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상기도 바이러스 감염 진단에서 혈중 MxA 검사의 유용성 평가

Usefulness of Blood Myxovirus Resistance Protein A Test for the Diagnosis of Upper Respiratory Viral Infections

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Background: Upper respiratory tract infections (URTIs) are very common and viruses are the most common cause of URTIs. Myxovirus resistance protein A (MxA) is induced by type 1 and type 3 interferons during viral infection, and inhibits viral replications. We investigated the usefulness of blood MxA in the diagnosis of viral URTIs for the first time in Korea.
Methods: We evaluated the clinical performance of the AFIAS MxA (Boditech Med, Inc., Korea) and proposed a new optimal cutoff using ethylenediaminetetraacetic acid (EDTA)- heparinized-, and capillary blood collected from URTIs patients (n=66) and healthy individuals (n=48). Allplex Respiratory Panels 1, 2, and 3 and Allplex SARS-CoV-2 Assay multiplex real-time RT-PCR (Seegene, Korea) were used to confirm viral infections using nasopharyngeal swab samples.
Results: The optimal cutoff values of EDTA blood revealed 47.57 ng/mL, 58.69 ng/mL, 48.28 ng/mL, and 35.05 ng/mL for AFIAS-1, AFIAS-3, AFIAS-6, and AFIAS-10, respectively. The corresponding cutoff values were 45.28 ng/mL for heparinized blood using AFIAS-6 and 65.54 ng/mL for capillary blood using AFIAS-1. The sensitivity and specificity were both 100% and 92%, respectively, regardless of the virus type (SARS-CoV-2, n=19; influenza A, n=11; influenza B, n=39; human rhinovirus, n=4), when AFIAS-6 was applied to EDTA blood using the manufacturer's recommended cutoff of 30 ng/mL.
Conclusions: The optimal cut-off values for several models of AFIAS and the three blood sample types were slightly higher than the manufacturer's recommended cut-off. AFIAS-MxA is useful for screening URTIs caused by various viruses.

Key Words: Myxovirus Resistance Proteins, MxA protein, Point-of-care, Upper respirarotry tract infections, Biomarker

INTRODUCTION

Upper respiratory tract infections (URTIs), including the common cold, pharyngitis, sinusitis, and bronchitis, are the most frequently encountered illnesses in medical practice. Although viruses are the predomiant causative agents of these URTIs, more than 50% of affected patients are prescribed antibiotics [1-3]. The overuse of antibiotics, not only increases healthcare costs, but also contributes to the growing problem of antibiotic resistance. As such, antibiotics should be used with prudence and reserved for confirmed or strongly suspected bacterial infections. Nevertheless, they continue to be frequently prescribed, without laboratory diagnostic evidence in most cases.

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In Korea, the government has established a national strategy and action plan (2016-2020) to address antibiotic resistance. As a core strategy, this plan calls for the development of a rapid diagnostic test to differentiate between bacterial and viral infections [4]. From this perspective, screening tests for viral infections are required, especially in primary care clinics where comprehensive laboratory diagnostic tests may not be available.

Myxovirus resistance protein A (MxA) is a 76-kDa antiviral protein induced by type I and III interferons in response to viral infections [5]. MxA plays a crucial role in the inhibition of viral replication at an early stage of its life cycle [6, 7]. Multiple studies have shown that elevated MxA levels indicate viral infection [8, 9]. In contrast, MxA tends to be low in healthy individuals or in those with bacterial infections making it a potentially useful biomarker for screening viral infections. Theoretically, identifying patients with URTIs via a positive MxA result could help reduce unnecessary antibiotic prescriptions, which aligns with the national strategy of controlling antibiotic resistance.

In this study, we measured blood MxA protein levels in patients with URTIs caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza virus (FLU), and human rhinovirus (HRV), using an immunofluorescence analyzer (IFA). We established the optimal cut-off using EDTA-, heparinized-, and capillary blood for the four different IFA models. We also evaluated the usefulness of MxA in diagnosing URTIs caused by various viruses.

MATERIALS AND METHODS

1. The participants

This study involved 66 patients who visited primary care clinics of otorhinolaryngology due to fever (≥37.5℃) or respiratory symptoms, such as cough, sneezing, rhinorrhea, sore throat, sputum, headache, rhonchi, nasal congestion, and myalgia in the last three days, during January to February 2024, in Changwon, Gyeongnam Province, Republic of Korea. Patients treated with interferon, oral corticosteroids, methotrexate, cyclosporine, antimetabolite, and anti-viral agents, or with a biotin prescription within 24 hours were excluded. Patients with severe trauma, burns, myocardial infarction, cerebrovascular infarction, or vaccination within 30 days were also excluded. Forty-eight healthy individuals without any symptoms or signs of respiratory tract infections were recruited as controls. Males comprised 45.5% and 29.2% of the study- and control groups, respectively. The median age was 34 years (standard deviation [SD]: 12 years) in the study group and 39 years (SD: 15 years) in the control group. Nine (13.6%) children (<18 years old) were in the study group and two (4.2%) were in the control group.

All participants voluntarily agreed to participate and provided written informed consent. Parental consent was received for the children to follow international ethics guideline. The confidentiality of all participants was maintained throughout the study. This prospective study was approved by the Institutional Review Board (IRB) of Gyeongsang National University Changwon Hospital (GNUCH) (IRB No. 2022-01-009).

2. IFA

AFIAS MxA is a fluorescent lateral-flow immunoassay coated with anti-MxA. First, 100 μL of blood was applied onto the AFIAS MxA cartridge. Once MxA in the blood was bound to anti-MxA and the test was run on an AFIAS IFA, the results were displayed on the screen within 12 minutes. MxA levels in EDTA blood were measured using four different AFIAS models (AFIAS-1, AFIAS-3, AFIAS-6, and AFIAS-10, BoditechMed, Inc., Chuncheon, Korea). The number after the AFIAS indicates the test capacity. Heparinized blood was used only for AFIAS-6, while capillary blood was applied only for AFIAS-1. Detection range of MxA of each model was between 10–300 ng/mL.

3. Blood samples

Approximately 5 mL of venous blood was collected from patients and normal controls. The blood samples were divided into K2-EDTA and Li-heparin tubes. These tubes were kept at 4℃ and were transported to GNUCH on the same day for measurement of MxA. In parallel, capillary blood (10 μL) was collected from the tip of index finger into a capillary tube and was tested at the point of care using AFIAS-1.

4. Nasopharyngeal swab samples

Nasopharyngeal swabs were collected from the participants by medical personnel for real-time PCR testing. The swab samples were suspended into viral transport media (305C FLOQSwabs UTM, Copan, Brescia, Italy, or CTM, NobleBio, Hwasung, Korea), and were transported to the laboratory on ice on the same day,

and stored at -80℃ until the samples were processed and RT-PCR was performed.

5. RT-PCR

The Allplex™ Respiratory Panel 1, 2, and 3 and Allplex™ SARS-CoV-2 Assay multiplex real-time RT-PCR kits (Seegene, Seoul, Korea) were used to detect viral pathogens in the nasopharyngeal swab specimens. Briefly, viral RNA was extracted from the nasopharyngeal swab samples using *ExiPrep*™48 Dx (Bioneer Daejeon, Korea), according to the manufacturer's instructions. RT-PCR was performed using the *Exicycler*™ 96 (Bioneer) and *ExiStation*™ Manager software (Bioneer).

6. Statistical analysis

Correlations between the measurements in the AFIAS models were assessed using Pearson's correlation coefficients. We estimated the sensitivity, specificity, and area under the receiver operating characteristic (AUROC) curve to assess the performance of the AFIAS models based on the manufacturer's recommended cut-off of 30 ng/mL. When we assessed the sensitivity and specificity of the AFIAS, RT-PCR was used as a confirmatory test for URTIs (gold standard). The optimal cut-off for each AFIAS model and blood sample type was estimated by determining the threshold with the highest sum of sensitivity and specificity. Statistical significance was set at $P<0.05$. Statistical analyses were performed using the R Statistical Software (ver. 4.4.2; R Core Team 2024).

RESULTS

When EDTA blood was used, the sensitivity (98-100%) and specificity (92-94%) of all AFIAS models were exceedingly high

Table 1. Clinical performance, AUROC curve, and optimal cutoff of the AFIAS MxA using EDTA blood for the diagnosis of viral upper respiratory tract infections

AFIAS MxA	RT-PCR		Sensitivity % (95% CI)	Specificity % (95% CI)	AUROC	Optimal cutoff
	Positive	Negative				
AFIAS-1						
Positive	65	3	98 (92-100)	94 (83-99)	0.987	47.57 ng/mL
Negative	1	45				
AFIAS-3						
Positive	66	4	100 (95-100)	92 (80-98)	0.997	58.69 ng/mL
Negative	0	44				
AFIAS-6						
Positive	66	4	100 (92-100)	92 (80-98)	0.996	48.28 ng/mL
Negative	0	44				
AFIAS-10						
Positive	66	4	100 (95-100)	92 (80-98)	0.996	35.04 ng/mL
Negative	0	44				

There are four distinct models of the AFIAS analyzer based on the sample loading capacity. RT-PCR of nasopharyngeal swab specimens was used to confirm viral upper respiratory tract infections.
Abbreviations: RT-PCR, real-time polymerase chain reaction; AUROC, area under the receiver operating characteristic curve; CI, confidence interval.

Table 2. Sensitivity and specificity of the AFIAS-1 MxA in EDTA and capillary blood samples

Sample type	RT-PCR		Sensitivity % (95% CI)	Specificity % (95% CI)	AUROC	Optimal cutoff
	Positive	Negative				
EDTA blood						
Positive	65	3	98 (92-100)	94 (83-99)	0.987	47.57 ng/mL
Negative	1	45				
Capillary blood						
Positive	65	4	98 (92-100)	92 (80-98)	0.993	65.54 ng/mL
Negative	1	44				

P value=0.59.
Abbreviations: RT-PCR, real-time polymerase chain reaction; AUROC, area under the receiver operating characteristic curve; CI, confidence interval.

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(Table 1). There were no statistically significant differences in sensitivity and specificity between the AFIAS models (all $P>0.32$). Additionally, the estimated optimal cutoff values of the AFIAS models (35.04-58.69 ng/mL) were all slightly higher than the suggested cutoff value (30 ng/mL) by the manufacturer. The cutoff of EDTA blood revealed 47.57 ng/mL, 58.69 ng/mL, 48.28 ng/mL, and 35.05 ng/mL for AFIAS-1, AFIAS-3, AFIAS-6, and AFIAS-10, respectively. The cutoff for heparinized blood AFIAS-6 was 45.28 ng/mL with 97% sensitivity, 92% specificity, and AUROC of 0.993 (data not presented).

The optimal cutoff value for capillary blood AFIAS-1 was 65.54 ng/mL (Table 2), with a sensitivity of 98% and a specificity of 92%.

MxA levels in the same EDTA blood samples were measured using different AFIAS models (1, 3, 6, and 10), and the correlations between the MxA levels in these models were evaluated (Fig. 1). Regardless of the AFIAS model, the MxA measurements of these

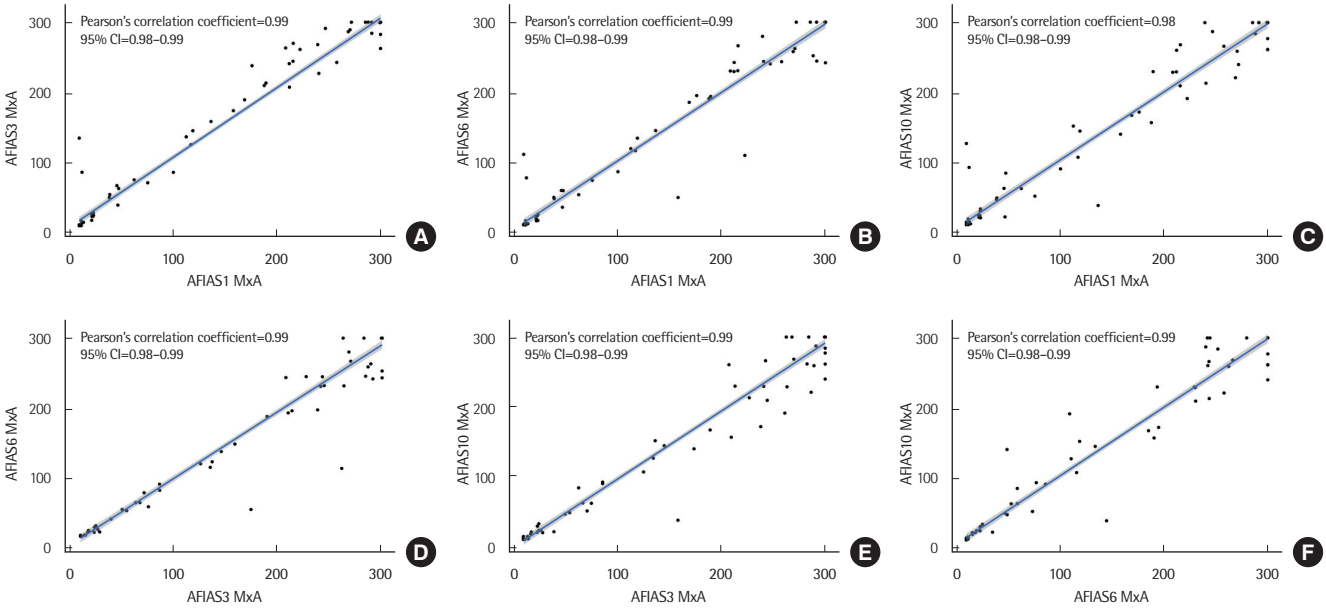

Fig. 1. Correlation analysis of four different AFIAS models, 1, 3, 6, and 10 for MxA measurement in EDTA blood.

Table 3. Sensitivity and specificity of the AFIAS-6 MxA for EDTA blood according to each respiratory virus

Virus	RT-PCR		Sensitivity % (95% CI)	Specificity % (95% CI)	AUROC %	Optimal cutoff
	Positive	Negative				
Overall						
Positive	66	4	100 (92-100)	92 (80-98)	99.6	48.28 ng/mL
Negative	0	44				
SARS-CoV-2						
Positive	19	4	100 (82-100)	92 (80-98)	99.1	48.36 ng/mL
Negative	0	44				
Influenza A						
Positive	11	4	100 (72-100)	92 (80-98)	99.6	48.28 ng/mL
Negative	0	44				
Influenza B						
Positive	39	4	100 (91-100)	92 (80-98)	99.9	98.5 ng/mL
Negative	0	44				
Human rhinovirus						
Positive	4	4	100 (40-100)	92 (80-98)	99.0	53.29 ng/mL
Negative	0	44				

Abbreviations: RT-PCR, real-time polymerase chain reaction; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

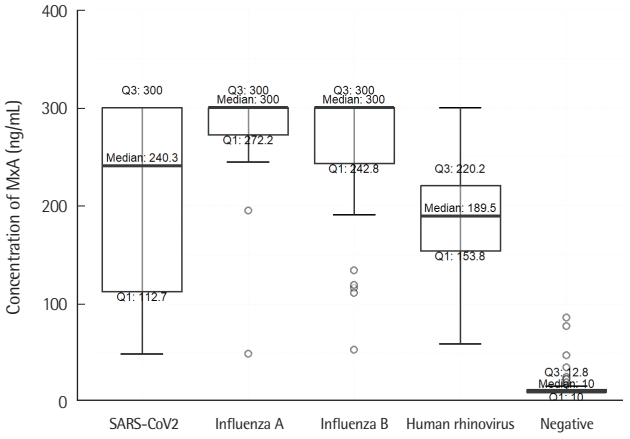

Fig. 2. Box-and-whisker plots showing MxA concentrations in EDTA blood measured by the AFIAS-6 test according to each virus.
Q1: First quartile; Q3: Third quartile.

models were all highly correlated to each other (correlation coefficients ≥0.98).

We further evaluated the differences in the performance of the AFIAS-6 model according to each virus (SARS-CoV-2, FluA, FluB, and HRV). Similarly, excellent sensitivity (100%) and specificity (92%) were confirmed, regardless of the virus type (Table 3).

The median and interquartile range values of the AFIAS-6 MxA for EDTA blood according to the positivity of each virus are presented in Fig. 2. The median AFIAS-6 MxA values were significantly higher than the cutoff value (30 ng/mL) among participants with viral infections, regardless of the virus type (240.3 ng/mL for SARS-CoV-2; 300.0 ng/mL for FluA; 300.0 ng/mL for FluB; 189.5 ng/mL for HRV). In contrast, the median AFIAS-6 MxA value was 10.0 ng/mL among participants not infected with the virus, which is the detection limit.

DISCUSSION

MxA has previously been shown to be a promising biomarker for diagnosing viral respiratory infections [10-13]. In this study, we evaluated the performance of AFIAS MxA in detecting viral URTIs. We demonstrated that the AFIAS MxA is useful for laboratory tests using EDTA-, heparinized-, or capillary blood. However, Iliopoulou et al. reported rather a lower sensitivity (79.7 %) and specificity (80.0 %) [14]. Interestingly, the observed optimal cutoff values (35.04-58.69 ng/mL) for the AFIAS models were slightly higher than the manufacturer-recommended cutoff value of 30 ng/mL. This discrepancy may be due to differences in the study populations, sample handling, or measurement conditions.

The evaluation of different blood sample types revealed that, while the sensitivity remained equally high for both EDTA and capillary blood samples using the AFIAS-1 model, the specificity was slightly lower for capillary blood. Chieux et al. demonstrated a strong correlation between the MxA values in capillaries and peripheral whole blood [15]. These findings suggest that although EDTA blood may be more reliable, capillary blood remains a viable alternative, especially for pediatric patients or in resource-limited countries. Analysis of the AFIAS-6 performance across different viral infections (SARS-CoV-2, FluA, FluB, and HRV) demonstrated excellent sensitivity (100%) and specificity (92%). This highlights the versatility of the AFIAS in detecting MxA levels across a range of viral infections, justifying its potential as a valuable tool for screening URTIs.

Recent studies have provided valuable insights into MxA as a biomarker for differentiating viral from bacterial respiratory infections. MxA is significantly higher in viral infections than in bacterial infections or among healthy controls [14, 16]. In a retrospective study of children with viral, bacterial, and mixed respiratory infections in China, MxA testing demonstrated an AUC of 0.8019 for distinguishing viral infections from bacterial infections [16]. While MxA is highly specific for viral infections, there are also other promising biomarkers, such as C-reactive protein (CRP) and procalcitonin, which are highly sensitive and specific for bacterial infections. Iliopoulou et al. [14] reported that combining MxA with CRP improved the differentiation between bacterial and viral infections, as bacterial infections tended to show lower MxA levels and higher CRP levels. Similarly, Metz et al. [12] highlighted that MxA levels alone may not always distinguish between viral and bacterial coinfections, suggesting that a combined biomarker approach could enhance diagnostic accuracy.

In conclusion, we investigated MxA levels in three different types of blood samples: EDTA-, heparinized-, and capillary blood, for the first time in Korea. We targeted URTIs because these infections are the most common in humans, and antibiotics are frequently prescribed. As the diagnosis of viral URTIs is not easy and can be expensive or time-consuming in the real world, a simple screening method, such as blood MxA measurement, may be valuable to physicians. This study confirmed that the clinical performance of AFIAS MxA was excellent compared to RT-PCR for

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detecting viral URTIs. These results support the proof-of-concept that blood MxA measurement may serve as a rapid and reliable screening method for viral URTIs. Additionally, the AFIAS-1 platform can be considered a practical point-of-care test using capillary blood samples.

요 약

배경: 상기도 감염은 매우 흔한 질환으로, 대부분 바이러스에 의해 감염된다. Myxovirus resistance protein A (MxA)는 바이러스 감염 시 제1형과 제3형 인터페론 자극에 의해 생성되어 바이러스 증식을 억제한다. 본 연구에서는 한국에서 최초로 바이러스성 상기도감염 진단을 위해 혈액 기반 MxA 유용성을 평가였다.

방법: 저자들은 AFIAS MxA (바디텍메드, 한국)의 임상성능평가를 시행하였으며, 상기도감염 환자 66명, 건강인 48명에 대해서 EDTA, 헤파린, 모세혈액 3종류 혈액에 대한 MxA의 적정 기준치를 제시하고자 하였다. 바이러스 감염 여부는 비인후도말을 채취하여 Allplex™ Respiratory Panel 1, 2, 3와 Allplex™ SARS-CoV-2 Assay multiplex real-time RT-PCR (씨젠, 한국)로 바이러스 유전자 증폭을 하여 확인하였다.

결과: AFIAS-1, AFIAS-3, AFIAS-6, AFIAS-10 모델에서 EDTA 혈액 MxA 적정 기준치는 각각 47.57 ng/mL, 58.69 ng/mL, 48.28 ng/mL, 35.05 ng/mL로 산정되었다. 또한 헤파린 혈액을 이용한 AFIAS-6의 MxA 기준치는 45.28 ng/mL, 모세혈을 이용한 AFIAS-1의 MxA 기준치는 65.54 ng/mL이었다. 확인된 바이러스는 SARS-CoV-2가 19명, A형독감 11명, B형독감 39명, 리노바이러스 4명이었다. EDTA 혈액을 사용하여 AFIAS-6에서 제조사 제시 기준치인 30 ng/mL를 적용했을 때, 모든 바이러스 감염군에서 민감도 100%, 특이도 92%를 보였다.

결론: 네 가지의 AFIAS 모델과 3가지 혈액 종류에 대해서 MxA 적정 기준치를 분석한 결과, 제조사 기준치보다 약간 높게 나왔다. AFIAS MxA는 다양한 호흡기 바이러스에 의한 상기도 감염의 선별 검사로 유용하게 사용할 수 있을 것으로 판단된다.

Conflicts of Interest

None declared.

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REFERENCES

1. Kim JA, Park J, Kim BY, Kim DS. The trend of acute respiratory tract infections and antibiotic prescription rates in outpatient settings using health insurance data. Korean J Clin Pharm 2017;27:186-94.
2. Higashi T and Fukuhara S. Antibiotic prescriptions for upper respiratory tract infection in Japan. Intern Med 2009;48:1369-75.
3. Li J, Song X, Yang T, Chen Y, Gong Y, Yin X, et al. A systematic review of antibiotic prescription associated with upper respiratory tract infections in China. Medicine (Baltimore) 2016;95:e3587.
4. Ryu S. The new Korean action plan for containment of antimicrobial resistance. J Glob Antimicrob Resist 2017;8:70-3.
5. Holzinger D, Jorns C, Stertz S, Boisson-Dupuis S, Thimme R, Weidmann M, et al. Induction of MxA gene expression by influenza A virus requires type I or type III interferon signaling. J Virol 2007;81:7776-85.
6. Haller O and Kochs G. Human MxA protein: an interferon-induced dynamin-like GTPase with broad antiviral activity. J Interferon Cytokine Res 2011;31:79-87.
7. Lehtinen O, Broman N, Waris M, Vuorinen T, Peltola V, Löyttyniemi E, et al. Association of human myxovirus resistance protein A with severity of COVID-19. BMC Infect Dis 2022;22:755.
8. Engelmann I, Dubos F, Lobert PE, Houssin C, Degas V, Sardet A, et al. Diagnosis of viral infections using myxovirus resistance protein A (MxA). Pediatrics 2015;135:e985-93.
9. Toivonen L, Schuez-Havupalo L, Rulli M, Ilonen J, Pelkonen J, Melen K, et al. Blood MxA protein as a marker for respiratory virus infections in young children. J Clin Virol 2015;62:8-13.
10. Nakabayashi M, Adachi Y, Itazawa T, Okabe Y, Kanegane H, Kawamura M, et al. MxA-based recognition of viral illness in febrile children by a whole blood assay. Pediatr Res 2006;60:770-4.
11. Tong-Minh K, van Hooijdonk S, Versnel MA, van Helden-Meeuwsen CG, van Hagen PM, van Gorp ECM, et al. Blood myxovirus resistance protein-1 measurement in the diagnostic work-up of suspected COVID-19 infection in the emergency department. Immun Inflamm Dis 2022;10:e609.
12. Metz M, Gualdoni GA, Winkler HM, Warenits AM, Stöckl J, Burgmann

H, et al. MxA for differentiating viral and bacterial infections in adults: a prospective, exploratory study. Infection 2023;51:1329-37.
13. Rhedin S, Eklundh A, Ryd-Rinder M, Peltola V, Waris M, Gantelius J, et al. Myxovirus resistance protein A for discriminating between viral and bacterial lower respiratory tract infections in children–the TREND study. Clin Microbiol Infect 2022;28:1251-7.
14. Iliopoulou K, Koufargyris P, Doulou S, Tasouli E, Katopodis S, Chachali SP, et al. Developing a tool for differentiation between bacterial and viral respiratory infections using myxovirus resistance protein A and C-reactive protein. Infect Dis Ther 2024;13:105-19.
15. Chieux V, Hober D, Chehadeh W, Harvey J, Alm G, Cousin J, et al. MxA protein in capillary blood of children with viral infections. J Med Virol 1999;59:547-51.
16. Zhu M, Chen L, Cao J, Cai J, Huang S, Wang H, et al. Clinical application of myxovirus resistance protein A as a diagnostic biomarker to differentiate viral and bacterial respiratory infections in pediatric patients. Front Immunol 2025;16:1540675.

https://doi.org/10.47429/lmo.2026.16.1.48