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A Decadal Trend Analysis of Measles Cases in Rajasthan and Future Prediction using ARIMA Model: An Observational Study

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ABSTRACT

Introduction: Measles, a highly transmissible disease marked by fever and a maculopapular rash, posed a substantial threat to life in the 1960s. Nevertheless, the advent of the measles vaccine had a profound impact, significantly diminishing its toll on mortality. Similarly, through effective influenza surveillance and early epidemic warning systems, public health officials can timely identify influenza trends and provide crucial scientific support for prevention and control measures. This proactive approach holds great public health significance.

Aim: To analyse the long-term trend of measles cases in Rajasthan, India, and the impact of Coronavirus Disease-2019 (COVID-19) on it, with future predictions using Auto-Regressive Integrated Moving Average (ARIMA) modelling.

Materials and Methods: The present study was a retrospective, descriptive observational study in which monthly diagnosed measles cases were collected from the Measles Rubella Laboratory, Department of Microbiology, Sawai Man Singh Medical College, Jaipur, Rajasthan, India, for the period of April 2010 to April 2023. An ARIMA model was developed using data from 2010 to 2020 to predict the monthly number of measles cases in 2021. The predicted values were then compared to the actual cases in 2021 to assess the model's accuracy.

Results: Out of the total positive cases, males were slightly more prone to acquire infection than females (1734 males, 54%; 1477 females, 46%). The monthly index for new measles cases ranged from 0.11 to 2.6. It reached its lowest point in July (0.106) and August (0.25) and peaked in March (2.594) and April (1.84). The overall trend was fluctuating; however, the incidence of measles cases clearly increased after the year 2021. The difference between observed cases and predicted cases for the period of April 2020 to December 2021 was not statistically significant (t-value=0.261 and p-value=0.797).

Conclusion: The fluctuating trend of measles was observed during the last decade; however, the observed cases of measles showed an upward trajectory during and after the COVID-19 outbreak. This study also highlighted the monthly index of the measles cases, which peaked in March to April and was lowest in July to August.

Keywords: Auto-regressive integrated moving average, Coronavirus disease-2019, Influenza-like illness, Monthly index

INTRODUCTION

Measles is a highly contagious disease caused by the Paramyxovirus of the genus Morbillivirus, primarily affecting the respiratory system [1]. It is mainly characterised by fever and a maculopapular rash and is spread by coughing and sneezing, with a secondary attack rate of 90% [2,3]. Measles was one of the major causes of mortality in the 1960s, before the introduction of vaccination for measles, with an estimated 135 million cases per year and 7-8 million deaths globally [4]. Vaccination had a major impact on the death rate, decreasing it by 79% from an estimated 6.5 lakh in the year 2000 to 1.3 lakh in the year 2015 globally [4].

India contributes significantly to the global death rate due to the higher prevalence of malnutrition and case fatality rates [5]. In the year 2015, India reported 61,255 measles cases, with Rajasthan accounting for 1,769 cases [6]. In 1985, measles vaccination was introduced in the Universal Immunisation Programme of India, but due to low routine coverage and the vaccine's effectiveness, large groups of children remained susceptible to it in subsequent years [7]. In 2010, as per the National Technical Advisory Group on Immunisation (NTAGI), the Government of India introduced the second dose of the measles vaccine for children under the National Immunisation Programme [8,9].

Studies indicate that measles eradication is technically feasible with available vaccines [10]. Despite the availability of vaccines up to the village level, provided free of cost to the end-user, and vaccination coverage of 78% as per the Rapid Survey on Children (RSOC-2013-14) [11], the country still grapples with the morbidity and mortality of measles, indicating a large cohort of children are left unvaccinated [12]. Therefore, the rationale of the study was to examine the trend of measles over the last decade and identify factors affecting the spread of the disease, including vaccine coverage.

The aim of the study was to analyse the long-term trends of measles cases in Rajasthan, India, the impact of COVID-19 on measles trends [3], and the prediction of expected cases in the future using ARIMA modelling.

MATERIALS AND METHODS

A retrospective, record-based, descriptive observational study was conducted at the Measles Rubella Laboratory, Department of Microbiology, Sawai Man Singh Medical College, Jaipur, Rajasthan, India. The Measles Rubella Laboratory, affiliated with SMS (Sawai Man Singh) Medical College, Jaipur, Rajasthan, stands as one of the largest laboratories in the state of Rajasthan (Lab ID- 265), under the World Health Organisation (WHO) surveillance project. It serves as the primary testing facility for measles and rubella cases, covering all districts (under the measles surveillance programme) within the state of Rajasthan. Serum samples from suspected cases of measles with presenting symptoms of fever and rash were received in the Measles Rubella Laboratory. These samples were accompanied by demographic information, clinical details, and vaccination history provided in a standardised Laboratory Requisition Form (LRF).

All received samples were tested by Enzyme-Linked Immunosorbent Assay (ELISA) for the presence of Anti-IgM antibodies for measles. In the period from 2010 to 2018, ELISA kits from "Siemens Pvt., Ltd.," and later from "Euromine Pvt., Ltd.," were used. Results were generated and reported within 48 hours of sample receipt, utilising the WHO software, previously in Epi and later in the Vaccine Preventable Diseases Surveillance Information Management System (VSIMS).

Data collection and analysis: A monthly number of diagnosed measles cases were taken from the records of the Measles Rubella Laboratory over the period from April 2010 to April 2023. The datasets of monthly new cases were divided into two segments [1]. The data spanning from April 2010 to April 2023 were utilised to analyse long-term trends, monthly variations/index in cases, and make predictions for expected cases of measles during and after COVID-19 [2]. Additionally, observed data for the monthly cases from April 2020 to December 2021 were used to compare the expected versus observed cases of measles.

The utilisation of the ARIMA model involved the analysis of time series data and forecasting of measles cases, with the goal of offering scientific evidence to support prevention and control efforts. This model has three stages that explain the methodology of the present study based on these three stages: model identification, model estimation and validation, and model application.

In the initial phase, the study evaluated the viability of differentiating monthly measles cases by investigating stationarity and seasonality. If seasonality is observed, we will opt for a seasonal ARIMA model. Ultimately, considering the clear manifestation of seasonal characteristics in the new measles cases and their classification as time series data, we affirm the ARIMA model as the most suitable approach for predictive analysis in our study [13].

STATISTICAL ANALYSIS

The data were input into Excel 2019, and the time series ARIMA model was constructed and analysed using Statistical Package for Social Sciences (SPSS) 28.0. Initially, the monthly incidence rate of measles cases was computed. To facilitate ARIMA modelling, the prerequisite of stationarity was examined. If the data series was determined to be non stationary during application, a process involving differencing and/or data conversion was applied to transform it into a stationary time series.

Following that, the ARIMA model was utilised for prediction and analysis, adopting the format ARIMA (P,D,Q), where 'P' denoted the autoregressive order, 'D' represented the difference order, and 'Q' signified the moving average order. The values of 'P' and 'Q' were determined through an examination of the Autocorrelation Function (ACF) diagram and Partial ACF (PACF) diagram derived from the stationary series. The fitted ARIMA model was identified using the expert modeller of SPSS software.

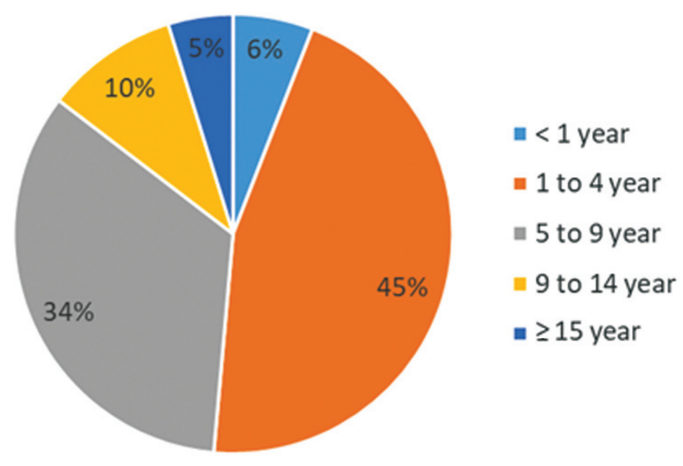
Next, the least square method was utilised to estimate the parameters of the selected model, and the significance of the Ljung-Box Q statistic was tested. A series of assessments, including goodness-of-fit tests, white noise tests, and parameter independence tests, were conducted to evaluate the fitting effect of the model. The parameter independence test was employed to assess the independence and randomness of the ACF and PACF.

In the last step, the data were adjusted according to the best-established ARIMA model, and a comparative analysis was carried out by contrasting it with the actual incidence to assess the predictive effectiveness of the model. The identification of the best-fitted ARIMA model was determined with the assistance of the expert modelling capabilities of the SPSS software (version 23).

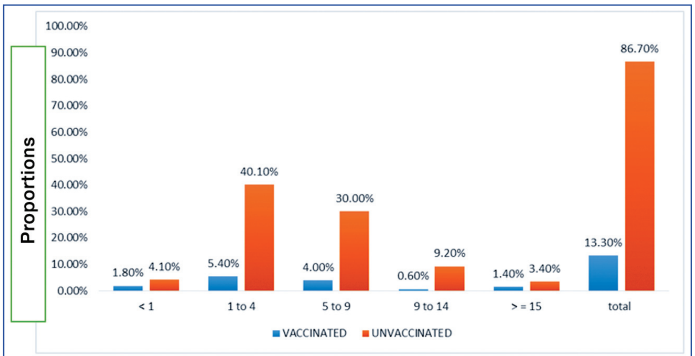
Ethical clearance: The study was conducted under the WHO surveillance project, and samples were received from different areas of the state with patient details in the LRF. Consent was obtained at the point of sample collection by the WHO surveillance team. Confidentiality has been maintained, and the information obtained has been used only for academic purposes. The last author (SKS) has been working as the Director of the WHO accredited laboratory at SMS Medical College, Jaipur, Rajasthan, India, under the WHO surveillance project for Measles and Rubella; hence, no ethical clearance was required.

RESULTS

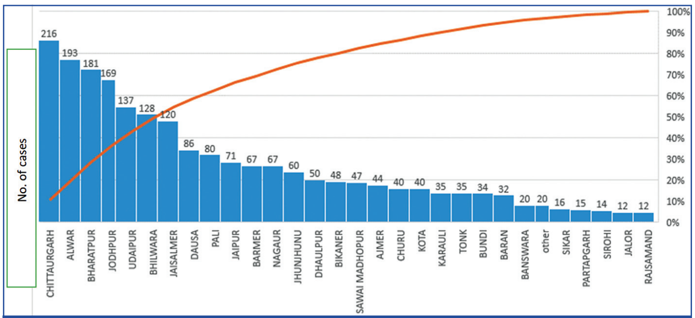
Out of a total of 10,285 samples, 3211 (31.22%) tested positive for anti-IgM antibodies against measles from April 2010 to April 2023. Among all 3,211 measles cases, 1,734 (54%) were males, while 1,477 (46%) were females. The overall attack rate was 25.7% over the period, ranging from 4% to 75%, with the maximum attack rate in 2011 followed by 2010 (73%) and 2015 (69%). The distribution of cases based on age, age with vaccination status, and geographical location is depicted in [Table/Fig-1-3], respectively.



[Table/Fig-1]: Distribution of cases as per age.



[Table/Fig-2]: Distribution of measles cases as per their vaccination status.

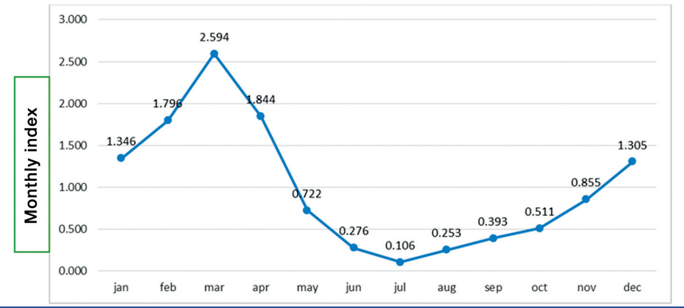


[Table/Fig-3]: Distribution of measles cases as per their geographical locations (districts).

Monthly variation of measles cases: The monthly index for new measles cases ranged from 0.11 to 2.6. It reached its lowest points in July (0.106) and August (0.25) and peaked in March (2.594) and April (1.84). [Table/Fig-4] illustrates the monthly indices for each month.

Trend Stabilisation

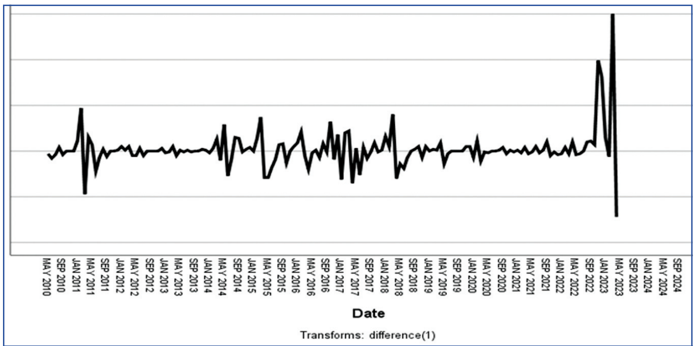
The time series diagram of monthly measles cases in Rajasthan state from April 2010 to April 2023 was plotted. It can be seen from the graph that the sequence of cases did not exhibit stationarity, and the overall trend was fluctuating. However, the incidence of measles



[Table/Fig-4]: Monthly index of new measles cases.

cases clearly increased after the year 2021. Trend stabilisation is essential before applying ARIMA models to time series data to ensure stationarity. This process simplifies modelling, enhances forecasting accuracy by focusing on short-term fluctuations, and improves model interpretability by separating long-term trends from short-term dynamics.

To meet the prerequisites (stationary data, constant variance) for ensuring the stability of model modelling, the heteroscedasticity of the data series was addressed by eliminating it, and the original data underwent differentiation to mitigate its impact. Considering the potential loss of original data resulting from the differentiation process, efforts were made to minimise the number of difference orders. After the first-order difference of the original sequence, the sequence tended to be stable at difference order D=1 [Table/Fig-5].



[Table/Fig-5]: Time series diagram of cases after first-order difference.

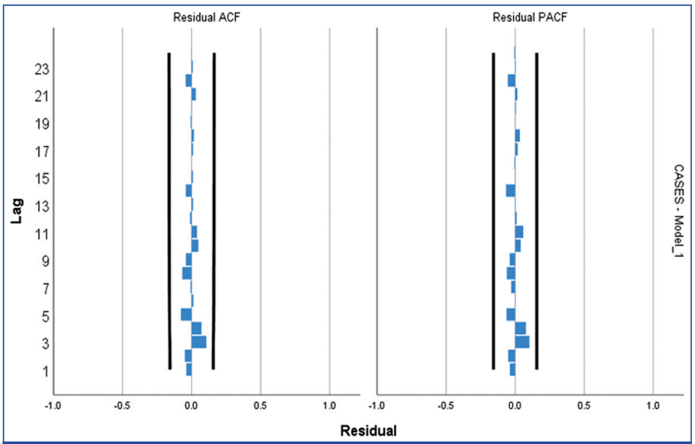
Model identification: The Expert Modeller feature within the SPSS software was utilised to identify the fitted ARIMA model, which was determined to be ARIMA (2, 1, 1) (1, 0, 1). Parameter estimation and the Ljung-Box Q statistic test were conducted for the alternative model, along with an assessment of goodness of fit.

The Bayesian Information Criterion (BIC) was employed to assess the fitting effect, where a smaller BIC value indicated a better fitting effect. In this study, the BIC value of 6.15 for the ARIMA (2,1,1) model was the smallest among all models, indicating the ARIMA (2,1,1) model as the most optimal one [Table/Fig-6]. Additionally, an autocorrelation diagram of the residual sequence revealed that both the ACF and PACF did not exceed the 95% confidence interval, suggesting an independent distribution of the residuals [Table/Fig-7]. The Ljung-Box Q statistics showed no statistical significance (p-value >0.05), accurately indicating that the residuals conformed to a white noise sequence. In conclusion, the ARIMA (2,1,1) model was considered the best-fitting model.

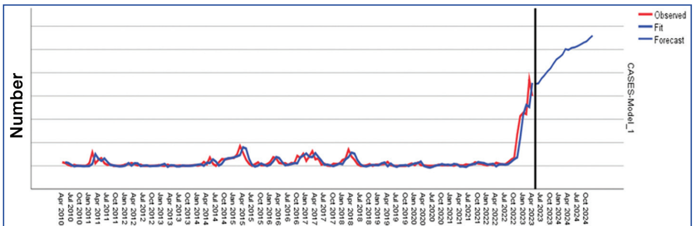
Model Statistics (model 1): ARIMA (2, 1, 1)						
Number of predictors	Model fit statistics		Ljung-Box Q (18)			Number of outliers
	Stationary R-squared	Normalised BIC	Statistics	DF	Sig.	
0	0.099	6.153	6.486	13	0.927	0

[Table/Fig-6]: Model statistics for ARIMA.

Model evaluation: The trend of measles cases over the period fluctuated. It exhibited relative stability from 2011 to 2015 and from 2018 to mid-2022. However, it showed an upward trajectory during and after the surge of the COVID-19 pandemic. The established ARIMA (2,1,1) model was used to predict the monthly measles cases in Rajasthan for the period after the pandemic, and the fitting effect diagram between the predicted value and the actual value was drawn [Table/Fig-8]. The difference between observed cases and predicted/expected cases for the period of April 2020 to December 2021 was not statistically significant (t-value=0.261 and p-value=0.797) [Table/Fig-9].



[Table/Fig-7]: Residual autocorrelation and partial autocorrelation diagrams.



[Table/Fig-8]: Observed and predicted cases of measles and forecasting of cases.

*This figure shows the long-term trend of measles cases. The observed cases are depicted by the red line, while the expected cases are represented by the blue line; #The black vertical line separates the observed period from the forecast period

In summary, the overall trend of the model's prediction results aligned with the actual situation, and the relative error was minimal. This suggests that the model effectively simulated the incidence of measles cases during that period. The observed cases of measles show an upward trajectory during and after the COVID-19 outbreak due to a significant increase in the number of tests for Influenza-Like Illness.

DISCUSSION

Measles is a disease of childhood as supported by the present study, where 79.5% of the cases were under nine years of age. This finding aligns with other studies; for instance, Singh K and Garg R reported 90% of cases in the age group under 10 years [12]. In India, a study revealed that 41% of cases were in the age group of 1-4 years and 37% in the age group of 5-9 years [14]. Reports from Madhya Pradesh noted two peaks: one in the age group of 2-3 years and another in the age group of 5-9 years [15]. Males were predominantly affected compared to females in the present study, consistent with studies from North East India [16] and Kerala [17]. This gender difference could be attributed to variations in gender ratios within the regions where the samples were collected or differences in parental attitudes or concerns towards their female children. In the present study, out of the total cases, 13.3% were vaccinated according to historical records, while the remaining 86.7% were not vaccinated. This finding contrasts with a study on outbreaks in Rajasthan, where 31% of cases detected were vaccinated [11]. Studies from North East India and South India reported 23.3% and 28.6% of cases being vaccinated, respectively [16,17]. This study clearly concludes that the disease is more common among the unvaccinated

Observed and predicted cases of measles									
Date_	Observed cases	Predicted cases	LCL	UCL	Date	Observed cases	Predicted cases	LCL	UCL
Mar 2020	3.00	12.24	-0.96	25.45	Aug 2022	16.00	3.63	-9.58	16.83
Apr 2020	2.00	4.86	-8.34	18.07	Sep 2022	27.00	20.34	7.13	33.54
May 2020	0.00	-0.42	-13.63	12.78	Oct 2022	34.00	26.34	13.13	39.54
Jun 2020	0.00	-3.73	-16.93	9.48	Nov 2022	133.00	133.97	120.76	147.17
Jul 2020	0.00	2.50	-10.70	15.71	Dec 2022	214.00	214.00	200.79	227.21
Aug 2020	1.00	0.77	-12.43	13.98	Jan 2023	228.00	238.76	225.56	251.97
Sep 2020	5.00	0.89	-12.32	14.09	Feb 2023	222.00	218.41	205.21	231.62
Oct 2020	2.00	3.99	-9.22	17.20	Mar 2023	372.00	368.41	355.21	381.62
Nov 2020	3.00	4.32	-8.89	17.52	Apr 2023	300.00	296.41	283.21	309.62
Dec 2020	2.00	4.58	-8.63	17.78	May 2023	NA	329.15	315.95	342.36
Jan 2021	3.00	-1.41	-14.61	11.80	Jun 2023	NA	354.75	336.07	373.42
Feb 2021	1.00	7.14	-6.06	20.35	Jul 2023	NA	390.52	367.64	413.39
Mar 2021	5.00	-2.25	-15.45	10.96	Aug 2023	NA	397.17	370.76	423.58
Apr 2021	2.00	5.37	-7.84	18.58	Sep 2023	NA	428.32	400.21	456.43
May 2021	1.00	0.15	-13.05	13.36	Oct 2023	NA	458.16	428.45	487.88
Jun 2021	6.00	2.66	-10.54	15.87	Nov 2023	NA	485.34	454.11	516.58
Jul 2021	4.00	4.04	-9.17	17.24	Dec 2023	NA	511.36	478.68	544.05
Aug 2021	5.00	5.24	-7.97	18.45	Jan 2024	NA	534.48	500.40	568.55
Sep 2021	15.00	6.08	-7.13	19.29	Feb 2024	NA	562.95	527.54	598.36
Oct 2021	10.00	13.11	-0.09	26.32	Mar 2024	NA	591.44	554.74	628.13
Nov 2021	9.00	10.34	-2.87	23.54	Apr 2024	NA	649.29	611.35	687.23
Dec 2021	5.00	8.74	-4.47	21.94	May 2024	NA	677.36	636.94	717.79
Jan 2022	2.00	2.91	-10.29	16.12	Jun 2024	NA	704.27	661.51	747.04
Feb 2022	6.00	2.19	-11.02	15.39	Jul 2024	NA	731.50	686.52	776.49
Mar 2022	3.00	7.67	-5.53	20.88	Aug 2024	NA	752.21	705.11	799.31
Apr 2022	13.00	3.03	-10.18	16.24	Sep 2024	NA	780.94	732.14	829.74
May 2022	9.00	12.92	-0.29	26.12	Oct 2024	NA	809.24	758.79	859.69
Jun 2022	6.00	9.61	-3.60	22.81	Nov 2024	NA	836.67	784.63	888.71
Jul 2022	6.00	6.61	-6.59	19.82	Dec 2024	NA	863.72	810.13	917.30

[Table/Fig-9]: Observed Vs predicted cases of measles during and after the surge of COVID-19.
*LCL: Lower control limit; and ULC: Upper control limit (the values are unusual above and below the control limit

population. The National Family Health Survey (NFHS-5) in 2020-21 showed an improvement in measles immunisation coverage, reaching around 85% in Rajasthan [18], but this was still insufficient to curb transmission.

The study revealed that overall attack rates ranged from 4% to 75%, with an average attack rate of 25.7% over 13 years. Monthly trend observations indicated that the monthly index for measles cases was higher in the months of March and April. Similarly, a study in Kerala showed higher cases in the winter and early spring months (January-April) [16]. Variations in attack rates depend on many factors, including the population at risk, vaccination status, and geographical factors. In a study conducted in Surat, the attack rate was 7.6% [10]; in periurban areas of Chandigarh over one year (1998-99), it ranged from 4-5% [19]; and among the migrant population in India, it was 7.7% overall and 21% in children below five years [20].

This study highlighted the monthly index of measles cases, which peaked in the months of March to April and was lowest in July to August. The study also indicated that the trend of measles cases fluctuated over time, showing an upward trajectory after the surge of the COVID-19 pandemic. In the initial years, a lesser number of samples were received in the laboratory, possibly because the system took some time to be fully implemented across all fronts. Since 2014, more than 300 samples have been received annually, and more recently, in 2021, 1,862 samples were received, followed by 3,430 samples in 2022, as the strategy for measles surveillance (sample collection) was changed. Initially, samples were collected from all suspected cases of measles, but later samples were collected from all cases presenting with fever and rash, leading to a reduction in percent positivity. This study also highlights the anticipated future trend of measles cases during and after the COVID-19 pandemic, projecting until the end of 2024.

Limitation(s)

The study's limitation lies in the absence of individual case tracking, which hinders an in-depth exploration of the disease complexities and complications associated with measles. Future research endeavours should include a comprehensive examination that integrates insights into the knowledge, attitudes, and practices of the local population to enhance our understanding.

CONCLUSION(S)

During the last decade, measles cases exhibited a fluctuating trend, but during and after the pandemic, they have shown an upward trajectory. This trend is expected to continue increasing in the near future, especially during the months of March to April, which are the months that typically experience a peak in cases due to seasonal patterns. Policy-makers should implement proactive measures before the peak season to mitigate the impact and prevent further spread of the disease. Moreover, there is an urgent need to enhance routine immunisation coverage, especially in high-risk areas, and to promote extensive vaccine coverage in regions where gender discrimination against female children persists. Reinforcement of surveillance is also crucial to effectively monitor and respond to outbreaks.

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- iThenticate Software: Apr 22, 2024 (4%)

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