Comparative evaluation of 25-Hydroxy vitamin D levels among women with polycystic ovarian syndrome and normal women of reproductive age group attending a tertiary care hospital

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Abstract
Background: Polycystic Ovary Syndrome (PCOS) has been termed as the most common endocrine entity encountered by the women of the reproductive age group. The aim of the study was to find the comparison between Vitamin D levels among Normal women and Women with PCOS in the reproductive age group at one of the largest maternity hospitals of Kashmir Valley.

Methods: The study was a cross-sectional study which was carried out at one of the largest maternity tertiary care hospitals of Kashmir Valley. Women in the reproductive age group, women diagnosed with PCOS using clinical or Ultrasound criteria. For comparison, women who attended the outpatient department for any cause other than PCOS were included in the study.

Results: The mean age of the patients was 28 ± 8 years in PCOS women and 27 ± 6 years among normal women without PCOS. Majority 99 (66%) of the patients without PCOS were having serum fasting insulin levels within normal range while 123 (82%) among PCOS were having increased levels of serum fasting insulin levels. Moreover, 148 (99%) of PCOS patients fall under any one of the categories of Vitamin D deficiency while the reverse was true for women without PCOS.

Conclusion: Fasting serum Insulin levels and Serum 25(OH) Vitamin-D levels were significantly lower in PCOS women than the normal women in the reproductive age group.

Keywords: PCOS, Ovarian Disease, 25(OH) D Levels, Insulin Levels.

Introduction
Polycystic Ovary Syndrome (PCOS) has been termed as the most common endocrine entity encountered by the women of the reproductive age group. Characteristics features of PCOS include dysfunction of ovaries which leads to oligomenorrhea and eventually anovulation, hirsutism due to hypersecreations of androgens and an ultrasound diagnosis of multiple cysts morphology of ovaries(1). Long term risk factors of PCOS include type 2 diabetes mellitus, carcinoma endometrium and cardiovascular diseases(2). Vitamin D is an important precursor and plays an important role in our body especially...
in the bones. The active form of Vitamin D (25-Hydroxy vitamin D) has a role in bone metabolism, calcium-phosphorus homeostasis and many other cell proliferation and differentiation processes\(^3\). Vitamin D is has also an important role in reproductive system including follicular development in the ovaries by signaling anti-Mullerian hormone pathways\(^4\). PCOS, a complex disorder causes defect in the metabolism and reproductive system\(^5,6\) and many studies have linked its pathogenesis to Vitamin D deficiency which eventually leads to metabolic syndrome\(^7,8\). Furthermore, some studies have even documented association of obesity with the decreased levels of Vitamin D in patients with PCOS\(^7,8\).

The deficiency of Vitamin D has been observed to be quite common among the population and studies have found vitamin D levels as low as 20 ng/ml in 10-60% of the adults\(^9\). The causes of Vitamin D deficiency include decreased skin synthesis of Vitamin D, hereditary disorders of vitamin D synthesis, kidney diseases etc. Other factors which reduced absorption from the skin include use of skin creams, skin pigmentation and skin grafts. Moreover, obesity causes reduced bioavailability of Vitamin D\(^10\). Many studies have compared Vitamin D Levels among normal women and women with PCOS. Some studies found no change in the levels of Vitamin D\(^11,12\) while some showed higher or lower levels of Vitamin D\(^11,12\). We conducted this study with the aim to find the comparison between Vitamin D levels among Normal women and Women with PCOS in the reproductive age group at one of the largest maternity hospitals of Kashmir Valley.

**Material & Methods**

**Study Design & Setting:** The study was a cross-sectional study which was carried out at one of the largest maternity tertiary care hospitals of Kashmir Valley.

**Study Period & Study Unit:** The study was conducted for a period of 2 months from October 2018-November 2018 among normal women and women with PCOS attending outpatient department of a tertiary care hospital.

**Sample Size:** Arbitrarily we included 150 normal women and 150 women with PCOS

**Inclusion Criteria:** Women in the reproductive age group, women diagnosed with PCOS using clinical or Ultrasound criteria. For comparison, women who attended the outpatient department for any cause other than PCOS were included in the study.

**Exclusion Criteria:** Women with known endocrine disorders, liver disease, renal disease, drug history of Vitamin D agonists or antagonists, women on Hormonal replacement therapy.

**Questionnaire:** A questionnaire was developed before the study to capture socio-demographic\(^13\) and clinical details.

**Procedure:** The patients were grouped into normal women without PCOS and women with PCOS and were explained the objectives of the study after taking informed consent. Fasting serum insulin levels and 25 Hydroxy Vitamin D levels were measured using enzyme linked Immunosorbant Assay (ELISA) with a normal range of 75-100 nmol/ml. The obtained levels of 25(OH)D were classified as < 25 nmol/ml as Severe Deficiency, 25-49.9 nmol/ml as Deficiency, 50-74.9 nmol/ml as Insufficiency and above 75 nmol/ml as normal. The responses were entered in the Excel Spreadsheet and later analyzed using SPSS v 20.0 statistical software.

**Statistical Analysis:** Data was presented as measures of central tendency. Categorical variables were analysed using Chi-square test. Ethical Issues: The study didn’t have any ethical issues related to human or animal experiments. The confidentiality of the participants was maintained as per study protocol.

**Results**

The study involved a total of 300 patients grouped into women with PCOS and normal women without PCOS. The mean age of the patients was 28 ± 8 years in PCOS women and 27 ± 6 years among normal women without PCOS. Majority of
the patients in the PCOS group were overweight (28%) and obese (51%). Such was not the case with women without PCOS. Majority of the study participants in our study belonged to upper middle and lower middle socioeconomic class as per Kuppuswamy Socioeconomic scale update 2018.[13] [Table 1]

Table 1: Socio-demographic characteristics of the study participants

| Age Involved | Group       | Women with PCOS n= (150) | Normal Women n= (150) |
|--------------|-------------|--------------------------|-----------------------|
| 14-18        | 54 (36%)    | 46 (31%)                 |
| 19-30        | 54 (36%)    | 64 (43%)                 |
| 31-40        | 32 (21%)    | 30 (20%)                 |
| >40          | 10 (7)      | 10 (7)                   |
| BMI          |             |                          |
| Lean         | 12 (8%)     | 20 (13%)                 |
| Normal       | 20 (13%)    | 36 (24%)                 |
| Overweight   | 42 (28%)    | 46 (31%)                 |
| Obese        | 76 (51%)    | 48 (32%)                 |
| Socioeconomic status |         |                          |
| Upper (I)    | 11 (7%)     | 9 (6%)                   |
| Upper Middle (II) | 58 (39%) | 55 (37%)                 |
| Lower Middle (III) | 45 (30%) | 48 (32%)                 |
| Upper Lower(IV) | 22 (15%) | 28 (19%)                 |
| Lower (V)    | 14 (9%)     | 10 (7%)                  |

Fasting serum Insulin levels are mentioned in Table 2 along with serum 25 (OH) D levels. Majority 99 (66%) of the patients without PCOS were having serum fasting insulin levels within normal range while 123 (82%) among PCOS were having increased levels of serum fasting insulin levels. The association was statistically significant. Moreover, 148 (99%) of PCOS patients fall under any one of the categories of Vitamin D deficiency while the reverse was true for women without PCOS and the association was statistically significant.

Table 2: Serum Fasting Insulin Levels & Serum 25(OH) D levels among PCOS and Non PCOS women

| PCOS Cases | Normal Cases | P-Value |
|------------|--------------|---------|
| Fasting Serum Insulin Levels |              |         |
| 3-9 miu/l | 27 (18%)     | 99 (66%) | <0.001* |
| >10 miu/l | 123 (82%)    | 51 (34%) |         |
| Serum 25(OH)D levels |              |         |
| Severely Deficient | 88 (59%) | 20 (13%) | <0.001* |
| Deficient | 45 (30%)     | 40 (27%) |
| In sufficient | 15 (10%) | 59 (39%) |
| Normal    | 2 (1%)       | 31 (21%) |

Discussion

The cross sectional study included 300 patients who were diagnosed PCOS cases and normal women (150 each) and inferences were drawn between the two groups. The mean age of the patients in PCOS group was 28 ± 8 years while mean age among non PCOS group was 27 ± 6 years. Most of the patients in PCOS group were found to be overweight (28%) and obese (51%). Such was not the case with non PCOS women group.[14] Majority of the study participants in our study belonged to upper middle and lower middle socioeconomic class as per Kuppuswamy Socioeconomic scale update 2018.[13] In this study we compared the serum fasting Insulin levels among the two group and found that 99 (66%) of the patients without PCOS were having serum fasting insulin levels within normal range while 123 (82%) among PCOS were having increased levels of serum fasting insulin levels. The association was statistically significant. This is in accordance with the studies published earlier where they found that the serum fasting insulin levels among the women with diagnosed PCOS was below normal values.[15-17]

Moreover we also compared serum 25(OH) D levels among the two groups. The results indicated that the level of 25(OH) D levels were significantly lower in PCOS women than in the non PCOS women. The association between the two was statistically significant. The results of our study are with agreement with the studies published by Elida et al.[18]. In their case control study, they found that there were higher levels of 25(OH) D levels among the control group containing non PCOS women than the cases group containing PCOS diagnosed women. Another study conducted by Li et al.[19] done on 25 women with PCOS found an inverse relationship between 25(OH) D levels and BMI. Majority (72%) women among the cases were having Vitamin D deficiency and almost half of them with severe deficiency. This is also in accordance with the results of our study. Wehr et al.[19] also reported lower serum Vitamin D levels among women with
PCOS compared to normal women without PCOS and their association was statistically significant. The result published by Wehr et al\(^{(19)}\) were in accordance with our study.

**Conclusion**

Fasting serum Insulin levels and Serum 25(OH) Vitamin-D levels were significantly lower in PCOS women than the normal women in the reproductive age group.

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