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ASSESSING THE ROLE OF INSULIN RESISTANCE IN INDIAN SUBJECTS WITH HIRSUTISM AND ACNE VULGARIS – A CROSS-SECTIONAL AND OBSERVATIONAL STUDY

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ABSTRACT

Background: Hirsutism and acne are commonly encountered conditions and are easy to treat. However, they pose a striking consequence on self-perception. The pathogenesis of hirsutism and acne are extensively studied with one being attributed to insulin resistance. However, these are not well understood.

Aim: The present study aimed to establish a relationship between acne vulgaris and hirsutism to insulin resistance and to assess the severity of two conditions with increased insulin resistance.

Methods: In included subjects, detailed clinical history was recorded followed by parameters including BMI, weight, and height along with the signs and symptoms of underlying insulin resistance. The severity of hirsutism was assessed using mFG (modified Ferriman Gallwey) score and acne was recorded using GAGS (global acne grading system). The data were analyzed to formulate results.

Results: 174 subjects were divided into 3 groups where acne only group with 154 subjects depicted a significant correlation between insulin resistance with recurrence and acne severity with $p<0.0001$. The hirsutism-only group with 12 subjects showed a strong correlation of HOMA-IR to mFG score and recurrence showing increased hirsutism severity with increased insulin resistance $p<0.0001$ and recurrence $p<0.007$. Combined hirsutism and acne group showed a positive correlation between BMI and insulin resistance and not severity.

Conclusion: The present study concludes that insulin resistance is a vital contributing factor in the pathogenesis of severe and resistant acne and hirsutism. Insulin resistance can have a significant impact on the psychological state of the affected subjects making it necessary to adopt a different approach for the management of these conditions.

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Keywords: Acne, global acne grading system, hirsutism, HOMA-IR, mFG

INTRODUCTION

Hirsutism and acne vulgaris are common dermatological concerns showing high prevalence globally including in India. The two conditions are commonly encountered in dermatological practice in Indian scenarios. The etiopathology and associated mechanisms for these entities are studied widely and are attributed to varied factors. Acne vulgaris is a chronic and complex inflammatory disease arising from the pilosebaceous unit and its etiology is attributed to various factors including genetics, host factors, and environmental factors. The etiology is also linked to the proliferation of *Cutibacterium acnes*, follicular hyperkeratinization, hyperplasia and hypertrophy of the sebaceous gland, and increased sebum production.[1]

Hirsutism is another dermatological issue that is the most distressing condition in female subjects. Especially those in the younger age groups. Hirsutism describes a condition where excessive terminal hairs are seen in female subjects resembling the male pattern, and involve areas like thighs, upper arms, lower back, upper back, pelvis, abdomen, chest, chin, and/or upper lips.[2]

Various theories are attributed to the pathogenesis of hirsutism and acne vulgaris. One such theory is the role of insulin resistance (IR) which has been accepted and studied by various clinicians and scholars recently. Insulin resistance with a decrease in circulating glucose uptake by the insulin-responsive tissues in the same concentration of insulin leads to a hyperglycemic state which, in turn, results in adverse micro and macrovascular consequences. With the increase in sedentary lifestyles and modern technologies, the prevalence of insulin resistance has increased widely.[3]

Insulin resistance not only leads to hirsutism or acne but also to various dermatological conditions including vitiligo vulgaris, androgenetic alopecia, psoriasis, and acanthosis nigricans. Insulin resistance is also correlated to different cardiovascular diseases like ischemic heart diseases and metabolic disorders like PCOS (polycystic ovarian syndrome), dyslipidemia, and diabetes mellitus. In addition to these consequences, there is a significant psychological impact associated with hirsutism and acne vulgaris in affected subjects.[4]

The present clinical study aimed to establish a relationship between acne vulgaris and hirsutism to insulin resistance and to assess the severity of two conditions with increased insulin resistance.

MATERIALS AND METHODS

The present cross-sectional observational study aimed to establish a relationship between acne vulgaris and hirsutism to insulin resistance and to assess the severity of two conditions with increased insulin resistance. The study was done at department of dermatology, venereology and leprosy after the clearance was given by the concerned Institutional Ethical Committee. The study population was recruited from the Department of Dermatology of the institute.

The study includes subjects visiting the Outpatient Department of Dermatology with hirsutism and acne vulgaris and following the exclusion and inclusion criteria for study participation. Verbal and written informed consent was taken from all the study subjects before participation. The exclusion criteria for the study were subjects on the use of alternative medications, hormonal

therapy, history of oral retinoid use, systemic inflammatory diseases affecting insulin metabolism, lactating females, pregnant females, malignancy, atherosclerotic vascular diseases, hypertension and thyroid dysfunction.

After final inclusion, detailed history was recorded for all the subjects followed by clinical examination. The demographic data were recorded for all the subjects including BMI (body mass index), weight, and height on the preformed structured proforma which also assessed symptoms and signs of underlying insulin resistance. The proforma had questions concerning recurrent infections of the bladder, vagina, skin, or gums, menstrual irregularities, voice deepening, excessive hair loss, seborrhea, decreased/increased appetite, weakness or fatigue, and rapid or unexplained weight loss or weight gain.

This was followed by an assessment of the fasting blood sugar (FBS) levels and fasting insulin levels to get the HOMA-IR (homeostatic model assessment for insulin resistance). The HOMA-IR value of >2.5 was considered significant and suggested insulin resistance. The severity of hirsutism was assessed using mFG (modified Ferriman Gallwey) scores and the severity of acne was assessed using GAGS (global acne grading system).

The data gathered were analyzed statistically using SPSS software version 21.0 and Pearson correlation coefficient to assess the correlation between hirsutism and acne to insulin resistance. The confidentiality of the data was kept throughout. The p-value of <0.05 was considered statistically significant.

RESULTS

The study included 174 subjects that were divided into 3 groups where Group I had 88.50% (n=154) subjects having only acne, Group II had 6.89% (n=12) study subjects having only hirsutism, and Group III had 4.59% (n=8) study subjects having both acne vulgaris and hirsutism respectively. The mean age of the study subjects was 24.81±4.32 years.

In Group I, the majority of the study subjects were of age <20 years with 49.35% (n=76). In groups II and III, the majority of the subjects were within 21-30 years with 58.33% (n=7) and 62.5% (n=5) respectively. There were 50.57% (n=88) females and 49.42% (n=86) males in the present study.

History of type 2 diabetes mellitus was positive in 14.94% (n=26) subjects in total with 14.28% (n=22) subjects, 16.6% (n=2), and 25% (n=2) study subjects respectively from Group I, II, and III. For insulin resistance, positive signs and symptoms of insulin resistance were seen in 64 male and 20 female subjects. Among 78 subjects with naïve acne, insulin resistance was seen in 27 study subjects and 76 subjects had recurrent acne, and insulin resistance was seen in 57 study subjects depicting a strong possibility of correlation.

Normal BMI range was seen in the majority of study subjects with 76 subjects having BMI in the range of 18.5 to 24.9 with mean BMI of 24.26. A significant association with insulin resistance was seen in 41.4% (n=32) of subjects. A 100% strong association of insulin resistance was seen in 11 study subjects of group I who have a BMI of >30. Among 40 subjects out of 46 subjects in the overweight category with a BMI of 25-30, had insulin resistance. Two subjects of 21 subjects in the underweight category of BMI <18.5 had insulin resistance.

The mean HOMA-IR, mean fasting insulin and mean fasting blood sugar were significantly high in the study. Recurrence, age, GAGS, and raised HOMA-IR showed a strong association with BMI in this group with $p<0.01$. A significant association was seen between age and BMI with $p<0.05$. However, no significant association was seen between BMI and gender with $p>0.05$ when assessed using Pearson's correlation coefficient as depicted in Table 1. In the majority of study subjects having insulin resistance, it was significantly seen in very severe, severe, and moderate acne groups with 59%, 88%, and 46% of study subjects respectively.

In group II, 12 females having confirmed diagnosis of hirsutism were assessed and insulin resistance was seen in 7 of those subjects. Among 5 subjects out of 7 having insulin resistance were naïve, whereas, other subjects had recurrent hirsutism. In subjects with hirsutism, the mean BMI was 24.26. Insulin resistance was seen in 1 subject having a BMI of >30. 4 subjects among 5 having a high BMI in the overweight range of 25-30 showed insulin resistance, whereas 3 subjects had insulin resistance in subjects having BMI in the normal range.

The only significant factor correlated with high BMI was age with $p<0.05$ when assessed using Pearson's correlation coefficient. 25% (n=3) of study subjects with high BMI were in the age range of 21-30 years, whereas, in 20.8% (n=3) study subjects with high BMI were in the age range of 31-40 years. A high BMI was correlated to a high HOMA-IR value of >2.5, recurrence and age in this group with $p<0.01$. However, no significant association was seen in mFG scores with $p >0.05$ as shown in Table 2.

In group III having both hirsutism and acne vulgaris, 8 female subjects had hirsutism and acne. Among these 8 subjects, 6 subjects had a new and recent diagnosis of hirsutism and acne, whereas, recurrent disease was seen in 2 subjects. Among 2 subjects having recurrent disease, 1 had insulin resistance. Among 7 naïve subjects, 3 had insulin resistance. A significantly high BMI was seen in subjects having insulin resistance with a mean BMI of 26.6. In 8 subjects of group III, Pearson's correlation showed no association of BMI to raised mFG scores or raised GAGS scores. Also, no correlation was seen between insulin resistance and increased severity of hirsutism or acne with $p>0.05$ as depicted in Table 3.

DISCUSSION

The present cross-sectional observational study aimed to establish a relationship between acne vulgaris and hirsutism to insulin resistance and to assess the severity of two conditions with increased insulin resistance. History of type 2 diabetes mellitus was positive in 14.94% (n=26) overall study subjects with 14.28% (n=22) subjects, 16.6% (n=2), and 25% (n=2) study subjects respectively from Group I, II, and III. For insulin resistance, positive signs and symptoms of insulin resistance were seen in 64 male and 20 female subjects. Among 78 subjects with naïve acne, insulin resistance was seen in 27 study subjects and 76 subjects had recurrent acne, and insulin resistance was seen in 57 study subjects depicting a strong possibility of correlation. These results were consistent with the studies of Gayen R et al[5] in 2021 and Ray S et al[6] in 2012 where authors reported similar demographics in the subjects of their studies.

The study results showed that a normal BMI range was seen in the majority of study subjects with 76 subjects having BMI in the range of 18.5 to 24.9 with a mean BMI of 24.26. A

significant association with insulin resistance was seen in 41.4% (n=32) of subjects. A 100% strong association of insulin resistance was seen in 11 study subjects of group I who have a BMI of >30. Among 40 subjects out of 46 subjects in the overweight category with a BMI of 25-30, had insulin resistance. Two subjects among 21 subjects in the underweight category of BMI <18.5 had insulin resistance. These results were in agreement with the findings of Balato N et al[7] in 2014 and Gonzalzaz- Gonzalzaz J et al[8] in 2016 where a similar association in BMI and insulin resistance was seen.

It was seen that mean HOMA-IR, mean fasting insulin, and mean fasting blood sugar were significantly high in the study. Recurrence, age, GAGS, and raised HOMA-IR showed a strong association with BMI in this group with $p<0.01$. A significant association was seen between age and BMI with $p<0.05$. However, no significant association was seen between BMI and gender with $p>0.05$ when assessed using Pearson's correlation coefficient. In the majority of study subjects having insulin resistance, it was significantly seen in very severe, severe, and moderate acne groups with 59%, 88%, and 46% of study subjects respectively. These findings were in line with the studies of Bloomgarden Z et al[9] in 2003 and Lymn D et al[10] in 2016 where authors reported a similar association of BMI to various factors was seen.

The study results showed that in group II, 12 females having confirmed diagnosis of hirsutism were assessed and insulin resistance was seen in 7 of those subjects. Among 5 subjects out of 7 having insulin resistance were naïve, whereas, other subjects had recurrent hirsutism. In subjects with hirsutism, the mean BMI was 24.26. Insulin resistance was seen in 1 subject having a BMI of >30. Four subjects among 5 having a high BMI in the overweight range of 25-30 showed insulin resistance, whereas 3 subjects had insulin resistance in subjects having BMI in the normal range. These results were comparable with the previous data of Abdelmawla M et al[11] in 2019 and Collier C et al[12] in 2008 where a similar association between hirsutism and BMI was seen.

It was also seen that the only significant factor correlated with high BMI was age with $p<0.05$ when assessed using Pearson's correlation coefficient. 25% (n=3) of study subjects with high BMI were in the age range of 21-30 years, whereas, in 20.8% (n=3) study subjects with high BMI were in the age range of 31-40 years. A high BMI was correlated to a high HOMA-IR value of >2.5, recurrence and age in this group with $p<0.01$. However, no significant association was seen in mFG scores with $p>0.05$. These results were similar to previous results of Munichandrappa P et al[13] in 2017 and Bhate K et al[14] in 2013 where authors reported a significant association of BMI was seen with age and HOMA-IR.

It was seen that in group III having both hirsutism and acne vulgaris, 8 female subjects had hirsutism and acne. Among these 8 subjects, 6 subjects had a new and recent diagnosis of hirsutism and acne, whereas, recurrent disease was seen in 2 subjects. Among 2 subjects having recurrent disease, 1 had insulin resistance. Among 7 naïve subjects, 3 had insulin resistance. A significantly high BMI was seen in subjects having insulin resistance with a mean BMI of 26.6. In 8 subjects of group III, Pearson's correlation showed no association of BMI to raised mFG scores or raised GAGS scores. Also, no correlation was seen between insulin resistance and increased severity of hirsutism or acne with $p>0.05$. These results were in line with the findings

of Wankhede V et al[15] in 2019 and Nagpal M et al[16] in 2013 where authors reported no correlation between BMI to mFG and GAGS as in the present study.

CONCLUSION

The present study, considering its limitations, concludes that insulin resistance is a vital contributing factor in the pathogenesis of severe and resistant acne and hirsutism. Insulin resistance can have a significant impact on the psychological state of the affected subjects making it necessary to adopt a different approach for the management of these conditions.

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TABLES

	Recurrent/Naive	**Gender**	**Age**	**GAGS**	**HOMA-IR**	**BMI**
Recurrent/Naive						
Pearson correlation	1	-0.016	0.002	0.363	0.277	0.384
p-value	-	**0.**73	**0.000**	**0.000**	**0.000**	
Number (n)	154	154	154	154	154	154
Gender						
Pearson correlation	-0.016	1	-0.037	0.001	0.055	-0.076
p-value	0.73	-	0.47	0.93	0.34	0.15
Number (n)	154	154	154	154	154	154
Age						
Pearson correlation	0.004	-0.037	1	0.093	0.101	0.184
p-value	0.95	0.47	-	0.08	0.05	**0.001**
Number (n)	154	154	154	154	154	154
GAGS						
Pearson correlation	0.34	0.001	0.07	1	0.749	0.625
p-value	**0.000**	0.73	0.07	-	**0.000**	**0.000**
Number (n)	154	154	154	154	154	154
HOMA-IR						
Pearson correlation	0.277	0.037	0.101	0.749	1	0.812
p-value	**0.000**	0.319	0.068	**0.000**	-	**0.000**
Number (n)	154	154	154	154	154	154
BMI						
Pearson correlation	0.384	0.076	0.184	0.625	0.812	1
p-value	**0.000**	0.171	**0.001**	**0.000**	**0.000**	-
Number (n)	154	154	154	154	154	154

Table 1: Pearson's correlation of various parameters in study subjects with acne vulgaris

	Recurrent/Naive	**mFG score**	**HOMA-IR**	**BMI**	**Age**
Recurrent/Naive					
Pearson correlation	1	0.473	0.535	0.632	0.318
p-value	-	**0.017**	**0.007**	**0.001**	**0.125**
Number (n)	12	12	12	12	12
mFG					
Pearson correlation	0.473	1	0.715	0.311	0.189
p-value	**0.017**	-	**0.000**	0.134	0.368
Number (n)	12	12	12	12	12
HOMA-IR					

Pearson correlation	0.535	0.715	1	0.491	0.336
p-value	**0.007**	**0.000**	-	**0.014**	0.105
Number (n)	12	12	12	12	12
BMI					
Pearson correlation	0.632	0311	0.491	1	0.489
p-value	**0.001**	0.134	**0.012**	-	**0.013**
Number (n)	12	12	12	12	12
Age					
Pearson correlation	0.318	0.189	0.336	0.489	1
p-value	0.125	0.368	0.105	**0.013**	-
Number (n)	12	12	12	12	12

Table 2: Pearson's correlation of various parameters in study subjects with hirsutism

	Recurrent/Naive	**mFG score**	**GAGS**	**HOMA-IR**	**BMI**	**Age**
Recurrent/Naive						
Pearson correlation	1	0.074	-0.064	0.176	0.317	0.269
p-value	-	0.786	0.815	0.505	0.217	0.302
Number (n)	8	8	8	8	8	8
mFG score						
Pearson correlation	0.074	1	-0.137	-0.248	0.237	-0.197
p-value	0.786	-	0.597	0.343	0.367	0.455
Number (n)	8	8	8	8	8	8
GAGS						
Pearson correlation	-0.064	-0.137	1	0.463	0.259	0.487
p-value	0.815	0.597	-	0.061	0.316	**0.047**
Number (n)	8	8	8	8	8	8
HOMA-IR						
Pearson correlation	0.176	-0.248	0.463	1	0.519	0.586
p-value	0.501	0.343	0.061	-	**0.032**	**0.012**
Number (n)	8	8	8	8	8	8
BMI						
Pearson correlation	0.317	0.237	0.259	0.519	1	0.157
p-value	0.217	0.367	0.316	**0.032**	-	0.551
Number (n)	8	8	8	8	8	8
Age						
Pearson correlation	0.269	-0.197	0.487	0.586	0.157	1
p-value	0.302	0.455	**0.047**	**0.012**	0.555	-
Number (n)	8	8	8	8	8	8

Table 3: Pearson's correlation of various parameters in study subjects with hirsutism and acne vulgaris both