

# Measles and Influenza A/H3N2 Coinfection in a Measles Suspected Infant from Iran

Alireza Esmaeiloghli<sup>1</sup>, kaveh sadeghi<sup>1</sup>, Nazanin Shafiei Jandaghi<sup>1</sup>, Vahid Salimi<sup>1</sup>, Jila Yavarian<sup>2</sup>, sevrin Zadheidar<sup>1</sup>, and Talat mokhtari-azad<sup>1</sup>

<sup>1</sup>Tehran University of Medical Sciences

<sup>2</sup>School of Public Health, Tehran University of Medical Sciences

March 07, 2024

## Abstract

Measles is an acute infectious disease which is highly contagious. This illness is caused by a negative sense, single-stranded RNA virus belonging to the Paramyxoviridae family. In spite of having a highly effective vaccine, measles is still a public health concern. In October 2019, Iran has achieved the status of measles elimination using effective vaccination strategies and surveillance system based on WHO recommendations. However, recent COVID-19 pandemic disrupted impeccable immunization services and altered health-seeking behaviors worldwide. Herein, we report a case of measles and influenza co-infection in a nine month-old infant from Bushehr province of Iran

## Introduction

Measles and influenza viruses both are infectious diseases which are transmitted among individuals through respiratory route. Measles virus is a single-stranded RNA virus belonging to the *Paramyxoviridae* family [1] which is a highly contagious virus with reproduction number (R0) of 15-18 . Therefore, it is classified as one of the most contagious viruses infecting humankind [2]. Because of the measles vaccination starting at 1968 and effective vaccination mass campaign started in 2003 and the ongoing procedure in Iran, the mortality rate has been reduced considerably to date[3-5], nevertheless measles is still a public health concern.

Influenza viruses belong to the *Orthomyxoviridae* family. These viruses cause annual epidemics worldwide. Before COVID-19 pandemic, in the United States 5% to 20% of the population were infected with these viruses every year.

The R values of different influenza viruses causing moderate number of illness are different from those causing a high number of illnesses. The median R value for seasonal influenza has been reported 1.28 (IQR:1.19–1.37) [6-8].

Since the beginning of the COVID-19 pandemic, on the one hand, the circulation of the other infectious agents transmitted through the respiratory tract have been reduced by observing quarantine, social distancing and wearing masks. On the other hand, COVID-19 has diverted a huge part of healthcare systems resources and efforts toward pandemic response, disrupted routine immunization services and altered health-seeking behaviors of people worldwide [9, 10].

In October 2019, Iran has achieved the status of measles elimination using effective vaccination strategies and surveillance system based on WHO recommendations[4] . However, during recent months, limited number of measles cases were identified by Iran Measles and Rubella national center. Herein, we report a case of measles and influenza co-infection in a nine month-old infant from Bushehr province of Iran.

## Case presentation and laboratory diagnosis

On November 4, 2021, a 9-month-old male infant presented a two-day fever and maculopapular rash, clinically suspected of measles virus infection, was admitted to Dashti Healthcare Center, Bushehr, Iran. He has not received the MMR vaccine, as the first shot of the vaccine administers to children who are 12 months old. There was no information available regarding the past medical or travelling history of the patient. Upon admission, a nasopharyngeal swab, urine and serum specimen were collected which the first two samples, were placed in VTM (viral transport media). These specimens were sent at a low temperature (4) to the National Measles and Rubella Center for measles virus serological, cellular and molecular examination according to the CDC and WHO protocols [11]. At first, Anti-Measles virus IgM Elisa test (EUROIMMUN, Germany) was performed on the serum specimen in which the Elisa test was positive. For further investigation, the nasopharyngeal sample was cultured in Vero-hSLAM cell line, to see the specific cytopathic effect (CPE) of measles virus –the syncytia. Then the molecular detection was performed, as the following: total genomic ribonucleotide acid was extracted using High Pure Viral Nucleic acid kit (Roche Diagnostics GmbH, Germany) according to the manufacturer's instructions. To confirm the serology result, the extracted RNA was tested for measles virus using the 1-step RT-PCR Master mix (Biotech rabbit, Germany) by using specific primers (MeV214 and MeV216). Gel electrophoresis of the PCR product showed an approximately 610 bp band which were assessed by sanger sequencing using Genetic analyzer (3130, Applied Biosystems, USA). Nucleotide analysis confirmed indicated that the measles virus belonged to the B3 strain (based on C-terminal of the nucleocapsid protein), which is currently circulating in Iran. Concurrently, we investigated the nasopharyngeal swab for influenza virus and SARS-CoV-2 to determine whether the patient had a co-infection. For influenza virus and SARS-CoV-2 detection, two separated real-time RT-PCR reactions using specific primers and probes and Invitrogen (USA) master mix were used. The results showed that, the patient was positive for influenza A virus with a cycle threshold of 32, and was negative for SARS-CoV-2. To find out the subtype of this influenza virus strain, another qRT-PCR (Invitrogen, USA) targeting the HA gene was performed, which results in influenza virus A/H3N2 identification.

## Discussion and conclusion

To the best of our knowledge, we report the first observation of measles and influenza co-infection in the world. Recently, co-infections of SARS-CoV-2 and measles have been reported in symptomatic measles patients. The mixed infection are clinically important as the patients referring to the hospital with measles may be silent carriers of other respiratory viruses such as SARS-CoV-2 and influenza virus. There is a report from Brazil in 2021 detecting a co-infection of measles and SARS-CoV-2 [12], but co-infection of measles and influenza virus case has not been reported elsewhere in the world. No studies have clearly investigated the impact of this simultaneous infection on the severity and transmissibility of these diseases.

In conclusion, all respiratory samples of patients suspected of measles infection should be screened for influenza virus and SARS-CoV-2 during the COVID-19 pandemic and influenza epidemic. These findings are critical for preventing and breaking the chain of infection in pandemic and epidemic circumstances that can provide new perspectives and insights regarding treatment strategies in patients with co-infections compared to those with single infection.

## References

1. Salimi, V., et al., *Molecular epidemiology of measles virus in Iran 2009–2010: First detection of measles genotype H1*. Journal of Medical Virology, 2011. **83** (12): p. 2200-2207.
2. Koch, A., et al., *Adult Measles - Case Reports of a Highly Contagious Disease*. Open Access Maced J Med Sci, 2019. **7** (18): p. 3009-3012.
3. Zahraei, S.M., et al., *Successful Control and Impending Elimination of Measles in the Islamic Republic of Iran*. The Journal of Infectious Diseases, 2011. **204** (suppl.1): p. S305-S311.
4. Namaki, S., et al., *The elimination of measles in Iran*. Lancet Glob Health, 2020. **8** (2): p. e173-e174.

5. Mirchamsy, H., *Measles immunization in Iran*. Reviews of infectious diseases, 1983. **5** (3): p. 491-494.
6. Leung, N.H., *Transmissibility and transmission of respiratory viruses*. Nature Reviews Microbiology, 2021: p. 1-18.
7. Biggerstaff, M., et al., *Estimates of the reproduction number for seasonal, pandemic, and zoonotic influenza: a systematic review of the literature*. BMC Infectious Diseases, 2014. **14** (1): p. 480.
8. Petersen, E., et al., *Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics*. The Lancet infectious diseases, 2020.
9. Dadashzadeh, N., et al., *Shadow of Measles and COVID-19 Outbreak; two related diseases: Opportunity Situation?* 2022.
10. Mansour, Z., et al., *Impact of COVID-19 pandemic on the utilization of routine immunization services in Lebanon*. PLOS ONE, 2021. **16** (2): p. e0246951.
11. Rota, P.A., D.A. Featherstone, and W.J. Bellini, *Molecular epidemiology of measles virus*. Curr Top Microbiol Immunol, 2009.**330** : p. 129-50.
12. Nascimento, J., et al., *Coinfection of SARS-CoV-2 and Measles morbillivirus in a front-line health worker in Rio de Janeiro, Brasil*.Rev Assoc Med Bras (1992), 2020. **66** (8): p. 1027-1029.

#### **AUTHOR CONTRIBUTIONS:**

**Alireza Esmaeiloghli:** Methodology; Writing-original draft; Writing-review and editing. **Kaveh Sadeghi:** Conceptualization; Methodology; Writing-original draft; Writing-review and editing. **Nazanin Zahra Shafiei-Jandaghi:** Writing-review and editing. **Vahid Salimi:** Writing-review and editing. **Jila Yavarian:** Writing-review and editing. **Simin Abbasi:**Methodology. **Sevrin Zadheidar:** Methodology. **Somayeh Yaghoobizad:** Methodology. **Talat Mokhtari-Azad:** Project administration; Resources; Supervision; Writing-review and editing.