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Study of Immune Response of Immune Mediator Interleukin (17 and 23) Against Dermatophytes Infection

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ABSTRACT

Dermatophytosis (superficial fungal infections) is a type of fungal infection that arises mostly on dead keratin found in the top layer of the skin, hair, and nail. Dermatophytes are classified into three genera: Trichophyton (which causes diseases on the skin, hair, and nails), Epidermophyton (which causes infections on the skin, hair, and nails), and Microsporum (which causes infections on the skin, hair, and nails) (causing infections on skin and hair). Molecular methods for the differentiation between the genotyping characteristics of the species of dermatophytes are more specific, precise, and rapid than traditional methods, and they can discriminate between closely related species while being less susceptible to interference from external factors such as temperature variations and chemotherapy, among others. Trichophyton rubrum is the most common fungi that causes dermatophytosis, Molecular diagnosis is the best and most accurate method for diagnosing fungi, There is a clear variation in the genetic structure of local and global fungal isolates. High rate of interleukins (IL17, IL23) with fungal infections Culture on Sabouraud's Dextrose Agar (SDA) , required for species identification, was positive in 30 (28.3 %) and negative in 76 (71.7 %) of cases. Among the 55 , culture-positive isolates , 60 (56.7 %) dermatophytes , 10 (9.4%) Aspergillus , and 6 (5.7 %) Candida were isolated . the residence was (55.7%) in rural and (44.3%) in urban, which recorded high cases of skin infection in a rural area (63.5 %) compared to an urban area (36.5 %). Most of the cases were in the age group of (11-20) years Where the percentage of infection was in the ages of less than or equal to 10 years; 15% of the infection was sexually distributed, 9.4% were males and 5.6% were females. Of these, 8.4% were rural and 6.6% were urban. The cases were in the age group of (21-30) years were 23.5% as (15% males and 8.4% females) and (12.2% Rural and 11.3% Urban). The cases were in the age group of (31-40) years was 18.8% as (8.4% males and 10.3% females) and (12.2% Rural and 11.3% Urban). The cases were in the age group of (41-50) years were 6.6% (3.7% males and 2.8% females) and (4.7% Rural and 1.8% Urban). The cases were in the age group of (more than 50) years were 7.5% (1.8% males and 5.6% females) and (3.4% Rural and 3.4% Urban)

Keywords: Dermatophytes, IL-23/IL17, Antifungal Immunity

1. Introduction

The pathogenesis of Dermatophytes is thought to be based on tight interactions between components of the innate and adaptive immune system (Junichiro Hiruma, et al, 2020), (Harden JL, et al, 2015), (Schakel K, et al, 2016), (Yu Sawada, et al, 2021), (Schon MP, et al, 2005). Several classical studies underscore the importance of T cells for the pathogenesis of Dermatophytes

The interleukin-17 (IL-17) family of cytokines, namely interleukin-17A (IL-17A), is recognized to be important in the host's defense against fungal infections; however, the role of the other members of the IL-17 family in anti-fungal immunity is still mostly unclear. (Harden JL, et al, 2015), I demonstrate that the expression of the interleukin-17C (IL-17C) gene was significantly increased in kidney epithelial cells after fungal infection.

Following the initial definition of the Th1/Th2 immune response paradigm in 1986, immunological responses, whether infectious or autoimmune in nature, were divided into these groups for more than two decades after that date. We found that this model had a slew of flaws over the course of testing. Th1 effector cytokine IFNg was found to be less important

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than Th1 inducing cytokine IL-12 in numerous disease conditions, which remains an unresolved conundrum (Steinman, 2007). Many of these distinctions were brought into focus and reconciled by the discovery of Th17 cells, which shifted the paradigm of CD4-mediated immunity. It is important to note that (1) IL-23 stimulates the production of IL-17 in T cells, and (2) the p40 component of IL-12 is shared with IL-23 and the IL-12Rb1 is a subunit of the IL-23R was found to be particularly crucial (Florian Sparber, et al, 2019). It is through this mechanism that animals lacking IL-12p40 or IL-12Rb1 are rendered weaker not only in terms of IL-12 (and consequently, Th1 cells), but also in terms of IL-23 (hence, lacking Th17 cells). As a result of this, it was discovered that the induction of Th17 cells by TGF-b, IL-6 and IL-1b, and that IL-23 is a significant component in Th17 cell maintenance and disease (Taoming Liu, et al, 2021).

In the last few years, this concept has been used to Candida albicans immunity considerably. IL-17R-deficient mice were inoculated intravenously with Candida albicans and displayed lower survival and higher kidney fungal burden as compared to WT counterparts, respectively, in 2004, when the role of the IL-17 axis in antifungal host defense was first shown (Fabio SY, et al, 2021). However, the preponderance of evidence supports the idea that IL-17 is protective in systemic candidemia, notwithstanding a disagreement in one study (Nesmond S, et al, 2019). (Fabio SY, et al, 2021). Experimental immunization with C. albicans adhesion protein Als3p and aluminum hydroxide adjuvant protected against systemic candidiasis through the establishment of Th17 and Th1 responses, according to the findings, which were also used in the study (Lin et al., 2009).

Using a Klebsiella pneumoniae infection model, early studies found that interleukin-17 strongly stimulates granulocyte production and neutrophil chemotaxis (Goepfert A, et al., 2021). Neutrophils are activated by IL-17 in response to infection, as demonstrated by several studies in a variety of infection situations, many of which were conducted before the discovery of Th17 cells. An increase in G-CSF and CXC chemokines in mucosal epithelial cells and the stroma around them is hypothesized to activate neutrophils via IL-17 (Khader et al., 2009).

Interleukin-17 receptor alpha (IL-17RA) is highly expressed in neutrophils, but the neutrophil coreceptor IL-17RC is missing, hence there is no evidence that interleukin-17 directly affects these cells (Pelletier et al., 2010). The migration of neutrophils to peripheral inflammatory regions appears to be a major mediator of IL-17's protective effects, but other antimicrobial pathways may also be involved.

Reductions in absolute neutrophil counts (ANCs) in peripheral blood were related with decreased neutrophil recruitment and MPO activity in the kidneys of IL-17R-deficient mice (Fabio SY, et al, 2021). For OPC, researchers found reduced neutrophil numbers in the oral mucosa of IL-23p19/ and IL-17R/ mice when compared to the resistant mouse strains. Genes that encode CXCL1 (KC, Groa), CXCL2 (MIP2), CXCL5 (LIX), and CSF3 (G-CSF) as well as others that function to enhance or attract neutrophils were shown to be activated by microarray analysis in tongue tissue (Cho JJ, et al ., 2019). In addition, Candida albicans can cause the release of CXCL8 (IL-8), another potent neutrophil chemoattractant, from oral epithelial cells (OECs) (Dongari-Bagtzoglou and Kashleva, 2003; Dongari-Bagtzoglou et al ., 2005). Neutrophil extracellular traps can capture and destroy both C. albicans yeast and hyphae, as well as other discoveries, according to a similar study (Lou F, et al ., 2006). The host's response to Candida albicans infection is believed to include the recruitment of neutrophils to the infection site by IL-17.

2. Methodology

Principledfs

These kits were developed using the Sandwich-Elisa concept. The antibody specific for Human IL-17 and IL-23 has already been pre-coated on the micro ELISA plate included in this kit, making it ready for use. Samples (or standards) are mixed with a specific antibody in the micro ELISA plate wells to obtain a positive result. For the detection of the antigen, an Avidin-Horseradish Peroxidase (HRP) combination is used in conjunction with a biotinylated anti-Human IL-17 and IL-23 antibody. Rinsing away the components that aren't needed is the only way to remove them. Each well receives an injection of the substrate solution. Human IL-17 and IL-23, a biotinylated detection antibody, and an Avidin-HRP conjugate are the only components in the other wells that will be blue in color. This change in color is due to a stop solution being added to the enzyme-substrate process. Spectrophotometric methods are employed to determine the optical density (OD) at 450 + 2 nm. Due to the fact that the concentrations of Human IL-17 and IL-23 in the sample are directly proportional to its OD value. The optical density (OD) of the samples can be compared to the standard curve to estimate the concentration of Human IL-17 and IL-23 in the samples(Taoming Liu, et al, 2020)..

Subtract the duplicate results for each standard and sample to arrive at the average optical density. The standard concentration and optical density (OD) should be plotted on the x- and y-axes of a four-parameter logistic curve,

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respectively. If the optical density (OD) of the sample exceeds the upper limit of the standard curve, the sample should be retested with a sufficient dilution. To get the actual concentration, multiply the computed concentration by the dilution factor.

It is important for each test to be performed with a standard curve, as OD values can vary depending on the conditions under which an assay is carried out (e.g., operator, pipetting technique, washing technique, or temperature impacts). Using these examples of standard curves and data, you can better understand the concepts being discussed (Taoming Liu, et al, 2020)..

4. Results and discussion

4.1 distribution of IL-17 level mean into controls and patients

The distribution of IL-17 level means into controls and patients IL-17 mean level control was 53.92 ± 0.75, and 83.47 ± 3.17 for the patients where the P-value was less than 0.05 as shown in table 4.6 and figure 3.

Table 4.6: shows the distribution of IL-17 level mean into controls and patients for probability less than 0.05.

Groups	IL-17 level mean ±SE	Probability
Control	53.92 ± 0.75	P < 0.05
Patients	83.47 ± 3.17	

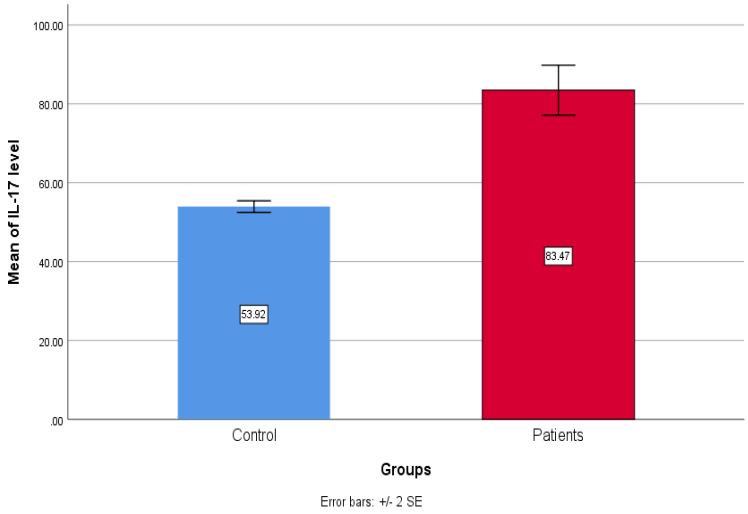

Figure (3) distribution of IL-17 level mean into controls and patients

4.2 the distribution of IL-23 level mean into controls and patients

The distribution of IL-23 level means into controls and patients, The IL-23 mean level control was 196.65 ± 1.84, and 269.90 ± 11.45 for the patients where the P-value was less than 0.05 as shown in table 1 and figure 4.

Table 4.7: shows the distribution of IL-23 level mean into controls and patients for probability less than 0.05.

Groups	IL-23 level mean ± SE	Probability
Control	196.65 ± 1.84	P < 0.05
Patients	269.90 ± 11.45	

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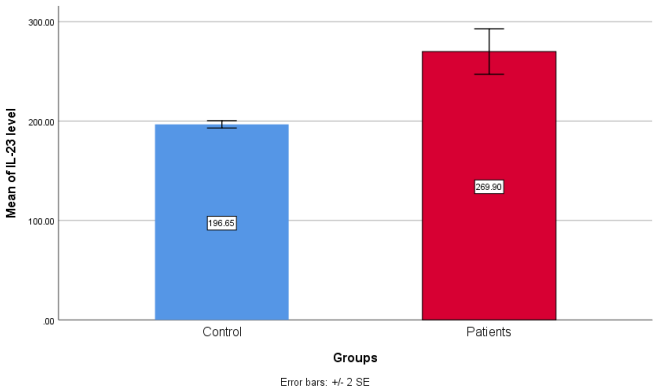

Figure (4) distribution of IL-23 level mean into controls and patients

4.3 distribution of Age mean into controls and patients

The distribution of Age means into controls and patients for probability their mean age was 25.80 ± 1.10 and 30.58 ± 3.34, with P-value greater than 0.05 respectively as shown in table 2 and figure 5.

Table 2: shows the distribution of Age mean into controls and patients for probability more than 0.05.

Groups	Age mean ± SE	Probability
Control	25.80 ± 1.10	P > 0.05
Patients	30.58 ± 3.34	

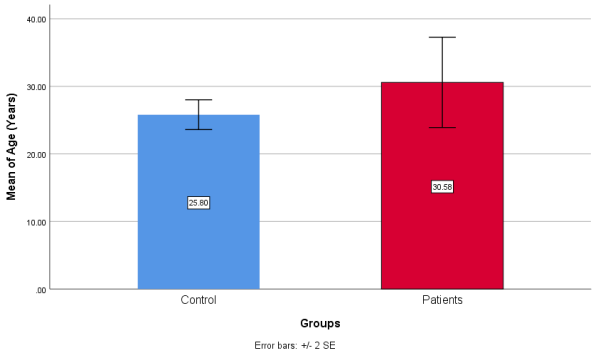

Figure (5) distribution of Age mean into controls and patients

4.4 **distribution of Percentage frequency of Gender patients and control.**

the distribution of Gender into controls and patients, 67 (67%) where males group distribution was 29 (64.4%) for Control and 28 (62.2%) for Patients, and 33 (33%) where females distribution was 16 (35.6%) for Control and 17 (37.8%) for Patients, P-value greater than 0.05, as shown in table 3 and figure 6. It is an approach to the results of (Nouh S. et al, 2020) where was their mean age was 30.2 ± 17.2 and 32.2 ± 16.5, respectively.

Table 3: shows the distribution of Gender into controls and patients for probability more than 0.05.

Groups	Gender		Probability
	Males No (%)	Females No (%)	
Control	29 (64.4)	16 (35.6)	P > 0.05
Patients	28 (62.2)	17 (37.8)	

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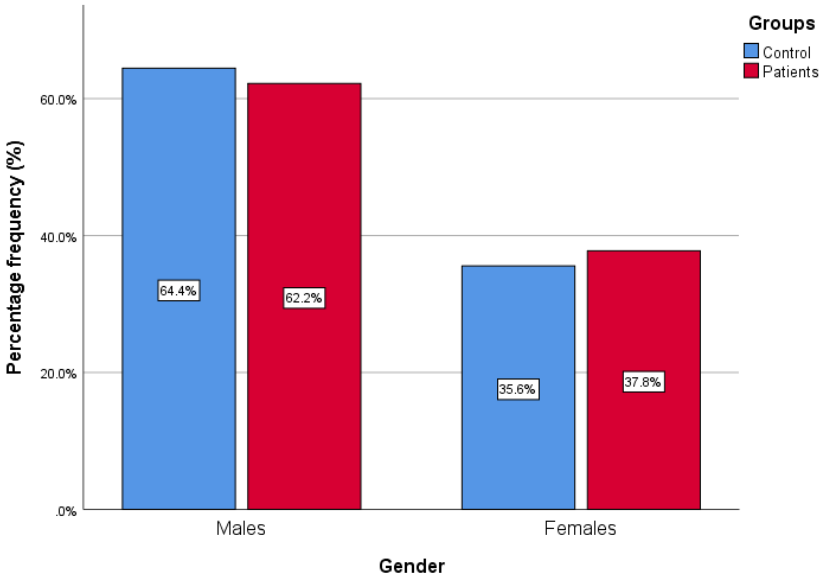

Figure (6) distribution of Percentage frequency of Gender patients and control.

4.5 distribution of injury severity into controls gender and patient's

the distribution of injury severity into controls gender and patient's gender. was 45 were in Control, the male group had 29 (64.4%) Nil and 16 (35.6%) Nil were Females. For the Patients 45 to, had a 28 Males group with 10 (35.7%) is a mild injury and 13 (46.4%) moderate injury and 5 (17.9%) severe. The Females group 17 were 8 (47.1%) is a mild injury and 9 (52.9%) was moderate injury, The Females hadn't any severe injury. As shown in Table 4 and Figure 7

Table 4: shows the distribution of injury severity into controls gender and patient's gender.

Groups	Control		Patients	
	Males No (%)	Females No (%)	Males No (%)	Females No (%)
Nil	29 (64.4)	16 (35.6)	0 (0.0)	0 (0.0)
+	0 (0.0)	0 (0.0)	10 (35.7)	7 (41.2)
++	0 (0.0)	0 (0.0)	13 (46.4)	9 (53)
+++	0 (0.0)	0 (0.0)	5 (17.9)	1 (5.8)

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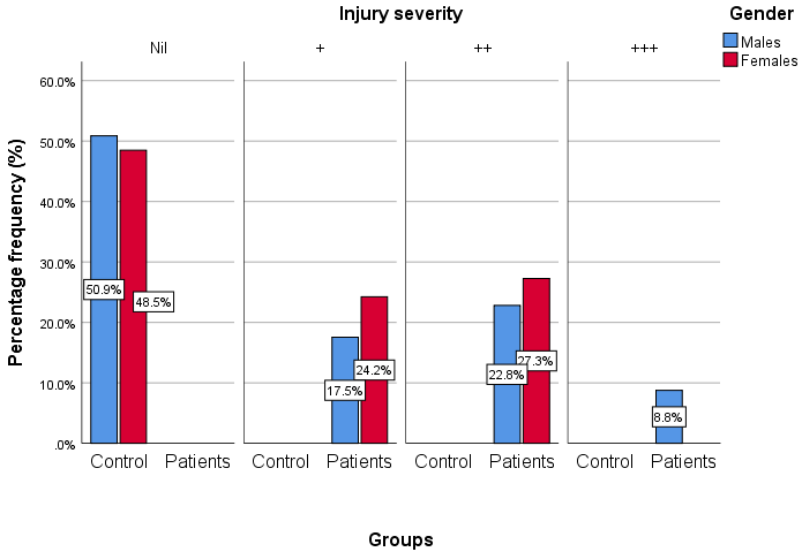

Figure (7) distribution of Percentage frequency of injury severity for Gender patients and control.

4.6 the correlation among the studied parameters in patients' group and control group

Table 5: the correlation among the studied parameters in patients' group and control group

		Groups	IL17	IL23	Age
Control	IL17	Pearson Correlation	1	-0.208	0.009
		Sig. (2-tailed)		0.170	0.954
	IL23	Pearson Correlation	-0.208	1	-0.039
		Sig. (2-tailed)	0.170		0.799
	Age	Pearson Correlation	0.009	-0.039	1
		Sig. (2-tailed)	0.954	0.799	
Patients	IL17	Pearson Correlation	1	-0.031	0.105
		Sig. (2-tailed)		0.840	0.496
	IL23	Pearson Correlation	-0.031	1	0.329*
		Sig. (2-tailed)	0.840		0.028
	Age	Pearson Correlation	0.105	0.329*	1
		Sig. (2-tailed)	0.496	0.028	

*. Correlation is significant at the 0.05 level (2-tailed).

It has been shown that persons who are weak in the IL-17 receptor signaling have a cell-intrinsic deficiency that causes them to be more susceptible than their healthy counterparts to systemic fungal infections. An increase in antifungal immunity was achieved by the release of GM-CSF by NK cells, which is essential for neutrophils' fungicidal action. For antifungal defense, natural killer cells (NK cells) are crucial, and cytokines from this family play a role in the development of NK cells. The IL-17-NK cell axis may have a role in the immune response to fungi, bacteria, viruses, and malignancies, as well as other pathogens.

A large body of evidence demonstrates that the interleukin (IL)-23 produced by myeloid cells is essential for the final differentiation and preservation of Th17 cells in naive precursor cells. Additional investigations have shown that in addition to IL-23-dependent IL-17A synthesis, there is an alternate route that is independent of IL-23, for example, for -T cells (a fraction of the so-called "unconventional" T-cells) or invariant natural killer cells. There is still a lot we don't know about how inhibiting IL-23 or IL-17 affects disease progression or the potential side effects that could result from this new approach.

5. Conclusion

High rate of interleukins (Il17, Il23) with fungal infections, Interleukin 17 (IL-17)-mediated immunity plays an important role in human defense against fungal infections. People lacking the IL-17 receptor or IL-17's ability to secrete it are more susceptible to systemic candidiasis (candidemia), however this study also showed that temporarily blocking the IL-17 pathway during an infection in wild-type humans had no effect on fungal control.

For fungal infections, it is thought that the interleukin-23/interleukin-17 axis improves pathogen survival while simultaneously inducing chronic inflammation. IL-17A and IL-23, which are produced in large quantities at the site of infection, both inhibit antifungal effector activities of neutrophils and activate their inflammatory program (i.e., the production of metalloproteinases and oxidants) despite evidence that IL-17A contributes to neutrophil mobilization in disseminated candidiasis. Neutrophils and dendritic cells (DCs) may create more interleukin 23 because to fungal persistence in this environment, which aids in the maintenance of inflammation and increases the production of interleukin-17A. Infection and chronic inflammation may be linked if bacteria do not reduce production of interleukin (IL) 23/IL-17.

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