Kerbala Journal of Pharmaceutical Sciences

ISSN: 2221-7207(Print) / **ISSN**: 3006-7189 (Online)

Measles Resurgence Amidst Declining Vaccination Rates: A Global Public Health Threat: A Review

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Received: 02/09/2025
Accepted: 27/10/2025
Published: 31/12/2025

Keywords: Measles, Immunity, re-emerging viruses, Vaccination

DOI: 10.62472/kjps.v16.i27.342-352

Abstract

Measles is still one of the leading causes of mortality for children globally and is the most contagious disease known to science. It is a highly contagious, and potentially fatal virus, which has resurfaced as a major global public health issue, even in highly industrialized nations. This comeback is mainly due to a worrying decrease in vaccination rates, which has been made worse by the COVID-19 pandemic's disruptions. Approximately three out of every 1,000 cases of measles result in death. Measles has no known cure, but vaccinations have been a preventive measure since the 1960s. Even though measles still causes a great deal of morbidity, and death worldwide, there has been a lot of progress. Measles killed an estimated 777,000 people worldwide annually just twenty years ago in 2000. It killed 128,000 people worldwide in 2021. According to the analysis, measles outbreaks were widespread in 37 nations in 2022 as opposed to 22 the previous year. There were outbreaks in 37 countries, with 28 in Africa, 6 in the eastern Mediterranean, 2 in Southeast Asia, and 1 in Europe. Despite the recent year's decline in measles infection, this year it has resurged, both around the world and in Iraq. According to the Control Disease Center (CDC), Iraq ranked number five of countries with the most measles outbreaks between August 2023 and January 2024. Nearly, in Iraq, the current number of cases is three times more than in all of 2008, since the beginning of the year around 1,000 cases continue to be recovered every week, while over than 22.000 children have been infected. At the end of March ninety-three children had perished. The rise is attributed to the low immunity of the reduced coverage population that has resulted from reduced coverage of routine vaccination during 2005-2008 due to insecurity. The spread of this disease among school students is being noticed across the Iraq governorates and health authorities. This article highlights the critical need for a reinvigorated worldwide commitment to measles vaccination programs, looks at the alarming rise in measles cases, and investigates the factors causing a reduction in vaccinations.

عودة ظهور الحصبة في ظل انخفاض معدلات التطعيم: تهديد للصحة العامة على مستوى العالم

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الخلاصة

لا تزال الحصبة أحد الأسباب الرئيسية لوفيات الأطفال على مستوى العالم وهي أكثر الأمراض المعدية المعروفة للعلم. إنه فيروس شديد العدوى، وربما قاتل، والذي عاد إلى الظهور كقضية صحية عامة عالمية رئيسية، حتى في الدول الصناعية العالية. وتعزى هذه العودة بشكل رئيسي إلى الانخفاض المقلق في معدلات التطعيم، والذي تفاقم بسبب اضطرابات جائحة كوفيد-19. ما يقرب من ثلاثة من كل 1000 حالة من حالات الحصبة تؤدي إلى الوفاة. الحصبة ليس لها علاج معروف، ولكن التطعيمات كانت إجراء وقائي منذ ستينيات القرن العشرين. على الرغم من أن الحصبة لا تزال تسبب قدرا كبيرا من المراضة والوفاة في جميع أنحاء العالم، فقد كان هناك الكثير من التقدم. قتلت الحصبة ما يقدر بنحو 777000 شخص في جميع أنحاء العالم سنويا قبل عشرين عاما فقط في عام 2000. قتل 128,000 شخص في جميع أنحاء العالم في عام 2021. وفقا للتحليل، كان تفشي الحصبة واسع الانتشار في 37 دولة في عام 2022 مقابل 22 دولة في العام السابق. كانت هناك فاشيات في 37 دولة، منها 28 في إفريقيا، و6 في شرق البحر الأبيض المتوسط، و2 في جنوب شرق آسيا، و1 في أوروبا. وعلى الرغم من انخفاض الإصابة بالحصبة في العام الأخير، فقد عادت إلى الظهور هذا العام، سواء في جميع أنحاء العالم أو في العراق. وفقا لمركز السيطرة على الأمراض (CDC)، احتل العراق المرتبة الخامسة من حيث البلدان التي شهدت أكبر عدد من تفشي الحصبة بين أغسطس 2023 ويناير 2024. في العراق تقريبا، يبلغ العدد الحالي للحالات ثلاثة أضعاف ما كان عليه في عام 2008 بأكمله، ومنذ بداية العام، يستمر تعافي حوالي 1000 حالة كل أسبوع، بينما أصيب أكثر من 22.000 طفل. وفي نهاية آذار/مارس، لقي ثلاثة وتسعون طفلا حتفهم. وتعزى هذه الزيادة إلى انخفاض مناعة السكان ذوي التغطية المنخفضة التي نتجت عن انخفاض تغطية التطعيم الروتيني خلال الفترة 2005-2008 بسبب انعدام الأمن. ويلاحظ انتشار هذا المرض بين طلاب المدارس في جميع أنحاء المحافظات العراقية والسلطات الصحية. يسلط هذا المقال الضوء على الحاجة الماسة إلى تنشيط الالتزام العالمي ببرامج التطعيم ضد الحصبة، وينظر في الارتفاع المقلق في حالات الحصبة، ويحقق في العوامل التي تسبب انخفاض التطعيمات.

1. Introduction

The measles virus (MV) belongs to the pramyxoviridia family and Morbillivirus genus, it is a negative-sense, enclosed, single-stranded, non-segmented RNA with at least six structural proteins encoded in its genome (Laksono et al., 2016). Measles is an acute, extremely contagious sickness that mainly affects children, and it is caused by the rubella virus, or MV (Perry & Halsey, 2004). Can occur in serious forms with non-pathognomonic clinical characteristics, especially in those with impaired or compromised cellular immunity individuals; such as cancer patients undergoing treatment, organ transplant recipients, AIDS patients, or those with any type of congenital immunodeficiency (El Najjar et al., 2014). It affects the upper respiratory tract before spreading to other sections of the body since it is a respiratory virus. After catching the virus, a person develops a systemic rash and becomes extremely contagious, able to infect others through simple airspace sharing, coughing, or sneezing (Paules et al., 2019). Measles may seem like a typical childhood rash, but it can lead to serious complications, especially in young children and those with weakened immune systems. Thankfully, there is a trustworthy vaccine available to prevent this disease (El Najjar et al., 2014; Perry & Halsey, 2004).

2. Measles Immunity

The immune response to the Measles virus is not understood entirely, measles virus replication takes place in lymphoid tissues, where CD150 acts as a receptor to facilitate T and B cells infection. Lymphocyte cells are reduced through the acute phase infection. However, the onset of the adaptive immune response causes a broad lymphocyte proliferation, T-cell production and antibodies specific to the Measles virus and a rash, and the removal of the viral infection. The nucleic acid viral (RNA) persists in lymphoid tissues in conjugation with germinal center proliferation, production of the secretory cells, and the maturation of ab avidity to create lifelong immunity, functionally distinct T-cell populations. On the other hand, concurrently declining memory and naive B cells, the spectrum of preexisting antibodies, and the sensitivity to new infections all increase susceptibility to infections in the future (Gordiienko et al., 2019). The measles virus (MV) encodes two surface glycoproteins, Hemagglutinin (H) and fusion (F); non-structural regulatory proteins V and C; and four internal proteins, matrix (M), phosphoprotein (P), nucleocapsid (N), and large polymerase (L). The hemagglutinin protein is the target of a neutralizing antibody, while the attachment protein is for cell entrance. It is observed on the vision's surface as a dimer of interacting non-covalently with fusion (F) (De Swart et al., 2007). Hemagglutinin (H) can interact with a range of receptors, including CD46 is a complement-regulatory protein, which expressed on all nucleoted cells, however, it is mostly used by measles virus vaccine strains. Nectin 4, is an adherens junction protein, which is expressed on the basolateral surface of epithelial cells and is used by wild-type (WT) measles virus strain and vaccination. CD150/ signaling lymphocyte activation molecule (SLAM), an immune-regulatory protein created on monocytes, dendritic cells, and lymphocytes that are utilized by both vaccine and WT viruses, is the primary receptor for WT MeV infection of lymphoid tissue and systemic virus transmission (de Vries, 2020). The measles viral infection is undetectable clinically throughout the incubation period, through the activated viral replication in lymphoid tissue and spreading systemically. Innate immune responses which are characterized by NF-κB, (IL-6), inflammasome (IL-1β, IL-18), and other factors, do not halt the reproduction and spread of viruses, even if type I IFN pathway activation is not evident in these responses (de Swart et al., 2008). Clearance is contingent upon the adaptive immune response. The maculopapular rash, which appears through (10–14) days after infection, and is a marker of the cellular immune response to infection, is brought on by lymphocyte infiltration into the viral replication sites in the epidermal epithelial cells. A week after the rash first emerges, blood tests show the presence of IgM antibodies and measles virus-specific IFN-γ-producing T cells as the rash starts to diminish. An IgM antibody specific to the measles virus is the main diagnostic test used to confirm a measles diagnosis. Although, antibodies will likely play a part measles virus-specific T-cell responses are required for virus clearance (Lin et al., 2012).

In summary, measles directly infects B and T cells that express CD150, hence interacting closely with the immune system. This results in a transient lymphocyte cell depletion, which is succeeded by immune activation that creates a lifelong defense against reinfection. Months after the infectious virus seems to have recovered and eradicated, MeV RNA is still present in lymphoid tissue and continues to trigger B and T cell responses unique to MeV. The production of IL-17 replaces IFN-γ by T cells, and the number of peripheral T cells increases. The proliferating germinal centers produce cells that secrete antibodies, which settle in the bone marrow and permanently maintain MeV antibody plasma levels. Conversely, a sustained increase in vulnerability to other diseases is likely brought about by a decrease in antibody levels.

3. The Importance of Vaccination

Before the measles vaccine was created, the infection killed a large number of people worldwide, and impacted nearly everyone by the time they were 15 years old. Around 135 million cases of measles infections and more than 6 million fatalities are reported each year due to the disease's global prevalence. The increased use of measles vaccinations throughout the world in the 1980s caused measles incidence and death rates to drop to extremely low levels. Global annual reported measles incidence per million people decreased by 66% between 2000 and 2018, as did the number of cases recorded, which decreased by 59%, and the estimated number of measles deaths, which decreased by 73%. Since vaccination became widely available in high-income nations in 1961, it has proven to be a safe and effective method of preventing and controlling measles. The absence of endemic measles transmission for at least 36 months is proof that substantial levels of community immunity have been established, which is necessary for the elimination of the disease (Di Pietrantonj et al., 2020, 2021; Masresha et al., 2020).

The global measles immunization campaign has significantly decreased the number of measles-related illnesses and fatalities around the globe. The foundation for the management and avoidance of measles has been routine MCV vaccination. MCV (Measles-containing –vaccine) is one of the most effective vaccinations ever created, with two doses being 97% effective in preventing measles. Less than 20% of recipients experience mild adverse events, and significant adverse events are incredibly uncommon. Since measles is one of the most contagious diseases in humans, maintaining high (≥95%) 2-dose MCV coverage is essential to stopping the disease's spread and achieving measles elimination. Nevertheless, the global MCV coverage plateaued for almost ten years, and the measles resurgence during 2023–2024 shows that there is still more work to be done. To reach a world free of measles, there must be international agreements to boost community access to and demand vaccines, as well as to develop innovations that can remove access hurdles and boost vaccine confidence (Gastañaduy et al., 2021b, 2021a).

4. Public Health Response

Measles is one of the most contagious illnesses, which can cause serious consequences or even death. A single sufferer may be able to infect twelve to eighteen other people. When an infected individual coughs, breathes, or sneezes, the infection spreads quickly. Nonetheless, measles is nearly completely avoidable with immunization; between 2000 and

2022, two doses of the vaccine avoided 57 million measles deaths worldwide. After verification of elimination, ongoing efforts to maintain measles infection control continue. Nonetheless, the eradication of measles carries noteworthy consequences for any public health system, necessitating high vaccination rates, elimination-standard surveillance in the face of nearly no disease, and maintaining physician awareness. As long as the global measles epidemic persists. To maintain the elimination of measles and respond to any cases that might not fit the standard cost-effectiveness standards used in another area of public health, this work must continue. These initiatives highlight how important it is to achieve 100% vaccination coverage and reduce the impact of imported measles. Convincing parents to vaccinate their children and encouraging professionals to screen patients with feverish rash illnesses for measles can be difficult, particularly in situations where there is no endemic measles virus. Maintaining laboratory proficiency and funding for a vaccination program is also challenging. A larger number of people can benefit from hearing about the experience of employing various containment techniques in nations that have long since eradicated measles (Gastañaduy et al., 2018). WHO is monitoring the epidemiological situation closely, vaccination coverage for rubella and measles, and surveillance performance in the region based on data from member states, and publishes a monthly published on rubella and measles situation in the region? According to the different studies, controlling the measles outbreak requires the following key activities to be implemented as part of strategies for outbreak, often necessitating, simultaneously coordinated responses by public health agencies: (Centers for Disease Control and Prevention, 2012; Ibrahim & Al Bar, 2009; Roush, 2017)**.**

- Organize a reaction committee or epidemic control team.
- Detected coverage in surrounding and affected areas.
- Promote surveillance, such as; finding active cases for further cases.
- Inform the appropriate and essential clinical health authorities.
- Educate and learn contacts and their patients about the transmission, and measuring techniques to minimize and reduce spread.
- Take the samples to a laboratory for viral detection and confirmation.
- Promote and implement activities of control to minimize viral transmission.
- Appropriate case management, including administration of vitamins like (A vitamin).
- Supply enough amounts of Measles vaccine to unvaccinated individuals.
- Assess immunity of contacts of cases, and offer post-exposure prophylaxis (vaccine, immunoglobulin) to those susceptible.
- Detected immunity of contacts of cases, by providing post-exposure prophylaxis (antibodies) to those susceptible.
- Isolation, implement quarantine, and exclusion in the household as required.
- Collect history details of outbreak response and cases.
- Summarize and analyze outbreaks, including data about vaccine coverage, and surveillance and vaccine coverage.

5. The Threat of Measles Outbreaks (WHO)

Measles is a highly contagious disease that is transmitted through the air by infected droplets. A person becomes infected 90% of the time if they are exposed without having had any vaccinations or exposure. In general, cases are dangerous for those who are unable to receive vaccinations, including those who are immunocompromised or have had immune systems weakened by transplant procedures, pregnant women, those with underlying medical disorders, and infants under a year old. Nine out of ten persons who are not vaccinated and are not protected will contract measles after coming into contact with the virus, and they are thought to be the source of infection that spreads to other people. When the number of confirmed cases of measles infection is elevated and exceeds the anticipated number of cases, an outbreak is proclaimed. Due to drops in measles vaccination coverage, measles cases have increased internationally during 2022 compared to 2021 by 18%, while deaths have increased by 43%. A recent WHO and US CDC report estimates that there are 9 million cases of measles worldwide, with 13600 deaths—mostly in children—resulting from the disease (Lee & Haidari, 2017; WHO, 2014). The risk of measles infection in children is nevertheless steadily rising. Compared to 22 nations in 2021, 37 countries have either seen a significant measles epidemic or disruption since 2022. Of the nations affected by the outbreak, 28 were in Africa, two were in South-East Asia, six were in the Eastern Mediterranean, and one was in Europe, according to the World Health Organization. It is alarming how much the number of measles outbreaks has increased recently, but this is not surprising considering the recent drop in vaccination rates. Anywhere there are measles cases, communities and nations with low vaccination rates are at risk. Nonetheless, the consideration of focused and timely measures is essential to preventing measles illness and fatalities. The vaccine is thought to be the most effective way to prevent measles; despite a little elevated coverage of vaccination worldwide between (2021 and 2022) 33 million children were still unable to receive the two doses of the vaccine. The first dosage of the vaccine was covered 83% of the time globally, and the second dose 74% of the time. This is still significantly less than the 95% coverage with two doses that are required to prevent outbreaks in communities (Centers for Disease Control and Prevention (CDC), 2003). The measles pandemic, which occurs in low-income nations because of a lack of recovery in vaccine coverage, is a warning sign for action. CDC and WHO urge nations to immunize every child against measles, and other infectious diseases that can be prevented by vaccination. They also call on international partners to support these nations' most vulnerable populations. All international health partners, as well as national, regional, and municipal governments, must make investments in improved and supportive surveillance systems as well as outbreak response capabilities to quickly detect, and contain outbreaks. Because of the COVID-19 pandemic-associated delays in supplemental immunization efforts, it is expected to be the most significant factor contributing to miss measles vaccination and declining coverage from 2020 to 2022. This raises the possibility of more significant global epidemics. This is mostly related to the COVID-19 pandemic, which caused lockdowns and mobility restrictions, which caused a delay in vaccine distribution ((CDC), 2003). The COVID-19 pandemic hinders surveillance and immunization programs. Furthermore, it has resulted in a global decline in immunization rates and the cessation of immunization programs, leaving millions of children susceptible to diseases like measles that can be prevented. Low immunization rates promote the virus's transmission, raising the possibility of outbreaks and putting all children who are not vaccinated at risk for infection; for this reason, we must meet and surpass regional targets for the eradication of measles. To provide two doses of the measles vaccine to every child on the planet, vaccination programs should be promoted and reinforced within primary healthcare. Moreover, nations should put in place effective surveillance systems to identify and reduce the immunity gap ((CDC), 2003; Centers for Disease Control and Prevention (CDC), 2003). Based on data from the UNHCR and the Iraqi Ministry of Health, we conducted descriptive analyses to examine the prevalence and resurgence of diseases in Iraq. Despite considerable early effects on the program of national immunization, the Ministry of Health (MoH) of Iraq, and humanitarian organizations were able to keep vaccine operations going, particularly for children. This involves organizing immunization drives to provide the measles, mumps, and rubella (MMR) vaccine to susceptible groups across the country, particularly remote and difficult-to-reach areas. Based on the National Immunization Schedule, children should get the (MMR) vaccine through the ages of four and six, as well as the measles vaccine at nine months and fifteen months. Measles, Mumps, and rubella outbreaks have been reported in Iraq; 30,321 cases of measles were reported in 2009, while 12,815 and 74,212 cases of mumps in 2004 and 2016, respectively, and 290 cases of rubella in 2004 (Lafta & Hussain, 2018). Lafta and Hussain conducted additional analyses to investigate the connection between national vaccination coverage and outbreaks of vaccine-preventable disease. They discovered that variations in vaccination coverage were the catalyst for outbreaks. From 2008–to 2009, Iraq experienced a major measles outbreak, with reported approximately 30,321 cases in 2009 alone. During the outbreak, eleven of the eighteenth governorates reported their highest incidence of the time series. While 8 governorates recorded occurrences greater than 120 per 100,000 people and ten governorates recorded incidences close to or less than 60 incidents per 100,000 people. The governorate that reported the lowest incidence, Dahuk, is the one that is located in the northwest. Its rate was 3.9 per 100,000. Wassit, which is located southeast of Baghdad, reported the highest incidence, 379.3 per 100,000. In 2004, a lesser outbreak was also detected, with 9,081 cases, mostly in the governorates in the south. The four governorates with the highest occurrence this year were Dahuk, Basrah, Muthanna, and Thi-Qar, Fig.1 (Thompson et al., 2023).

6. Measles Resurgence in Iraq: 2016-2024

Iraq has grappled with a significant resurgence of measles since 2016. Several factors contributed to this outbreak, including (Abdulrazzaq et al., 2012; Freidl et al., 2018; Jawad et al., 2021):

- Why Low vaccination rates: Vaccination programs were disrupted nationwide due to civil turmoil and instability. This resulted in a high number of vulnerable people, particularly kids.
- Population displacement: Attempts to vaccinate were made more difficult by internal displacement brought on by conflict. Communities that had been uprooted frequently lacked access to medical care, which increased their susceptibility to measles outbreaks.
- Misinformation and vaccine hesitancy: Misinformation about vaccines and hesitancy to vaccinate children also played a role in the resurgence.

Here's a possible timeline of the measles outbreak in Iraq according to WHO, Konema, CDC, and the Iraqi Ministry of Health:

- **2016:** A rise in measles cases is reported across Iraq, particularly in areas with low vaccination coverage.
- **2018:** A major outbreak occurs, with thousands of cases reported. The government implements emergency vaccination campaigns.
- **2020:** The COVID-19 pandemic disrupts healthcare services, including routine vaccinations, raising concerns about a resurgence of measles.
- **2021-2023:** Continued efforts to control the outbreak with vaccination campaigns, but challenges persist due to vaccine hesitancy and logistical difficulties Fig.2.

- **2024:** The current situation (as of March 2024) is 11595 from one January to 12 March of 2024 therefore being the fifth country in resurgence of measles cases worldwide according to CDC Table1. However, Iraqi health authorities likely continue efforts to control the outbreak through vaccination and public awareness campaigns.

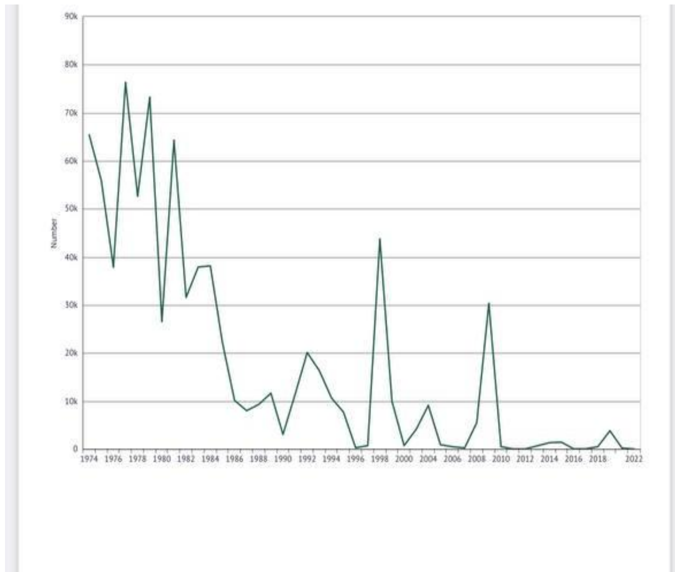

Figure1: Measles Cases In Iraq From 1974 To 2022

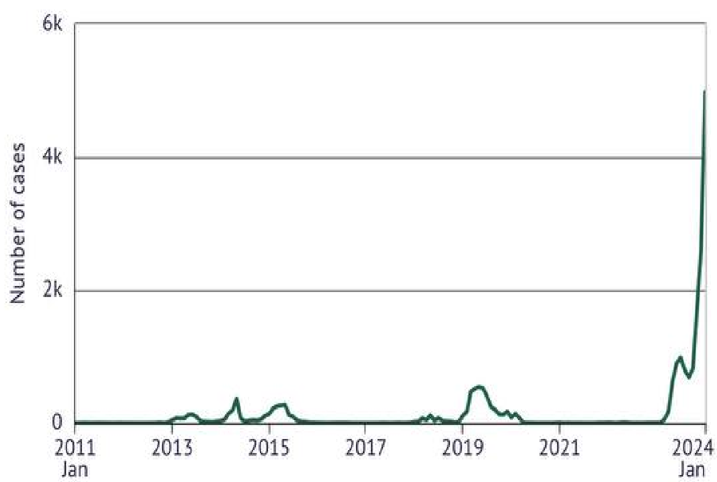

Figure2: Measles Case Resurgence in Iraq During 2024

Table1: Show the Top 10 Countries with Measles Outbreak

Rank	Country	No. of Cases
One	Kazakhstan	21,740
Two	Azerbaijan	13,720
Three	Yemen	13,676
Four	India**	13,220
Five	Iraq	11,595
Six	Ethiopia	9,042
Seven	Kyrgyzstan	7,601
Eight	Russian Federation	7,594
Nine	Pakistan	5,812
Ten	Indonesia	5,648

7. Why Measles Cases Are Rising Right Now

There are several reasons why measles cases are increasing at the moment including; herd immunity, the fact that 95% of people are expected to be vaccinated, even though most nations have been below that threshold for years, and the fact that not enough youngsters are receiving vaccinations. 86% percent of children worldwide had received a vaccination by the time they turned two, but in 2021 that percentage fell even lower to 81% percent. The United States has seen a decline in vaccination rates and a gradual increase in vaccination exemption rates. 93% of kindergarten students received measles vaccinations by the end of the 2021–2022 school year, according to CDC data. Therefore, promoting vaccination of more children is the best strategy to stop further epidemics. Due to tight programs in some countries that require vaccinations of children at specific times, many youngsters are still not inoculated and may find it difficult to become immunized later in life if they miss their window (Bednarczyk et al., 2016; Gambrell et al., 2022).

8. Conclusion

Iraq is currently dealing with a measles outbreak that is spreading due to a decline in vaccination rates. This decline can be attributed to several factors, including vaccine hesitancy, disruptions in healthcare services, and population displacement. The measles outbreak poses a serious threat to public health, especially for young children, so Iraq needs to prioritize raising vaccination rates through public awareness campaigns, better access to healthcare, and addressing vaccine hesitancy.

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