Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

APPRAISING THE FUNCTIONS OF AS A BIOMARKER OF INSULIN RESISTANCE IN VITILIGO VULGARIS PATIENTS

Dr. Satish Adulkar

Assistant Professor, Department of Dermatology, Venereology & Leprosy, Santosh Medical College, Ghaziabad, Uttar Pradesh

Email id: dr.satish.adulkar@gmail.com

How To Cite: Adulkar S. Appraising the Functions of as a Biomarker for Insulin Resistance In Vitiligo Vulgaris Patients. International Research Journal Of Pharmacy 2018,9:6:228-233.

DOI: 10.7897/2230-8407.096121

==========

ABSTRACT

Background: Vitiligo is a prevalent skin disorders that affects a wide population. It is characterised by the selective death of melanocytes. There is a dearth of information in the literature about trustworthy indicators of insulin resistance in vitiligo patients.

Aim: The purpose of this study was to evaluate the role of blood desnutrin as an insulin resistance biomarker in vitiligo vulgaris patients.

Methods: Ninety people with vitiligo vulgaris of both genders were evaluated and tested against ninety age- and gender-matched controls. In addition to measuring serum desnutrin, fasting serum insulin, LDL, VLDL, HDL, triglycerides, cholesterol, and FBG (fasting blood glucose), a thorough cutaneous and general examination was performed on each individual. Also, HOMA-IR (Homeostasis Model Assessment + insulin resistance) was done for all the participants.

Results: The participants with vitiligo vulgaris showed a statistically significant difference ($p<0.001$) in serum desnutrin, HOMA-IR, fasting insulin, FBG, and HDL when compared to the controls. Additionally, there was a p-value of less than 0.05 for desnutrin and HOMA-IR, fasting insulin, VLDL, LDL, and FBS. There was a non-significant but favourable connection between HDL and desnutrin levels ($p=0.06$).

Conclusion: The current study concludes that subjects with vitiligo vulgaris exhibit suppressed serum desnutrin levels, which are a biomarker of insulin resistance in these subjects due to elevated serum insulin and glucose levels that cause insulin resistance and hyperlipidemia.

Keywords: Desnutrin, hyperlipidemia, insulin resistance, vitiligo, vitiligo vulgaris

INTRODUCTION

A common skin condition called vitiligo is characterised by selective death of melanocytes and depigmentation. There is growing evidence of vitiligo vulgaris in the Indian population, a condition that affects people worldwide. The etiopathogenesis of vitiligo vulgaris has been attributed to a number of factors, with an autoimmune disorder being a major factor. This disorder is correlated with genetic and environmental predisposing factors as well as cell-detachment, oxidative stress, and metabolic abnormalities.[1]

Globally, vitiligo vulgaris affects around 0.5% to 2% of people. Data from earlier research clearly imply that vitiligo can show in a variety of systemic ways in addition to its skin-related symptoms. Additionally, vitiligo vulgaris has been connected to a number of metabolic disorders, such as glucose intolerance and lipid abnormalities. The systemic presentations in people with vitiligo vulgaris can be attributable to the combined effects of all these variables. Melanocytes found in adipose tissue have been shown to help prevent metabolic syndrome by reducing inflammation, oxidative stress, and oxidative damage.[2]

One member of the protein family that can aid in the lipolysis of adipose tissues is desnurin. When fasting, desnutrin is reversibly activated and then decreases after meals. Adipose triglyceride lipase, or ATGL, is another name for desnutrin. The body's adipose tissues are the main location for desnutrin, which is characterised by high substrate, particularly in situations of TAG (triacylglycerol).[3]

One major lipase that is thought to catalyse the hydrolysis of triacylglycerol in the body's adipose tissues is called desnutrin. Adipocyte hypertrophy is triggered by the buildup of triacylglycerol that results from the ablation of desnutrin. Overexpression of desnutrins causes adipocyte TAG to decrease, which in turn lessens diet-induced obesity.[4]

Additionally, desnutrin-mediated lipolysis mimics the oxidation of fatty acids and their reesterification in adipocytes. Whatever the mechanism behind changes in adipose tissue lipolysis, TAG is stored and rise in free fatty acid level. Insulin resistance, hypertension, cardiovascular problems, type 2 diabetes, and other metabolic illnesses might result from these individuals who have vitiligo vulgaris are more likely to have elevated insulin and glucose levels, which may further lower serum desnutrin and contribute to insulin resistance.[5]

Therefore, the purpose of the current clinical investigation was to evaluate blood desnutrin levels and their relationship to insulin resistance in vitiligo vulgaris patients.

MATERIALS AND METHODS

The current cross-sectional case-control clinical investigation set out to evaluate blood desnutrin levels and their relationship to insulin resistance in vitiligo vulgaris patients. Research evaluated 90 vitiligo vulgaris patients of both sexes who were compared to 90 gender- and age-matched controls. After receiving approval from the relevant institutional ethical committee, the study was carried out Department of Dermatology, Venereology & Leprosy, Santosh Medical College, Ghaziabad, Uttar Pradesh. Prior to their involvement in the study, all individuals provided their written and verbal informed consent.

Subjects with vitiligo vulgaris who were willing to participate in the study and who were at least eighteen years old met the inclusion criteria for the research. The study's exclusion criteria included people who had not provided informed consent to participate, women who were nursing or pregnant, hypertensive, diabetic, obese, younger than eighteen, and those who had segmental vitiligo.

Following the research subjects' final inclusion, each subject's complete medical history was documented, along with demographic information. Every participant underwent a clinical examination after that, during which their gender, age, marital status, employment, education, and habits were documented. Assessments were made of the illness history, vitiligo family history, past vitiligo treatments, disease activity, and disease duration. The measurement of disease activity evaluates the emergence of new lesions or the growth of preexisting lesions. Every patient underwent a comprehensive checkup, which included measurements of height in meters, weight in kilogrammes and BMI (kg/m2).

In dermatological assessment, the activity of vitiligo, extension of vitiligo, anatomical site, and Fitzpatrick's phenotype were assessed. The Vitiligo Area Scoring Index[6] was used to evaluate vitiligo extension, and the Vitiligo Disease Activity Score was used to evaluate vitiligo activity.[7]

Both the research participants and the controls underwent laboratory examination following a general, clinical, and dermatological assessment. Each individual had 5 ml of venous blood drawn under rigorous aseptic and sterile conditions for laboratory testing. After allowing the blood to coagulate for 30 minutes at room temperature, the blood was centrifuged for 15 minutes at 2000–3000 rpm. Following the collection of the supernatants, the serum was divided into three aliquots.

Triglycerides (TG), cholesterol, fasting blood glucose (FBG), LDL (low-density lipoprotein), HDL (high-density lipoprotein), and very low-density lipoprotein (VLDL) were all measured using the first aliquot. The levels of fasting

serum insulin were measured using the second aliquot. Using the formula fasting glucose level (mg/dl) X fasting insulin level (mU/ml)/405, insulin resistance was measured using the HOMA-IR (Homeostasis Model Assessment + Insulin Resistance) method. A HOMA-IR of ≤2.9 for early insulin resistance and >2.9 for substantial insulin resistance was used to measure it.8 Using a desnutrin commercial human ELISA kit, the quantitative ELISA approach was utilised to evaluate the third aliquot employed for desnutrin detection.

The collected data were statistically analysed using the Mann Whitney U test, Chi-square test, and Pearson correlation test using SPSS software version 21.0 (IBM Corp., Armonk, NY, USA). The mean and standard deviation of the data were reported. At $p<0.05$, the significance threshold was maintained.

RESULTS

The current cross-sectional case-control clinical investigation set out to evaluate blood desnutrin levels and their relationship to insulin resistance in vitiligo vulgaris patients. 90 participants with vitiligo vulgaris of both genders were evaluated in the research and compared to 90 gender- and age-matched controls. Participants in the study had mean ages of 37.85±13.97 years for controls and 43.14±14.74 years for cases; the difference was not statistically significant (p=0.08). The controls consisted of 51.1% (n=46) females and 48.8% (n=44) men, whereas the cases had 46.66% (n=42) females and 53.3% (n=48) males. The difference between the two groups was not statistically significant (p=0.65). BMIs of patients and controls were 26.69±3.31 kg/m2 and 25.97±3.91 kg/m2, respectively (p=0.17). At 163.14±7.19 m and 164.12±7.26 m, respectively, the heights of the controls and cases were non-significant (p=0.37).

Weight differences between study participants and controls were non-significant, with p=0.15, at 72.05±11.35 and 69.31±11.91 kg, respectively (Table 1). In terms of clinical features, the Koebner phenomenon was observed in 0 out of 88.8% (n = 80) and 1 out of 11.1% (n = 10) of the participants. In 8.88% (n=8), 22.2% (n=20), 17.7% (n=16), 26.6% (n=24), 20% (n=18), and 4.44% (n=4) research individuals, respectively, the VIDA scores were -1, 0, 1, 2, 3, and 4. The study subjects' mean VASI score was 1.65±0.12. The average duration of vitiligo was 6.05±8.69 years. 15.5% (n=14) and 84.4% (n=76) of the research participants had stationary and progressive causes, respectively. According to Table 2, the beginning of the disease was abrupt in 48.8% of the cases (n = 44) and progressive in 51.1% of the subjects (n = 46).

When several lipid variables were compared between the two research groups, the test and control participants' levels of cholesterol, TG (triglycerides), LDL (low-density lipoprotein), and VLDL (very low-density lipoprotein) were found to be similar, with corresponding p-values of 0.24, 0.08, 0.23, and 0.16. Table 3 indicates that the test group's HDL levels were 38.89±4.22 mmol/L, a statistically significant difference with p=0.01 from the control group's much higher HDL values of 42.8±14.65 mmol/L.

Desnutrin, HOMA-IR, fasting insulin, and fasting blood glucose were compared between the two study groups. Results showed that desnutrin was substantially greater in the control group (19.56±4.7 ng/ml) than in the study group (11.82±3.53 ng/ml; $p<0.001$).

Test individuals had considerably greater HOMA-IR ($p<0.001$) than controls. The study group's fasting insulin was substantially greater ($p<0.001$) than the controls'. Table 4 shows that the test group had higher fasting blood glucose levels ($p<0.001$) than the control group. The study's findings demonstrated that 32 participants in the test group and none in the control group had substantial insulin resistance patterns. With $p<0.001$, this difference was statistically significant. 34 participants from the control group and 36 participants from the test group showed early insulin resistance, which was significant ($p<0.001$). There were 34 and 68 patients in total from the test and control groups, respectively. The results showed that p=0.81 was statistically not significant (Table 5).

With respect to the relationship between desnutrin and HOMA-IR, fasting insulin levels, VLDL, LDL, and fasting blood glucose in vitiligo patients, the correlation was statistically significant, with corresponding p-values of <0.001, <0.001, 0.006, 0.01, and <0.001. Table 6 illustrates that, nevertheless, the connection between insulin resistance and HDL, triglyceride, and cholesterol levels was not statistically significant (p=0.05, 0.05, and 0.13, respectively).

DISCUSSION

It was observed that the Koebner phenomenon was present in 1 in 11.1% (n = 10) and 0 in 88.8% (n = 80) of the participants with regard to clinical features. In 8.88% (n=8), 22.2% (n=20), 17.7% (n=16), 26.6% (n=24), 20% (n=18), and 4.44% (n=4) research individuals, respectively, the VIDA scores were -1, 0, 1, 2, 3, and 4. The study subjects' mean VASI score was 1.65±0.12.

The average duration of vitiligo was 6.05±8.69 years. 15.5% (n=14) and 84.4% (n=76) of the research participants had stationary and progressive causes, respectively. In 51.1% (n=46) of the participants, the sickness started gradually, while in 48.8% (n=44) of the subjects, it started suddenly. These findings aligned with research conducted in 2006 by Kershaw EE et al[8] and Langin D,[10] who noted comparable clinical traits in vitiligo patients to those in the current investigation. The study's findings demonstrated that, when different lipid variables were compared between the two study groups, the levels of cholesterol, TG (triglycerides), LDL (low-density lipoprotein), and VLDL (very low-density lipoprotein) were found to be similar in test and control subjects, with corresponding p-values of 0.24, 0.08, 0.23, and 0.16.

Subjects in the control group had considerably higher HDL levels (42.8±14.65 mmol/L) than those in the test group (38.89±4.22 mmol/L), a difference that was statistically significant (p=0.01). These results corroborated those of Ergin C et al.[11] in 2017 and Demir B et al.[12] in 2014, whose findings indicated similar lipid profiles in vitiligo patients as seen in our investigation.

Desnutrin, HOMA-IR, fasting insulin, and fasting blood glucose were compared between the two study groups. Results showed that desnutrin was substantially greater in the control group (19.56±4.7 ng/ml) than in the study group (11.82±3.53 ng/ml; p<0.001). Test individuals had considerably greater HOMA-IR (p<0.001) than controls.

The study group's fasting insulin was substantially greater (p<0.001) than the controls'. Additionally, the test group's fasting blood glucose levels were greater (p<0.001) than the controls'. These findings were in line with those of Pietrzark A et al. (2000) and Burge MR. (2004), whose authors hypothesised that controls had noticeably greater levels of desnutrin than vitiligo patients. The study's findings demonstrated that 32 participants in the test group and none in the control group had substantial insulin resistance patterns. With p<0.001, this difference was statistically significant. 34 participants from the control group and 36 participants from the test group showed early insulin resistance, which was significant (p<0.001).

The total number of individuals in the control and test groups was 34 and 68, respectively. This difference in number was not statistically significant (p=0.81). These results were similar to those of studies conducted in 2006 by Birol A et al. and in 2003 by Brunn JM et al., who found that people with and without vitiligo had similar levels of insulin resistance. Desnutrin levels and HOMA-IR, fasting insulin levels, VLDL, LDL, and fasting blood glucose were found to be statistically significantly correlated when study parameters and desnutrin levels were evaluated in vitiligo subjects. The corresponding p-values were <0.001, <0.001, 0.006, 0.01, and <0.001. However, there was no significant connection (p=0.05, 0.05, and 0.13, respectively) between insulin resistance and HDL, triglyceride, and cholesterol levels. The present study's outcomes aligned with the research conducted by Akrem J et al. (2007) and Gopal KV et al. (2007), which proposed a substantial role of desnutrition in vitiligo.

CONCLUSION

Taking into account its limitations, the current study comes to the conclusion that lower levels of serum desnutrin, which are associated with insulin resistance and hyperlipidemia, are observed in people with vitiligo vulgaris due to elevated levels of blood insulin and glucose. Therefore, in individuals with vitiligo vulgaris, decreased blood desnutrin levels can serve as a biomarker of insulin resistance. To avoid metabolic and cardiovascular problems, it is essential to use a multidisciplinary approach in the early detection of diabetes mellitus, hyperlipidemia, and insulin resistance in vitiligo vulgaris patients.

REFERENCES

1. Sharma YK, Bansal P, Menon S, Prakash N. Metabolic syndrome in vitiligo patients among a semi-urban Maharashtrian population: A case-control study. Diabetes Metab Syndr 2017;11:77-80.
2. Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. Vitiligo: A comprehensive overview Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. J Am Acad Dermatol. 2011;65:473-91.
3. Villena JA, Roy S, Sarkadi-Nagy E, Kim KH, Sul HS. Desnutrin, an adipocyte gene encoding a novel patatin domain-containing protein, is induced by fasting and glucocorticoids: Ectopic expression of desnutrin increases triglyceride hydrolysis. J Biol Chem 2004;279:47066-75.
4. Pietrzak A, Bartosińska J, Hercogová J, Lotti TM, Chodorowska G. Metabolic syndrome in vitiligo. Dermatol Ther 2012;25:41-3.

5. Bergqvist C, Ezzedine K. Vitiligo: A review. Dermatology 2020;236:571-92.
6. Zimmermann R, Strauss JG, Haemmerle G, Schoiswohl G, Birner-Gruenberger R, Riederer M, *et al*. Fat mobilization in adipose tissue is promoted by adipose triglyceride lipase. Science 2004;306:1383-6.
7. Ahmadian M, Abbott MJ, Tang T, Hudak CS, Kim Y, Bruss M, *et al*. Desnutrin/ATGL is regulated by AMPK and is required for a brown adipose phenotype. Cell Metab 2011;13:739-48.
8. Ahmadian M, Duncan RE, Varady KA, Frasson D, Hellerstein MK, Birkenfeld AL, *et al*. Adipose overexpression of desnutrin promotes fatty acid use and attenuates diet-induced obesity. Diabetes 2009;58:855-66.
9. Kershaw EE, Hamm JK, Verhagen LA, Peroni O, Katic M, Flier JS. Adipose triglyceride lipase: Function, regulation by insulin, and comparison with adiponutrin. Diabetes 2006;55:148-57.
10. Langin D. Adipose tissue lipolysis as a metabolic pathway to define pharmacological strategies against obesity and metabolic syndrome. Pharmacol Res 2006;53:482-91.
11. Ergin C, Demir B, Ucak H, Cicek D, Aydin S, Dertlioglu SB, *et al*. Serum desnutrin levels in patients with psoriasis and their relationship with metabolic syndrome and insulin resistance. Dermatol Clin Res 2017;3:118-20.
12. Demir B, Ucak H, Cicek D, Aydin S, Erden I, Dertlioglu SB. Changes in serum desnutrin levels in patients with acne vulgaris. Eur J Dermatol 2014;24:589-93.
13. Pietrzak A, Lecewicz-Toruń B, Urban J. Comparison of serum lipid in girls affected with vitiligo and control group. Ann Univ Mariae Curie Sklodowska Med 2000;55:269-74.
14. Burge MR, Carey JD. Vitiligo associated with subcutaneous insulin lispro infusion in type 1 diabetes. Diabetes Care 2004;27:275-6.
15. Birol A, Kisa U, Kurtipek GS, Kara F, Kocak M, Erkek E, *et al*. Increased tumor necrosis factor-alpha (TNF-alpha) and interleukin 1 alpha (IL1-alpha) levels in the lesional skin of patients with nonsegmental vitiligo. Int J Dermatol 2006;45:992-3.
16. Bruun JM, Verdich C, Toubro S, Astrup A, Richelsen B. Association between measures of insulin sensitivity and circulating levels of interleukin-8, interleukin-6 and tumor necrosis factor-alpha. Effect of weight loss in obese men. Eur J Endocrinol 2003;148:535-42.
17. Akrem J, Baroudi A, Aichi T, Houch F, Hamdaoui MH. Profile of vitiligo in the south of Tunisia. Int J Dermatol 2008;47:670-4.
18. Gopal KV, Rama Rao GR, Kumar YH, Appa Rao MV, Vasudev P, Srikant. Vitiligo: A part of a systemic autoimmune process. Indian J Dermatol Venereol Leprol 2007;73:162-5.

S. No	Characteristics	Controls		Cases		p-value
		n=90	%	n=90	%	
1.	**Mean age (years)**	37.85±13.97		43.14±14.74		0.08
2.	**Gender**					
3.	Females	46	51.11	42	46.66	0.65
4.	Males	44	48.88	48	53.3	
5.	**BMI (kg/m2)**	25.97±3.91		26.69±3.31		0.17
6.	**Height (m)**	163.14±7.19		164.12±7.26		0.37
7.	**Weight (kg)**	69.31±11.91		72.05±11.35		0.15

Table 1: Comparison of demographic data in two groups of study subjects

S. No	Disease-related data	Number (n)	Percentage (%)
1.	**Koebner phenomenon**		
a)	0	80	88.8
b)	1	10	11.1
2.	**VIDA**		
a)	-1	8	8.88
b)	0	20	22.2
c)	1	16	17.7
d)	2	24	26.6

e)	3	18	20
f)	4	4	4.44
3.	**Mean VASI**	1.65±0.12	
4.	**Mean duration**	6.05±8.69	
5.	**Cause**		
a)	Stationary	14	15.5
b)	Progressive	76	84.4
6.	**Onset**		
a)	Gradual	46	51.1
b)	Sudden	44	48.8

Table 2: Disease-related data in study participants

S. No	Variables	Controls (n=45)	Tests (n=45)	p-value
1.	**VLDL**	19.64±3.6	21.89±6.83	0.24
2.	**LDL**	51.66±17.97	61.24±23.10	0.08
3.	**HDL**	42.8±14.65	38.89±4.22	**0.01**
4.	**TG**	97.04±19.37	145.27±163.14	0.23
5.	**Cholesterol**	124.6±88	120.26±24.42	0.16

Table 3: Comparison of lipid profile in control and test study subjects

S. No	Variables	Controls (n=45)	Tests (n=45)	p-value
1.	**Desnutrin (ng/ml)**	19.56±4.7	11.82±3.53	**<0.001**
2.	**HOMA-IR**	1.79±0.54	2.9±0.97	**<0.001**
3.	**Fasting insulin (IU/ml)**	9.29±2.45	12.33±3.59	**<0.001**
4.	**Fasting blood glucose (mg/dl)**	78.27±7.68	86.47±10.86	**<0.001**

Table 4: Comparison of Desnutrin, HOMA-IR, fasting insulin, and fasting blood glucose in two study groups

S. No	IR (insulin resistance)	Controls (n=45)	Tests (n=45)	p-value
1.	**Significant resistance**	0	32	**<0.001**
2.	**Early resistance**	34	36	**<0.001**
3.	**Total**	34	68	0.81

Table 5: Comparison of insulin resistance pattern in two groups of study subjects

S. No	IR (insulin resistance)	Pearson correlation/ Spearman correlation	p-value
1.	**HOMA-IR**	-0.625	**<0.001**
2.	**Fasting insulin**	-0.583	**<0.001**
3.	**VLDL**	-0.256	**0.006**
4.	**LDL**	-0.213	**0.01**
5.	**HDL**	0.164	0.05
6.	**TG**	-0.173	0.05
7.	**Cholesterol**	-0.127	0.13
8.	**FBG**	-0.444	**<0.001**

Table 6: Correlation of study parameters and desnutrin levels in subjects with vitiligo