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Original research

Mass immunisation to eradicate Japanese encephalitis: Real-world evidence from Guizhou Province in 2005–2021

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ABSTRACT

Objectives: To explore epidemiological changes of Japanese encephalitis (JE) in a long-time span and evaluate the impact of mass immunisation.
Method: Data on JE cases from hospitals and the county Centers for Disease Control and Prevention in Guizhou Province was collected between 2005 and 2021. Epidemiological changes were analyzed according to a series of policy implementations and the coronavirus disease 2019 (COVID-19) pandemic.
Results: A total of 5138 JE cases and 152 deaths were reported in Guizhou Province during 2005–2021. The average incidence and case fatality rates were 0.83/100,000 and 2.96%, respectively. The JE prevalence showed a declining trend over the years with the reduced incidence gap between age groups and narrowing of the high-epidemic regions. During the COVID-19 pandemic, the JE activity reached its nadir in 2020. The inclusion in the Expanded Program on Immunization of the JE vaccine and catch-up immunisations showed a significant impact on the JE declining incidence rate.
Conclusions: The implementation of JE immunisation programs has played a crucial role in controlling its spread. Continued efforts should be made to maintain high coverage of the JE vaccine and strengthen disease surveillance systems, ensuring JE effective control and eventual elimination.

1. Introduction

Japanese encephalitis (JE) is a mosquito-borne viral disease caused by the Japanese encephalitis virus (JEV), which is a member of the *Flaviviridae* family.[1] The transmission of JEV to humans is mainly through the bite of infected *Culex* species (mainly *Culex tritaeniorhynchus*) mosquitoes.[2] *Culex* species mosquitoes breed in irrigated rice paddies and take aquatic birds and pigs as reservoir and amplifying hosts, respectively.[3] JE was initially recorded in 1871 in Japan and gradually spread to South-East Asia and Western Pacific regions.[4,5] It is still a public health concern around the world.[6] More than three billion people live in areas with JEV transmission risk. Children under 15 years of age are particularly at risk, while surveillance reports in recent years have demonstrated that adults can also be infected.[7,8] JE has high

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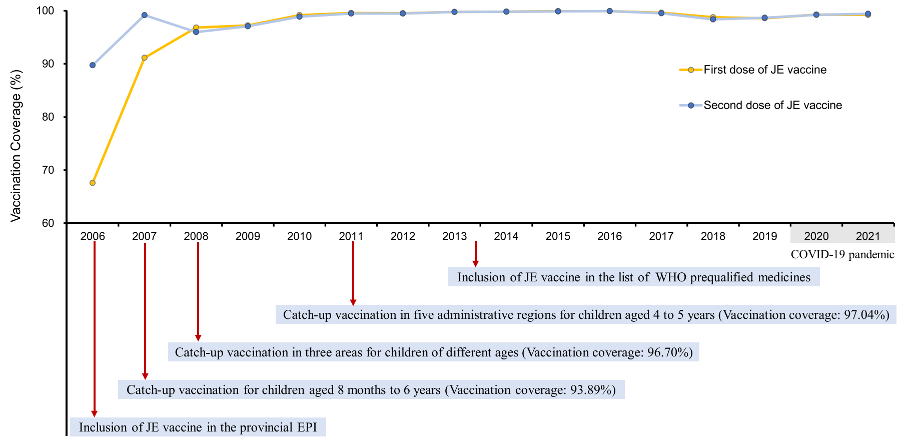

Fig. 1. History of the Japanese encephalitis (JE) prevention, control and vaccination in Guizhou Province. The yellow line and dots represent vaccination coverage of the first dose of JE vaccine. The blue line and dots represent the vaccination coverage of the second dose of JE vaccine.

Table 1
Demographic characteristics of Japanese encephalitis (JE) cases during 2005–2021 in Guizhou Province.

Characteristics	Total		Laboratory-confirmed cases		Clinically-diagnosed cases	
	No. of cases	Incidence rate (/100,000)	No. of cases	Incidence rate (/100,000)	No. of cases	Incidence rate (/100,000)
Overall, n (%)	5138	0.83	3019 (58.76)	0.49	2119 (41.24)	0.34
Gender, n (%)						
Male	3212 (62.51)	1.01	1878 (62.21)	0.59	1334 (62.95)	0.42
Female	1926 (37.49)	0.65	1141 (37.79)	0.38	785 (37.05)	0.26
Age group, years, n (%)						
<3	1341 (26.10)	5.07	714 (23.65)	2.70	627 (29.59)	2.37
3–6	1686 (32.81)	6.87	960 (31.80)	3.91	726 (34.26)	2.96
6–10	1339 (26.06)	3.59	839 (27.79)	2.25	500 (23.60)	1.34
≥10	772 (15.03)	0.15	506 (16.76)	0.10	266 (12.55)	0.05
Region, n (%)						
Bijie	1371 (26.68)	1.20	603 (19.97)	0.53	768 (36.24)	0.67
Qianxinanzhou	545 (10.61)	1.09	440 (14.57)	0.88	105 (4.96)	0.21
Anshun	391 (7.61)	0.98	211 (6.99)	0.53	180 (8.49)	0.45
Zunyi	944 (18.37)	0.86	484 (16.03)	0.44	460 (21.71)	0.42
Qiannanzhou	474 (9.23)	0.80	297 (9.84)	0.50	177 (8.35)	0.30
Liupanshui	384 (7.47)	0.77	279 (9.24)	0.56	105 (4.96)	0.21
Tongreng	389 (7.57)	0.70	274 (9.08)	0.49	115 (5.43)	0.21
Qiandongnanzhou	409 (7.96)	0.65	288 (9.54)	0.45	121 (5.71)	0.19
Guiyang	214 (4.17)	0.29	129 (4.27)	0.17	85 (4.01)	0.11
Others	17 (0.33)		14 (0.46)		3 (0.14)	
Classification, n (%)						
Scattered children	3019 (58.76)		1699 (56.28)		1320 (62.29)	
Kindergarten Children	231 (4.50)		135 (4.47)		96 (4.53)	
Students	1729 (33.65)		1071 (35.48)		658 (31.05)	
Others	159 (3.09)		114 (3.78)		45 (2.12)	

Note: JE, Japanese encephalitis.

mortality and disability rates, as it primarily affects the central nervous system and may result in permanent neurological disorder.[9] As there is no specific treatment immunisation is the most effective means to reduce JE.

JE has been prevalent in China for a long time. The first case in mainland China was documented in 1940.[10] Since 1951, JE cases have been legally reported annually through the monitoring system.[11] The morbidity peak occurred in 1971, when there were more than 170,000 cases reported.[12] Immunization with the JE vaccine was initially conducted in some economically developed provinces in 1968, and gradually extended to some high-epidemic areas since the first live-attenuated vaccine was licensed in 1988.[13] In 2008, the JE vaccine was included in the Expanded Program on Immunization (EPI) in China, administering the first dose to infants aged eight months, followed by a booster dose at two years.[14] After the implementation of immunisation and a series of control measures, JE national morbidity and mortality rates drastically decreased.[15] However, cases are mainly concentrated in the southwestern provinces of China, where they represent one of the serious public health issues.

The incidence rate of JE in Guizhou Province ranks among the highest in China, and has always exceeded the national average rate since 1978.[16] Its subtropical monsoon climate with a high relative humidity and heavy precipitation provides an optimal environment for mosquito breeding.[16,17] As a high-incidence province for JE, it integrated the JE vaccine into the provincial EPI in 2006 and carried out several catch-up immunisations, targeting key populations in high-endemic areas.[18] However, few studies have analyzed the JE epidemiological characteristics in Guizhou Province over a long period, and evaluated the impact of these catch-up immunization programs on JE activity.[19] In addition, the coronavirus disease 2019 (COVID-19) pandemic has had an impact on many infectious diseases, but no studies have assessed the JE incidence during the pandemic in China.[20]

Table 2
Demographic characteristics of Japanese encephalitis fatality cases during 2005–2021 in Guizhou Province.

Characteristics	No. of fatal cases	Case fatality rate (%)	OR (95% CI)	P
Overall, n (%)	152	2.96		
Gender, n (%)				
Male	90 (59.21)	2.80	Reference	
Female	62 (40.79)	3.22	1.12 (0.80–1.55)	0.50
Age group, years, n (%)				
<3	41 (26.97)	3.06	Reference	
3-6	54 (35.53)	3.20	1.13 (0.75–1.72)	0.56
6-10	33 (21.71)	2.46	1.26 (0.69–2.25)	0.44
≥10	24 (15.79)	3.11	1.69 (0.79–3.54)	0.17
Region, n (%)				
Bijie	56 (36.84)	14.58	1.39 (0.75–2.84)	0.32
Anshun	11 (7.24)	5.14	Reference	
Qiannan	14 (9.21)	3.60	1.06 (0.47–2.41)	0.90
Qianxinan	19 (12.50)	3.49	1.21 (0.58–2.66)	0.62
Tongreng	14 (9.21)	3.42	1.25 (0.56–2.88)	0.58
Zunyi	15 (9.87)	3.16	0.55 (0.25–1.25)	0.14
Liupanshui	6 (3.95)	1.53	0.51 (0.17–1.36)	0.19
Qiandongnan	15 (9.87)	1.09	1.30 (0.59–2.93)	0.52
Guiyang	2 (1.32)	0.21	0.32 (0.05–1.20)	0.14
Classification, n (%)				
Scattered children	100 (65.79)	3.31	Reference	
Kindergarten children	6 (3.95)	2.60	0.84 (0.32–1.80)	0.68
Students	39 (25.66)	2.26	0.58 (0.32–1.04)	0.07
Others	7 (4.61)	4.40	1.10 (0.39–2.77)	0.85

Note: JE, Japanese encephalitis; OR, odds ratio.

Therefore, research on the trend of JE prevalence is needed to evaluate and adjust current prevention strategies.

We have performed this study to explore JE epidemiological changes over a long time span and evaluated the impact of mass immunisation, providing real-world evidence for the eradication progress of the JE epidemic.

2. Method

2.1. Study site

Guizhou Province is located in Southwest China with a population of approximately 38 million and a gross domestic product of nearly 2 trillion yuan. It has nine prefectural administrative regions (Guiyang, Anshun, Bijie, Liupanshui, Qiannan, Qiandongnan, Qianxinan, Tongren, and Zunyi) and 88 counties.

2.2. Data resource and management

Implemented in 2005, the National Notifiable Disease Reporting System (NNDRS) collected JE cases from hospitals and the county Centers for Disease Control and Prevention (CDC) to the national CDC, through a web-based computerized reporting system. Cases were diagnosed according to the diagnostic criteria for JE (WS214-2008).[21] A clinically diagnosed JE case is defined as follows: (1) inidividuals with onset of symptoms living in JE endemic area or who have been to a JE endemic area within 25 days before the onset of symptoms during the mosquito breeding season; (2) individuals with symptoms of acute onset, such as fever, headache, projectile vomiting, and varying degrees of disturbance of consciousness after 2−3 days of fever onset; (3) individuals with an absence of superficial reflexes, enhanced hyperreflexia, meningeal irritation, pathological reflexes, spastic paralysis, decerebrate rigidity, alteration of pupil size, elevated blood pressure, and decreased heart rate; (4) individuals with a high white blood cell count ($10–20 \times 10^9$/L), with neutrophils accounting for more than 80%, increased intracranial pressure, and clear cerebrospinal fluid (CSF) appearance. A clinically diagnosed JE case whose serological testing with JEV-specific IgM in a single CSF or serum sample is positive, virus isolation confirmsing JEV, or a reverse transcriptase PCR showing specific JEV nucleic acid can be defined as a laboratory-confirmed case.

Data including clinically diagnosed and laboratory-confirmed JE cases in Guizhou Province between 2005 and 2021 was derived from the NNDRS. Demographic data including gender, age, region, and classification was collected from each patient. Population data was collected from the Guizhou Province Statistics Yearbook. This research project was approved by the Institutional Review Board of the Guizhou CDC (Q2023-10).

2.3. Data analysis

Categorical variables were summarized as frequencies and proportions. The overall incidence rate was all ages and defined as the number of both clinically diagnosed and laboratory-confirmed JE cases per 100,000 population per year. Age and gender-specific incidence rates were calculated as the number of JE cases in each group divided by the population of each group. The overall case fatality rate was calculated as the number of fatal cases divided by the number of all cases diagnosed per year. Age- and gender-specific case fatality rates were calculated as the number of fatal cases in each group divided by the number of all cases diagnosed in each group. Seasonal and annual trends of JE cases were analyzed and graphed using time-series plot, broken down into the general population, different gender and age groups. A joinpoint analysis with the Joinpoint Regression Program (version 4.1.1.1) from the Surveillance Research Program of the US National Cancer Institute (http://surveillance.cancer.gov/joinpoint) was used to model rates and to calculate the estimated Annual Percent Change (APC) with 95% confidence interval (CI). Statistically significant changes (joinpoints) in trend were estimated by APC. APC values that were positive or negative represented an upward or declining trend, respectively.

The JE yearly-specific incidence rate at a county level was mapped using the ArcGIS10.2.2 software. Moran's I spatial autocorrelation statistics was then calculated using global spatial autocorrelation analysis to determine if the JE incidence rate at the county level was clustered, dispersed, or random. We used the Getis-Ord Gi* spatial autocorrelation tool to measure the level of spatial interdependence between the county level incidence rate, and the nature and strength of that interdependence.

We have compared the JE incidence rate during different time periods by using the rate ratio (RR) and 95% CI to demonstrate the impact of a series of policy implementations and the COVID-19 pandemic. To evaluate the association between demographic variables (gender, age groups, region, and classification) and case fatality rate, a logistic regression model was performed to calculate the adjusted odds ratio (OR) and 95% CI. All statistical tests were two-sided, and statistical significance was determined using a level of $P < 0.05$.

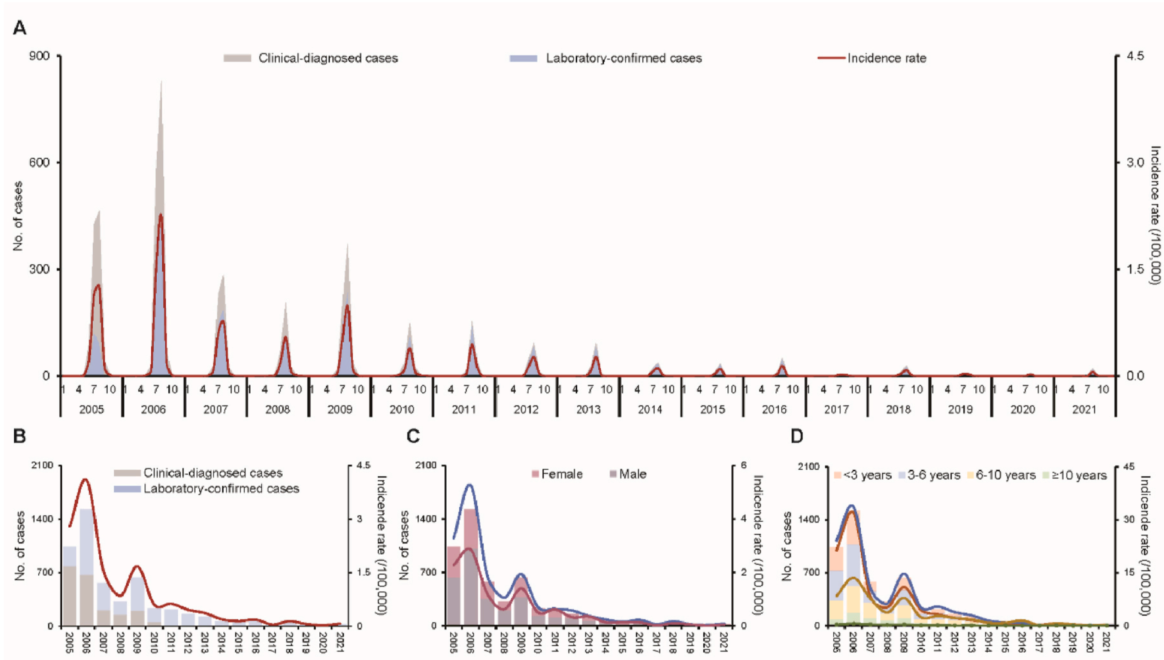

Fig. 2. Japanese encephalitis (JE) incidence rate in Guizhou Province from 2005 to 2021. (A) Overall incidence rate by month among the overall population. Incidence rates included all ages and based on all JE cases. (B) Incidence rate of JE by year among the overall population. Incidence rates included all ages and based on all JE cases. (C) Gender-specific incidence rate of JE in males and females. Gender-specific incidence rates were calculated as the number of all males or females JE cases divided by the male or female population of Guizhou Province every year. (D) Age-specific incidence rate of JE in different age groups. Age-specific incidence rates were calculated as the number of all JE cases in each age group divided by the population of every age group in Guizhou Province every year.

3. Results

3.1. History of JE prevention, control and JE immunisation in Guizhou Province

The JE vaccine was added into the provincial EPI in 2006, and since then vaccination coverage of the target population has remained at a high level, close to 100% (Fig. 1). There were three JE vaccine catch-up immunization campaigns in Guizhou Province. The first one was carried out in the whole province during May-June 2007, targeting children aged 8 months to 10 years. Among them, rural children aged 8 months to 6 years were vaccinated free of charge and the catch-up vaccination coverage was 93.89%. In April 2008, the second JE vaccine catch-up immunization campaign was implemented for children aged 8 months to 10 years in 31 counties. The specific implementation was to immunise children aged 8 months to 10 years in five counties, those aged 8 months to 6 years in eight counties and those aged 7–10 years in 18 counties for free. The catch-up vaccination coverage was 96.70% in 2008. In April 2011, the last round of catch-up vaccination was conducted for free in five administrative regions for the children born in 2006 and 2007 (aged 4−5 years), with a catch-up vaccination coverage of 97.04%. All vaccines in the routine and catch-up immunizations were live attenuated. The World Health Organization (WHO) added the JE vaccine to its list of prequalified medicines at the end of 2013.

3.2. Characteristics of JE cases and deaths

During 2005–2021, a total of 5138 JE cases was reported in Guizhou Province, of which 58.76% (3019/5138) were laboratory confirmed (Table 1). The overall incidence rate was 0.83/100,000, and males had a higher incidence rate (1.01/100,000) than females (0.65/100,000). Children aged 3-6 years had the highest incidence rate (6.87/100,000), followed by those under three years of age (5.07/100,000), while individuals aged over ten years had the lowest rate (0.15/100,000). The three cities with the most cases were Bijie (1371, 26.68%), Zunyi (944, 18.47%), and Qianxinan (545, 10.61%). Most cases were scattered children (3019, 58.76%).

Among 5138 JE cases, there were 152 fatalities with a case fatality rate of 2.96% (**Table 2**). Males (90, 59.21%), those aged 3-6 years (54, 35.53%), those living in Bijie and scattered children represented the majority of deaths.

Most cases occurred during the months of July–August (Fig. 2A). The JE incidence rate had an undulating trend during 2005–2009, with peaks observed in 2006. A slight rebound was observed in 2009. Then the incidence rate dropped and remained consistently low (Fig. 2B). The incidence rate in males was higher than that in females during 2005–2021 (Fig. 2C). Incidence rates in children aged under three years and 3-6 years were relatively high in 2005 and 2006, and close to those of other age groups after 2006. Gaps in the JE incidence rates among different age groups gradually narrowed and finally tended to be similar (Fig. 2D).

The joinpoint regression model showed a continued declining trend of the JE incidence rate in Guizhou Province during 2005–2021 (Fig. 3A). A significant decline was observed between 2005 and 2017 with a negative APC of 26.4% (95% CI -31.7%, -20.8%). Before the age of four years, the incidence rate increased with age (APC 36.9%, 95% CI: -15.0%, 120.3%) (Fig. 3B). Afterwards it decreased with increasing age, with the APC of -18.0% (95% CI: -33.7%, 1.4%), -74.0% (95% CI: -89.9%, -32.6%), and -16.4% (95% CI: -24.7%, -7.3%) for the age of 4–9 years, 9−25 years and above 25 years, respectively.

The geographical distribution in Guizhou Province illustrates the regional differences of JE prevalence (Fig. 4). Cases occurred in all counties, especially in 2005 and 2006. Before 2008, prevalence was mainly concentrated in counties with a previous epidemic. In 2009, epidemics had emerged in many low incidence counties. Since then, the number of counties with JE cases had gradually decreased. The global Moran's I index (0.493, $P < 0.001$) indicated spatial structure in the JE prevalence. Spatial statistical analysis of each period showed that JE cases mainly emerged in the southwestern part of Guizhou Province (Fig. S1).

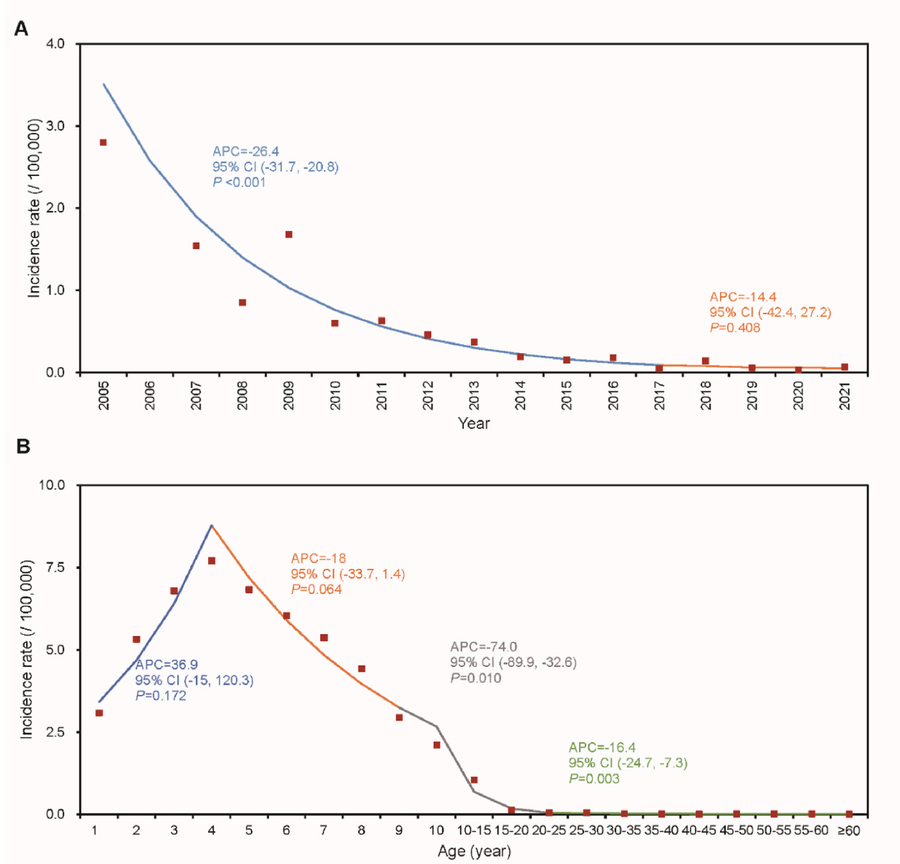

Fig. 3. The joinpoint regression of annual incidence rate of Japanese encephalitis (JE) and age-specific incidence rate in different age groups. (A) Joinpoint regression of annual incidence rate from 2005 to 2021. (B) Joinpoint regression of age-specific incidence rate in different age groups. Age-specific incidence rates of different age groups were defined as the cumulative number of JE cases in that age group divided by the cumulative population of that age group in Guizhou Province between 2005 and 2021.

3.3. Comparison of JE incidence and case fatalityratest over different periods

According to the history of JE prevention and control and the COVID-19 pandemic, JE cases and fatal cases were divided into four groups, respectively. The incidence of JE cases was significantly higher during 2005–2006 compared to that during 2007–2013, 2014–2019 and 2020–2021 (Fig. 5A). Differences in gender and age groups were further analyzed and the same trend in incidence rates of all JE cases was observed (Fig. 5B and C).

Unlike the continuing downward trend in the incidence rate, the case fatality rate in all cases maintained an upward trend in the first three periods and decreased during 2020–2021 except for those aged 3-6 years (Fig. 6). There were few fatal cases during 2014–2019 and 2020–2021, and most of them were clinically-diagnosed ones, particularly in the latter three periods.

3.4. Impact of the JE catch-up immunissation programs on its prevalence

The JE incidence rate has changed significantly over the implementation periods of the policy of catch-up vaccinations (Fig. 7). When the province's large-scale vaccination policy was first implemented during May-June 2007 and partially implemented during April 2008, the incidence rate in rural and urban children aged 8 months to 6 years dropped sharply, from 22.36/100,000 to 4.98/100,000 (RR = 0.22, 95% CI 0.20−0.25, P < 0.001), and 2.10/100,000 to 0.75/100,000 (RR = 0.36, 95% CI 0.32−0.40, P < 0.001), respectively (Fig. 7A and Table S2). However, the epidemic rebounded when catch-up vaccination was halted in 2009, which was more pronounced among rural children.

After analyzing the JE incidence rate in children of different age groups when the catch-up vaccination had been implemented during April 2008, it was observed that the rate in children who had received the catch-up vaccination continued to decline while it rebounded in children who had not received the catch-up vaccination (Fig. 7B). The incidence rate in different age groups after catch-up immunization dropped sharply during the catch-up vaccination, from 30.69/100,000 to 10.23/100,000 (RR = 0.33, 95% CI 0.24−0.46, P < 0.001), 15.79/100,000 to 5.47/100,000 (RR = 0.35, 95% CI 0.27−0.45, P < 0.001) and 31.93/100,000 to 9.51/100,000 (RR = 0.30, 95% CI 0.23−0.39, P < 0.001) for children aged 8 months to 6 years, children aged 7−10 years, and children aged 8 months to 10 years, respectively.

The JE incidence rate in children aged 4−5 years who had received the catch-up vaccination in 2011 continued to decrease (7.01/100,000 from July 2010 to June 2011, 5.47/100,000 from July 2011 to June 2012, and 3.08/100,000 from July 2012 to June 2013) (Fig. 7C), while the JE rate in children aged 4−5 years who had not received the catch-up vaccination in 2011 increased and then decreased slightly (3.87/100,000 from July 2010 to June 2011, 7.75/100,000 July 2011 to June 2012, and 6.46/100,000 July 2012 to June 2013).

4. Discussion

The JE incidence rate in Guizhou Province showed a significantly declining trend during 2005-2021, while a slight declining trend of JE case fatality rate was observed during 2005–2019. Children aged 3-6 years had the highest JE incidence rate but the gap in JE incidence rates among different age groups was gradually decreasing. The geographical distribution of JE cases is gradually shrinking. Mass

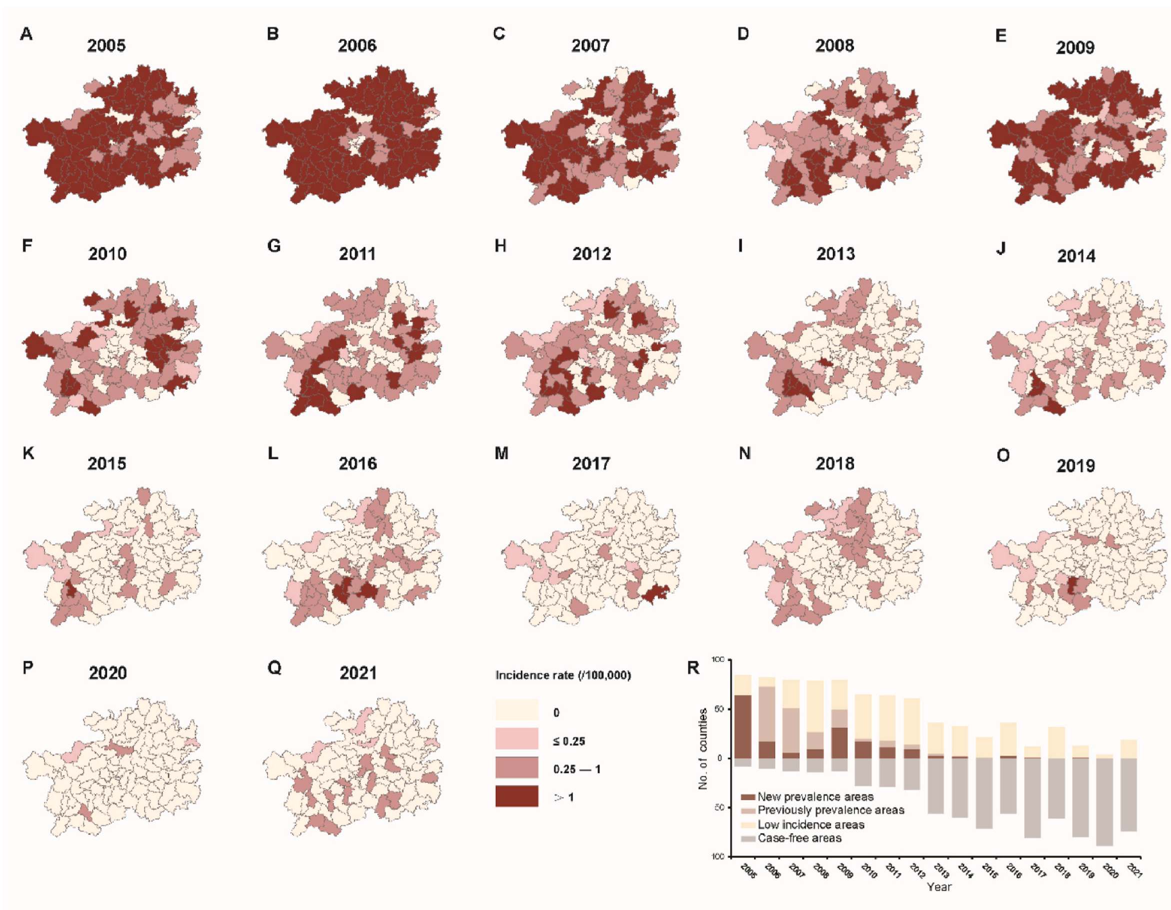

Fig. 4. **Geographical distribution of Japanese encephalitis (JE) cases in Guizhou Province.** (A–Q) Annual geographical distribution of the overall incidence rate from 2005 to 2021. (R) Number of counties with different prevalence levels per year. The JE incidence rate was divided into four levels (0, ≥0.25/100,000, 0.25/100,000–1/100,000 and > 1/100,000). Areas with an incidence rate greater than 1/100,000 are classified as prevalence areas. Areas with an incidence rate between 0.25/100,000 and 1/100,000 and less than 0.25/100,000 are classified as low incidence areas. Areas with no cases are classified as case-free areas.

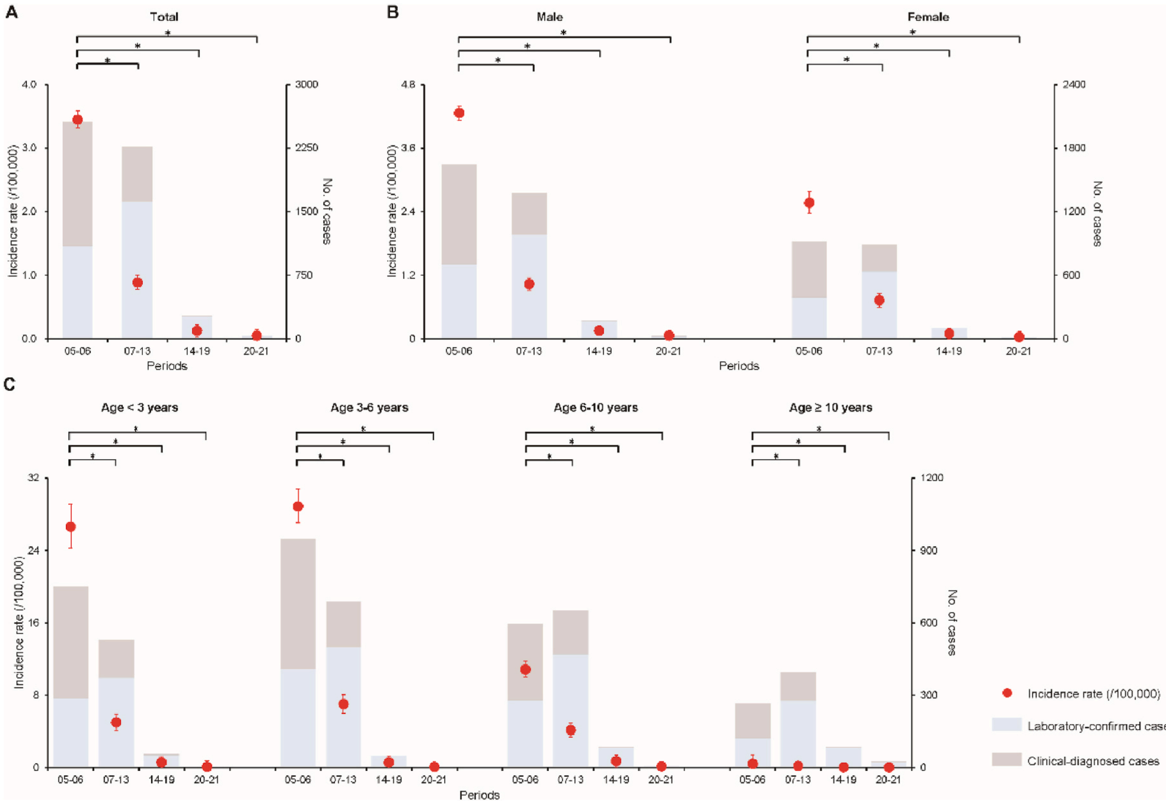

Fig. 5. Dynamics of the incidence rate of Japanese Encephalitis (JE) during four time periods. (A) Overall incidence rate of JE cases during four time periods among the overall population. (B) Gender-specific incidence rate of JE cases during four time periods among males and females. (C) Age-specific incidence rate of JE cases during four time periods among different age groups.

immunization has played an important role in eradicating JE. A catch-up vaccination targeted in the high-epidemic regions has shown a significant impact on the decline of JE incidence.

JE has been a significant public health concern in Guizhou Province for a while.[16,17,22] A series of intervention programs including routine and catch-up vaccination, enhanced surveillance, and diagnosis ability, have been implemented and were effective in eliminating JE.[13,23] The he JE vaccine has been shown to prevent the disease. In China, the JE incidence decreased significantly, with a marked reduction in the incidence rate after the inclusion of the JE vaccine in the EPI (4.072/100, 000 during 1970–2007 *vs*. 0.122/100,000 during 2008–2020).[24] In other countries, JE vaccination has been associated with a decline in JE incidence.[25,26]

Due to those control measures, the JE epidemiological characteristics in Guizhou Province have changed, especially in the reduction of JE cases and changes in age structure. Children under 15 years are the high-risk group and the key population for immunization over the years.[7] Substantial reduction in the incidence rate of the high-risk group confirms the effectiveness of vaccination and makes JE elimination just around the corner.[13] However, the age structure of has changed slightly as the incidence rates in all age groups are close to each other, indicating that the older age groups may now be at more risk since they were not emphasized in the vaccination programs.[5] Studies conducted in other provinces in China and other countries have observed a modest shift of age prevalence towards adults.[8,27,28] A change in the immunization policy in Guizhou Province, focusing upon all age groups needs to be brought to our attention. In addition to strengthening JE vaccination among children and adults whose occupation is related to mosquito exposure and farming in high-risk areas such as Bijie, Zunyi, and Qianxinan, should be encouraged. In addition, it should be noted that although the number of deaths in recent years was small, most of them were clinically-diagnosed cases, and it is urgent to improve the medical capacity of diagnosis and treatment in the areas where deaths were located.

JE cases have been reported in all the counties in Guizhou Province. Every year, its regional distribution undergoes some changes, which is reflected in the fact that some areas alternately become the new prevelance areas of the year. Although the areas where JE cases occur are gradually shrinking, there are also cases observed in areas without previous cases in recent years. The implementation of immunization and other preventive and control measures is still an important issue that cannot be ignored.[22]

Studies have confirmed that humans can develop protective neutralizing antibodies after receiving primary immunization with the JE vaccine which can be effectively maintained for more than five years.[29,30] Since the vaccine was included into the provincial EPI in 2006, it has enabled susceptible populations to continuously build immune responses and help prevent disease. However, routine immunization is aimed at children born after 2006, and there are still a large number of susceptible people who have not been immunized. The three waves of the province's large-scale catch-up vaccination programs have been carried out for this part of the susceptible population. In 2007, free catch-up immunization for children aged 8 months to 6 years in rural areas achieved great success, and the effect of reducing morbidity is more significant than that of urban areas. This is due to the fact that there were many high-risk populations in rural areas and the coverage of catch-up vaccination was relatively higher. On the basis of the catch-up immunization in 2007, the catch-up vaccination for different age groups in specific high-epidemic areas in 2008 also showed remarkable effects, and the decrease of incidence rates was most pronounced in the expanded age group (8 months–10 years). However, an obvious rebound of the incidence rate in children who had not been in the catch-up vaccination program was observed. While the catch-up vaccination in 2011 showed a longer lasting effect in JE reduction it has been suggested

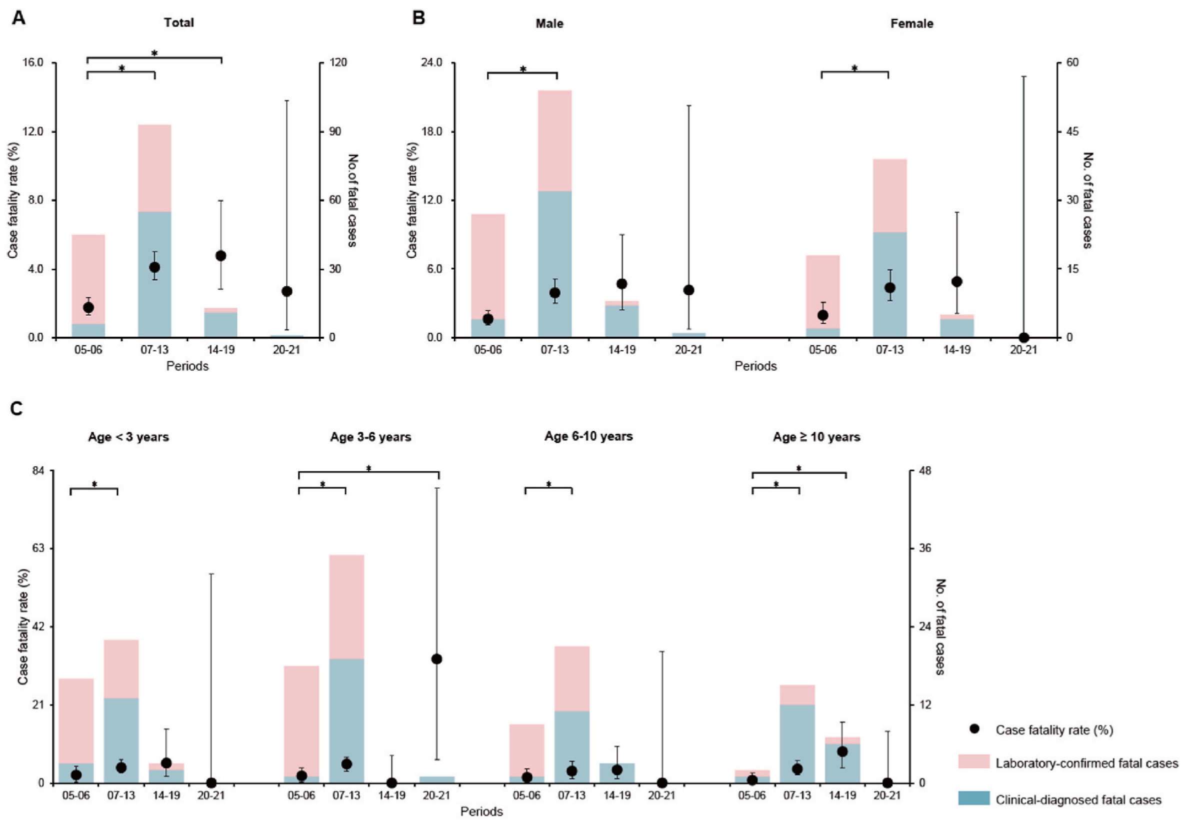

Fig. 6. Dynamics of the case fatality rate of Japanese encephalitis (JE) during four time periods. (A) Case fatality rate in all cases during four time periods among the overall population. (B) Gender-specific case fatality rate in all cases during four time periods among males and females. (C) Age-specific case fatality rate in all cases during four time periods among different age groups.

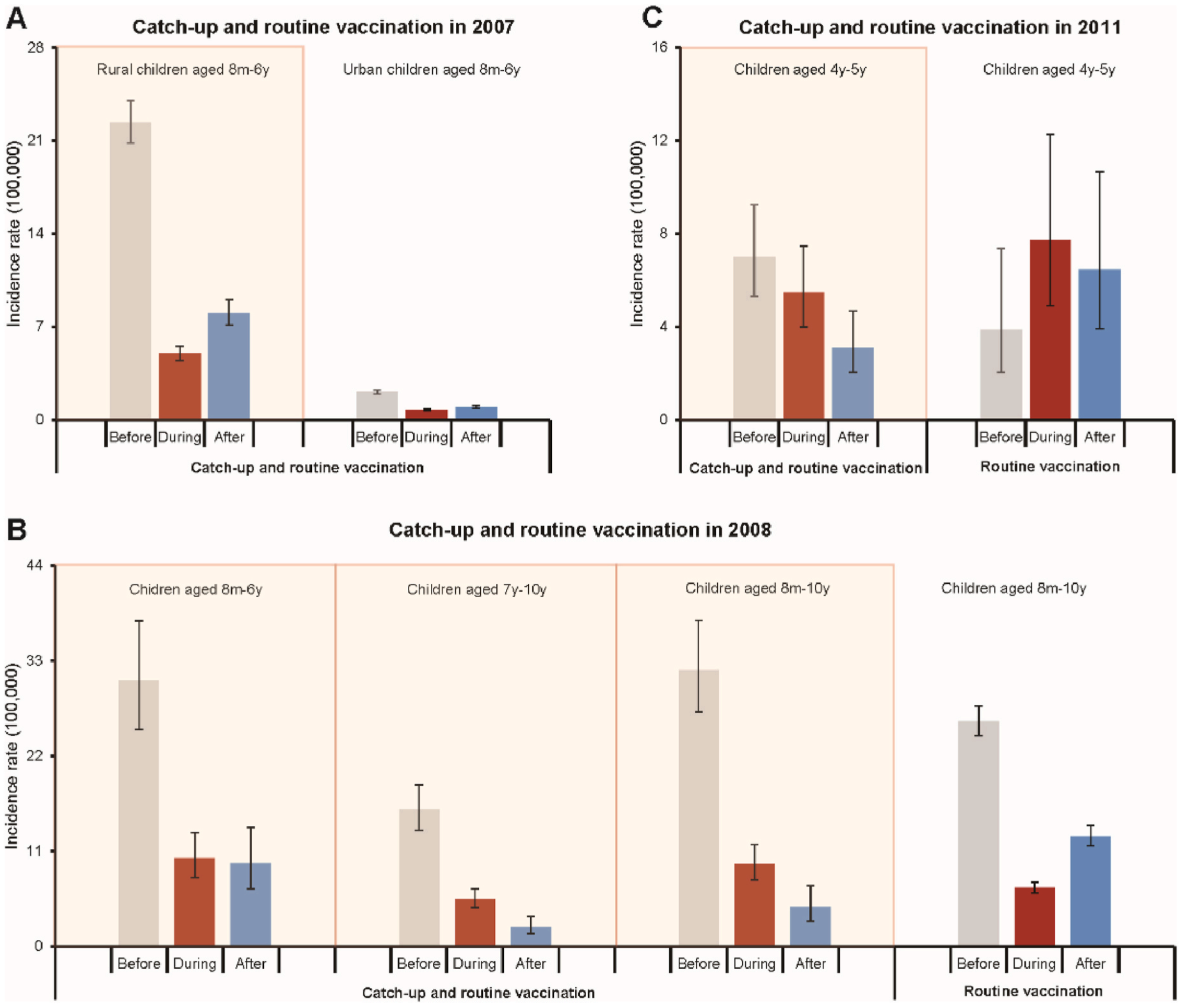

Fig. 7. Dynamics of the incidence rate of Japanese encephalitis (JE) during catch-up vaccinations. (A) Incidence rate of rural and urban children aged 8 months to 6 years. 'Before' refers to the period from July 2006 to June 2007, 'during' refers to the period from July 2007 to June 2009 and 'after' refers to the period from July 2009 to June 2010. (B) Incidence rate of JE in catch-up and routine vaccination and routine vaccination age groups. 'Before' refers to the period from July 2006 to June 2007, 'during' refers to the period from July 2007 to June 2009 and 'after' refers to the period from July 2009 to June 2010. (C) Incidence rate in children aged 4−5 years in catch-up and routine vaccination and routine vaccination area. 'Before' refers to the period from July 2010 to June 2011, 'during' refers to the period from July 2011 to June 2012 and 'after' refers to the period from July 2012 to June 2013.

that the establishment of immunity in susceptible populations is a long process. Cessation of the catch-up vaccination programs in 2009 may have resulted in previously unimmunized populations becoming infected during the JE epidemic season.[17] In addition to vaccination, the JEV activity is affected by ecological, environmental, climatic, and behavioral factors in humans.[31] Enhanced surveillance of these associated factors before and after the epidemic season, and supervision of the implementation of routine vaccination are crucial for JE elimination.

The non-pharmaceutical interventions against the COVID-19 pandemic implemented worldwide have slowed or even stopped the spread of several infectious diseases.[20,32,33] In this study, we have found that the JE incidence rate in Guizhou Province dropped to its nadir after the outbreak of COVID-19 in 2020, but a slight rebound occurred in 2021. During the initial stages of the COVID-19 pandemic, the limitation in people's movements resulted in a decrease in JE transmission. However, some studies have reported that the vaccination against diseases other than COVID-19 dropped in the early months of the pandemic.[34,35] It is possible that the same problem also emerged in JE immunisation programs, which implies that the number of children and adults who are not protected against JEV may have escalated. This could be one of reasons for the rebound of the incidence rate in 2021. It suggests that the risk of a JE epidemic occurring is still high and preventive measures in Guizhou Province must not be disregarded.

There are several limitations to our study. It was a retrospective analysis, based on surveillance data. Therefore, there were some unmeasured biases and causal inferences cannot be assumed. The JE incidence rate in Guizhou Province may be underestimated since somecases were asymptomatic and have subclinical symptoms, leading to an underreporting in the passive surveillance system. Besides, the COVID-19 pandemic has shifted the focus to COVID-19 prevention and control, neglecting JE surveillance to some extent.

5. Conclusion

The incidence of JE has significantly decreased and its geographic distribution narrowed with the addition of the JE vaccine to the EPI and catch-up vaccinations and other control measures. The JE implementation vaccination programs have played a crucial role in controlling the disease spread, with substantial progress being made towards eliminating it entirely. The ongoing efforts to keep high vaccine coverage and to strengthen the disease surveillance systems must continue to ensure that JE remains under control, and eventually, is eliminated.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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CRediT authorship contribution statement

Wan-Xue Zhang: Data curation, Formal analysis, Methodology, Visualization, Writing – original draft. **Suye Zhao:** Data curation, Formal analysis, Methodology, Visualization, Writing – original draft. **Chunliu Pan:** Data curation, Formal analysis, Methodology, Visualization, Writing – original draft. **Yiguo Zhou:** Data curation, Writing – review & editing. **Chao Wang:** Data curation, Writing – review & editing. **Liping Rui:** Data curation, Writing – review & editing. **Juan Du:** Data curation, Writing – review & editing. **Ting-Ting Wei:** Data curation, Writing – review & editing. **Ya-Qiong Liu:** Data curation, Writing – review & editing. **Ming Liu:** Conceptualization, Formal analysis, Supervision, Writing – review & editing. **Qing-Bin Lu:** Conceptualization, Funding acquisition, Methodology, Supervision, Validation, Writing – review & editing. **Fuqiang Cui:** Conceptualization, Funding acquisition, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

None.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jve.2024.100366.

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