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Original article

Measurement of Serum YKL 40 Level in Patients with Vitiligo and Its Relation with Disease Severity

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Abstract

Background: The selective destruction of melanocytes characterizes the persistent skin disorder known as vitiligo. A small percentage of the global population (0.5–2.0%) suffers from vitiligo, an acquired depigmentation disorder. Since it typically shows up on the face and other noticeable areas, it could be psychologically upsetting. One of the conserved families of mammalian chitinases is YKL-40, or chitinase-3-like protein 1. **Aim of the Work**: This study was set out to determine how vitiligo patients' serum levels of the inflammatory biomarker YKL-40 (CH3L1) varied with disease severity. **Patients and Methods:** Two groups were involved in this study: Forty vitiligo patients comprised the first group. They ranged in age from eighteen to fifty-nine and included both men and women. Forty healthy people served as control cases in the second group. They ranged in age from sixteen to fifty years old and included both boys and ladies.

Results: As none of the vitiligo cases we looked at had any comorbidities, including skin or systemic diseases, our results suggest that YKL-40 may play a role in the etiology of vitiligo disease and demonstrate the clear elevation of this parameter in vitiligo patients. While a greater YKL-40 level may indicate systemic inflammation in vitiligo patients, it does not appear that YKL-40 concentration directly correlates with the degree of skin alterations. Additionally, YKL-40 seems to be a highly sensitive indicator of illness in vitiligo patients. After calculating the ideal serum YKL-40 cut-off value using the ROC curve, we found that this parameter was 100% sensitive and specific within our patient group. **Conclusion:** The fact that YKL-40 levels are higher in vitiligo patients raises the possibility that it plays a role in the onset of the disease.

1. Introduction:

Vitiligo is a persistent skin condition characterized by the selective death of melanocytes. [1]. Vitiligo affects 0.5% to 2.0% of the worldwide population and is often psychologically distressing due to its manifestation on the face and other conspicuous regions. [2].

The etiology of vitiligo remains unclear, despite the proposal of different possibilities. Autoimmunity is believed to significantly contribute to the pathophysiology of vitiligo. The condition may arise from the interaction of many pathogenic variables, including autoimmunity, brain dysregulation, and heightened oxidative stress in genetically susceptible people. [3].

The evolution of vitiligo is erratic, marked by intervals of disease quiescence alternating with phases of gradual or accelerated depigmentation, often signifying a worse prognosis and extended treatment duration. [4].

The conserved family of mammalian chitinases has 18 members, one of which is chitinase-3-like protein 1 (YKL-40), a glycosyl hydrolase. Because it does not catalyze any reactions, the exact biological role of this protein is unknown. [5].

Inflammation, proliferation, and angiogenesis are all areas where YKL-40 is known to play a significant role.

Studies on this protein have focused on a range of inflammatory diseases, such as inflammatory bowel disorders, rheumatoid arthritis, osteoarthritis, viral hepatitis, cardiovascular disease, and cancer. [6].

2. Aim of the Work:

The purpose of this research was to determine the relationship between vitiligo severity and YKL 40 levels in patients.

3. Subjects and Methods:

Subjects

From July 1, 2021, to February 1, 2022, researchers from Beni-Suef University Hospital's dermatology outpatient clinic conducted a case-control study. eighty people, forty of whom had vitiligo and forty who served as controls. This research included two groups: The first cohort included 40 individuals diagnosed with vitiligo. The second group had 40 unaffected people serving as control cases. All patients provided informed consent to engage in this study. The local ethics commission at Beni-Suef University accepted the study.

Inclusion criteria:

Adult patients of both sexes with vitiligo, aged 18 to 60 years.

Exclusion criteria:

Everyone with an inflammatory ailment, such as IBD, RA, ILD, osteoarthritis, viral hepatitis, heart disease, cancer, or any other inflammatory disorder, would not be included in the study.

Methodology:

All subjects were subjected to the following:

Detailed medical history (including gender, age, health status, and family medical history). Assessment of vitiligo disease activity employing grading and digital imaging measurement of affected body surface area for a comprehensive clinical evaluation. Area Severity Index for Vitiligo (VASI): Hand units measure the percentage of vitiligo, with one hand unit approximately equal to one percent of the total body surface area. [7]. The closest required percentage was used to determine the level of pigmentation. Complete erasure of pigmentation (100%), sparse pigmentation (90%), greater depigmentation than pigmented area (75%), equal depigmentation and pigmented area (50%),pigmented area is greater than depigmented area (25%) and a few isolated spots of depigmentation (10%) are seen. [8].

The whole body vitiligo extent tensity index(VETI) is computed using a

formula incorporating contributions from all anatomical areas. VETI rating: (percentage of cranial involvement × intensity grade) + (percentage of torso involvement × intensity grade) 4 + (percentage of upper limb involvement × intensity grade) 2 + (percentage of lower limb participation × intensity grade) 4 + (percentage of genital involvement × degree of tension) 0.1 The coefficients presented in this formula are derived from the percentage of skin surface according to the rule of nines. The coefficient for the head is 1 (9:9=1), for the trunk and lower limb is 4 (36:9=4), for the upper limb is 2 (18:9=2), and for the genitalia is around 0.1 (1:9=0.1).

VETI: (Ph×Th) +(Pt × Tt) 4 + (Pu × Tu) 2+ (Pl × Tl)4 + (Pg × Tg) 0.1

5 + 20 + 10 + 20 + 0.5 = 55.5

The maximum score of VETI is 55.5.

Statistical Analysis:

It was into IBM SPSS version 20 that the data was entered once it had been edited, coded, and collected. Numbers and percentages were used to represent the qualitative data. Meanwhile, when the quantitative data followed a parametric distribution, it was shown as means, standard deviations, and ranges. The significance of the P-value was determined by comparing it to the thresholds of non-significance (NS) and significance ($P < 0.05$).

4. Results:

Table 1: Comparison between Control (n. =40) and Patient (n. =40) regarding Age and Sex.

		Control	Patient	Test value	P-value	Sig.
		No.= 40	No.= 40			
Age	Mean ± SD	38.55 ±13.43	39.03±13.08	-0.**160**•	0.873	NS
	Range	18 – 50	18 – 59			
Sex	Female	27 (67.5%)	24 (60.0%)	0.487*	0.485	NS
	Male	13 (32.5%)	16 (40.0%)			

P-value > 0.05: Non-significant (NS); P-value < 0.05: Significant (S); P-value < 0.01: highly significant (HS)

*: Chi-square test, • : Independent t-test

As can be seen from the previous table, there was no statistically significant difference between the two groups when it came to age, and the same held true for sex.

Table 2: Comparison between Control (n=40) and Patient (n=40) regarding YKL 40 (ng/ml).

		Control	Patient	Test value	P-value	Sig.
		No.= 40	No.= 40			
YKL 40(ng/ml)	Mean ± SD	39.84 ± 12.93	525.88 ± 153.19	-19.996•	0.000	HS
	Range	25.67 - 98.55	318.2 - 930.5			

P-value > 0.05: Non-significant (NS); P-value < 0.05: Significant (S); P-value < 0.01: highly significant (HS)

*: Chi-square test, • : Independent t-test

The prior table reveals a statistically significant difference when comparing the two groups with respect to YKL 40(ng/ml).

Table 3: Relation between YKL 40(ng/ml) and Family history.

		YKL 40(ng/ml)		Test value	P-value	Sig.
		Mean ± SD	Range			
Family history	No	497.67 ± 141.27	318.2 - 857.6	-1.529•	0.135	NS
	Yes	572.88 ± 165.43	393 - 930.5			

According to the data in the preceding table, there is no correlation between YKL 40(ng/ml) and genetics.

Table 4: Distribution of the studied cases according to Patterns of vitiligo.

Patterns of vitiligo	No.	%
Generalised	28	70.0%
Vulgaris	15	53.6%
Acrofacial	9	32.1%
Universal	4	14.3%
Localised	12	30.0%
Focal	12	100.0%
Segmental	0	0.0%

Table 5: Relation between YKL 40(ng/ml) and Patterns of vitiligo.

Patterns of vitiligo	**YKL 40(ng/ml)**		**Test value**	**P-value**	**Sig.**
	Mean ± SD	**Range**			
Generalised	525.94 ± 157.86	318.2 – 930.5	-0.004	0.997	NS
Universal	650.88 ± 234.92	398.1 – 857.6			
Acrofacial	523.34 ± 183.63	319.7 – 930.5			
Vulgaris	494.19 ± 106.87	318.2 – 728.2			
Localised	525.72 ± 148.43	394.1 – 903.3			
Focal	525.72 ± 148.43	394.1 – 903.3			

No statistically significant association was discovered between YKL 40(ng/ml) and patterns of vitiligo, as shown in the preceding table.

Table 6: Correlation between YKL 40(ng/ml) With Age, Duration of vitiligo disease (years), Duration of last lesion (months), VASI score, and VETI score.

	YKL 40(ng/ml)	
	r	**P-value**
Age	0.017	0.919
Duration of vitiligo disease (years)	-0.250	0.120
Duration of last lesion (months)	0.223	0.166
VASI score	-0.128	0.430
VETI score	0.014	0.932

According to the data in the preceding table, YKL 40(ng/ml) did not correlate significantly with age, vitiligo disease duration (years), last lesion duration (months), VASI score, or VETI score.

Table 7: Cut off, sensitivity, and specificity of YKL 40(ng/ml) in the detection of vitiligo

	Cut-off point	**AUC**	**Sensitivity**	**Specificity**	**+PV**	**-PV**
YKL 40(ng/ml)	> 98.55	1.000	100.0	100.0	100.0	100.0

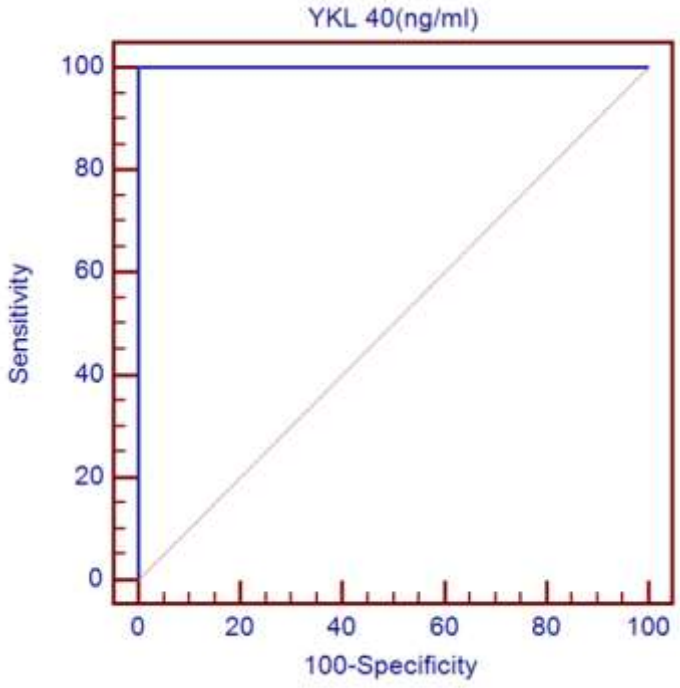

Figure 1: ROC curve (Control and Patient) group regarding YKL 40(ng/ml).

With a sensitivity of 100%, specificity of 100%, positive protective value (PPV) of 100%, negative protective value (NPV) of 100%, and overall accuracy of 100%, the receiver operating characteristic curve (ROC) suggests that the optimal cutoff point of YKL 40(ng/ml) to identify the patient group is > 98.55.

5. Discussion:

Vitiligo is a depigmentation condition of the skin, clinically marked by the emergence of disfiguring, confined skin macules. [9]. The condition primarily arises from the loss of melanocytes or blocking the melanin production pathway. The pathophysiology of vitiligo is complex, yet the underlying components seem to be progressively clarified. This may assist in identifying potential therapeutic targets. [10]. Upcoming years will see the initiation of new clinical studies predicated on this scientific advancement.

In both prokaryotes and eukaryotic species, CHI3L1 (YKL-40) is a prevalent non-enzymatic chitinase-like protein (CLP). further on, it was found in the culture supernatant of the MG63 osteosarcoma cell line. It was further demonstrated that human chondrocytes, synoviocytes, and vascular smooth muscle cells contained it. Macrophages, fibroblast-like cells, endothelial cells, hepatic stellate cells, and neoplastic cells are some of the cell types that generate CHI3L1.[6]**.**

In dermatological disorders as psoriasis [11], atopic dermatitis (AD) and others, YKL-40 has been the subject of multiple investigations. [12], alopecia areata [13], and vitiligo [14]; however, the findings thus far are inconsistent, and the biological functions of CHI3L1 in numerous skin diseases remain unexplored. Consequently, we resolved to investigate this issue and ascertain if YKL-40 may be significant in the patho-mechanisms of vitiligo.

Forty individuals diagnosed with vitiligo and forty healthy controls, identical in age and gender, were included in this case-control study at dermatology clinics affiliated with Beni-Suef University hospitals.

The average age of the participants was 32.10 ± 9.49 years, and their average duration of illness was 9.43 ± 8.35 years. The ages of the participants varied from eighteen to fifty-nine. Previous epidemiological studies on vitiligo have found that the average age of onset is 25.9 ± 16.6 years, and that there are two overlapping subgroups depending on start age, which is in line with the results of this study. The average age at which a subset of vitiligo patients first appears is 10.3 ± 5.6 years, and this group accounts for around 38% of all instances. The average age of onset for a subset of late-onset vitiligo, which accounts for about 62% of cases, is 34.0 ± 14.5 years. [15].

Numerous studies have been conducted globally to ascertain vitiligo's clinical and epidemiological characteristics.

Only a limited number of studies have sought to distinguish these results between males and females, and notably, some statistically significant differences were observed. The current study followed a female predominance in vitiligo cases, with a female-to-male ratio of 2.1:1. This ratio, while higher, is comparable to the reported 1.38:1 ratio in an epidemiological study aimed at identifying gender-based differences in the clinic-epidemiological patterns of vitiligo [16]. This gender disparity may be elucidated by the documented evidence that specific gene polymorphisms are linked to vitiligo in females. [17].

In the current research, 37.5% of patients had a positive family history of vitiligo. Sh et al. [14] discovered that 25 out of 40 patients (62.5%) had a favorable family history.

Our research revealed a median VASI score of 2.25, ranging from 0.5 to 1.5. In contrast, the VETI score exhibited a median of 5.04, spanning from 0.5 to 20. In accordance with our research, the VASI score in Sh et al. [14] varied from 0.5 to 14.25, with a median of 2, whereas the VETI score ranged from 0.5 to 20.5, with a median of 4.75.

All of our patients had progressing illness. Consistent with our research, Sh et al. [14] demonstrate that 92.5% of the examined patients had active disease.

In this research, the upper limb was the most prevalent location of vitiligo, accounting for 47.0% of cases. Consistent with our findings, Sh et al. [14] indicated that the predominant area of vitiligo was the upper limb (42.5%).

None of our patients had concomitant cutaneous or systemic illnesses. Sh et al. [14] found the same findings, since none of the individuals had a history of related disorders or prior therapy.

The research indicated that YKL-40 serum levels are considerably higher in vitiligo patients than in healthy controls, suggesting its potential involvement in the pathomechanisms of vitiligo. The results of the studies conducted so far are consistent with one another. A recent case-control study compared the blood levels of YKL-40, hs-CRP, and ESR in patients with vitiligo to normal controls. The results showed that vitiligo patients had significantly higher serum YKL-40 levels than the control group [14]. The inflammatory biomarker YKL-40 (CH3L1) protein was measured in the blood of 40 vitiligo patients and 40 healthy controls in a separate study. The blood CH3L1 levels of vitiligo patients were significantly greater than those of

the healthy control group, according to the researchers. [18].

The present investigation revealed no statistically significant correlations between YKL-40 serum levels and the individuals' age, gender, illness duration, or family history. In the same context, Hemida et al. discovered a statistically significant positive linear link between illness duration and YKL-40 blood levels. Still, no statistically significant associations were found between YKL-40 and age, gender, or family history [18].

The current investigation found no significant link between YKL-40 serum levels and VASI or VETI scores. This research evaluates the link between YKL-40 and VASI and VETI scores.

Vitiligo is recognized as an illness that impacts the skin and may predispose individuals to systemic symptoms. Numerous systemic diseases, mostly of autoimmune origin, have been shown to have a strong association with vitiligo. A potential common patho-mechanism underlying these disorders is inflammation.

Using serum YKL-40 levels as a metric, Ezzat et al. [21] compared 50 vitiligo patients with 50 healthy controls. There was a positive association between YKL-40 levels and the severity of the disorder, and the vitiligo group exhibited noticeably greater levels than the control group. The authors propose that YKL-40 could be valuable as a biomarker for disease activity in vitiligo.

Everyone knows CHI3L1 plays a significant role in controlling Th2 inflammation and M2 macrophage activation. Several skin diseases, including vitiligo, are associated with M2 macrophages. The current thinking on what causes vitiligo is that it is an autoimmune disorder that starts with dendritic cells that present antigens and then activate and bring cytotoxic T lymphocytes that attack melanocytes in the skin. Macrophages' function in the immunological modulation of vitiligo has not been well examined until lately. The findings of this study suggest the involvement of YKL-40 in the pathogenesis of vitiligo and demonstrate a significant increase in this parameter among patients with vitiligo who have no comorbidities (none of the examined vitiligo cases exhibited associated skin or systemic diseases). It should be emphasized that elevated YKL-40 levels may only indicate systemic inflammation in vitiligo patients, since its concentration does not directly correlate with the degree of skin alterations. Furthermore, YKL-40 appears to be a highly sensitive

indicator of the disease in patients with vitiligo. Within our patient cohort, we established the optimal cut-off value for serum YKL-40 from the ROC curve, revealing this parameter to be elevated with 100% sensitivity and specificity among the subjects examined.

Based on our literature assessment, this research is an inaugural investigation evaluating the diagnostic utility of serum YKL-40 levels in diagnosing vitiligo.

6. Conclusion:

One important factor in Th2-mediated inflammation and allergy sensitivity is chitinase 3-like 1 (CHI3L1), which is also known as YKL-40. Despite CHI3L1's association with asthma and other diseases characterized by inflammation, cell death, and tissue remodeling, its role in vitiligo is unknown.

YKL-40 is significant in the development of many diseases. Limited prior research has described the function of YKL-40 in vitiligo, leaving its involvement in disease pathogenesis unconfirmed; our present investigation found an elevated blood level of YKL-40 in vitiligo patients compared to healthy controls. This result may initiate further study using diverse methodologies and a bigger sample size to investigate the disparity in YKL-40 regulation between vitiligo and healthy skin.

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