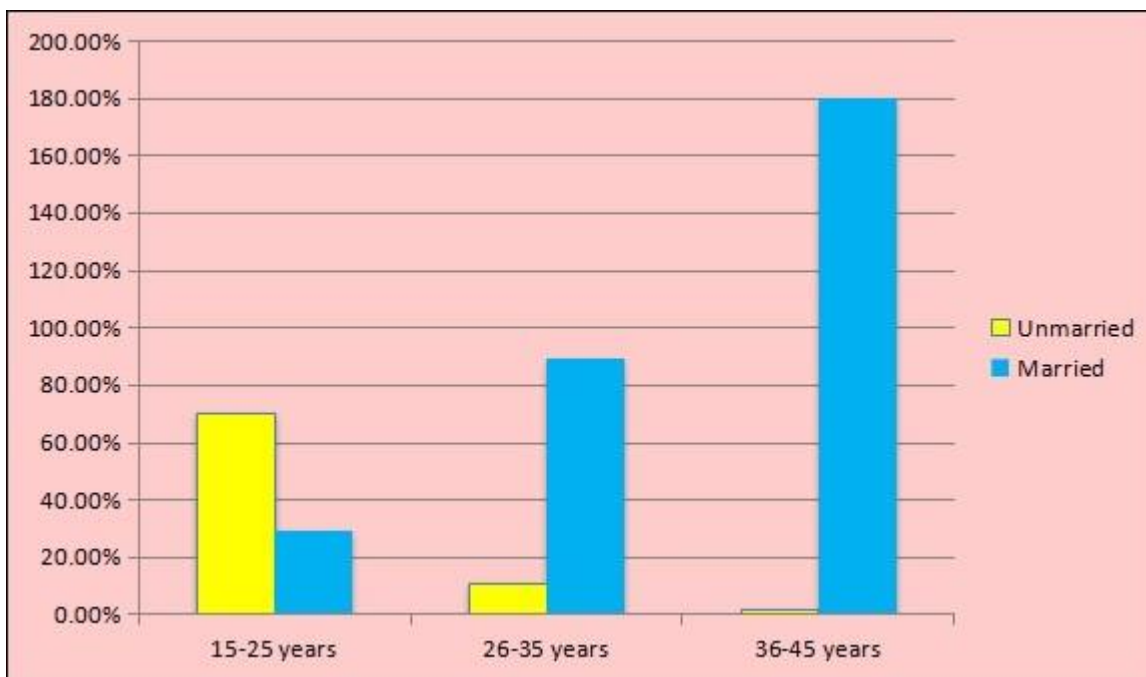


Fig. 3: Age Group Wise Distribution Of Subjects Bases On Marital Status.

CONCLUSION

- One of the most prevalent endocrine disorders in women of reproductive age is PCOS/PCOD .One in ten people have PCOD, a disorder caused by hormonal imbalance.
- Prevalence estimates range greatly, from 2.8% to as high as 39%, due to discrepancies in the diagnostic criteria used.

- Initially, it was believed that PCOD was related to a number of physical health problems.
 - It is now known to be connected to mental health problems as well.
 - Such variables as infertility, obesity, acne, and hirsutism can cause unwelcome stress on a female with PCOD and result in poorer self-esteem and a poor quality of life.
 - The prevalence of clinical problems in PCOD was shown to be statistically significant for irregular menstrual periods (34.19%), acne (22.23%), and hirsutism (12.05%), among different age groups.
 - This study's participants had a 20.80% prevalence of obesity, according to calculations and observations.
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