

Retrospective analysis of an outbreak of scarlet fever in United Arab Emirates

Eman Khalifa Sobh¹, Thiyagaraj A Kumarasamy² and Zahraa Khalifa Sobh²

¹Paediatric Department, Kanad Hospital, Al Ain, United Arab Emirates. ²Faculty of Medicine, Alexandria University, Egypt (Correspondence to Zahraa Sobh: z_khalifa2017@yahoo.com; zahraa.sobh@alexmed.edu.eg).

Abstract

Background: Scarlet fever is an infectious disease caused by *Streptococcus pyogenes*. However, there is limited data regarding the disease in the Arab World, including the United Arab Emirates.

Objective: To analyse a scarlet fever outbreak in United Arab Emirates.

Methods: This retrospective cross-sectional study included scarlet fever cases diagnosed at the Kanad Hospital, Al Ain, United Arab Emirates in 2022 and 2023. Data were retrieved from the hospital records and analysed using SPSS version 23.0. Chi-Square, Mann-Whitney, and Monte Carlo tests were applied.

Results: Two hundred and twenty-two cases (13.5% in 2022 and 86.5% in 2023) were confirmed ($P < 0.001$). Majority (67.1%) of the patients were aged 3–6 years, with a mean age of 4.56 ± 1.99 years. Rash, fever and sore throat were observed in 100%, 99.1%, and 82.0% of cases, respectively. The majority (85.1%) were managed as outpatients and 77.0% responded to oral penicillin. Patients' age was not significantly associated with nonresponse to penicillin and in-hospital admission. The outbreak had winter and summer peaks, with the highest incidence occurring during January and February 2023.

Conclusion: This study serves as a valuable reference for other studies, which should include antimicrobial susceptibility testing and the prevailing genetic variance of *Streptococcus pyogenes*.

Keywords: Scarlet fever, *Streptococcus pyogenes*, outbreak, infectious disease, Kanad Hospital, United Arab Emirates, Arab World

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Introduction

Streptococcus pyogenes (group A *Streptococcus*) is a highly virulent sub-type of the *Streptococcus* family and one of the most fatal bacterial pathogens worldwide (1). The virulence of *S. pyogenes* is influenced by the sub-type of *Streptococcal* M protein, which exhibits high genetic variability. The M protein envelops group A *Streptococci* and serves as the principal antigen, playing a crucial role in type-specific immunity. The M protein is vital for group A *Streptococcus* virulence, offering antiphagocytic functions crucial for survival in human tissues and body fluids (2).

Scarlet fever, or scarlatina, is an acute bacterial respiratory infection caused by *S. pyogenes*. *S. pyogenes* secretes infectious erythrogenic toxins, resulting in characteristic red coloured skin rashes caused by increased cytokine production during the early stages of the fever (3).

In the mid-19th Century, scarlatina was a leading cause of childhood mortality (4,5). The discovery and creation of antibiotics (penicillin) in 1928 and 1941, respectively; and improved sanitation, markedly reduced scarlet fever-related deaths by the mid 20th Century (6,7). However, scarlet fever re-emerged in the 21st Century as an escalating public health problem in some countries (8–10). For example, the World Health Organization (WHO)

noted an increasing trend in scarlet fever cases in some European countries in 2022 and 2023 (11), more than what would usually be expected in those geographical locations, communities or seasons (12).

Limited data are available on confirmed cases of scarlet fever in the Eastern Mediterranean Region, including the United Arab Emirates (UAE). Our study aimed to document the physiopathology, epidemiology and clinical features of a scarlet fever outbreak that occurred in Al-Ain, Abu Dhabi, United Arab Emirates in 2022 and 2023.

Methods

We conducted a retrospective cross-sectional study of scarlet fever cases diagnosed at Kanad Hospital, Al-Ain, Abu Dhabi, from January 2022 to December 2023. We chose to use data from this hospital because of its longstanding reputation for excellence (13). We used a simplified set of inclusion criteria derived from the diagnostic criteria for scarlet fever provided by the United States Centers for Disease Control and Prevention (US CDC) (14). These criteria include: general symptoms (fever, sore throat and painful swallowing, headache or body ache, gastric pain, nausea or vomiting); physical signs in the throat and neck (whitish coating on the tongue during early days, red and bumpy tongue, red throat and swollen tonsils,

white patches or streaks of pus on the tonsils, tiny red spots on the roof of the mouth, enlarged cervical lymph nodes); cutaneous signs (red rash that feels rough like sandpaper; red skin in the axillary, elbow, and groin creases; pale area around the mouth; skin peeling upon rash fading).

Ethical approval was obtained from the Kand Hospital Research Ethics Committee. All patient data were collected confidentially and stored in a secure database.

Using our diagnostic search criteria, we collated data on demographics, clinical signs and symptoms, treatment type, and outcome (discharge or death). With permission, we searched the electronic medical records of Kanad Hospital to find cases of scarlet fever reported from January 2022 until December 2023. All extracted data were collated and analyzed using SPSS version 23.0. We used the Chi-square test and Monte Carlo analyses to compare groups for categorical variables, while the Mann-Whitney test was used to compare quantitative variables that exhibited non-normal distributions.

Results

We identified 222 reported cases of scarlet fever at the Kanad Hospital–in Al-Ain, UAE: 30 (13.5%) in 2022 and 192 (86.5%) in 2023. Given that the number of cases did not begin to spike until November 2022, we observed a higher prevalence of cases during 2023 ($\chi^2 = 118.216$, $P < 0.001$). The prevalence of scarlet fever was significantly higher in all months during 2023 than in 2022 ($P < 0.001$), except July, October, November, and December. We used a chi-square test to compare the number of patients. There were two seasonal peaks.

The first peak began in November 2022 and reached the summit during January and February 2023. Prevalence then gradually declined and reached a trough in July. The second peak was in August and September 2023, with a much lower peak than the first wave (Figure 1).

As shown in Table 1, there was a similar number of cases in each age range by gender. Age range for cases was between 1 and 11 years, with a mean age of 4.56 ± 1.99 . Males had a mean age of 4.57 ± 2.02 and females had a mean age of 4.55 ± 1.98 . Consistent with these average ages, we observed that the majority of cases, 149 (67.1%), were in the 3 to 6-year-old age groups. There was no significant difference between the mean age of both sexes

(Mann-Whitney U (1, N = 90) = 6 155.50; $P > 0.05$). Gender was not found to be associated with the distribution of scarlet fever cases in the different age categories (χ^2 (5, N = 222) = 2.63; $P > 0.05$).

Clinical signs and symptoms of scarlet fever

Rash was present in all the 222 cases. Rash location by case was distributed as follows: generalized rash (102; 45.9%), face (106; 47.7%), torso (62; 27.9%), chest (28; 12.6%), arm (4; 1.8%), abdomen (4; 1.8%), perineum (3; 1.4%) and hands (2; 0.9%). Nearly all (220; 99.1%) the patients presented with fever ($> 38^\circ\text{C}$), 182 (82.0%) had a sore throat, 119 (53.6%) had a cough, and 121 (54.5%) had tonsillar exudate (pus or white spots visible on the tonsils). Some patients presented with vomiting (69; 31.1%), nasal congestion (63; 28.4%), cervical lymphadenopathy (55; 24.8%), abdominal pain (49; 22.1%), and lethargy (43; 19.4%).

Treatment regimen for scarlet fever cases

Table 2 shows that 189 (85.1%) of cases were managed as outpatients, whereas 33 (14.9%) required hospitalisation due to disease severity or oral penicillin resistance. Neither penicillin resistance nor hospitalisation were associated with patient age ($\chi^2 = 2.95$, $P > 0.05$; $\chi^2 = 5.73$, $P > 0.05$). For cases that showed resistance to oral penicillin, doctors used a variety of antibiotics, depending on the severity of the clinical signs and symptoms and whether the patient required hospitalisation: (i) intravenous co-amoxiclav (23; 45.1%); (ii) intravenous ceftriaxone (10; 19.6%); (iii) intramuscular ceftriaxone (8; 15.7%); (iv) oral azithromycin 4; 7.8%); (v) intravenous clindamycin (4; 7.8%); and (vi) oral clindamycin (2; 3.9%).

Discussion

We reported a retrospective cross-sectional study of an outbreak of 222 cases of scarlet fever, which began in November 2022 and ended in September 2023, in Al-Ain, Abu Dhabi, United Arab Emirates. We highlighted the role of seasonal weather changes as well as the transmission and infection peaks and troughs associated with in-school children. There were two seasonal peaks in this outbreak (Figure 1). The first occurred in February 2023, which corresponded to the winter months, school terms and rises in cases after school holidays in December and January. There was another small peak of cases in April and May 2023, which roughly corresponded to the period

Table 1 Age and gender of identified cases of scarlet fever from Kanad Hospital, UAE, 2022-2023

Age (Years)	Female (n=110) No, %	Male (n=112) No, %	Total (n=222) No, %
1-2	20 (18.2)	18 (16.1)	38(17.1)
3-4	38 (34.5)	38 (33.9)	76(34.2)
5-6	34 (30.9)	39 (34.8)	73(32.9)
7-8	16 (14.5)	14 (12.5)	30(13.5)
9-10	2 (1.8)	1 (0.9)	3 (1.4)
≥ 11	0 (0)	2 (1.8)	2 (0.9)

Table 2 Association between age, responsiveness to treatment with oral penicillin and disease severity for identified scarlet fever cases at Kanad Hospital, UAE, 2022–2023

Age (years)	Penicillin susceptible No, %	Penicillin resistant No, %	Out-patient treatment No, %	In-patient treatment No, %
1–2	26 (68.4)	12 (31.6)	28 (73.7)	10 (26.3)
3–4	61 (80.3)	15 (19.7)	64 (84.2)	12 (15.8)
5–6	57(78.1)	16 (21.9)	64(87.7)	9(12.3)
7–8	23(76.7)	7(23.3)	28 (93.3)	2 (6.7)
9–10	2(66.7)	1(33.3)	3(100)	0(0)
≥11	2 (100)	0 (0)	2 (100)	0 (0)
Total (all ages)	171 (77.0)	51 (23)	189 (85.1)	33 (14.9)

children went back to school after celebrating Ramadan. There was a trough in cases during the summer months and school holidays, with a short peak roughly 3–4 weeks following the beginning of new school session in September 2023.

Similarly, Ma et al. had reported a scarlet fever outbreak in China with two seasonal peaks annually in relation to school semesters (15). In the United Kingdom, 57 primary school children developed scarlet fever in March 2009, both a winter month and mid-term period for school children (16). In Germany, school physicians reported 18 cases of scarlet fever during January and February 2020, which corresponded to both winter months and school term after winter holidays (17). Hong Kong registered an increase in cases of scarlet fever in June 2011 after the Easter school holidays in April (18).

The mean age of children infected with scarlet fever in this study was 4.56 years, which agrees with the findings of Ryu et al that the median age of scarlet fever cases was 4.2 years (19). Our finding that more children were infected in the 3–6-year age groups corresponds to data from Lu et al., who reported 86.42% cases in the 3–9-year age groups, in Zhejiang Province, China, from 2004–2018 (20). We found 2 studies that reported higher incidence rate of scarlet fever among older children (21,22), but we

did not find this outcome in our analysis. We also found the number of scarlet fever cases to be equally distributed between genders, coinciding with one study conducted in Beijing, China in 2006–2011 (23). However, other evidence from Zhejiang Province, China showed that the incidence of scarlet fever was significantly higher among males (20).

Case reports of clinical assessments in our study revealed that all patients exhibited the characteristic rash of scarlet fever. Similarly, case reports from London confirmed rash was the most common symptom of scarlet fever (24). Also, we reported that 99.1% of patients had fever, but fewer cases had a sore throat, cough, or tonsillar exudate, which agrees with published literature (8,20,23,24).

We found that 14.9% of scarlet fever cases were hospitalised, which is much higher than figures from Poland, where only 1.1% of cases required hospitalisation during the outbreak in 2009 (25). We suggest that the relatively high number of scarlet fever patients requiring hospitalisation in our study indicates high virulence of type A *Streptococcus* in our geographical region. We did not find age to be associated with the need for hospital admission or penicillin resistance. Therefore, we suggest that clinical resistance to β-lactams and the need for

Figure 1 Scarlet fever cases recorded at Kanad Hospital, UAE, 2022–2023



hospitalisation are both factors which are more likely to be associated with the organism's virulence than age or gender.

General consensus on group A Streptococcus is that it is universally susceptible to β -lactams, oral penicillin being the antibiotic of choice for managing scarlet fever (26,27). However, literature is beginning to emerge reporting β -lactam resistance in this group. Emerging resistance may be due to the high genetic variation of the M pathogen genome, among other factors (28-31). At Kanad Hospital, all patients were initially treated with oral penicillin, and over three-quarters of them recovered. Nearly 15% of cases needed another antibiotic, including co-amoxiclav, ceftriaxone, azithromycin, and

clindamycin, requiring longer periods of hospitalisation than reported in other studies.

One limitation of our retrospective analysis is that we could only assess the response to antimicrobial therapy on a clinical basis, as antimicrobial susceptibility testing is not routinely done for patients with scarlet fever at Kanad Hospital. Thus, we recommend that future prospective studies should be conducted to investigate antibiotic susceptibility of suspected or confirmed cases and the potential for β -lactams resistance due to high genetic variability and increasing virulence of *Streptococcus pyogenes* in the UAE.

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Competing interests: None declared.

Analyse rétrospective d'une flambée de scarlatine aux Émirats arabes unis

Résumé

Contexte : La scarlatine est une maladie infectieuse causée par *Streptococcus pyogenes*. Cependant, il existe peu de données à ce sujet dans le monde arabe, et notamment aux Émirats arabes unis.

Objectif : Analyser une flambée de scarlatine survenue aux Émirats arabes unis.

Méthodes : La présente étude transversale rétrospective a inclus des cas de scarlatine diagnostiqués à l'hôpital Kanad, à Al Ain, aux Émirats arabes unis en 2022 et 2023. Les données ont été extraites des dossiers d'hôpital et analysées à l'aide du logiciel SPSS version 23.0. Les tests de khi carré, de Mann-Whitney et de Monte-Carlo ont été appliqués.

Résultats : Deux cent vingt-deux cas (13,5 % en 2022 et 86,5 % en 2023) ont été confirmés ($p < 0,001$). La majorité des patients (61,7 %) étaient âgés entre trois et six ans, l'âge moyen étant de $4,56 \pm 1,99$ ans. Des éruptions cutanées, de la fièvre et des maux de gorge ont été observés dans 100 %, 99,1 % et 82 % des cas respectivement. La majorité des personnes touchées (85,1 %) ont été prises en charge en ambulatoire et 77,0 % ont répondu à la pénicilline par voie orale. L'âge des patients n'était pas significativement associé à la non-réponse à la pénicilline et à l'hospitalisation. La flambée a connu des pics en hiver et en été, l'incidence la plus élevée s'étant produite en janvier et février 2023.

Conclusion : Cette étude sert de référence précieuse pour d'autres études, qui devraient inclure des tests de sensibilité aux antimicrobiens et la variance génétique prévalente de *Streptococcus pyogenes*.

تحليل وصفي لفاشية الحمى القرمزية في الإمارات العربية المتحدة

إيمان خليفة صبح، ثياجاراج أديمولام كوماراسامي، زهراء خليفة صبح

الخلاصة

الخلفية: إن الحمى القرمزية مرضٌ مُعد تسببه المكورات العقدية المقيحة. ولكن توجد بيانات محدودة عن هذا المرض في العالم العربي، ومنه الإمارات العربية المتحدة.

الأهداف: هدفت هذه الدراسة إلى تحليل فاشية الحمى القرمزية في الإمارات العربية المتحدة.

طرق البحث: شملت هذه الدراسة المقطعية الاسترجاعية حالات الحمى القرمزية التي سُخِّصت في مستشفى كند في مدينة العين بالإمارات العربية المتحدة في عامي 2022 و 2023. واستُرجعت البيانات من سجلات المستشفى، وحُللت ببرنامج SPSS، الإصدار 23.0. وطُبِّقت اختبارات مربع كاي، ومان ويتني، ومونت كارلو.

النتائج: رُصدت 222 حالة مؤكدة (13.5% منها في عام 2022 و 86.5% في عام 2023) (القيمة الاحتمالية: $P < 0.001$). وتراوحت أعمار غالبية المرضى (67.1%) بين 3 و 6 سنوات، وبلغ متوسط أعمارهم 4.56 ± 1.99 سنوات. ولوحظت أعراض الطفح الجلدي والحمى والتهاب الحلق في 100% و 99.1% و 82.0% من الحالات على الترتيب. وقُدِّم العلاج لغالبية المرضى (85.1%) في العيادات الخارجية، واستجاب 77.0% منهم للبنسلين الفموي. ولم ترتبط أعمار المرضى ارتباطاً ملحوظاً بعدم الاستجابة للبنسلين والحاجة إلى دخول المستشفى. وبلغت الفاشية ذروتها في الشتاء وفي الصيف، وحدثت أعلى معدلات الإصابة خلال شهري يناير/ كانون الثاني وفبراير/ شباط 2023.

الاستنتاجات: تعد هذه الدراسة مرجعاً قيماً لدراسات أخرى، وهي الدراسات التي ينبغي أن تشمل اختبارات بشأن الحساسية لمضادات الميكروبات والتباين الجيني للسائد للمكورات العقدية المقيحة.

References

1. Brouwer S, Rivera-Hernandez T, Curren BF, Harbison-Price N, De Oliveira DMP, Jespersen MG, et al. Pathogenesis, epidemiology and control of Group A Streptococcus infection. *Nat Rev Microbiol.* 2023;21(7):431-47. DOI: 10.1038/s41579-023-00865-7
2. Metzgar D, Zampolli A. The M protein of group A Streptococcus is a key virulence factor and a clinically relevant strain identification marker. *Virulence.* 2011;2(5):402-12. DOI: 10.4161/viru.2.5.16342
3. Michael Trent H, Rebecca C, Basel K, Amrit Kaur P, Lipi B, Theresa L, et al. Clinical management and impact of scarlet fever in the modern era: findings from a cross-sectional study of cases in London, 2018–2019. *BMJ Open.* 2021;11(12):e057772. DOI: 10.1136/bmjopen-2021-057772
4. Hardy, Anne, 'Scarlet Fever', *The Epidemic Streets: Infectious Diseases and the Rise of Preventive Medicine 1856–1900* (Oxford, 1993; online edn, Oxford Academic, 3 Oct. 2011), <https://doi.org/10.1093/acprof:oso/9780198203773.003.0004>, accessed 30 Apr. 2024.
5. Duncan CJ, Duncan SR, Scott S. The dynamics of scarlet fever epidemics in England and Wales in the 19th century. *Epidemiol Infect.* 1996;117(3):493-9. DOI:10.1017/S0950268800059161.
6. Duncan SR, Scott S, Duncan CJ. Modelling the dynamics of scarlet fever epidemics in the 19th century. *Eur J Epidemiol.* 2000;16(7):619-26. DOI: 10.1023/a:1007645110006
7. Tan SY, Tatsumura Y. Alexander Fleming (1881-1955): Discoverer of penicillin. *Singapore Med J.* 2015;56(7):366-7. DOI: 10.11622/smedj.2015105.
8. Park DW, Kim S-H, Park JW, Kim M-J, Cho SJ, Park HJ, et al. Incidence and characteristics of scarlet fever, South Korea, 2008–2015. *Emerg Infect Dis.* 2017;23(4):658. DOI: 10.3201/eid2304.160773
9. Liu Y, Chan TC, Yap LW, Luo Y, Xu W, Qin S, et al. Resurgence of scarlet fever in China: a 13-year population-based surveillance study. *Lancet Infect Dis.* 2018;18(8):903-12. DOI: 10.1016/S1473-3099(18)30231-7
10. Lamagni T, Guy R, Chand M, Henderson KL, Chalker V, Lewis J, et al. Resurgence of scarlet fever in England, 2014–16: a population-based surveillance study. *Lancet Infect Dis.* 2018;18(2):180-7. DOI: 10.1016/S1473-3099(17)30693-X
11. World Health Organization. Increased incidence of scarlet fever and invasive Group A Streptococcus infection - multi-country 2023. Available from: <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON429> (Accessed 30 April 2024)
12. World Health Organization. Disease outbreaks. Available from: <https://www.who.int/teams/environment-climate-change-and-health/emergencies/disease-outbreaks> (Accessed 30 April 2024)
13. UAE Official Press. Kanad Hospital: The story of the Al Ain hospital where Sheikh Mohamed was born. 2021. Available from: <https://gulfnews.com/uae/year-of-the-50th/kanad-hospital-the-story-of-the-al-ain-hospital-where-sheikh-mohamed-was-born-1.79714052> (Accessed 30 April 2024)
14. Centres for Disease Control and Prevention C. Group A Streptococcal (GAS) Disease, Scarlet Fever. Available from: <https://www.cdc.gov/groupastrep/diseases-hcp/scarlet-fever.html> (Accessed 30 April 2024)
15. Ma Y, Gao S, Kang Z, Shan L, Jiao M, Li Y, et al. Epidemiological trend in scarlet fever incidence in China during the COVID-19 pandemic: A time series analysis. *Front Public Health.* 2022;10:923318. DOI: 10.3389/fpubh.2022.923318
16. Lamden K. An outbreak of scarlet fever in a primary school. *Arch Dis Child.* 2011;96(4):394-7. DOI: 10.1136/adc.2010.189944
17. Saad N, Muller N, Walter J, Murajda L. Scarlet fever outbreak in a primary and middle school in Germany: importance of case ascertainment and risk communication. *Epidemiol Infect.* 2020;148. DOI: 10.1017/S0950268820002642
18. Luk E, Lo J, Li A, Lau M, Cheung T, Wong A, et al. Scarlet fever epidemic, Hong Kong, 2011. *Emerg Infect Dis.* 2012;18(10):1658-61. DOI: 10.3201/eid1810.111900
19. Ryu S, Chun B. Investigation of scarlet fever outbreak in a kindergarten. *Infect Chemother.* 2018;50(1):38-42. DOI: 10.3947/ic.2018.50.1.38
20. Lu Q, Wu H, Ding Z, Wu C, Lin J. Analysis of epidemiological characteristics of scarlet fever in Zhejiang Province, China, 2004–2018. *Int J Environ Res Public Health.* 2019;16(18):3454. DOI: 10.3390/ijerph16183454
21. Tang J, Tseng T, Chan T. Detecting spatio-temporal hotspots of scarlet fever in Taiwan with spatio-temporal G_i^* statistic. *PLoS One.* 2019;14(4):e0215434. DOI:10.1371/journal.pone.0215434
22. Chen M, Cai J, Davies M, Li Y, Zhang C, Yao W, et al. Increase of emm1 isolates among group A Streptococcus strains causing scarlet fever in Shanghai, China. *Int J Infect Dis.* 2020;98:305-14. DOI: 10.1016/j.ijid.2020.06.053
23. Yang P, Peng X, Zhang D, Wu S, Liu Y, Cui S, et al. Characteristics of group A Streptococcus strains circulating during scarlet fever epidemic, Beijing, China, 2011. *Emerg Infect Dis.* 2013;19(6):909-15. DOI: 10.3201/eid1906.121020
24. Herdman M, Cordery R, Karo B, Purba A, Begum L, Lamagni T, et al. Clinical management and impact of scarlet fever in the modern era: findings from a cross-sectional study of cases in London, 2018–2019. *BMJ Open.* 2021;11(12):e057772. DOI: 10.1136/bmjopen-2021-057772
25. Czarkowski M, Kondej B, Staszewska E. Scarlet fever in Poland in 2009. *Przegl Epidemiol.* 2011;65(2):209-12. Available from: <https://pubmed.ncbi.nlm.nih.gov/21913461/> (Accessed 30 April 2024)
26. Plainvert C, Doloy A, Loubinoux J, Lepoutre A, Collobert G, Touak G, et al. Invasive group A streptococcal infections in adults, France (2006–2010). *Clin Microbiol Infect.* 2012;18(7):702-10. DOI: 10.1111/j.1469-0691.2011.03624.x

27. Basetti S, Hodgson J, Rawson TM, Majeed A. Scarlet fever: a guide for general practitioners. *London journal of primary care.* 2017;9(5):77-9. DOI: 10.1080/17571472.2017.1365677
28. Musser JM, Beres SB, Zhu L, Olsen RJ, Vuopio J, Hyyryläinen HL, et al. Reduced In Vitro Susceptibility of *Streptococcus pyogenes* to β -Lactam Antibiotics Associated with Mutations in the *pbp2x* Gene Is Geographically Widespread. *J Clin Microbiol.* 2020;58(4):1993-19. DOI: 10.1128/JCM.01993-19.
29. William P Hanage, Samuel A Shelburne, *Streptococcus pyogenes* With Reduced Susceptibility to β -Lactams: How Big an Alarm Bell?, *Clin. Infect. Dis.* 2020;71:205–6. DOI:10.1093/cid/ciz1006
30. Yu D, Zheng Y, Yang Y. Is There Emergence of β -Lactam Antibiotic-Resistant *Streptococcus pyogenes* in China? *Infect Drug Resist.* 2020;13:2323-7. DOI: 10.2147/idr.s261975.
31. Sun. L, Xiao. Y, Huang. W, Lai. J, Lyu. J, Ye. B, et al. Prevalence and identification of antibiotic-resistant scarlet fever group A *Streptococcus* strains in some paediatric cases at Shenzhen, China. *J Glob Antimicrob Resist.* 2022;30:199-204. DOI: 10.1016/j.jgar.2022.05.012