Egyptian Journal of Medical Microbiology Volume 34 / No.4 / October 2025 201-209 Online ISSN: 2537-0979

ORIGINAL ARTICLE

The possible roles of miRNA 155-5p, miRNA 146a and miRNA 342-3P in regulating serum levels of Interleukin-6 (IL-6) in Immunosuppressed Patients with Fungal Infections

[1]Duaa H. Salim, [1]Maan H. Salih*, [2]Milad A. Mizher
[1]Department of Biology, College of Sciences, Tikrit University, Tikrit, Salah Al Deen, Iraq.
[2]Department of Biology, College of Education for Pure Sciences, Tikrit University, Tikrit, Salah Al Deen, Iraq.

Key words:
Immunosuppressed, Fungi, miRNA, IL6

Corresponding Author:
Maan H. Salih.
Department of Biology, College of Sciences, Tikrit University, Tikrit, Salah Al Deen, Iraq
Tel.: 009647703768011
maan.hasan@tu.edu.iq

ABSTRACT

Background: *Background: Pathogenic fungi can infect immunocompromised patients, raising global public health concerns. Objective: The current study aims to assess miRNA expression differences and their relation to IL6 levels in immunosuppressed patients during fungal infections.* ***Methodology:*** *This study included 44 cancer patients with fungal infections, 22 cancer patients without infections, and 24 healthy controls. Fungal species were identified by culture, microscopy, and 18S rRNA gene sequencing. IL-6 levels were measured using ELISA, and microRNA gene expression was analyzed via qRT-PCR.* ***Results****: Patients infected with yeasts displayed a significant decrease in IL6 levels ($p < 0.001$) and those with mold also have lower levels compared to healthy individuals ($p < 0.001$). The levels of miRNA 155-5p were lower in yeast-infected patients ($p < 0.001$) and mold-infected patients ($p < 0.001$), compared to healthy controls. In contrast, miRNA 146a expression was significantly higher in yeast ($p = 0.001$) and mold infection groups ($p = 0.016$) than in controls. Additionally, miRNA 342-3P expression increased in yeasts ($p < 0.001$) and mold patients ($p < 0.001$) in contrast to healthy individuals. Positive correlation between IL6 and miRNA 155-5p was detected and negative correlations between IL6 levels and miRNA 146a/ miRNA 342-3p were also detected.* ***Conclusion:*** *miR-155, miRNA 146a, and miRNA 342-3P may have important roles in regulating IL6 serum levels in immunosuppressed patients with fungal infection.*

INTRODUCTION

Over 500 fungal species are considered infectious to humans, even though, there are countless fungal species in the world. Most fungi may be found in the environment and are also found in both humans and animals as typical flora[1]. Fungal infections have garnered attention from public and industrial communities as a new worldwide health problem. As a result of their growing significance, the World Health Organization (WHO) released the first-ever Fungal Priority Pathogens List in 2022[2]. The most common invasive fungal pathogens include molds (mainly Aspergillus spp.) and yeasts (mainly Candida spp.), while other fungal pathogens occur in much lower frequencies[3].

Over the last few years, the prevalence of immunocompromised patients in the general population has been raised markedly[4]. Globally, invasive fungal infections are considered one of alarming problems due to their substantial infection and death rates[5]. Although invasive fungal infections can cause morbidity and mortality in immunocompromised patients, non-neutropenic adult individuals hospitalized in intensive care units (ICU) can also be infected with invasive fungi[6]. In individuals with a competent immune system, most fungal infections are either asymptomatic or lead to non-specific signs and symptoms that typically resolve without treatment[7].

Cytokine deregulation has a vital role in various diseases, including cancer diseases, infectious diseases, and autoimmune diseases[8]. Cytokines have the potential to treat various diseases due to their immunomodulatory properties. Understanding their roles in immunity and disease mechanisms is essential to developing effective therapeutic interventions. Interleukin 6 (IL6) is a multifunctional cytokine that plays a dual role in the immune system, attributed to both pro-inflammatory and anti-inflammatory effects. Its impact varies depending on the specific context of the immune response[9]. To coordinate the immune response with infections, immune cells release extracellular vehicles (EVs) that contain an adapted cocktail of proteins and microRNAs (miRNAs)[10]. MicroRNAs are essential in

regulating immune functions by guiding the development of immune cell subsets like B cells and T cells. They influence the development and function of lymphocyte cells[9,11]. During a fungal infection, different tissues, cells, and extracellular vesicles release miRNAs differently, which modulates the host immune response and either promotes or inhibits antifungal effects[12].

Published research has demonstrated a relationship between the regulated immune response via miRNA and the fungal infection mechanism[13,14]. Due to the limited number of studies exploring pathogens and the immune and molecular responses in various patient groups, this study focused on two groups of immunosuppressed patients with yeast and mold infections. Additionally, it included a group of cancer patients who had no reported fungal infections, in order to more accurately assess patient responses. Therefore, the current study's objective is to evaluate differences in the miRNA expression and its relation to IL6 levels in immunosuppressed patients during infection with yeasts and molds. These findings may help in developing future strategies to eliminate or inhibit invasive fungus during infection.

METHODOLOGY

Population study:

The study population comprised a total of 24 healthy volunteers, characterized by their lack of any evident disease symptoms, absence of infections, and no documented family history of diabetes or cancer. This healthy cohort was critically important to establish a baseline for comparison. In contrast, the patient group consisted of 64 individuals diagnosed with various types of cancer, all of whom were classified as immunosuppressed. This immunosuppression made them more vulnerable to infections, which was a primary focus of the study. To investigate potential yeast and fungal infections, a series of diagnostic tests were done, resulting in the stratification of the patient population into three distinct groups. The first group included 22 patients diagnosed specifically with yeast infections. The second group comprised 22 patients identified with mold infections. Finally, the third group included 22 cancer patients who exhibited no signs of yeast or mold infections. Demographic data, any comorbidity and final diagnosis of various cancers were collected from patient's records.

Sample collection:

A total of 5 mL of blood was drawn from patients and healthy volunteers. For the ELISA test, 3 mL was sampled in a gel tube for serum isolation. For gene expression analysis, 200 µL of the blood sample was combined with 800 µL of Trizol (Thermo Fisher Scientific, Waltham MA USA) in a 2 mL Eppendorf tube.

Fungi identification:

Samples taken from blood cases were cultured on the Brain Heart Infusion Agar and then on Sabouraud Dextrose Agar medium supplemented with amoxicillin (250 mg/L). DNA extraction from the growing colonies of fungi was conducted using the DNeasy t Kit (QIAGEN, Germany). The ITS region was amplified at 95°C for 5 min, followed by 35 cycles of 95°C for 30 seconds, 49°C for 30 seconds, and 72°C for 2 min, and final steps at 72°C for 5 min [15]. The amplified ITS-rDNA gene was sent sequencing service (Macrogen, Seoul, South Korea).

Detection of Serum Levels of Interlekon-6:

Serum levels of IL-6 were performed by Enzyme Linked Immunoassay following the manufacturer's protocols (Sunlong, China). The absorbance was precisely measured at 450 nm using a Bio-Rad Laboratories, Inc. microplate reader. The concentration of IL6 in serum samples was quantified using standard curves.

Gene expression analyses:

RNA was extracted using the miRNA universal extraction Kit (QIAGEN, USA) following the manufacturer's protocol. RNA quantitative and quality were accurately determined with the NanoDrop ND-1000 (NanoDrop Technologies, Waltham, MA, USA). We utilized a specialized kit (QIAGEN, USA) for first-strand cDNA synthesis targeting poly(A) microRNA (miRNA), which provided all essential raw materials for miRNA poly(A) tailing and reverse transcription reactions. The amplification of cDNA samples corresponding to miRNAs was effectively evaluated using RT-PCR. All amplification reactions were conducted with Power SYBR Green (Applied Biosystems; Thermo Fisher Scientific, Waltham, MA, USA). All amplification reactions were conducted with Power SYBR Green The amplification conditions included 95°C for 10 minutes, followed by 40 cycles of 95°C for 10 seconds, and 60°C for 1 minute, concluding with a final dissociation stage to ensure the specificity of the amplification according to manufacture condition Kit (Thermo Fisher Scientific, Waltham, MA, USA). The target genes and details of the primer sequences that are complementary to them are described in Table 1.

Table 1: The primer sequences were chosen for current study.

Genes		Nucleotides sequence	Source
ITS	F	TCCGTAGGTGAACCTGCGG	[15]
	R	TCCTCCGCTTATTGATATGC	
miRNA 155-5p	F	ACCACCGTTAATGCTAATCGTGATA	New design for the current study
miRNA 146a	F	AACACGTGTGAGAACTGAATTCCAT	
miRNA 342-3P	F	AACAATTCTCACACAGAAATCGCAC	
Universal	R	CAGTGCAGGGTCCGAGGT	
U6		GTGCTCGCTTCGGCAGCA	
		CAAAATATGGAACGCTTC	

Statistical Analysis:

GraphPad Prism version 10.4.1. was used to perform statistical analysis. The results are presented as mean ± standard deviation, and median (interquartile range). To compare the statics variation between the two groups, we used Student's T-test. While detecting statics variation among multiple groups, a one-way analysis of variance (ANOVA) was followed by Tukey's test. The receiver operating characteristic (ROC) curve was used to characterize and compare the ability to distinguish between immunosuppressed patients with fungal infections and healthy individuals. Additionally, Pearson correlation analysis was performed to measure the correlation coefficient that measures the linear correlation between two variables. If the p-value is less than 0.05, it is judged as statistically significant.

RESULTS

Following diagnostic testing to ascertain whether fungal infections were present in immunosuppressed patients, 24 samples were chosen from patients without a documented fungal infection, 22 samples were selected from patients with yeast infections, and 22 samples were from patients with molds infections, based on the results of culture, microscopic examination, and DNA sequencing. Figure 1 shows Candida parapsilosisas a sample for a yeast infection while Figure 2 shows Arthroderma amazonicum as a sample for a mold infection. Demographic and clinical data of tested groups are summarized in Table 2.

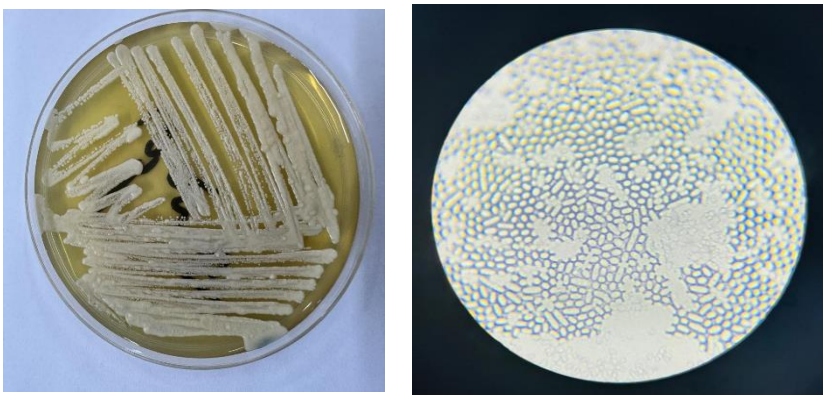

Fig. 1: Microscopic identification of Candida parapsilosisas a sample for a yeast infection.

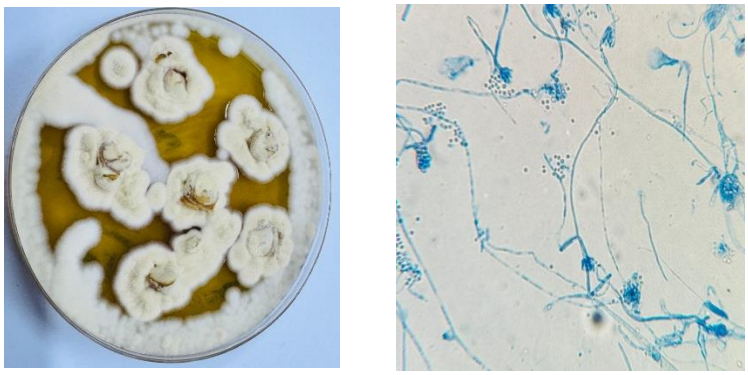

Fig. 2: Microscopic identification of Arthroderma amazonicum as a sample for a mold infection.

Table 2: Represent demographic and clinical data of patients' and healthy groups.

	Yeast infection	Molds infections	Cancer patients Without infection	Control
Number	22	22	22	24
Age (mean ± SD)	62.64± 11.38	58.73±14.93	59.05± 8.313	51.54±10.26
Cancer duration				
1-12 months	35%	25%	41%	-
1-6 years	65%	75%	59%	-
Family history of cancer patients	19%	15%	21%	No
Surgery	10%	12%	5%	-
Comorbidity				
Diabetes	20%	22%	10%	8.3 %
Hypertension	17%	26%	31%	12.5%
Diabetes with Hypertension	25%	27%	15%	8.3%
Without Comorbidity	38%	25%	44%	70.9 %

The relative miRNA 155-5p gene expression analysis was calculated using the 2-ΔCt method and compared to healthy individuals as controls. As shown in Figure 3A. The folding of miRNA 155-5p was decreased in patients infected with yeast [mean ± SD: 0.8354 ± 0.2494, median (IQR): 0.7692 (0.6330, 0.9880), p < 0.001]; and mold [mean ± SD:0.8853 ± 0.2977, median (IQR): 0.8693 (0.6716, 1.118), p < 0.001]; respectively with control groups [mean ± SD: 1.824 ± 0.6288, median (IQR): 1.874 (1.184, 2.411] and patients without fungi infection [mean ± SD: 1.322± 0.3683, median (IQR): 1.220 (1.042, 1.588)]. No significant difference (p=0.979) was detected when comparing the folding of miRNA 155-5p between yeast and mold infection. The Area Under the Curve (AUC) for miRNA-155-5p is 0.9261 (95% Confidence Interval (CI) of 0.8643 -0.9879), which indicates its effectiveness in distinguishing between patients (mold and yeast infection) and control subjects. The sensitivity of the test is 81.82%, meaning it accurately identifies 81.82% of patients with mold and yeast infections. The specificity is 91.67%, indicating that it correctly identifies 91.67% of healthy as not having mold and yeast infections, as seen in Figure 3B.

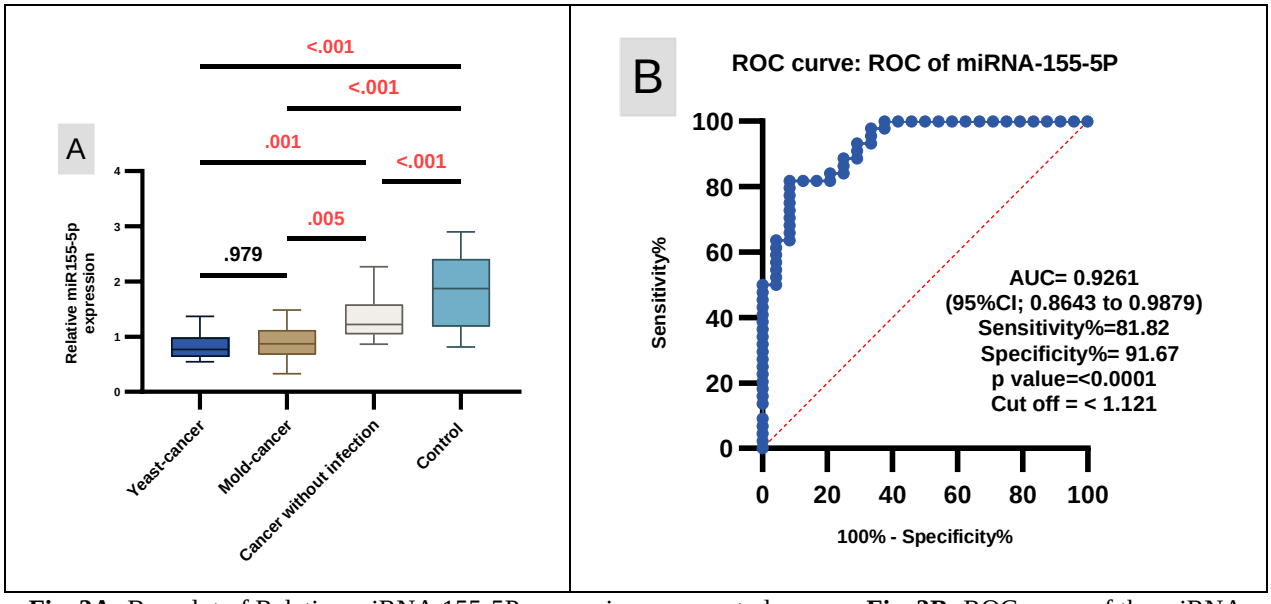

Fig. 3A: Box plot of Relative miRNA 155-5P expression among study group. **Fig. 3B:** ROC curve of the miRNA 155-5P expression between patients with fungi infection and healthy group.

The expression levels of the miRNA 146a gene were analyzed using the 2-ΔCt method, with healthy individuals serving as the control group. According to Figure 4A, the expression of miRNA 146a was significantly increase in patients infected with yeast (mean ± SD: 1.577± ٠.٥٢٤٣; median (IQR): 1.556 (١.١١١, 1.899); p = 0.001) and in those infected with mold (mean ± SD: 1.467± 0.5048; median (IQR): 1.542 (1.126, 1.٧٤٨); p = 0.٠١٦) compared to the health group [mean ± SD: 1.824 ± 0.6288, median (IQR): 1.874 (1.184, 2.411] and patients without fungal infection [mean ± SD: 1.055± 0.3741, median (IQR): 1.112 (0.7249, 1.304]. Moreover, there was non significant difference (p = 0.858) in the expression of miRNA 155-5p between yeast and mold infections. The AUC of miRNA 146a is 0.7645 (95% Confidence Interval (CI): 0.6528 - 0.8763), indicating it's a fairly good ability to distinguish between patients with mold or yeast infections and healthy subjects. The test exhibits a sensitivity of 56.82%, accurately identifying 56.82% of patients with these infections. Its specificity is 84%, showing it correctly identifies 84% of healthy individuals as not having mold or yeast infections, as illustrated in Figure 4B.

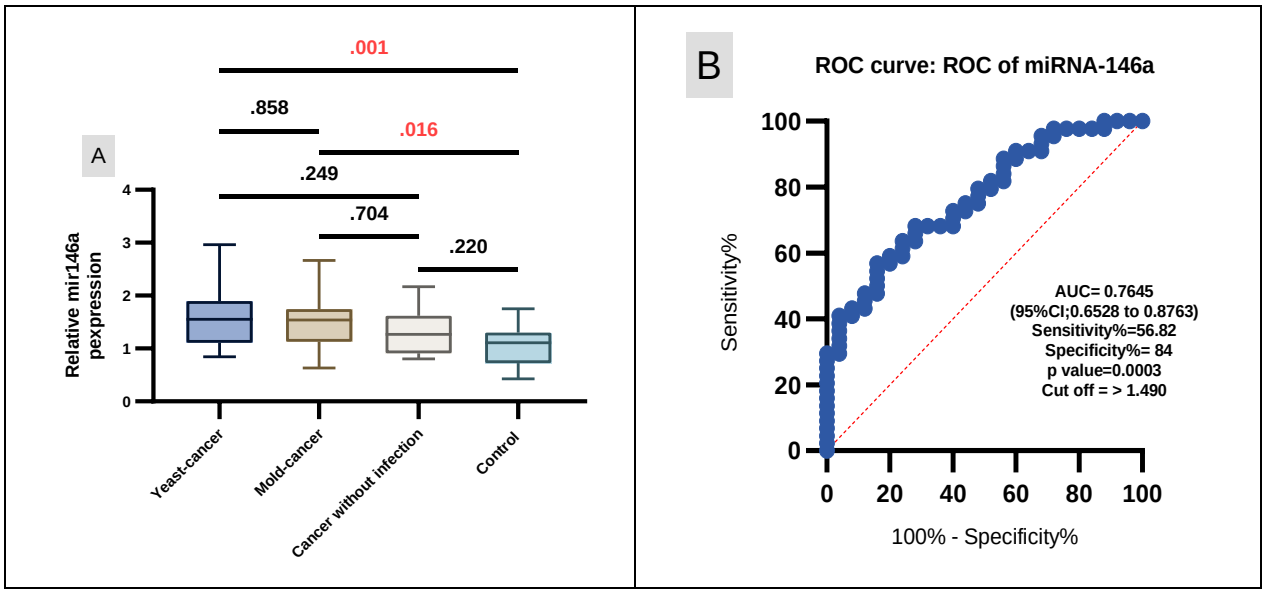

Fig. 4A: Box plot of Relative miRNA 146a expression among study group. **Fig.4B:** ROC curve of the miRNA 146a expression between patients with fungi infection and healthy group.

The miRNA 342-3P gene's expression levels were analyzed using the 2-ΔCt method, with healthy individuals serving as a control group. As illustrated in Figure 5A, we found a significant increase in the expression of miRNA 342-3P among patients infected with yeast (mean ± SD: 2.393 ± 0.4857; median [IQR]: 2.430 [2.148, 2.733]; p < 0.001) and those afflicted by mold (mean ± SD: 1.862 ± 0.4979; median [IQR]: 1.773 [1.470, 2.343]; p < 0.001) when compared to the healthy group (mean ± SD: 1.277 ± 0.4018; median [IQR]: 1.191 [0.9259, 1.588]) and patients without fungi infection [mean ± SD: 1.277± 0.4018, median (IQR): 1.191 (0.9259, 1.588]. Furthermore, our analysis revealed a significant difference (p = 0.033) in the expression of miRNA 342-3P between yeast and mold infections. Remarkably, the AUC for miRNA 342-3P stands at 0.8797 (95% Confidence Interval [CI]: 0.8002 - 0.9593), it has a high ability to differentiate between patients suffering from mold or yeast infections and healthy individuals. The test boasts a sensitivity of 72.73%, identifying the patients with these infections. Additionally, its specificity is an impressive 78.5%, effectively recognizing 78.5% of healthy individuals as free from mold or yeast infections, as demonstrated in Figure 5B.

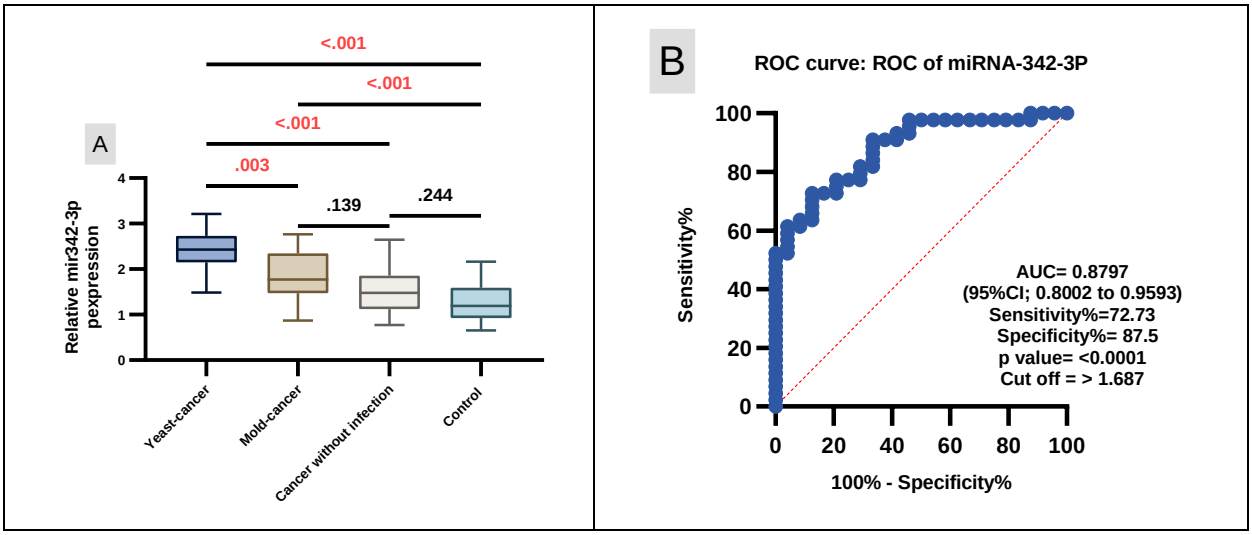

Fig. 5A: Box plot of Relative miRNA 342-3P expression among study group. **Fig. 5B:** ROC curve of the miRNA 342-3P expression between patients with fungi infection and healthy group.

The IL6 levels were analyzed among the patient group, with healthy individuals as a control group. As shown in Figure 6, we noted a remarkable decrease in IL-6 levels among patients infected with yeast (mean ± SD: 113.4± 28.12; median [IQR]: 109.0 [97.16, 135.0]; $p < 0.001$) and those affected by mold (mean ± SD: 145.2± 74.52; median [IQR]: 145.1 [114.9, 181.0]; $p < 0.001$) when compared to the healthy group (mean ± SD: 220.6± 0.4018; median [IQR]: 210.9 [160.0, 284.5]). Additionally, our analysis revealed a significant difference in level IL6 between yeast and mold infections ($p = 0.001$).

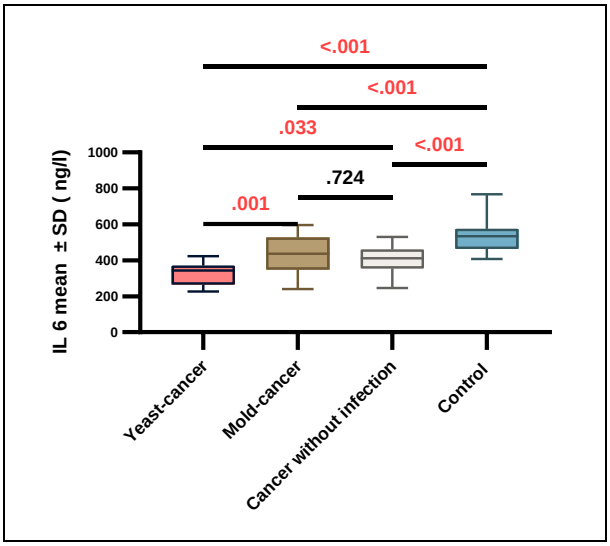

Fig. 6: Box plot of IL 6 level among study group.

To evaluate the overall correlation between changes in interleukin-6 (IL6) levels and microRNAs between patients infected with yeast and mold vs the healthy group, Pearson's correlation analysis was conducted. The results, shown in Figure 7A, indicate that the Pearson correlation coefficient was a moderate positive correlation between IL6 and miRNA 155-5p ($p=0.0004$, $r = 0.5089$). Conversely, IL6 levels exhibited negative correlations with miRNA 146a and miRNA 342-3p ($r = -0.4544$, p-value $=0.0019$ and $r = -0.3238$, $p=0.0320$ respectively), Figure 7B and 7C.

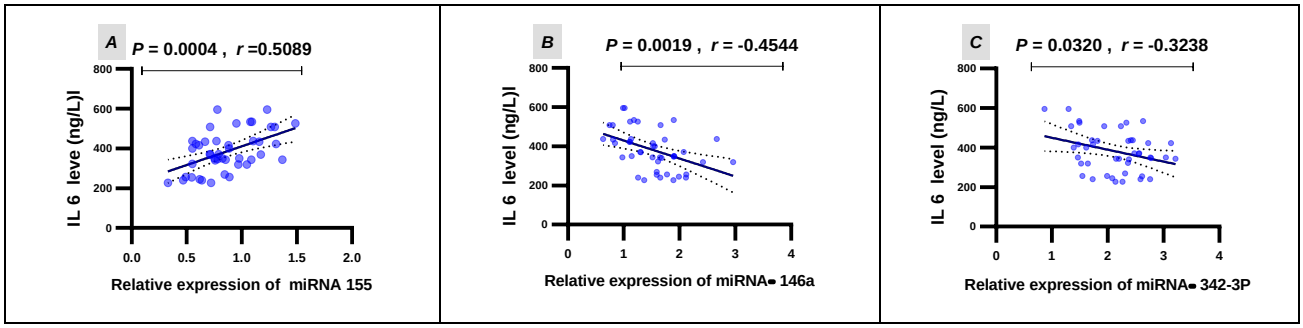

Fig. 7A: correlation between miRNA 155 and IL 6 in patients with fungi infection, **Fig.7B:** correlation between miRNA 146a and IL 6 in patients with fungi infection, **Fig. 7C:** correlation between miRNA 342-3P and IL 6 in patients with fungi infection

DISCUSSION

In the current study, we found that yeast and mold infections can reduce the expression of miR-155 and increasing in folding of the miRNA 146a and miRNA 342-3P. In addition, our data showed reduced IL-6 levels in patients with fungal infection.

Communication between immune cells through extracellular vesicle-associated miRNAs was reported to be crucial for regulating immune responses[10]. Following a fungal infection, miRNAs appear in varied expression responses, influencing the host immune response through a variety of cellular mechanisms[16]. Our study showed downregulation in miR-155 and upregulation of both miR-146a miRNA 342-3P in the two groups of immunosuppressed patients infected with molds and yeasts compared to the two groups of patients without fungi infected and healthy groups. miR-155 was transcribed from the B cell integration cluster, promoting inflammation and the overexpression of important oncogenic microRNAs (oncomiRs) in a variety of human malignancies[17]. The mycotoxin ochratoxin A (OTA), which is produced by fungi, significantly increases miR-155-5p[18]. However, the interpretation most consistent with the current results is that confirmed by previous studies that reported down-regulation of miR-155-5p is associated with advanced tumor stages, indicating its potential role as a tumor suppressor[19,20]. A significant increase in interleukin (IL)-8 cytokine production and IL-6 secretion during inflammation were the outcomes of increased miR-155-5p expression[21].

As for the results of the MiR-146a, they are consistent with previous studies that led to the fact that miR-146a regulates inflammation during Aspergillus fumigatus infection, where overexpression reduces TNF-α and IL-6, while downregulation increases these cytokines[22]. another study also indicated During fungal infection, MiR-146a regulates the immune response by inhibiting the NF-κB pathway then reducing IL-6 and TNFα after Dectin-1 activation by Candida albicans[23].

To our knowledge, no previous study has linked miR-342-3p expression with fungal infection. However, prior research has detailed the role of miR-342-3p in the immune response and its primary function in regulating IL-6. Overexpression of miR-342-3p reduces inflammatory cytokines TNF-α, cyclooxygenase-2, IL-6, and IL-1β in T2DM[24]. Previous studies on irradiated mice suggest that the upregulation of miR-342-3p affects IL-6 levels, indicating a potential regulatory relationship, but it does not confirm an inverse correlation with IL-6[25]. The miR-342-3p levels were significantly lower in Rheumatoid Arthritis patients and inversely correlated with IL-6, suggesting that the downregulation of miR-342-3p is associated with increased IL-6 levels[26].

As for the interpretation of the results of IL 6, they are consistent with the results of previous studies in several aspects. IL-6 inhibition was associated with the activation of T- and NK-cells, which countered the immunosuppressive environment created by tumors[27]. Accordingly, it has been demonstrated that IL-6 helps to suppress the growth of opportunistic fungi, such as cryptococcal infection[28] also IL-6 deficiency increases susceptibility to Candida albicans infection, as IL-6-/- mice show lower survival rates and higher fungal loads[29]. which may explain the decreased IL6 levels with fungal infection in the current study. In addition, the infection can reach multiple organs and systems in the body. In mice models, A lack of IL-6 increases the growth of cryptococcal cells in the blood, which may allow fungi to enter the central nervous system and be linked to higher mortality[30].

Our study reveals findings that, somewhat similar to previous research on the regulation of IL-6 in immunosuppressed individuals with fungal infections, contribute novel insights. We not only support earlier work but also enhance it by highlighting the critical role of this cytokine in cancer patients who are infected with yeast and molds, in contrast to patients without fungal infections and healthy controls. Additionally, we demonstrate the possible regulatory roles of miRNA

155-5p, miRNA 146a, and miRNA 342-3p with IL-6, both directly or indirectly, during fungal infections.

The present results revealed moderate positive correlation between IL6 and miRNA 155-5p while negative correlations were detected between IL6 levels with miRNA 146a and miRNA 342-3p. These findings suggest that miR-155, miRNA 146a, and miRNA 342-3P are critical in regulating the inflammatory response in immunosuppressed patients with fungal infections.

Unfortunately, the study included a relatively small sample. Further researches are needed to examine more closely the links between IL6 gene regulation and fungal infection, especially in mice and human samples

CONCLUSION

The present study reported downregulation of miR-155 and upregulation of miR-146a and miRNA 342-3P in immunosuppressed patients infected with molds and yeasts compared to non-infected and healthy groups. Additionally, IL6 levels were significantly decreased in yeast and mold-infected patients compared to healthy individuals. The evidence from this study suggests that IL6 has a vital role in the immune response to fungal infection in immunosuppressed patients. Also, miR-155, miRNA 146a, and miRNA 342-3P may have important roles in regulating IL6 serum levels in immunosuppressed patients with fungal infections.

Conflict of Interest

No Conflict of Interest

Ethical consideration

All procedures conducted in studies involving human participants adhered to the 1975 Helsinki Declaration and its subsequent amendments or comparable ethical standards. Before initiating the study, ethical approval was obtained from the College of Science at Tikrit University in Iraq (3/7/1403 in 17/3/2014).

REFERENCES

1. Pathakumari B, Liang G, Liu W. Immune defence to invasive fungal infections: A comprehensive review. *Biomedicine and Pharmacotherapy*. 2020;130. doi:10.1016/j.biopha.2020.110550
2. Denning DW. Global incidence and mortality of severe fungal disease. *Lancet Infect Dis*. 2024;24(7). doi:10.1016/S1473-3099(23)00692-8
3. Low CY, Rotstein C. Emerging fungal infections in immunocompromised patients. *F1000 Med Rep*. 2011;3(1). doi:10.3410/M3-14
4. Azoulay E, Schellongowski P, Darmon M, et al. The Intensive Care Medicine research agenda on critically ill oncology and hematology patients. *Intensive Care Med*. 2017;43(9). doi:10.1007/s00134-017-4884-z
5. WHO. *WHO Fungal Priority Pathogens List to Guide Research, Development and Public Health Action*. Vol 1.; 2022.
6. Ostrosky-Zeichner L, Al-Obaidi M. Invasive Fungal Infections in the Intensive Care Unit. *Infect Dis Clin North Am*. 2017;31(3). doi:10.1016/j.idc.2017.05.005
7. Llenas-García J, González Beiro R, Ramos-Rincón JM, Wikman-Jorgensen P. Imported Systemic Endemic Mycoses in Spain 1997–2021: An Analysis of a National Hospital Database. *Mycoses*. 2025;68(1). doi:10.1111/myc.70021
8. Bhol NK, Bhanjadeo MM, Singh AK, et al. The interplay between cytokines, inflammation, and antioxidants: mechanistic insights and therapeutic potentials of various antioxidants and anti-cytokine compounds. *Biomedicine and Pharmacotherapy*. 2024;178. doi:10.1016/j.biopha.2024.117177
9. Aliyu M, Zohora FT, Anka AU, et al. Interleukin-6 cytokine: An overview of the immune regulation, immune dysregulation, and therapeutic approach. *Int Immunopharmacol*. 2022;111. doi:10.1016/j.intimp.2022.109130
10. Halder LD, Babych S, Palme DI, et al. Candida albicans Induces Cross-Kingdom miRNA Trafficking in Human Monocytes To Promote Fungal Growth. *mBio*. 2022;13(1). doi:10.1128/MBIO.03563-21
11. Khameneh SC, Razi S, Lashanizadegan R, et al. MicroRNA-mediated metabolic regulation of immune cells in cancer: an updated review. *Front Immunol*. 2024;15. doi:10.3389/fimmu.2024.1424909
12. Shrivastava M, Pandey D, Sharma P, Singh R. MicroRNA regulation and host interaction in response to Aspergillus exposure. *Biocell*. 2022;46(2). doi:10.32604/biocell.2022.016822
13. Kumar M, Topno RK, Kumar R. RNAi: antifungal therapy against Invasive pulmonary aspergillosis (IPA) in humans. *Indian Journal of Microbiology Research*. 2023;10(3). doi:10.18231/j.ijmr.2023.022
14. Yang A, Chen H, Lin J, et al. Comprehensive analysis of peripheral blood non-coding RNAs identifies a diagnostic panel for fungal infection after transplantation. *Bioengineered*. 2022;13(2). doi:10.1080/21655979.2022.2032963
15. White TJ, Bruns T, Lee S, Taylor J. AMPLIFICATION AND DIRECT SEQUENCING OF FUNGAL RIBOSOMAL RNA GENES FOR PHYLOGENETICS. In: *PCR*

Protocols. ; 1990. doi:10.1016/b978-0-12-372180-8.50042-1

16. Croston TL, Lemons AR, Beezhold DH, Green BJ. MicroRNA regulation of host immune responses following fungal exposure. *Front Immunol*. 2018;9(FEB). doi:10.3389/fimmu.2018.00170
17. Quinn SR, Mangan NE, Caffrey BE, et al. The role of Ets2 transcription factor in the induction of microrna-155 (miR-155) by lipopolysaccharide and its targeting by interleukin-10. *Journal of Biological Chemistry*. 2014;289(7). doi:10.1074/jbc.M113.522730
18. Rhee KH, Yang SA, Pyo MC, Lim JM, Lee KW. MiR-155-5p Elevated by Ochratoxin A Induces Intestinal Fibrosis and Epithelial-to-Mesenchymal Transition through TGF-β Regulated Signaling Pathway In Vitro and In Vivo. *Toxins (Basel)*. 2023;15(7). doi:10.3390/toxins15070473
19. Ysrafil Y, Astuti I, Anwar SL, et al. MicroRNA-155-5p diminishes in vitro ovarian cancer cell viability by targeting HIF1α expression. *Adv Pharm Bull*. 2020;10(4). doi:10.34172/apb.2020.076
20. Zare A, Alipoor B, Omrani MD, Zali MR, Alamdari NM, Ghaedi H. Decreased miR-155-5p, miR-15a, and miR-186 expression in gastric cancer is associated with advanced tumor grade and metastasis. *Iran Biomed J*. 2019;23(5). doi:10.29252/.23.5.338
21. Cazzanelli P, Lamoca M, Hasler J, et al. The role of miR-155-5p in inflammation and mechanical loading during intervertebral disc degeneration. *Cell Communication and Signaling*. 2024;22(1). doi:10.1186/s12964-024-01803-7
22. Tong J, Duan Z, Zeng R, et al. MiR-146a Negatively Regulates Aspergillus fumigatus-Induced TNF-α and IL-6 Secretion in THP-1 Macrophages. *Mycopathologia*. 2021;186(3). doi:10.1007/s11046-021-00538-0
23. Du L, Chen X, Duan Z, et al. MiR-146a negatively regulates dectin-1-induced inflammatory responses. *Oncotarget*. 2017;8(23). doi:10.18632/oncotarget.16958
24. Ray SL, Coulson DJ, Yeoh MLY, et al. The role of miR-342 in vascular health. Study in subclinical cardiovascular disease in mononuclear cells, plasma, inflammatory cytokines and PANX2. *Int J Mol Sci*. 2020;21(19). doi:10.3390/ijms21197217
25. Wei W, Bai H, Zhang T, et al. Regulation of Circulating miR-342-3p Alleviates the Radiation-Induced Immune System Injury. *Radiat Res*. 2023;200(6). doi:10.1667/RADE-23-00125.1
26. Zhou Q, Liu J, Sun Y, Chen X, Zhang X, Ding X. Expression of miR-342-3p in rheumatoid arthritis patients and its effect on synovial fibroblast inflammation and migration. *Nan Fang Yi Ke Da Xue Xue Bao*. 2022;42. doi:10.12122/j.issn.1673-4254.2022.11.16
27. Patel SA, Nilsson MB, Yang Y, et al. IL6 Mediates Suppression of T- and NK-cell Function in EMT-associated TKI-resistant EGFR-mutant NSCLC. *Clinical Cancer Research*. 2023;29(7). doi:10.1158/1078-0432.CCR-22-3379
28. Munzen ME, Gomez MR, Hamed MF, et al. Palmitoylethanolamide shows limited efficacy in controlling cerebral cryptococcosis in vivo. *Antimicrob Agents Chemother*. 2023;67(10). doi:10.1128/aac.00459-23
29. Van Enckevort FHJ, Netea MG, Hermus ARMM, et al. Increased susceptibility to systemic candidiasis in interleukin-6 deficient mice 1. *Med Mycol*. 2008;37(6). doi:10.1111/j.1365-280x.1999.00247.x
30. Reguera-Gomez M, Munzen ME, Hamed MF, Charles-Niño CL, Martinez LR. IL-6 deficiency accelerates cerebral cryptococcosis and alters glial cell responses. *J Neuroinflammation*. 2024;21(1):242. doi:10.1186/s12974-024-03237-x