Clinical Study
Meibomian Gland Dysfunction: Endocrine Aspects

Ozlem G. Sahin, Elçin Kartal, and Nusret Taheri

1 Department of Ophthalmology, College of Health Sciences, Middle East Technical University, 06800 Ankara, Turkey
2 Department of Statistics, Middle East Technical University, 06800 Ankara, Turkey
3 Department of Biochemistry, College of Health Sciences, Middle East Technical University, 06800 Ankara, Turkey

Correspondence should be addressed to Ozlem G. Sahin, ozlem1158@yahoo.com

Received 15 July 2011; Accepted 21 August 2011

Purpose. To compare the hormone levels of patients with seborrheic meibomian gland dysfunction with controls. Procedures. This is a retrospective case-control study involving 50 patients and 50 controls. Blood workup for hormones was studied in both groups by using macroELISA (enzyme-linked immunosorbent assay). Statistical evaluation was done by using SPSS 15.0 independent samples t-test. Results. There were statistically significant differences of serum testosterone and dehydroepiandrosterone sulphate levels between patients and controls (P = 0.000). Female gender showed statistically significant differences of serum thyroid-stimulating hormone and prolactin levels between patients and controls (P = 0.014 and P = 0.043), in addition to serum testosterone and dehydroepiandrosterone sulphate levels (P = 0.000 and P = 0.001). However, male gender showed statistically significant differences of only serum testosterone and dehydroepiandrosterone sulphate levels between patients and controls. (P = 0.003 and P = 0.003 resp.). Conclusions. Increased serum levels of testosterone and dehydroepiandrosterone sulphate in both genders should be considered as diagnostic markers for seborrheic meibomian gland dysfunction.

1. Introduction
Meibomian gland dysfunction (MGD) is considered to be a discrete disease entity without prominent inflammatory alterations of the lid margins and a frequent cause of wetting deficiencies of the ocular surface leading to dry eye disease [1]. MGD is grouped as obstructive and seborrheic dysfunction [2, 3]. Obstructive MGD is characterized by hyperkeratinization of the ductal epithelium and increased viscosity of the meibum resulting in obstruction of the meibomian gland duct and orifice [1, 2]. Obstructive MGD is reported to be much more frequent in the general population and increases with age [2]. Seborrheic MGD is characterized by hypersecretion of meibum [3]. Proposed diagnostic criteria for seborrheic MGD include ocular symptoms and lid margin abnormalities [3]. Age, hormonal disturbances, and environmental influences have been considered in the pathogenesis of both obstructive and seborrheic MGD [2]. The effect of androgens on meibomian gland function has been studied in a group of patients with an average of 70.9 years, and androgen deficiency is considered as a critical factor in the pathogenesis of MGD and dry eye [4, 5]. Very little information exists concerning the correlation of serum levels of sex hormones, thyroid hormones, thyroglobulin, cortisol, and prolactin with seborrheic MGD between 20–30 years of age. The purpose of this study is to compare the serum levels of dehydroepiandrosterone sulphate (DHEAS), testosterone, estriol, 17-hydroxyprogesterone (17-OH-Prog), prolactin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), bound and unbound thyroid hormones (T3, T4), thyroglobulin, and cortisol between patients with seborrheic MGD and controls in a gender-based design between 20–30 years of age.

2. Methods
This is a retrospective case-control study involving 50 patients, 31 male and 19 female with a mean ± standard deviation (SD) of 23.92 ± 5.73 years, and 50 controls 19 male and 31 female with a mean age of 23.36 ± 4.61 years.
Table 1: Descriptive statistics of serum hormone levels in both genders with respect to patients with seborrheic meibomian gland dysfunction and controls.

| Hormones               | Groups      | N  | Mean               | SD    |
|------------------------|-------------|----|-------------------|-------|
| TSH (mIU/mL)           | Patient     | 50 | 1,9188            | 1,11642|
| Control                | 50          | 1,7696       | 1,00285         |
| Bound-T3 (nmol/L)      | Patient     | 50 | 1,5930            | 32533 |
| Control                | 50          | 1,7884       | 1,42732         |
| Bound-T4 (nmol/L)      | Patient     | 50 | 81,0106           | 9,74157|
| Control                | 50          | 83,3822      | 10,77266        |
| Unbound-T3 (pmol/L)    | Patient     | 50 | 4,9398            | 0,75224|
| Control                | 50          | 4,8162       | 0,80606         |
| Unbound-T4 (pmol/L)    | Patient     | 50 | 14,4654           | 2,17048|
| Control                | 50          | 14,4144      | 2,42574         |
| FSH (mIU/mL)           | Patient     | 50 | 4,2894            | 1,95526|
| Control                | 50          | 4,1122       | 3,37226         |
| LH (mIU/mL)            | Patient     | 50 | 3,8674            | 2,64136|
| Control                | 50          | 3,8062       | 2,40230         |
| 17-OH-Prog (ng/mL)     | Patient     | 50 | 2,2484            | 3,90230|
| Control                | 50          | 3,8628       | 6,99213         |
| Estrodiol (pg/mL)      | Patient     | 50 | 69,2948           | 56,87763|
| Control                | 50          | 79,4172      | 63,27935        |
| Prolactin (ng/mL)      | Patient     | 50 | 17,9796           | 9,88949|
| Control                | 50          | 18,3808      | 8,63390         |
| Testosterone (ng/mL)   | Patient     | 50 | 4,7764            | 3,66869 |
| Control                | 50          | 2,2714       | 2,71801         |
| Cortisol (ng/mL)       | Patient     | 50 | 147,0022          | 55,22128|
| Control                | 50          | 130,5280     | 53,70375        |
| DHEA-S μg/mL           | Patient     | 50 | 370,7088          | 146,50287|
| Control                | 50          | 238,5034     | 97,72012        |
| Thyroglobulin (IU/mL)  | Patient     | 50 | 11,9058           | 8,16335 |
| Control                | 50          | 11,0008      | 14,74698        

DHEA-S: Dihydroepiandrosterone-sulphate, 17-OH-Prog: 17 Hydroxysterone, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, N: Number, TSH: thyroid stimulating hormone, T3: triiodothyronine, T4: thyroxine, SD: Standard deviation.

The study is approved by the Human Studies Committee of the Middle East Technical University (Ankara, Turkey) and were conducted in accordance with guidelines established by the Declaration of Helsinki. Ocular symptoms including ocular fatigue, discharge, foreign body sensation, dryness, discomfort, sticky sensation, pain, epiphora, itching, redness, heavy sensation, glare, excessive blinking, and history of chalazion or Hordeolum were scored from 0 to 4 according to the number of symptoms present [3]. Lid margin abnormalities including irregular lid margin, vascular engorgement, plugged meibomian gland orifices, and anterior or posterior replacement of mucocutaneous junction, were scored from 0 to 4 depending on the number of abnormalities present [3]. Superficial punctate keratopathy (SPK) in the cornea was scored from 0 to 3 [3, 6]. The tear film break-up time (BUT) was measured consecutively three times after instillation of fluorescein 1% (fluoresceite injection) and the median value was adopted [6]. Assessment of meibomian gland function was done by using two techniques: observation of meibomian gland orifices by using biomicroscopy and transillumination observation techniques by using a light probe (meibography) [7, 8]. Meibography was performed by using a transillumination device for vitrectomy with a 20-gauge fiberoptic light probe (Bausch and Lomb Millennium, Rochester, NY) including tungsten-halogen ad metal halide. Meiboscore for upper and lower eyelids was used as previously described: grade 0 (no loss of meibomian glands), grade 1 (loss of less than one-third of the total area of the meibomian glands), grade 2 (loss of between one-third and two-thirds of the total area), and grade 3 (loss of over two-thirds of the total area) [7, 8]. Meibomian gland expression was evaluated by applying moderate digital pressure on the tarsus of the upper eyelid, and the degree of ease with which meibum secretion was induced was evaluated as grade 0 (clear meibum, easily expressed), grade 1 (cloudy meibum, expressed with mild pressure), grade 2 (cloudy meibum expressed with more than moderate pressure), and grade 3 (no meibum expressed even with hard pressure) [9]. The procedure was performed by the same ophthalmologist. Tear film production was evaluated using the Schirmer test without application of topical anesthetics. A diagnosis of seborrhoeic MGD was made on the basis of an ocular symptom score of 3 or more and a lid margin score of 2 or more [3, 6]. Patients with meiboscore 1 or more, a Schirmer value of 5 mm or less, the tear break-up time of less than 5 seconds, and SPK score of 1 or more, were excluded from the study. The controls had no evidence of blepharitis, seborrhoeic MGD, or corneal diseases. They have only refractive errors and are otherwise healthy. Exclusion criteria for both groups include ocular allergies, contact lens wearing, history of eye surgery, and systemic or ocular diseases that might interfere tear film production or function [10]. Patients displayed ocular symptoms for at least 3 months and received no topical or systemic therapy for at least 4 weeks. Morning fasting values of testosterone, LH, FSH, DHEA-S, 17-OH-Prog, TSH, bound and unbound T3 and T4, prolactin, thyroglobulin, and cortisol were determined in 1 milliliter (mL) serum of patients and controls on the same day by using Vidas PC (bioMerieux, France) with macroELISA technique. Statistical evaluation was done by using SPSS 15.0 independent samples t-test.

3. Results
The mean score of ocular symptoms of patients with seborrhoeic MGD was 9.48 over 14.0, and the mean score of lid margin abnormalities was 2.98 over 3.0. SPK was not detected in both groups. The tear film BUT was in the normal range, and there were no loss of the meibomian glands in both groups. The patients had the score of meibomian gland expression either grade 0 or grade 1. Table 1 discloses mean and standard deviation (SD) of serum levels of TSH, bound and unbound T3 and T4, FSH, LH, 17-OH-Prog, estrodiol, prolactin, testosterone, DHEA-S, cortisol, and thyroglobulin of the patients and controls in both genders. The mean (SD) of serum testosterone level was 2.27 (2.72) ng/mL in controls.
Table 2: Descriptive statistics of serum hormone levels in female gender with respect to patients with seborrheic meibomian gland dysfunction and controls.

| Sex | Group | N | Statistic | Mean | Std. Error | SD |
|-----|-------|---|-----------|------|------------|----|
|     | Control |     |          |      |            |    |
| F   | TSH (µIU/mL) | 31 | 1,636     | 1,160 | 0.89308    |
|     | Bound-T3 (nmol/L) | 31 | 1,837     | 0.3235 | 1,80170    |
|     | Bound-T4 (nmol/L) | 31 | 83,425    | 1,77369 | 9,87551   |
|     | Unbound-T3 (pmol/L) | 31 | 4,526     | 0.1068 | 0.59474    |
|     | Unbound-T4 (pmol/L) | 31 | 13,842    | 0.3013 | 1,67762    |
|     | FSH (mIU/ml) | 31 | 4,5674    | 0.34349 | 1,91249 |
|     | LH (mIU/ml) | 31 | 4,330     | 0.57185 | 3,18394 |
|     | 17-OH-Prog (ng/ml) | 31 | 5,438     | 0.84706 | 7,08447 |
|     | Estrodiol (pg/ml) | 31 | 99,389    | 0.84706 | 7,08447 |
|     | Prolactin (ng/ml) | 31 | 4,567     | 0.84706 | 7,08447 |
|     | Testosterone (ng/ml) | 31 | 3,687     | 0.02907 | 7,16186 |
|     | Cortisol (ng/ml) | 31 | 125,961   | 0.95027 | 5,57449 |
|     | DHEA-S (µg/ml) | 31 | 212,070   | 0.155036 | 8,652082 |
|     | Thyroglobulin (IU/ml) | 31 | 12,684    | 0.730031 | 7,38753 |
| Patients | TSH (µIU/mL) | 19 | 2,459     | 0.32201 | 1,40359 |
|     | Bound-T3 (nmol/L) | 19 | 1,424     | 0.06133 | 0.26734 |
|     | Bound-T4 (nmol/L) | 19 | 78,541    | 2.61172 | 11,38422 |
|     | Unbound-T3 (pmol/L) | 19 | 4,429     | 0.13957 | 0.60835 |
|     | Unbound-T4 (pmol/L) | 19 | 13,550    | 0.54541 | 2,37738 |
|     | FSH (mIU/ml) | 19 | 4,455     | 0.34066 | 1,48492 |
|     | LH (mIU/ml) | 19 | 6,215     | 1.04083 | 4,53688 |
|     | 17-OH-Prog (ng/ml) | 19 | 4,362     | 1.33275 | 5,80933 |
|     | Estrodiol (pg/ml) | 19 | 113,8679  | 16,43153 | 4,62339 |
|     | Prolactin (ng/ml) | 19 | 23,512    | 0.275322 | 1,20099 |
|     | Testosterone (ng/ml) | 19 | 0.6895    | 0.07690 | 0,33520 |
|     | Cortisol (ng/ml) | 19 | 146,729   | 0.137991 | 7,54498 |
|     | DHEA-S (µg/ml) | 19 | 325,5653  | 0.3252678 | 141,78094 |
|     | Thyroglobulin (IU/ml) | 19 | 13,640    | 2,23048 | 9,72246 |

DHEA-S: dihydroepiandrosterone-sulphate, 17-OH-Prog: 17-hydroxyprogesterone, F: female, FSH: follicle stimulating hormone, LH: luteinizing hormone, N: number, Std: standard, SD: standard deviation, TSH: thyroid stimulating hormone, T3: triiodothyronine, T4: thyroxine.
Table 3: Descriptive statistics of serum hormone levels in male gender with respect to patients with seborrheic meibomian gland dysfunction and controls.

| Sex | Group | N | Statistic | Mean | Std. Error | SD | Statistic |
|-----|-------|---|-----------|------|------------|----|-----------|
| M   | Control TSH (µIU/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | Bound-T3 (nmol/L) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | Bound-T4 (nmol/L) | 19 | 83,3116 | 2,84108 | 12,38399 |
|     | Unbound-T3 (pmol/L) | 19 | 5,2895 | 2,84108 | 12,38399 |
|     | Unbound-T4 (pmol/L) | 19 | 15,3474 | 2,84108 | 12,38399 |
|     | FSH (mIU/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | LH (mIU/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | 17-OH-Prog (ng/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | Estriol (pg/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | Prolactin (ng/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | Testosterone (mg/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | Cortisol (mg/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |
|     | DHEA-S (µg/mL) | 19 | 8,2532 | 1,34430 | 1,50077 |
|     | Thyroglobulin (IU/mL) | 19 | 1,9874 | 1,7089 | 1,2643 | 34 | 1,15225 |

Patients

| TSH (µIU/mL) | 31 | 1,5874 | 1,34430 | 1,50077 |
| Bound-T3 (nmol/L) | 31 | 1,6965 | 1,34430 | 1,50077 |
| Bound-T4 (nmol/L) | 31 | 82,5239 | 1,34430 | 1,50077 |
| Unbound-T3 (pmol/L) | 31 | 5,2526 | 1,34430 | 1,50077 |
| Unbound-T4 (pmol/L) | 31 | 15,0265 | 1,34430 | 1,50077 |
| FSH (mIU/mL) | 31 | 1,2926 | 1,34430 | 1,50077 |
| LH (mIU/mL) | 31 | 1,2926 | 1,34430 | 1,50077 |
| 17-OH-Prog (ng/mL) | 31 | 1,2926 | 1,34430 | 1,50077 |
| Estriol (pg/mL) | 31 | 1,2926 | 1,34430 | 1,50077 |
| Prolactin (ng/mL) | 31 | 1,2926 | 1,34430 | 1,50077 |
| Testosterone (ng/mL) | 31 | 7,2813 | 1,34430 | 1,50077 |
| Cortisol (ng/mL) | 31 | 147,1694 | 9,83788 | 54,77501 |
| DHEA-S (µg/mL) | 31 | 398,3774 | 25,97363 | 144,61507 |
| Thyroglobulin (IU/mL) | 31 | 10,8429 | 1,25798 | 7,00414 |

DHEA-S: dihydroepiandrosterone-sulphate, 17-OH-Prog: 17 hydroxyprogesteron, FSH: follicle stimulating hormone, LH: lutenizing hormone, M: male, N: number, TSH: thyroid stimulating hormone, T3: triiodothyronine, T4: thyroxine, Std: Standard, SD: Standard deviation.

in female gender with respect to patients with seborrheic MGD and controls ($P = 0.001, 95\% CI 0.15, 0.49$; Table 4). The data mean of serum DHEA-S level in female gender of both patients and controls was 255.20 (122.70) µg/mL. The mean value of DHEA-S in female controls was 212.07 (86.32) µg/mL and in female patients with seborrheic MGD was 325.57 (141.78) µg/mL (Table 2). There was statistically significant difference of mean serum values of DHEA-S in female gender with respect to patients with seborrheic MGD and controls ($P = 0.001, 95\% CI 0.15, 0.49$; Table 4). Table 3 shows the mean (SD) of serum hormone levels in male gender with respect to the patients with seborrheic MGD and controls. The data mean of serum testosterone level in male gender of both patients and controls was 6.56 (2.28) ng/mL (Table 4). The mean value of serum testosterone in male patients with seborrheic MGD was 7.281 (2.20) ng/mL (Table 3). There was statistically significant difference of mean serum values of testosterone in male gender with respect to patients with seborrheic MGD and controls ($P = 0.003, 95\% CI 0.68, 3.14$; Table 4).

The data mean of serum DHEA-S level in male gender of both patients and controls was 354.0 (141.10) µg/mL. The mean value of serum DHEA-S level in male patients with seborrheic MGD was 398.38 (144.6) µg/mL, and in controls was 281.63 (102.0) µg/mL. There was statistically significant differences of mean serum levels of DHEA-S in male gender with respect to patients with seborrheic MGD and controls ($P = 0.003, 95\% CI 0.68, 3.14$; Table 4). No statistically significant differences of mean serum levels of the hormones including bound and unbound T3 and T4, FSH, LH, 17-OH-Prog, estriol, cortisol, and thyroglobulin in both genders were found between the patients with seborrheic MGD and controls ($P > 0.05$).

4. Discussion

This is the first time a case-control comparative study has been undertaken to assess the endocrine aspects of seborrheic MGD in a gender-based design. It represents the first
report of increased serum levels of testosterone and DHEA-S in both genders with seborrheic MGD and increased serum levels of TSH and prolactin only in female gender with seborrheic MGD. Meibomian gland is considered as an androgen target organ [11]. Androgens (testosterone) are reported to control meibomian gland function, regulate the quality and/or quantity of lipids produced by this tissue, and promote the formation of the tear film’s lipid layer [5, 11]. Previous studies related to androgen deficiency revealed significant and striking alterations in the lipid patterns of meibomian gland secretions, and it was considered to be an important etiologic factor in the pathogenesis of evaporative dry eye [4, 5]. However, testosterone excess is considered to provoke or aggravate seborrhea at a significance rate of \( P < 0.01 \) [12]. The effect of androgens on human skin is reported to increase sebaceous gland growth and differentiation, produce acne and seborrhea [13]. We demonstrated statistically significant increase of serum levels of testosterone in both genders with seborrheic MGD with respect to control genders. The mean score of ocular symptoms of the patients with seborrheic MGD was 9.48 over 14.0, and the mean score of lid margin abnormalities was 2.98 over 4.0. The value of serum testosterone was considered to be a significant factor affecting the severity of seborrheic MGD in both genders. Adrenal glands secrete large amounts of DHEA and DHEA-S which are then converted into potent androgens (testosterone and dehydrotestosterone) or estrogens by stereogenic enzymes in the peripheral sites that permit target tissues to adjust the formation and metabolism of androgens and estrogens to local requirements [14]. Increased serum levels of DHEA-S have been reported in patients with seborrheic dermatitis, acne vulgaris, alopecia, and hirsutism [15–17]. The aging process is paralleled by a dramatic decline in the serum concentrations of DHEA and DHEA-sulphate [14]. Serum levels of DHEA is reported to decrease from the age of 30 years [18]. In addition, there is a marked decline in the circulating levels of DHEA in post-menopausal women [18]. Our study includes the patients with seborrheic MGD at young age, mean age of 23, and age-matched controls. We demonstrate significant increase in serum levels of DHEA-S in both genders of patients with respect to control genders. We consider increase in serum values of DHEA-S in patients with seborrheic MGD could be used as diagnostic marker, and could be correlated with severity of the disease. Estrogens, glucocorticoids, and prolactin are also considered to influence sebaceous gland function by stimulating proliferation of sebocyte [19, 20]. Previous studies demonstrated that tear production in humans is correlated with prolactin [21]. The effect of prolactin on meibomian gland function has not been reported before. Our study revealed significant increase in serum levels of prolactin in female gender of patients with seborrheic MGD as compared to control gender. However, there was no significant increase in serum levels of prolactin in male patients with seborrheic MGD as compared to control gender. The correlation of serum prolactin level with seborrheic MGD remains to be determined. The function of TSH on sebocytes has not been reported before. Our study revealed significant increase in serum levels of prolactin in female gender of patients with seborrheic MGD as compared to control gender. The correlation of serum levels of TSH with seborrheic MGD also remains to be determined in larger cohorts. No significant difference of serum levels of other hormones including bound and unbound T3 and T4, FSH, LH, progesterone, estrodiol, cortisol and thyroglobulin were found between patients with seborrheic MGD and controls in both genders. In conclusion: Increased serum levels of testosterone and DHEA-S in both genders should be considered as diagnostic markers for seborrheic MGD and may affect severity of the disease. However, the correlations of serum levels of TSH and prolactin with seborrheic MGD need to be further investigated.

**Conflict of Interests**

The authors have no proprietary or commercial interests in any concept or product discussed in this paper.
References

[1] E. Knop, N. Knop, H. Brewitt et al., “Meibomian glands: part III. Dysfunction- argument for a discrete disease entity and as an important cause of dry eye,” Ophthalmologe, vol. 106, no. 11, pp. 966–979, 2009.
[2] E. Knop and N. Knop, “Meibomian glands: part IV. Functional interactions in the pathogenesis of meibomian gland dysfunction (MGD),” Ophthalmologe, vol. 106, no. 11, pp. 980–987, 2009.
[3] R. Arita, K. Itoh, S. Maeda et al., “Proposed diagnostic criteria for seborrheic meibomian gland dysfunction,” Cornea, vol. 29, no. 9, pp. 980–984, 2010.
[4] K. L. Krenzer, M. R. Dana, M. D. Ullman et al., “Effect of androgen deficiency on the human meibomian gland and ocular surface,” Journal of Clinical Endocrinology and Metabolism, vol. 85, no. 12, pp. 4874–4882, 2000.
[5] D. A. Sullivan, B. D. Sullivan, J. E. Evans et al., “Androgen deficiency, meibomian gland dysfunction, and evaporative dry eye,” Annals of the New York Academy of Sciences, vol. 966, pp. 211–222, 2002.
[6] J. Shimazaki, M. Sakala, and K. Tsubota, “Ocular surface changes and discomfort in patients with meibomian gland dysfunction,” Archives of Ophthalmology, vol. 113, no. 10, pp. 1266–1270, 1995.
[7] W. D. Mathers, W. J. Shields, M. S. Sachdev, W. M. Petroll, and J. V. Jester, ”Meibomian gland dysfunction in chronic blepharitis,” Cornea, vol. 10, no. 4, pp. 277–285, 1991.
[8] J. Shimazaki and K. Tsubota, ”Evaluation of meibomian gland dysfunction via meibography,” Atarashii-Ganka, vol. 10, pp. 1031–1034, 1993.
[9] J. Shimazaki, E. Goto, M. Ono, S. Shimmura, and K. Tsubota, ”Meibomian gland dysfunction in patients with Sjögren syndrome,” Ophthalmology, vol. 105, no. 8, pp. 1485–1488, 1998.
[10] R. Arita, K. Itoh, S. Maeda et al., ”Efficiency and diagnostic criteria for the differential diagnosis between obstructive meibomian gland dysfunction and aqueous deficiency dry eye,” Japanese Journal of Ophthalmology, vol. 54, pp. 387–391, 2010.
[11] D. A. Sullivan, B. D. Sullivan, M. D. Ullman et al., ”Androgen influence on the meibomian gland,” Investigative Ophthalmology & Visual Science, vol. 41, pp. 3732–3742, 2000.
[12] M. Placzek, B. Arnold, H. Schmidt et al., ”Elevated 17-hydroxyprogesterone serum values in male patients with acne,” Journal of the American Academy of Dermatology, vol. 53, no. 6, pp. 955–958, 2005.
[13] C. C. Zouboulis, W. C. Chen, M. J. Thornton, K. Qin, and R. Rosenfield, ”Sexual hormones in human skin,” Hormone and Metabolic Research, vol. 39, no. 2, pp. 85–95, 2007.
[14] F. Labrie, A. Belanger, V. Luu–The et al., ”DHEA and intracrine formation of androgens and estrogens in peripheral target tissues: its role during aging,” Steroids, vol. 63, no. 5-6, pp. 322–328, 1998.
[15] B. J. Kim, J. Y. Kim, H. C. Eun, O. S. Kwon, M. N. Kim, and B. I. Ro, ”Androgenic alopecia in adolescents: a report of 43 cases,” Journal of Dermatology, vol. 33, no. 10, pp. 696–699, 2006.
[16] F. Vitale and P. Ruggieri, ”LHRH analogues and PCO disease: validity of the use of enantone depot in the treatment of the disease,” Acta Europaea Fertilitas, vol. 23, no. 6, pp. 293–295, 1992.
[17] U. Cirkel, L. Belkien, J. P. Hanker, K. W. Schwerppe, and H. P. Schneider, ”Effects of a chlormadione acetate-containing ovulation inhibitor on androgenization pictures and liver and lipid metabolism in young females,” Geburtshilfe Frauenheilkd, vol. 46, pp. 439–443, 1986.
[18] F. Labrie, ”DHEA, important source of sex steroids in men and even more in women,” Progress in Brain Research, vol. 182, pp. 97–148, 2010.
[19] C. C. Zouboulis, ”The sebaceous gland,” Hautarzt, vol. 61, no. 6, pp. 467–477, 2010.
[20] C. C. Zouboulis, ”Acne and sebaceous gland function,” Clinics in Dermatology, vol. 22, no. 5, pp. 360–366, 2004.