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Original Research Article

Acne Vulgaris- Associated Cutaneous Findings, PCOS and Hormonal Changes

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Abstract: Acne vulgaris is a common skin condition which can present as a part of metabolic syndrome called polycystic ovarian syndrome(PCOS). This study was done to determine the associated cutaneous findings in acne, its association with PCOS and the hormonal changes in acne vulgaris. A prospective study was done on 50 female patients who presented with acne. Presence of associated clinical manifestations like Hirsutism, Acanthosis nigricans, Menstrual Dysfunction and Androgenetic Alopecia were noted. Pelvic Ultrasonography of the pelvis was done to look for Polycystic Ovaries. Hormonal Investigations done were Serum Dehydroepiandrosteronesulfate (DHEAS) levels, Serum Follicle stimulating hormone (FSH) levels, Serum Leuteinizing hormone (LH) levels, Serum Prolactin levels, Serum Testosterone and Serum Insulin levels. In our study,14% patients demonstrated Acanthosis nigricans, 24% had menstrual dysfunction and 12 % had Androgenetiic alopecia. PCOD was seen in 44% patients on ultrasonography. LH/FSH ratio was deranged in 12 % patients, raised serum insulin levels were seen in 12% cases, raised levels of Dehydroepiandrosterone sulphate(DHEAS) was seen in 12 % patients and raised Prolactin levels were seen in 8 % of the cases and 2% demonstrated raised testosterone levels. Patients with acne vulgaris may show clinical features like Acanthosis nigricans, androgenetic alopecia and hirsutism. A major group may show underlying PCOD and hormonal derangements. Hence, all female patients with acne should be screened with Ultrasonography and hormonal studies for optimal management.

Keywords: Acne, Hirsutism, Acanthosis nigricans, Androgenetic alopecia, PCOD, Hormonal derangement

INTRODUCTION

Acne vulgaris is a common skin condition, affecting 85-100% of people at some time during their lives. It is caused by changes in the pilosebaceous units, skin structures consisting of a hair follicle and its associated sebaceous gland via androgen stimulation. It is characterized by non-inflammatory follicular papules or comedones and by inflammatory papules, pustules and nodules in its most severe forms. Acne occurs most commonly during adolescence, and often continues into adulthood. In adolescence, acne is usually caused by a disturbance in hormonal levels in puberty [1]. For most people, acne diminishes over time and tends to disappear or reduce by age 25 [2]. The pathogenesis of acne is multifactorial and complex. There are four major factors in the etiology of acne which are seborrhea, comedo formation, colonization of sebaceous duct with Propionibacterium Acnes and inflammation. Acne can also present itself as a part of metabolic syndrome called polycystic ovarian syndrome. PCOS is a common disorder, affecting 5-10% of women [3] with multiple aetiologies and a variable clinical presentation. Symptoms and signs include menstrual dysfunction, acne, hirsutism, obesity, infertility, insulin resistance, and polycystic ovaries. Onset of the menstrual disorder begins peri pubertally and has been associated with childhood antecedents of low birth weight and premature pubarche [4, 5]. Definition of PCOS requires 2 of the 3 criteria (Revised 2003 Rotterdam criteria) to be met -oligoanovulation or anovulation, hyperandrogenemia (elevated levels of circulating androgens) or hyperandrogenism (clinical evidence of androgen excess) or polycystic ovaries by ultrasound(either 12 or more follicles measuring 2-9mm

in diameter, or increased ovarian volume (>10cm³). PCOS, a heterogenous syndrome, is the most frequently encountered endocrine disturbance in women of reproductive age. Its prevalence ranges from 5% to 10% [6, 7]. It affects all ethnic groups, and it is not only a reproductive disorder but a metabolic one. Not many studies have been done in our population correlating the presence of acne with associated clinical features, PCOD and hormonal changes. Hence, the present study was undertaken to determine the same in our population.

MATERIALS AND METHODS

A prospective, open labelled randomized study was done in the department of Dermatology and venereology at Dr. R.N Cooper Municipal General Hospital. Study Population included 50 newly diagnosed female patients with acne in the age group of 12 years to 40 years. Patients of acne already on treatment, pregnant and lactating females were excluded from the study. The study was approved by the local ethics committee and written informed consent was obtained from all the patients.

Patient demographic data, age, weight height, body mass index (BMI) and menstrual history was recorded in a predesigned proforma. Location of lesions, associated systemic diseases and complications were also noted. All patients of Acne were examined for presence of androgenic signs like hirsutism, Acanthosis nigricans, and androgenetiic alopecia. Blood pressure was recorded in each case.

Ultrasonography of the pelvis was done in all subjects trans abdominally using a 3.5 MHz probe. The ovarian morphology was carefully seen. Diagnosis of PCO was done when either 12 or more follicles measuring 2-9mm in diameter were present, or an increased ovarian volume of (>10cm³) was seen. The best time to perform an ultrasound of the pelvis is in the early follicular phase (day 3–6 of the menstrual cycle) in women who have regular menses. Anovulatory women who have oligoamenorrhea may be scanned at random or 3 to 5 days after a progestin-induced withdrawal bleed. Hence, accordingly the patients were instructed to undergo ultrasonography examination.

Hormonal assays done were Serum Dehydroepiandrosteronesulfate (DHEAS) levels, Serum Follicle stimulating hormone (FSH) levels, Serum Leuteinizing hormone (LH) levels, Serum Prolactin levels, Serum Testosterone- free and total levels and Serum Insulin levels. Measurement of the hormones were done by chemiluminiscence method.

In view of the circadian cyclicity of many hormones, the best time to draw blood is in the early morning, and in those who patients who have regular menses between days 3 and 8 of the menstrual cycle. Hence blood collection was done between 3 and 8 days of the menstrual cycle and early morning sample was collected. A correlation was done between the androgenic signs, hormonal changes and presence of PCO in patients of acne.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS 15 software. Percentages were calculated for the various categories. Chi- square and Fisher Exact test was used to compare the various groups and a *p*-value <0.05 was considered as significant.

RESULTS

A study was done on 50 patients present with acne. Patients history was taken followed by clinical examination, ultrasonography and hormonal assessment. Table-1 shows the age distribution of our patients enrolled in our study.

Table 1: Age Distribution of Acne

Age Group	No. of Patients	%
11-15	3	6
16-20	27	54
21-25	13	26
26-30	5	10
31-35	2	4
Total	50	100

In our study maximum (54%) patients were in the age group of 16-20years followed by (26 %) in the age group of 21-25 years. Table 2 shows the number of Patients with salient features of PCOS. There were 12 patients (24%) of acne with abnormal menstruation. A raised BMI was seen in 7 (14%) patients. Hirsutism (Fig 1), Acanthosis nigricans (Fig 2) and androgenic alopecia (Fig 3) was found in 11 cases (22%),7 cases (14%) and 6 cases (12%) respectively. Raised blood pressure was found in only 4(8%)of the cases. In our study 22 of 50 (44%) patients demonstrated presence of polycystic ovaries on pelvic ultrasound imaging (Fig 4). Table 3 shows the hormonal profile of acne patients. Abnormal levels of hormones were seen in 15 out of 50 cases (30%) cases. A raised LH/FSH ratio of > 1.5% was seen in 6 patients (12%). Prolactin levels were raised in 4 patients (8%) while DHEAS level was elevated in 6 cases (12%). Total testosterone was raised in one case and free testosterone was raised in 2 cases. High levels of insulin were found in 6 (12%) cases. Two groups of acne were studied one with presence of PCOS and others without it. A correlation was done between presence of PCOS with BMI, androgenic signs and hormonal abnormality. Out of 7 patients with raised BMI, 6 showed presence of PCOS. There were 9 patients of PCOD who presented with hirsutism while only 2 patients of hirsutism had normal ovaries on ultrasonography. 6 pts with Acanthosis nigricans had

PCOS while only 1 showed normal ultrasonography findings.11 out of 12 patients presenting with menstrual dysfunction had PCOS. Statistical analysis of the above parameters between 2 groups, showed that the association between PCOS with menstrual dysfunction (with p value 0.00017), high BMI, Hirsutism (with p value 0.00611), Acanthosis nigricans (with p value 0.03448) and acne was statistically significant. Also, the association between BMI and ultrasonographic finding of polycystic ovaries was statistically significant (with p value 0.034). The association of PCOS with other parameters and hormonal levels was not found to be statistically significant.

Table 2: Salient Features in patients of acne

Findings in Patients of Acne	No of cases
Menstrual Dysfunction	12(24%)
Hypertension	4(8%)
Raised BMI	7(14%)
Hirsutism	11(22 %)
Acanthosis nigricans	7(14 %)
Androgenic alopecia	6(12 %)
Polycystic ovaries	22(44%)

Table 3: Hormonal Profile in patients of acne

Hormone	Low	Normal	Raised
FSH	10(20%)	40(80%)	0
LH	3(6%)	44(88%)	3(6%)
LH/FSH ratio	0	43(86%)	7(14%)
Prolactin	2(4%)	44(88%)	4(8%)1
DHEAS	19(38%)	25(50%)	6(12%)
Total Testosterone	34(68%)	15(30%)	1(2%)
Free Testosterone	16(32%)	32(66%)	2(4%)
Insulin	0	44(88%)	6(12%)

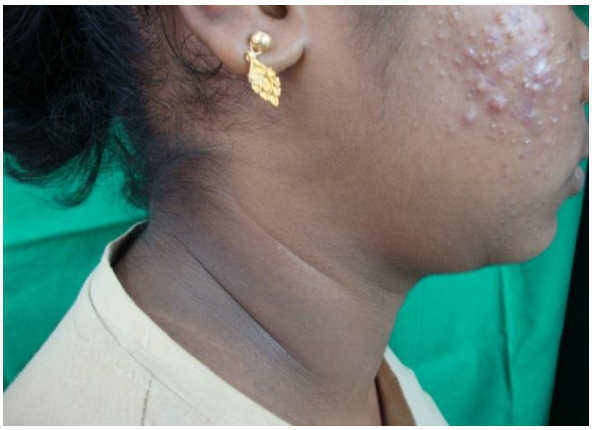

Fig-1: Acne with Acanthosis nigricans

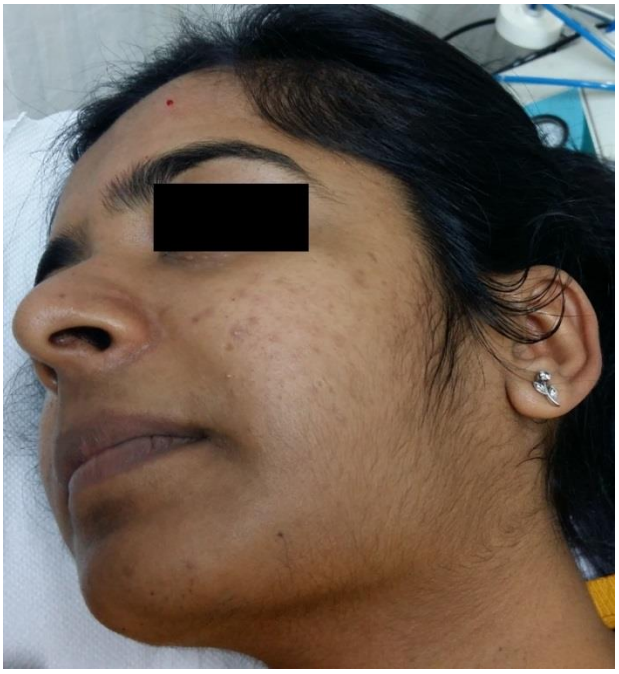

Fig-2: Acne with Androgenetic Alopecia

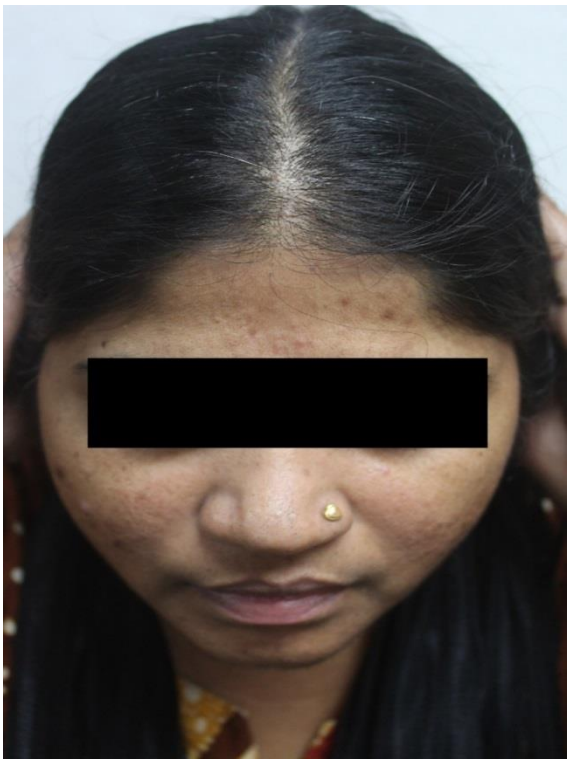

Fig-3: Acne with Hirsutism

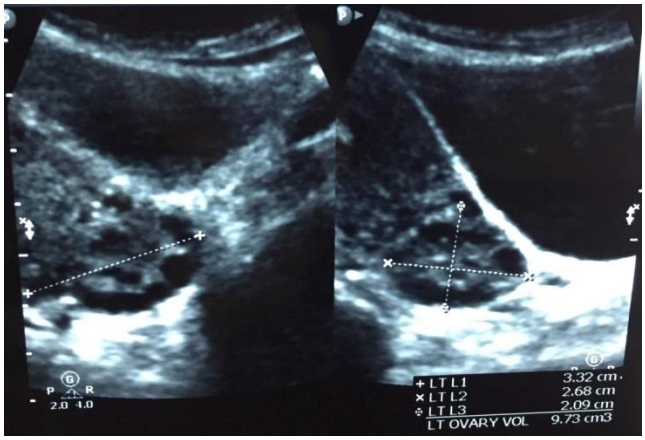

Fig-4: Ultrasonography of Polycystic Ovaries

DISCUSSION

Acne vulgaris is a pilosebaceous gland disease that usually affects people from puberty to young adulthood. The pathogenetic factors involved in acne formation are hyperplasia of sebaceous glands, increased sebum production, hyperkeratinization of pilosebaceous ducts, propionibacterium acnes colonization and periglandular dermal inflammation. A study was conducted on 50 female patients of acne in the department of dermatology along with abdominal USG examination and hormonal profile.

In our study a high proportion of patients (80%)were seen in the 16-25 years age group. Nazan et al have found maximum cases of acne in their study to be between 15 to 17 years age group while Adityan *et al* reported 79.2% cases in 16 to 25 years age which is similar to our study [8, 9]. This age group is involved due to spurt in androgen levels in puberty. There were 14% of acne cases in the present study who were adults in the age group between 26 to 35 years. Law et al have reported cases of acne in adults [10]. Menstrual dysfunction was present in 24% of our cases while 39.2 % of the cases had menstrual dysfunction in the study conducted by Timpatanapong *et al* [11], Reingold *et al* have found an association between acne, hirsutism and menstrual disturbances in their study on acne. A raised BMI was seen in 14% of the cases [12], Slayden *et al* have reported that acne was more common in obese women [13]. Del petri m *et al* have reported a high BMI in patients with acne as compared to the control group [14]. Signs of hyperandrogenemia found in our study were hirsutism (22 %), Acanthosis nigricans (14%), Androgenic alopecia (12%). Adityan *et al* have reported a higher incidence of hirsutism (76.4 %) and Acanthosis nigricans (52.9 %) in their study. They have reported androgenic alopecia in 11.7 % of their cases which is similar to our study [9]. PCO were found in 44 % of our cases. Cibulla *et al* have reported polycystic ovaries in 50 % of their cases of acne while Padova *et al* have reported in 45.3 % of their cases which is similar to our study [15, 16]. PCOS shows presence of hyperandrogenism with polycystic ovaries. Acne is a common occurrence in these patients as they have high levels of IGF-1 and androgens. IGF (insulin like growth factor) induces the production of androgens from the ovary while simultaneously inhibiting the hepatic synthesis of sex hormone binding globulin. Therefore, the bioavailability of androgens increases. The comedogenic effect of IGF-1 and high androgen level are thought to be responsible for the acne seen in PCOS [13].

The Hormonal Profile of our patients showed abnormal hormones in 15 % patients. A low FSH was found in 20 % of the cases while raised LH was found in 6 % of the cases. Hence, a raised LH/FSH was found in 14 % of the patients. Similar findings have been reported in a study by Timpatanapong *et al* [11]. It has been suggested that the elevated LH level stimulates androgen production from theca cells of ovary as the FSH level is low the aromatisation of androgen to estrogen is not complete, therefore, androgen is in excess. However, there is a pulsatile secretion of LH, hence, a single hormonal assay may not reflect true LH level.

Hyperprolactinemia has been found in 8 % of our cases. Zacur *et al* have reported that elevated prolactin in POS patients can vary from 3.2 to 66.7 % [17]. However, the definite role of prolactin in acne aetiology is still not clear [18]. A Study by Timpatanapong *et al* have reported higher mean levels of prolactin in patients of acne as compared to the normal control group [11]. Prolactin is supposed to increase the level of DHEAS by acting on the adrenals [19, 20].

DHEAS levels were raised in 6 % of our patients while Testosterone was elevated in 6 % of the cases. Slayden *et al* have reported hyperandrogenemia in patients of acne in their study. They concluded that Hyperandrogenemia was evident in a majority of nonhirsute acneic patients studied, their data suggested

that androgen suppression may be useful in treating acne in many of these patients [13].

Rahman *et al* conducted a study to find the correlation between testosterone levels and acne formation. They found a statistically significant association between the two. Androgen stimulates production of sebum, growth of sebaceous glands and hyperkeratinisation [21].

A raised insulin level was found in 12 % of our cases. Nazan *et al* studied insulin resistance in severe acne cases and compared it with the control group. They reported that the fasting blood glucose levels were similar in both groups but, a significantly higher level of insulin was found in the study group. Up to 50 % of the women with PCOS have a genetic defect coding for serine phosphorylation of insulin receptors. The resulting increased insulin levels directly and indirectly, increase androgen production [22]. In a study conducted by Smith *et al* it was found that the IGF-1 stimulates sebaceous gland lipogenesis. This increased sebum production is one of the etiology of acne [23].

Statistically in our study a significant correlation was found between acne vulgaris and clinical features such as hirsutism, Acanthosis nigricans, menstrual dysfunction with ultrasonographic evidence of polycystic ovaries. Also, the association between BMI and polycystic ovaries was significant.

CONCLUSION

Hence this study statistically shows a significant co-relation between Acne vulgaris and clinical features such as Hirsutism, Acanthosis nigricans, androgenetic alopecia and Menstrual dysfunction with ultrasonographic evidence of polycystic ovaries. Also, the association between BMI and ultrasonographic finding of polycystic ovaries was statistically significant. It is mandatory to screen these patients for polycystic ovaries by ultrasonography and do the hormonal profile. So, the correct diagnosis of PCOD in patients with acne will lead to treatment of the underlying cause.

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