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Research Article

Cytokine Profiles and Disease Severity in Measles: A Prospective Observational Study

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A B S T R A C T

Introduction: Measles is a significant global health concern that causes substantial morbidity and mortality, particularly in infants and children.

Aim: This study aimed to evaluate the levels and balance of pro-inflammatory (TNF-α and IL-6) and anti-inflammatory (IL-4) cytokines in the serum of infants and children with measles, based on disease severity.

Methods: A prospective observational study was conducted involving 21 infants and children aged 1 month to 14 years with moderate or severe measles, along with a control group of 25 healthy children. Serum cytokine concentrations were measured using ELISA, and acute-phase biomarkers (C-reactive protein and procalcitonin) were evaluated.

Results: The experimental group showed significantly higher TNF-α and IL-6 levels than the control group ($P<0.05$). IL-4 levels were also elevated in the experimental group, particularly in severe cases ($P<0.001$). Correlation analysis revealed positive associations between cytokine levels and disease severity (IL-4: $r=0.52$, IL-6: $r=0.64$, TNF-α: $r=0.48$). Negative correlations were observed between cytokine and lymphocyte counts, whereas inverse relationships were found with C-reactive protein and procalcitonin levels.

Conclusion: These findings suggest that the complex interplay between pro-inflammatory and anti-inflammatory cytokines contributes to the immunopathology of measles, with higher levels of TNF-α, IL-6, and IL-4 being associated with increased disease severity.

Keywords: Measles, Cytokines, Inflammation, Immunopathogenesis, Interleukins, Proinflammatory

Introduction

Measles is a highly communicable viral illness caused by the measles virus. It spreads through respiratory droplets and remains contagious on surfaces for up to two hours. Symptoms include fever, cough, conjunctivitis, runny nose, and a maculopapular rash spreading from the face downward. Complications such as pneumonia, blindness, and encephalitis are common in children under five years of age with poor immunity or nutrition.[1,2]

Measles remains widespread worldwide, affecting over seven million individuals annually and causing more than 100,000 deaths.[3,4] In 2023, approximately 107,500 people, mainly children under the age of five, died from measles.[5] These deaths occur due to secondary infections resulting from the immunosuppressive effects of measles. The disease weakens immunity by erasing immune memory, making individuals vulnerable to infections after the initial infection.[6,7] This immunosuppression occurs through lymphocyte dysfunction and immune memory cell destruction, hampering the body's ability to fight new infections.[6-8]

The inflammatory response to measles infection engages both the innate and adaptive immune systems through cytokine networks. Pro-inflammatory cytokines, such as tumour necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and IL-6, released by activated macrophages and monocytes, facilitate chemotaxis by recruiting granulocytes, monocytes, and lymphocytes to infection sites, creating inflammatory conditions for viral elimination.[9,10]

Cytokine surge initiates the production of regulatory cytokines, such as IL-2, IL-12, and interferon-γ (IFN-γ).[9,11] IL-12 promotes type 1 T helper (Th1) immune responses by inducing IFN-γ in CD8+ cytotoxic and CD4+ T helper cells.[9-11] Early measles response involves significant Th1 cytokine production for viral control.[9,12] Fatal measles cases show high levels of pro-inflammatory cytokines (TNF-α, IL-1β, IL-12p70, IL-2, IFN-γ) but reduced IL-4, indicating a cytokine imbalance that worsens the prognosis.[9]

During infection progression, a "second wave" of anti-inflammatory cytokines emerges to reduce the tissue damage. IL-4, released by T helper 2 CD4+ T cells, becomes prominent during this phase.[12,13] IL-4 opposes pro-inflammatory cytokines and promotes M2 macrophage polarisation, supporting tissue repair and humoral immunity regulation.[12–14] Studies in Zambian children have revealed that while IL-4 and IL-13 levels increase post-measles rash, IL-5 levels remain low, leading to decreased eosinophils and serum IgE levels, suggesting complex Th2 response regulation.[12]

Pro-inflammatory and anti-inflammatory cytokine interactions are influenced by cytokine cascades an signalling redundancies. Cytokines use overlapping pathways to modulate immune responses.[13,15] Anti-inflammatory IL-1Ra and IL-10 levels increase during measles, potentially explaining the weakened hypersensitivity responses during recovery.[10-12]

Procalcitonin (PCT) serves as a clinical biomarker in the acute phase and increases during severe systemic inflammation to identify serious cases. Its role differs from that of traditional cytokine mediators.[9] PCT triggers monocytes and macrophages to release proinflammatory cytokines, such as tumour necrosis factor α and IL-6, which boost calcitonin 1 gene expression across cells, resulting in widespread PCT production.[16] PCT stimulates monocytes and macrophages to release proinflammatory cytokines, including tumour necrosis factor α, IL-1β, and IL-6.[17]

Measles inflammation involves a dynamic balance in which pro-inflammatory cytokines clear the virus, followed by regulatory phases (including IL-4) that reduce inflammation. Disruptions in these processes lead to adverse outcomes.[9-13] This cytokine network defines measles immunopathogenesis and remains central to immunological research.[9–12] Despite extensive research on measles immunity mechanisms over the past six decades, many aspects, particularly self-limiting and persistent infections, remain unresolved. Cytokines, as mediators of inflammation and immunity, may hold clinical and prognostic importance in measles infections among infants and children; however, these areas remain poorly understood.

This study aimed to evaluate the levels and balance of pro-inflammatory (TNF, IL-6) and anti-inflammatory (IL-4) cytokines in the blood serum of infants and children with measles, based on disease severity.

Materials and Methods

Between 2018 and 2019, a prospective observational study was conducted at the Republican Clinical Infectious Diseases Hospital in Bishkek, Kyrgyz Republic. The interleukin levels were analysed in the laboratory of the Research Institute of Molecular Biology and Medicine at the National Centre for Cardiology and Therapy under the Ministry of Health of the Kyrgyz Republic.

The study involved 21 infants and children aged 1 month to 14 years who were clinically diagnosed with moderate or severe measles and formed the experimental group. Diagnosis was confirmed using polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA). Additionally, a control group of 25 healthy children, matched by age and without measles symptoms, was also assessed. The experimental group was divided into two subgroups based on disease severity: Group 1 included 10 children with moderate measles, and Group 2 included 11 children with severe measles.

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The inclusion criteria were as follows: confirmed measles infection through clinical and laboratory evidence, age range of 1 month to 14 years, and moderate or severe disease presentation. The exclusion criteria were as follows: adults with measles, mild measles cases, and the presence of other infectious diseases. A composite clinical severity score was used to evaluate disease severity. This score included factors such as fever duration and intensity (≥39°C for >3 days), complications (pneumonia, croup, respiratory failure), haematologic indicators (leukopenia and elevated C-reactive protein), the need for intensive care, and the patient's nutritional or immunologic status before illness. Patients were categorised as having moderate or severe disease based on these criteria.

Blood samples were collected during the acute phase of the illness. Serum cytokine concentrations of TNF-α, IL-6, and IL-4 were measured using ELISA kits (Vector-Best, Novosibirsk, Russia). The assays were conducted using a Human HumaReader HS ELISA Microplate Reader (Human Diagnostics, Wiesbaden, Germany), and absorbance was recorded at 450 nm. All results were expressed in picograms per millilitre (pg/mL). Furthermore, acute-phase biomarkers, including C-reactive protein (CRP) and PCT, were evaluated using standard laboratory methods to assess systemic inflammatory responses and their correlations with cytokine dynamics.

The Bioethics Committee of I.K. Akhunbaev Kyrgyz State Medical Academy granted ethical approval (Protocol No. 2, dated April 19, 2017). Written informed consent was obtained from the parents or legal guardians of the participating children. Verbal assent was obtained from children aged ≥ 7 years, following the institution's ethical guidelines.

Data analysis was conducted using version 11.5 of the Statistical Package for the Social Sciences. Descriptive statistics are presented as mean±standard deviation. Student's t-test was used to identify statistical differences between groups. Pearson's correlation coefficients (r) were calculated to evaluate the association between cytokine levels and clinical or laboratory parameters. Statistical significance was established at three levels: $P < 0.05$, $P < 0.01$, and $P < 0.001$, which correspond to confidence intervals of 95%, 99%, and 99.9%, respectively.

Results

This study examined pro-inflammatory and anti-inflammatory cytokines in patients with measles receiving care at Republican Clinical Infectious Diseases Hospital, Bishkek, Kyrgyzstan, during 2018-2019. The study included 21 patients with measles, of whom 61.9% were confirmed via ELISA testing and 38.1% were diagnosed using clinical and epidemiological methods.

The age distribution showed that infants under one year constituted 47.6% (10 individuals), while those children over one year constituted 52.4% (11 individuals). Boys comprised 57.1% of the group. Additionally, 57.1% of patients were from urban areas, and 95.2% were from unorganised families. Contact with measles patients confirmed in 61.9% of the cases. Only 9.5% of the children had a positive vaccination history, while the others were not vaccinated against measles.

Examining diagnoses made at referral and admission revealed a concerning lack of awareness among pre-hospital doctors regarding the clinical signs of measles in children. Measles is often misdiagnosed as other conditions, such as enterovirus infection or acute respiratory viral infection with an allergic rash. Of the infants and children studied, 47.6% (10 individuals) had moderate measles (Group 1), whereas 52.4% (11 individuals) had severe measles (Group 2) based on clinical and laboratory criteria.

Pneumonia was the most common complication in children with measles, affecting 90.5% of the cases. Croup complicated measles in 23.8% of the cases (5 children), while bronchial obstruction syndrome occurred in 9.5% of the cases. Additionally, 14.3% developed stomatitis. Regarding severity, 28.6% (6 individuals) required intensive care hospitalisation. Among them, 9.5% (2 individuals) had cerebral edema, and 23.8% developed disseminated intravascular coagulation. Among the associated pathologies, anaemia, urinary tract infections, and thymomegaly were observed in 42.9 %, 9.5%, and 4.8% of cases, respectively.

Among patients with measles, 76.2% had a high fever. During the catarrhal stage, 52.4% of the patients exhibited loose stools, similar to secretory diarrhoea. Catarrhal symptoms included conjunctivitis (76.2%), cough (76.2%), runny nose (71.4%), scleritis (76.2%), photophobia (76.2%), and throat redness. Filatov-Belsky-Koplik spots were observed in 66.7% of the cases. The rash was maculopapular, but in 14.3% of cases, haemorrhages occurred alongside it. The rash appeared in a descending pattern over 3-4 days, without itching.

In the experimental group, laboratory tests showed increased serum levels of proinflammatory cytokines (Table 1): TNF-α by 2.2 times and IL-6 by 3.6 times compared to the control ($P<0.05$).

The findings suggest group 1 and group 2 patients show elevated levels of proinflammatory cytokines IL-6 and TNF-α in the bloodstream during the initial stages of illness. These cytokines trigger an acute inflammatory response. Additionally, the anti-inflammatory cytokine IL-4 remained higher in the experimental group than in the control group (7.4 versus 2.3) ($P <0.05$), indicating a link between IL-4 levels and infection progression characteristics. A comparative

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study assessed the pro- and anti-inflammatory cytokine levels in the blood of group 1 and group 2 patients based on disease severity. The findings are presented in Table 2.

Table 1.Levels of pro-inflammatory and anti-inflammatory cytokines (IL-4, IL-6, TNF-α) in the serum of the experimental group compared to the control group

Parameters	Experimental group (n=21)	Control group (n=25)	P
IL-4			
Min	7.4±2.0	3.2±0.8	<0.05*
Max	2.17±9.6		
IL-6			
Min	5.2±1.5	1.44±0.64	<0.05*
Max	1.8±8.0		
TNF-α			
Min	11.6±2.5	5.2±1.9	<0.05*
Max	3.0±22		

Values are expressed as the mean±standard deviation. IL-4 – Interleukin-4, IL-6 – Interleukin-6, TNF-α – Tumor necrosis factor-α, Min – Minimum, Max – Maximum. *P <0.05; **P <0.01, ***P <0.001

Table 2.Analysis comparing cytokine levels (IL-4, IL-6, TNF-α) based on the severity of measles

Cytokines (pg/mL)	Group 1 (n=10)	Group 2 (n=11)	Control group	P
IL-4			3.2±0.8	P_{1-2}>0.05*
Min	6.4±2.1	8.4±1.2		P_{1-3}>0.05*
Max	2.1±1.1	5.6±1.4		P_{2-3}<0.001***
IL-6			1.44±0.64	P_{1-2}>0.05*
Min	4.1±1.2	6.1±1.2		P_{1-3}<0.05*
Max	1.8±0.8	4.5±1.2		P_{2-3}<0.001***
TNF-α			5.2±1.9	P_{1-2}>0.05*
Min	9.6±3.2	13.5±3.5		P_{1-3}>0.05*
Max	3.0±1.2	8.2±2.1		P_{2-3}<0.05*

Values are expressed as the mean±standard deviation. IL-4 – Interleukin-4, IL-6 – Interleukin-6, TNF-α – Tumor necrosis factor-α, Min – Minimum, Max – Maximum. *P <0.05; **P <0.01, ***P <0.001.

Table 2 reveals that the levels of proinflammatory cytokines IL-6 and TNF-α in the blood serum of group 2 patients were significantly higher than those in the control group (P_{2-3}<0.001, P_{2-3}<0.05). Elevated levels of these cytokines were also observed in group 1 patients (P_{1-3}>0.05).

The IL-6 levels in group 1 patients were 2.8 times higher than those in the control group, while in those with group 2 patients, the levels were elevated by 4.2 times. TNF-α levels showed an increase in group 1 patients by 1.8 times and in group 2 patients by 2.6 times compared to the control group (P <0.05). These findings suggest that the experimental group experienced a significant activation of innate immunity, as evidenced by the marked rise in early proinflammatory cytokines IL-6 and TNF-α, highlighting the active role of epithelial cells in the immune response to the measles virus.

Regarding the IL-4 cytokine, the study observed the following: there was a 2.6-fold increase in IL-4 levels in the blood serum of group 2 patients (Table 1) and a 2-fold increase in those with group 1 patients, compared to the baseline values found in the control group (P_{2-3}<0.001). This suggests that the IL-4 levels in the serum of the experimental group were relatively elevated at the onset of the disease, and as the clinical severity increased, the levels tended to rise further, linked to the activity of type 2 T-helper cells. Consequently, children with measles exhibit significant alterations in cytokine status, characterised by the activation of key pro-inflammatory (IL-6 and TNF-α) and anti-inflammatory cytokines (IL-4), reflecting the intensity of antiviral defence in measles.

Drawing from the research findings mentioned above, it is evident that cytokines can effectively act as indicators of inflammation, mirroring the intensity, type, and outcome of the infectious process of measles. The nature of the systemic cytokine response plays a significant role in determining the severity of clinical symptoms and repercussions in children with measles. A correlation analysis was performed between certain blood parameters of measles patients and the levels of proinflammatory cytokines (IL-6 and TNF-α) and anti-inflammatory cytokines (IL-4). The analysis of the relationship between cytokine levels in the serum and clinical and laboratory parameters in measles patients, based on disease severity, revealed the following (Table 3).

Table 3.Paired samples test illustrating the association between the severity of measles and serum cytokine concentrations (IL-4, IL-6, and TNF-α)

-	Paired differences			t	r	Two-sided P
	m±M	SEM	95% CI (Lower, upper limits)			
Severity – IL-4	-4.92±1.79	0.39	-5.73, -4.10	-12.5	0.52	0.015
Severity – Il-6	-2.65±1.31	0.28	-3.25, -2.05	-9.28	0.64	0.002
Severity – TNF-α	-9.12±3.90	0.85	-10.90, -7.34	-10.70	0.48	0.024

Values are expressed as the m±M = Mean±Standard deviation, SEM – Standard error of the mean, 95% CI – 95% confidence interval, t – Student's t-test, r – Pearson correlation coefficient. IL-4 – Interleukin-4, IL-6 – Interleukin-6, TNF-α – Tumor necrosis factor-α. *P <0.05; **P <0.01, ***P <0.001.

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Group 2 patients exhibited higher levels of IL-4, IL-6, and TNF-α in the serum than those in group 1 and the control group. As shown in Table 3, a correlation was identified between the serum concentrations of IL-4, IL-6, and TNF-α and the clinical severity classification of measles, which was determined by factors such as the duration of fever, presence of complications, inflammatory markers, and requirement for intensive care. With an increase in disease severity, cytokine levels also increased, exhibiting correlation coefficients of +0.52, +0.64, and +0.48, respectively. This suggests that pro-inflammatory and anti-inflammatory cytokine levels could serve as markers for assessing disease severity and treatment efficacy.

In group 1 and group 2, IL-6 showed a negative correlation (r=-0.18) and IL-4 (r=-0.02, respectively) with leukocyte counts, supporting IL-4's anti-inflammatory role. The negative IL-6 correlation between leukocytes may be due to reduced IL-6 concentration after detoxification therapy. In children with measles, TNF-α levels showed a positive correlation with leukocyte counts (r=0.038), indicating systemic inflammation. At admission, a negative correlation existed between IL-6 (r=-0.05), TNF-α (r=-0.10), and IL-4 (r=-0.11) cytokines and segmented neutrophil percentage, reflecting viral infection suppression of leukopoiesis. At discharge, IL-6 (r=0.23), TNF-α (r=0.28), and IL-4 (r=0.17) showed a positive correlation with segmented neutrophil percentage. As measles progressed with increased symptoms and rash, changes in the cytokine profile indicated the activation of pro-inflammatory and anti-inflammatory mechanisms.

In the early days of measles, pro-inflammatory cytokines IL-6 (r=0.03), TNF-α (r=0.07), and anti-inflammatory IL-4 (r=0.08) correlated positively with lymphocyte percentage during admission, indicating viral-stimulated leukopoiesis. At discharge, IL-6 (r=-0.24), TNF-α (r=-0.33), and IL-4 (r=-0.12) showed a negative correlation with lymphocytes. The measles virus targets epithelial and immune cells, causing lymphopenia through CD3+, CD4+, and CD8+ reduction while activating immunity. Analysis showed negative correlations between cytokines and erythrocyte sedimentation rate: IL-6 (r=-0.62), TNF-α (r=-0.39), and IL-4 (r=-0.43), demonstrating their inhibitory effects.

Additionally, acute inflammation markers, such as CRP and PCT, were assessed, showing a significant negative correlation of IL-4 (r=-0.35), IL-6 (r=-0.42), and TNF-α (r=-0.34) with PCT levels at admission and discharge (Table 4).

In the experimental group, there is a reduction in the release of proinflammatory mediators, such as TNF-α and IL-6, triggered by PCT. This suggests a viral inflammatory process, which is crucial for determining treatment approaches. Correlation analysis demonstrated a direct relationship between CRP and IL-6 (r=1.00), aligning with the understanding that these are markers of inflammation. IL-6, in particular, serves as a proinflammatory cytokine and is the primary driver of the liver's production of acute-phase inflammatory proteins (Table 5).

Values are expressed as the m±M = Mean±Standard deviation, SEM – Standard error of the mean, 95% CI – 95% confidence interval, r – Pearson correlation coefficient, t – Student's t-test. IL-4 – Interleukin-4, IL-6 – Interleukin-6, TNF-α – Tumor necrosis factor-α, CRP – C-reactive protein. *P <0.05; **P <0.01, ***P <0.001.

IL-4 exhibited a negative correlation with CRP levels (r=-1.00), reinforcing its anti-inflammatory role. TNF-α also showed a negative correlation with CRP (r=-1.00), suggesting a diverse protein composition in the late acute phase response in patients with measles. Regarding outcomes, 61.9% of patients recovered, 33.3% showed improvement, and 4.8% experienced fatal outcomes.

Table 4.Paired analysis of serum pro- and anti-inflammatory cytokines and blood PCT levels in the experimental group

Pairs of inflammatory markers	Paired differences			t	r	Two-sided P
	m±M	SEM	95% CI (Lower, upper limits)			
IL-4 – PCT	6.18±2.71	0.85	4.24, 8.12	7.20	-0.35	0.317
IL-6 - PCT	3.89±2.99	0.94	1.74, 6.03	4.10	-0.42	0.221
TNF-α - PCT	11.14±5.37	1.70	7.29, 14.98	6.55	-0.34	0.327

Values are expressed as the m±M = Mean±Standard deviation, SEM – Standard error of the mean, 95% CI – 95% confidence interval, t – Student's t-test, r – Pearson correlation coefficient. IL-4 – Interleukin-4, IL-6 – Interleukin-6, TNF-α – Tumor necrosis factor-α, PCT – Procalcitonin. *P <0.05; **P <0.01, ***P <0.001.

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Table 5. Association between serum cytokine levels (IL-4, IL-6, TNF-α) and blood CRP concentrations in the experimental group

Pairs of inflammatory markers	Paired differences			t	r	Two-sided P
	m±M	SEM	95% CI (Lower, upper limits)			
IL-4 – CRP	4.49±1.25	0.89	-6.81, 15.79	5.04	-1.00	0.000
IL-6 – CRP	2.64±0.198	0.14	0.86, 4.41	18.85	1.00	0.000
TNF-α –CRP	7.69±1.11	0.79	-2.34, 17.72	9.73	-1.00	0.000

Discussion

Despite the availability of effective vaccines, measles remains a major public health issue. The disease causes fever, cough, runny nose, conjunctivitis, and maculopapular rash, with serious complications possible in young children and in immunocompromised individuals. Worldwide outbreaks continue to cause significant mortality.[18] Elimination efforts require addressing vaccine coverage and outbreak monitoring challenges.[19,20]

Various methods have been used to investigate measles, including clinical studies with diagnosed patients. Diagnosis confirmation is achieved through laboratory tests such as ELISA. Epidemiological research has monitored measles transmission and identified infection risk factors.[19,20] These studies involve gathering data on measles cases, vaccination coverage, and demographics.[20] To explore the inflammatory response, scientists assessed cytokine levels in the blood samples of infected individuals. ELISA techniques quantify specific cytokine levels. Additionally, animal models are used to examine disease pathogenesis and test potential treatments.[21]

The immunopathology of measles involves changes in cytokine levels, affecting disease progression. During infection, the pro-inflammatory cytokines TNF-α and IL-6 are elevated, indicating immune responses. The anti-inflammatory cytokine IL-4 shows complex regulation of disease severity. Studies have shown that severe cases have higher TNF-α and IL-6 levels than controls, whereas patients who died had higher TNF-α and lower IL-4 levels than survivors.[9] Strong macrophage and T cell activation produces Th1 cytokines in severe cases.[9] TNF-α and IL-6 mediate acute-phase reactions, causing fever and inflammation in severe measles.[9]

The anti-inflammatory response, measured by IL-4 levels, during severe measles, IL-4 levels are lower, indicating predominant Th1/pro-inflammatory responses.[9,22] In milder cases or recovery, IL-4 levels increase, showing a shift to Th2 responses that aid immunosuppression and recovery.[12,23] This IL-4 increase is related to suppressed cell-mediated immunity and susceptibility to secondary infections post-measles.[23] The IL-4 pattern is biphasic: reduced during acute illness but elevated during recovery.

In vaccine-modified measles, children show early increases in Th1 cytokines with decreased IL-4, followed by IL-4 elevation during recovery.[22] This pattern suggests that balanced modulation between pro- and anti-inflammatory pathways enables optimal outcomes. The balance between TNF-α/IL-6 and IL-4 indicates disease severity, where high pro-inflammatory cytokines with low IL-4 suggest severe outcomes, whereas restored anti-inflammatory cytokines signal recovery.[22,23]

Research has shown that measles infection leads to significant alterations in cytokine levels, reflecting the intensity of the antiviral defence. A study by Chechetova et al. in Kyrgyzstan showed that group 1 to group 2 patients had decreased CD4+ and CD8+ T cells, indicating T-cell immunity deficiency.[24] The immunoregulatory index was lower, showing a correlation between admission and hospital stay values in group 1 patients. The number of CD16+ T cells increased upon admission, indicating innate immune activation. These changes indicate weakened adaptive immunity and increased cytotoxic activity in group 2 patients, highlighting immune dysregulation and the need for immune parameter monitoring to predict disease severity.

The resurgence of measles highlights the need to enhance vaccine coverage and surveillance.[18] Addressing vaccine hesitancy and ensuring fair access are crucial for preventing outbreaks. Further research is needed to understand the immune responses to measles and identify therapeutic targets.[21-25] It is vital to explore the long-term consequences of measles infection, including secondary infections and complications.[25]

By combining clinical, epidemiological, and immunological methods, researchers can advance their knowledge of measles and devise effective prevention strategies.

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This collaboration is crucial for eradicating measles and protecting vulnerable populations.[19,20]

The results showed complex immune dynamics in children with measles, with increased pro-inflammatory responses (TNF-α and IL-6) and compensatory IL-4 elevation in group 2 patients. Changes in cytokine levels and T-cell subsets indicate disrupted immunity, affecting disease progression. Given the relationship between cytokine profiles and disease severity, monitoring these biomarkers could improve the prognosis and treatment of patients. Future research should explore these pathways to develop targeted therapies for severe paediatric measles infection.

Conclusions

Children suffering from moderate to severe measles have higher levels of pro-inflammatory cytokines (IL-6 and TNF-α) and the anti-inflammatory cytokine IL-4 than those in the control group. These results show that cytokine profiles indicate the immune response intensity during measles infection. While differences existed between moderate and severe cases, the limited sample size restricted subgroup comparisons. Cytokines such as IL-6, TNF-α, and IL-4 could be valuable biomarkers for evaluating inflammation and disease progression in children with measles. Larger studies are needed to validate these associations and investigate their roles in clinical decision-making.

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References

1. Goldhaber-Fiebert JD, Lipsitch M, Mahal A, Zaslavsky AM, Salomon JA. Quantifying child mortality reductions related to measles vaccination. PLoS One. 2010 Nov 4;5(11):e13842. [Google Scholar] [Pubmed]
2. Griffin DE, Lin WH, Pan CH. Measles virus, immune control, and persistence. FEMS microbiology reviews. 2012 May 1;36(3):649-62. [Google Scholar] [Pubmed]
3. World Health Organization [Internet]. Measles; [2024 Dec 26]. Available from: https://www.who.int/news-room/fact-sheets/detail/measles
4. Dabbagh A. Progress toward regional measles elimination—worldwide, 2000–2017. MMWR. Morbidity and mortality weekly report. 2018;67. [Google Scholar] [Pubmed]
5. Portnoy A, Jit M, Ferrari M, Hanson M, Brenzel L, Verguet S. Estimates of case-fatality ratios of measles in low-income and middle-income countries: a systematic review and modelling analysis. The Lancet Global Health. 2019 Apr 1;7(4):e472-81. [Google Scholar] [Pubmed]
6. Mina MJ, Kula T, Leng Y, Li M, De Vries RD, Knip M, Siljander H, Rewers M, Choy DF, Wilson MS, Larman HB. Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. Science. 2019 Nov 1;366(6465):599-606. [Google Scholar] [Pubmed]
7. Mina MJ, Metcalf CJ, De Swart RL, Osterhaus AD, Grenfell BT. Long-term measles-induced immunomodulation increases overall childhood infectious disease mortality. Science. 2015 May 8;348(6235):694-9. [Google Scholar] [Pubmed]
8. Griffin DE. Measles virus-induced suppression of immune responses. Immunological reviews. 2010 Jul;236(1):176-89. [Google Scholar] [Pubmed]
9. Lin WH, Nelson AN, Ryon JJ, Moss WJ, Griffin DE. Plasma cytokines and chemokines in Zambian children with measles: innate responses and association with HIV-1 coinfection and in-hospital mortality. The Journal of Infectious Diseases. 2017 Mar 1;215(5):830-9. [Google Scholar] [Pubmed]
10. Ten Oever J, Riza A, Sabou M, Cismaru C, Netea MG, Slavcovici A. Characterization of the acute inflammatory response in measles infection. Journal of the Pediatric Infectious Diseases Society. 2014 Sep 1;3(3):197-200. [Google Scholar] [Pubmed]
11. Guo Y, Cao W, Zhu Y. Immunoregulatory functions of the IL-12 family of cytokines in antiviral systems. Viruses. 2019 Aug 22;11(9):772. [Google Scholar] [Pubmed]
12. Moss WJ, Ryon JJ, Monze M, Griffin DE. Differential regulation of interleukin (IL)–4, IL-5, and IL-10 during measles in Zambian children. The Journal of infectious diseases. 2002 Oct 1;186(7):879-87. [Google Scholar] [Pubmed]
13. Opal SM, DePalo VA. Anti-inflammatory cytokines. Chest. 2000 Apr 1;117(4):1162-72.[Google Scholar] [Pubmed]
14. Junttila IS. Tuning the cytokine responses: an update on interleukin (IL)-4 and IL-13 receptor complexes. Frontiers in immunology. 2018 Jun 7;9:888. [Google Scholar] [Pubmed]
15. Lively S, Schlichter LC. Microglia responses to pro-inflammatory stimuli (LPS, IFNγ+ TNFα) and reprogramming by resolving cytokines (IL-4, IL-10). Frontiers in cellular neuroscience. 2018 Jul 24;12:215. [Google Scholar] [Pubmed]
16. Xu HG, Tian M, Pan SY. Clinical utility of procalcitonin

and its association with pathogenic microorganisms. Critical Reviews in Clinical Laboratory Sciences. 2022 Feb 17;59(2):93-111. [Google Scholar] [Pubmed]
17. Leclerc F, Cremer R, Noizet O. Procalcitonin as a diagnostic and prognostic biomarker of sepsis in critically ill children. Pediatric Critical Care Medicine. 2003 Apr 1;4(2):264-6. [Google Scholar] [Pubmed]
18. Chen HL, Tang RB. Measles re-emerges and recommendation of vaccination. Journal of the Chinese Medical Association. 2020 Jan 1;83(1):5-7. [Google Scholar] [Pubmed]
19. Coughlin MM, Beck AS, Bankamp B, Rota PA. Perspective on global measles epidemiology and control and the role of novel vaccination strategies. Viruses. 2017 Jan 19;9(1):11. [Google Scholar] [Pubmed]
20. Goodson JL, Chu SY, Rota PA, Moss WJ, Featherstone DA, Vijayaraghavan M, Thompson KM, Martin R, Reef S, Strebel PM. Research priorities for global measles and rubella control and eradication. Vaccine. 2012 Jul 6;30(32):4709-16. [Google Scholar] [Pubmed]
21. Suwanmanee S, Ghimire S, Edwards J, Griffin DE. Infection of pro-and anti-inflammatory macrophages by wild type and vaccine strains of measles virus: Nlrp3 inflammasome activation independent of virus production. Viruses. 2023 Jan 17;15(2):260. [Google Scholar] [Pubmed]
22. Pillet S, Svitek N, Von Messling V. Ferrets as a model for morbillivirus pathogenesis, complications, and vaccines. Measles: Pathogenesis and Control. 2009:73-87. [Google Scholar] [Pubmed]
23. Griffin DE, Ward BJ. Differential CD4 T cell activation in measles. Journal of Infectious Diseases. 1993 Aug 1;168(2):275-81. [Google Scholar] [Pubmed]
24. Chechetova S, Kadyrova R, Dzholbunova Z, Khalupko E, Mainazarova E, Vityala Y, Tagaev T. Immunological features of measles in children. Journal of Communicable Diseases. 2021;53(3):11-5. [Google Scholar]
25. Griffin DE. Measles virus persistence and its consequences. Current opinion in virology. 2020 Apr 1;41:46-51. [Google Scholar] [Pubmed]

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