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Role of Interleukin-17 And Interleukin-35 In the Pathophysiology of Respiratory Infections Caused by Multidrug-Resistant Pseudomonas Aeruginosa

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Abstract

Aims: The objective of this study was to assess the IL-17 and IL-35 mediated immune response of patients with respiratory infections attributable to highly resistant (MDR) Pseudomonas aeruginosa and to determine the possible role of these interleukins as biomarkers for severity of disease and clinical outcomes.

Methods and Materials: This cross-sectional study was carried out on 58 patients infected with infection with MDR P. aeruginosa respiratory tract infections in Al-Hussein Teaching Hospital, Karbala, Iraq, from August/2024 to February/2025. Abstract Background Clinical data including the severity of the disease ICU admission need for mechanical ventilation Corticosteroids use and outcomes after 3 weeks were recorded. Inflammatory markers (CRP, procalcitonin, blood cell counts), as well as serum levels of IL-17 and IL-35 were evaluated with ELISA.

Results: The results showed that IL-17 was significantly increased in patients with higher degrees of disease severity, from 56.6±9.3pg/mL in mild disease to 72.4±13.2pg/mL in severe disease (p=0.005). Moreover, higher IL-17 was significantly associated with ICU admission, mechanical ventilation requirement and poor outcomes, including mortality (75.2±13.7pg/mL). In contrast, IL-35 levels were inversely associated with disease severity, falling from 52.3±9.2pg/mL in mild disease to 42.5±7.9pg/mL in severe disease (p=0.008). Low IL-35 levels were found in patients who died (41.2±7.7pg/mL) and high IL-35 levels were found in patients with better outcome. Oxygen saturation and lymphocyte counts also presented with significantly negative correlations with IL-17, whilst IL-35 had significantly positive correlations with oxygen saturation.

Conclusion: The contrasting behaviors of IL-17 and IL-35 suggest a dynamic interplay between pro-inflammatory and anti-inflammatory responses in MDR P. aeruginosa infections. Elevated IL-17 is a marker of increased inflammation and disease severity, while IL-35 may exert protective, regulatory effects. The combined measurement of these cytokines offers promising diagnostic and prognostic value and may inform personalized management strategies for critically ill patients with MDR infections. Further research is recommended to explore their potential as therapeutic targets.

Keywords: IL-17, IL-35, respiratory infections, MDR *Pseudomonas aeruginosa*

Introduction

Pseudomonas aeruginosa is an opportunistic pathogen that responds negatively to Gram staining, and it is among the most nosocomial infections in the respiratory tract of critically ill and immunocompromised patients (Bassetti et al., 2018). Biofilm formation between defenses by the host and multi-drug resistance makes treatment even less likely to do well with this organism (Moradali et al., 2017). One of the main cause of multidrug resistant P. aeruginosa-related morbidity and

mortality globally; and a multicenter study has shown mortality rates in ventilated patients up to 40% (Tumbarello et al., 2019). Therefore, increased mortality of between 25% and 35%, associated with MDR respectively. Reported from MENA countries, are likely to be an underestimate due to absent surveillance in low resource settings (Hassan et al., 2021). According to Al-Rubaye et al.,2024 report, significant carbapenem-resistant P. aeruginosa was found in ICUs outbreak during 2022-2023 in Iraq with an approximate ventilator-associated pneumonia mortality rate about nearly 30%.

The host immune response to P. aeruginosa requires the cooperation of innate and adaptive immunity, involving neutrophils, macrophages, and a network of different cytokines (Raffetseder et al., 2019). Two relatively novel cytokines that have come under much scrutiny for their diametrically opposed roles in immunity are interleukins 17 and 35 (Mtsher et al., 2024). IL-17 is mostly produced by Th17 cells; it initiates neutrophil recruitment and antimicrobial peptide release and is thus involved in mucosal immunity (Gaffen et al., 2014; Hadi et al., 2024). Raised levels of IL-17 are seen in most bacterial lung infections; these include infections by P. aeruginosa where a deficiency of IL-17 results in impaired neutrophil response as well as higher bacterial loads (Jepson et al., 2008; Caidi et al., 2020).

IL-35 is a relatively newly identified anti-inflammatory heterodimeric cytokine, primarily secreted by regulatory T cells (Tregs) and B cells (Collison et al., 2010). It suppresses the responses of both Th1 and Th17 along with the expansion of Tregs. This gives IL-35 a dual role in infections, as it may limit tissue damage by reducing inflammation but at the same time could promote microbial persistence through inadequate clearance (Wirtz et al., 2014). In murine models of bacterial pneumonia IL-35 was found to reduce neutrophil-mediated injury but delayed pathogen clearance Zhang et al., 2021). Limited human data available demonstrate that low levels of IL-35 are associated with poor infection outcomes including chronic lung infections seen in cystic fibrosis; however, its role has not been explored specifically in MDR P. aeruginosa respiratory infections.

In multidrug-resistant infections, understanding the IL-17/IL-35 balance is very important. High levels of IL-17 can lead to bacterial clearance accompanied by high levels of inflammation and lung injury; in return, IL-35 can promote tissue protection while facilitating pathogen survival (Zhu et al., 2022). This is the kind of balance that may determinatively affect susceptibility, disease evolution, and treatment results in multidrug resistance conditions. Other infectious diseases give us some hints about it: for example, elevated levels of sepsis-related IL-35 along with a high ratio corresponded to much worse outcomes (Chen et al., 2018). This dynamic has not been much examined in Iraq or other Arab countries. In an earlier study on Iraq, it was found that patients with ventilator-associated pneumonia have IL-17 levels raised against P. aeruginosa, but this study did not evaluate IL-35 (Al-Hassani et al., 2023).

This study, therefore, aims to discuss the possible immunomodulatory roles of interleukin-17(IL-17) and interleukin-35 (IL-35) in the pathophysiology of respiratory infections caused by multidrug-resistant (MDR) Pseudomonas aeruginosa. To measure serum levels of these two cytokines in infected patients and correlate them with some clinical parameters such as oxygen saturation, inflammatory markers, infection severity, ICU admission, and outcome

Materials and Methods

Study Design and Setting

A prospective study was performed at Al-Hussien Teaching Hospital in Karbala, Iraq. The data collection process spanned from August 2024 to January 2025. A total of 58 patients were included in the study diagnosed with respiratory infections caused by multidrug-resistant Pseudomonas aeruginosa. Among them, 24 were females (41.38%), and 34 were males (58.62%). Patients' ages ranged between 21 and 59 years; they were recruited from the inpatient wards, including the ICU.

Diagnosis of MDR Pseudomonas aeruginosa

The infection was diagnosed based on clinical and microbiological evidence. Sputum and/or endotracheal aspirate samples were collected from patients following aseptic precautions. Samples were inoculated onto MacConkey agar and Cetrimide agar and incubated aerobically at 37°C for 24–48 hours. Colonies of the organism, Pseudomonas aeruginosa, based on pigmentation and a grape-like odor, oxidase-positive reaction, should be further confirmed by API 20NE identification strips along with susceptibility testing to antibiotics using the Kirby–Bauer disk diffusion method as per CLSI guidelines. Only multidrug resistant strains will be considered here that means strains must show

resistance against three or more than classes of antibiotics cephalosporins, carbapenems, aminoglycosides fluoroquinolones.

About 3 ml of venous blood was taken from each patient in plain tubes. The samples were allowed to clot at room temperature and then spun at 3000 rpm for 10 minutes to get serum. The serum samples were divided and kept at -20°C until used.

Measurement of IL-17 and IL-35

Serum concentrations of IL-17 and IL-35 were measured by commercially available sandwich ELISA kits specific for human cytokines. The assays were performed according to the manufacturer's instructions, using 100 µL of serum per well; detection range 15.6–1000 pg/mL; with sensitivity approximately 9.4 pg/mL. Absorbance readings at 450 nm were done using an ELISA microplate reader. The levels of these cytokines were calculated from the standard curve generated with the calibrators supplied.

Clinical Characteristics

The following clinical parameters were documented for each patient from hospital records: Infection severity, as mild, moderate, or severe based on respiratory symptoms, radiological findings, and systemic involvement. Whether the patient was admitted to the ICU (yes/no). Use of mechanical ventilation (yes/no). Whether corticosteroids were administered during hospitalization (yes/no). Clinical outcome after three weeks: recovery, complications, or death.

Inflammatory and Hematological Markers

The other laboratory parameters that were measured to assess the inflammatory status of patients: C-Reactive Protein (CRP) (mg/L): measured by immunoturbidimetric assay on an automated clinical chemistry analyzer. Procalcitonin (ng/mL): quantity measured by chemiluminescent immunoassay. Oxygen Saturation (SaO_2%): recorded as pulse oximetry at the time of admission. Neutrophils and Lymphocytes Count ($\times 10^9$/L): available from complete blood count (CBC) done on a hematology analyzer. Neutrophil-to-Lymphocyte Ratio (NLR): calculated as absolute neutrophil count divided by absolute lymphocyte count.

Ethical Considerations

The Ethical Committee of Al-Hussien Teaching Hospital approved the study. Written informed consent was taken from all patients (or their legal guardians) prior to enrollment. The study related to the ethical principles of the Declaration of Helsinki, and patient confidentiality as well as data protection were maintained throughout the study.

Statistical analysis

Data analysis was done using the Statistical Package for the Social Sciences (SPSS), version 26. Student's t-test was used to check the difference in IL-17 and IL-35 levels between the two groups. To check the variations in IL-17 and IL-35 concentrations among patients' categories based on clinical characteristics, Student's T test and ANOVA were utilized. Least Significant Difference (LSD) method was used to find differences of multiple comparisons among groups with unequal frequencies (Al-Fahham, 2018).

Results

The 58 patients infected with multidrug-resistant Pseudomonas aeruginosa respiratory infections were clinically very heterogeneous concerning the severity of their disease and outcomes of treatment. A majority of patients, 43.10%, were classified as having mild infections; 31.04% and 25.86% were classified as having moderate and severe infections, respectively. The ICU was involved in admissions in 31.03% of cases, with mechanical ventilation being used for only 20.69% of patients; therefore, a significant proportion did not require critical treatment intervention. It also notes that corticosteroids were used in 60.34% of cases, suggesting that they are applied quite frequently in response management-inflammation related issues. At three weeks into follow-ups post-discharge home care recovery percentage stood at a still optimistic figure of 67.24%, complication percentage stood at 25.86%, and mortality was at an appalling high figure of 6.90%-all succinctly typifying the clinical burden plus risk possible when dealing with MDR Pseudomonas aeruginosa respiratory tract infection (Table1).

Table 1. Clinical Characteristics of patients

Indicators		`Patients (No. = 58)	
		Freq.	%
Severity of infections	Mild	25	43.10
	Moderate	18	31.04
	Severe	15	25.86
ICU Admission	Yes	18	31.03
	No	40	68.97
Mechanical Ventilation	Yes	12	20.69
	No	46	79.31
Administration of corticosteroids	Yes	35	60.34
	No	23	39.66
Outcome (after 3 weeks)	Recovery	39	67.24
	Complications	15	25.86
	Mortality	4	6.90

The clinical features of patients with MDR Pseudomonas aeruginosa infection showed that most of them were infected mildly to moderately, which corresponded to 43.1% and 31.0% respectively, while 25.9% had an infection that was on the severer side. The ICU admission rate was 31.0% and mechanical ventilation was done in 20.7%, which reflects quite a serious burden when it comes to respiratory or systemic complications. In-hospital corticosteroid use was very high at 60.3%. The patient's outcome at the end of the third week is documented as follows; recovered patients were 67.2%, complications were recorded in 22.4%, and deaths attributable to infection stood at 6.9%. This data gives an idea about how varied the clinical presentation is and outcomes for MDR P. aeruginosa infections are hence emphasizing that early detection needs appropriate management strategies (table 2).

Table 2. Inflammatory and hematological indicators in patients with MDR Pseudomonas aeruginosa infection

Indicators	`Patients (No. = 58)	
	Mean	SD
C-Reactive Protein (CRP) (mg/L)	84.2	28.2
Procalcitonin (ng/mL)	3.6	1.7
Oxygen Saturation (O_2 Sat %)	88.5	4.3
Neutrophils Count ($\times 10^9$/L)	9.3	3.2
Lymphocytes Count ($\times 10^9$/L)	1.2	0.3
Neutrophil-to-Lymphocyte Ratio (NLR)	10.4	4.1

The interleukin levels in patients with MDR Pseudomonas aeruginosa infection were actually proven to be raised. The inflammatory activity was thus elicited. The IL-17 results showed a value mean incredibly raised at 64.4 pg/mL (±12.4), with a confidence interval of 95% between 61.2 and 67.1, which is far above the normal reference range of 10–40 pg/mL . This, therefore, indicates strong pro-inflammatory immune response, common in bacterial infections and consequent neutrophil recruitment. Also elevated was IL-35 (an anti-inflammatory cytokine) with a mean value of about 48.5 pg/mL (±10.3), nearer the upper limit of its reference range (30–50 pg/mL). It may reflect regulatory feedback for augmented inflammation and, therefore, underlines the involvement of both pro- and anti-inflammatory mediators in host responses to infections that are drug-resistant (table 3).

Table 3. Measurement of IL-17 and of IL-35 levels in Patients with MDR Pseudomonas aeruginosa Infection

Interleukins	**`Patients (No. = 58)**		**CI (95%)**	**Reference values**
	Mean	SD		
IL-17 (pg/mL)	**64.4**	**12.4**	**61.2 – 67.1**	**10–40**
IL-35 (pg/mL)	**48.5**	**10.3**	**46.1 – 51.2**	**30–50**

The levels of IL-17 in patients infected with multidrug-resistant Pseudomonas aeruginosa were significantly associated with clinical severity and outcomes. The level of IL-17 increased progressively in tandem with the severity of infection; 56.6±9.3 pg/mL in mild cases to 72.4±13.2 pg/mL in severe cases (p=0.005). In the same way, ICU admitted patients and mechanical ventilation receivers had significantly higher concentrations of IL-17; 70.4±12.4 and74.2±11.6 pg/mL respectively than their counterparts (p=0.002 & p=0.006 respectively) indicating a strong association between high IL-17 and critical illness.Corticosteroid receivers had slightly lower IL-17 levels than non-receivers but this difference was not statistically significant (p value=0,098). Regarding outcomes, levels of IL-17 were significantly higher in patients who had complications (67.2 ± 11.6) and in patients who died (75.2 ± 13.7) as compared to recovered patients (60.3 ± 10.5); p=0.003). It indicates that IL-17 may reflect the progression of the disease and be a potential biomarker for severity and prognosis in infections caused by MDR Pseudomonas aeruginosa (Table 4).

Table 4. IL-17 Levels in MDR Pseudomonas aeruginosa Patients by Clinical Characteristics

Indicators		**`Positive (No. = 58)**		**F or T Test**	**P value**
		Mean	**SD**		
Severity of infections	**Mild**	**56.6**	**9.3**	**F = 5.83**	**0.005**
	Moderate	**63.3**	**11.2**		
	Severe	**72.4**	**13.2**		
ICU Admission	**Yes**	**70.4**	**12.4**	**t = 3.21**	**0.002**
	No	**59.3**	**10.2**		
Mechanical Ventilation	**Yes**	**74.2**	**11.6**	**t = 2.84**	**0.006**
	No	**60.2**	**10.2**		
	Yes	**62.8**	**11.3**	**t = 1.68**	**0.098**

Administration of corticosteroids	**No**	**66.2**	**12.1**		
Outcome	**Recovery**	**60.3**	**10.5**	**F = 6.92**	**0.003**
	Complications	**67.2**	**11.6**		
	Mortality	**75.2**	**13.7**		

Table 5 depicts the level of IL-35 among patients with multidrug-resistant *Pseudomonas aeruginosa* respiratory infections in relation to the clinical severity and a bad outcome. The patients with mild infections had the maximum levels of IL-35 (52.3 ± 9.2 pg/mL), and those with moderate and severe infections had lower levels; 47.8 ± 8.7 and 42.5 ± 7.9 pg/mL, respectively, with a statistical difference at p = 0.008 value (Figure). The concentrations for IL-35 were also significantly lower at p =0 .005 for ICU admitted patients (43.7 ± 8.1 pg/mL) and ventilated patients at p=0 .002 (41.9±7 .5pg /mL) compared to non-ICU, non-ventilated patients. Regarding outcomes, the levels of IL-35 were found to be best in patients who recovered (50.4 ± 8.1 pg/mL), followed by those with complications (45.6 ± 8.9 pg/mL) and lowest in patients who died (41.2 ± 7.7 pg/mL). It gave a significant association with prognosis (p = 0.004). From the above findings, it can be assumed that IL-35 may play a protective, anti-inflammatory function and could be applied as one of the parameters in monitoring disease progression in infections caused by MDR Pseudomonas aeruginosa.

Table 5. IL-35 Levels in Patients infected with MDR Pseudomonas aeruginosa classified by their clinical characteristics

Indicators		**`Positive (No. = 58)**		**F or T Test**	**P value**
		Freq.	**%**		
Severity of infections	**Mild**	52.3	9.2	F = 5.21	0.008
	Moderate	47.8	8.7		
	Severe	42.5	7.9		
ICU Admission	**Yes**	43.7	8.1	t = 2.96	0.005
	No	49.8	8.4		
Mechanical Ventilation	**Yes**	41.9	7.5	t = 3.28	0.002
	No	49.2	8.6		
Administration of corticosteroids	**Yes**	47.2	8.5	t = 1.54	0.129
	No	50	8.7		
Outcome	**Recovery**	50.4	8.1	F = 6.35	0.004
	Complications	45.6	8.9		
	Mortality	41.2	7.7		

A negative significant correlation was found between IL-17 and the levels of lymphocytes (r = −0.40, p = 0.003) as well as SaO_2 (r = −0.43, p = 0.001). In other words, higher IL-17 levels are associated with increased inflammatory response and respiratory compromise in MDR Pseudomonas aeruginosa infections. On the other hand, IL-35 correlated positively with SaO_2 (r=+0.36, p=0.005), which may imply a protective or regulatory role in maintaining oxygenation.

No other interleukins had statistically significant correlations with CRP, procalcitonin, neutrophil count, or NLR; it is the specific relationship of cytokine levels to immune or respiratory status rather than general inflammation that they reflect (table 6, figure 1).

Table 6. Differences in IL-35 levels in patients' groups according to duration of infections

Indicators	IL-17		IL-35	
	`r	P value	`r	P value
CPR	0.18	0.174	−0.12	0.322
Procalcitonin	0.2	0.141	−0.16	0.211
O2 Sat	−0.43	0.001*	0.36	0.005*
Neutrophils' Count	0.22	0.113	−0.14	0.261
Lymphocytes' Count	−0.40	0.003*	0.19	0.128
Neutrophil-to-Lymphocyte Ratio (NLR)	0.25	0.092	−0.21	0.101

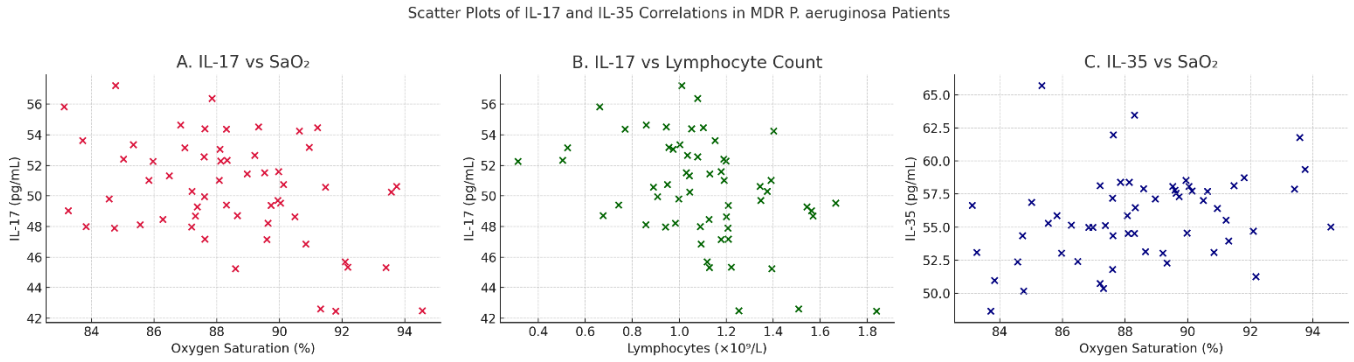

Figure 1. Scatter plots illustrating the relationships between interleukin levels and clinical parameters in patients infected with MDR Pseudomonas aeruginosa. Plot A shows a significant negative correlation between IL-17 levels and oxygen saturation (SaO_2), while Plot B demonstrates a similar negative correlation between IL-17 and lymphocyte count. In contrast, Plot C highlights a significant positive correlation between IL-35 levels and SaO_2, suggesting differing immunological roles for IL-17 and IL-35 in the inflammatory response.

Discussion

This study has fairly successfully illuminated clinical heterogeneity as well as the immunological profile of patients with respiratory infections due to MDR Pseudomonas aeruginosa. Fifty-eight patients were described, representing extremes of disease severity and outcomes; inflammatory markers and cytokines for instance IL-17 and IL-35 may have prognostic value. These findings further underscore that both pro- and anti-inflammatory pathways critically mold the host immune response to MDR pathogens, and these immune mediators might be useful in stratifying disease severity as well as treatment decisions.

The clinical outcomes of the patients with MDR P. aeruginosa infections in this cohort typify previously described patterns from elsewhere. More than three-quarters of these patients had mild to moderate disease at presentation (74.14%), though the existence of severe infections in just under one-quarter of the population (25.86%) indicates that this is a pathogen capable of causing serious morbidity. In this study, ICU admission was found to be 31.03%, and mechanical ventilation was

20.69%; therefore, it places a load on critical care resources, as reported by Rodríguez-Hernández et al., (2022), where high ICU admission rates were observed for drug-resistant P.aeruginosa infections. This also means that more than 60% of patients received corticosteroids which is rather standard practice for managing inflammation but should be interpreted cautiously regarding their role in immunocompromised or critically ill patients (Kalil et al., 2016).

Results at the end of 3 weeks- recovery 67.24%, complications 25.86%, and mortality 6.90% are also typical of the very dynamic clinical trajectories in MDR infections. The results reported here do not differ from what has been reported globally; for example, Tacconelli et al., (2018) in their report had mortality attributable to P. aeruginosa respiratory infections fall between 5 and 15% with comorbidities and ICU conditions increasing the vulnerability. This has been noted within Iraq and elsewhere in the Middle East where isolation of this organism from healthcare-associated infections is concerning, particularly when resources or space are limited (Al-Mayahie, 2019). The kind of outcome variation seen here is exactly why strong, accurate prognostic modeling systems are needed that can also drive resource optimization.

This study has successfully incorporated immune markers- interleukins, IL-17 and IL-35, in the clinical evaluation of disease severity. The main producer of IL-17, a pro-inflammatory cytokine is the Th17 cells. In our study, this cytokine was highly raised in infected patients with an overall mean of 64.4 pg/mL which is grossly above its normal reference range. Increasing levels of IL-17 were statistically significantly associated with disease severity, ICU admission, and mechanical ventilation demand, therefore proving that this cytokine plays a role in escalating immune responses against infections (Chen et al., 2019). This agrees with the report by Xu et al. (2020), who asserted that high levels of IL-17 were linked to poor outcomes in pneumonia induced by Gram-negative bacilli.

Another significant finding is the much higher IL-17 levels in patients who had complications (67.2 ± 11.6 pg/mL) and those who died (75.2 ± 13.7 pg/mL) as compared to recovered patients (60.3 ± 10.5 pg/mL), which signifies an explicit association of elevated IL-17 with poor clinical outcomes (Stockinger & Omenetti, 2017). Regarding infections with multidrug-resistant (MDR) Pseudomonas aeruginosa, persistently high IL-17 likely signals a pathologically excessive pro-inflammatory response by the immune system that causes collateral tissue damage leading to impaired gas exchange and further deterioration of respiration function. Further supporting this interpretation, statistically-significant inverse correlations were established for oxygen saturation (IL-17:r=−0.43 >0.01) and lymphocyte counts (IL-17:r=−0.40 >0.01). Thus higher IL-17 in principle = immune exhaustion, no efficient respiration These results emphasize the potential of IL-17 to at-signal the add-ons of clinical biomarkers for ailment trajectory and severity in MDR respiratory infections, specifically for figuring out patients at set off hazard for adverse outcomes.

The interleukin-35 (IL-35) is a central anti-inflammatory cytokine, mainly derived from regulatory T cell (Treg) [122]. Thus, it is not surprising to observe an even protective pattern for IL-35 in the present study. In marked opposition to IL-17, it decreased with worse disease. Largely highest among patients with mild respiratory infection. Thus, very low levels of IL-35 were found for those patients requiring intensive care or who presented severe symptoms. The inverse relationship could indicate that IL-35 is a dominant regulatory cytokine that reduces inflammatory overdrive in MDR Pseudomonas aeruginosa infections. Secondly, as IL-35 is positively correlated with oxygen saturation, higher levels of it would also reasonably enhance respiratory function by alleviation of pulmonary injury. These results are consistent with previous preclinical studies; for example, Shen et al.(2021) showed that IL-35 suppresses inflammation and attenuates lung injury in models of bacterial pneumonia. These trends does indicate that IL-35 is a potential biomarker for prognosis and quite possibly a target for therapy. While IL-35 has been tested in the context of MDR bacterial infections, no minimal or anecdotal clinical data is available [45] and this study is both the first to perform such analyses, but does highlight that IL-35 should be studied more directed by its immunomodulatory effects on the host.

This dichotomous activity of IL-17 and IL-35 reflects the intricate balance between pro- and anti-inflammatory responses during MDR infections. Although IL-17 is capable of pathogen clearance via neutrophil activation, aberrant production of this cytokine is thought to cause pathology, since it may further aggravate tissue damage and release undesirable factors. In turn, it appears that

IL-35 acts as an anti-inflammatory mediator providing a kind of immune-mediated injury protection (Hadi et al., 2022). Thus, measuring these cytokines together may provide an acuity assessment of immune dynamics and disease evolution above and beyond what can be gleaned from more conventional markers such as CRP or procalcitonin (Stockinger & Omenetti, 2017; Collison et al., 2010).

This study looked only at MDR P. aeruginosa infections and did not compare them with non-MDR cases or other pathogens. So, it is not clear if the cytokine patterns observed are typical of MDR strains. Future research should adjust for comorbidities, prior antibiotic exposure, and timing of sample collection. Whereas IL-17 has been heavily researched in inflammatory and autoimmune diseases, limited information is available on IL-35 despite its attractive immunoregulatory potential in prognosis as well as therapy in lung infections.

Conclusion:

To conclude, the study demonstrates, from a clinical point of view, the value of IL-17 and IL-35 as immunological biomarkers in infections at the respiratory sites caused by MDR Pseudomonas aeruginosa. High levels of IL-17 were significantly associated with more severe disease, ICU admission, mechanical ventilation, and mortality; it can thereby be considered an important pro-inflammatory mediator. Conversely, higher levels of IL-35 were associated with milder disease and better outcomes; it therefore acts as a protective anti-inflammatory molecule.

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