Trends and determinants of pertussis mortality in Sabah, Malaysia

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ABSTRACT

Introduction: Pertussis remains a major cause of infant morbidity and mortality despite widespread vaccination. Sabah, Malaysia, has consistently reported the nation's highest pertussis burden. This study described the epidemiology of pertussis and identified factors associated with mortality among confirmed cases in Sabah.

Material and Methods: A retrospective registry-based study was conducted using data from the Communicable Disease Control Information System (CDCIS) for all confirmed pertussis cases reported between January 2023 and December 2024. Sociodemographic, vaccination, and clinical variables were extracted. Univariable and multiple logistic regressions were performed to determine factors associated with death; variables with $p < 0.25$ were entered into the multivariable model. Adjusted odds ratios (aOR) with 95 % confidence intervals (CI) were reported.

Results: A total of 287 confirmed pertussis cases were recorded, including 35 deaths (case-fatality rate = 12.2 %). Most deaths occurred in infants < 2 months and among non-Malaysian or unvaccinated children. In the multivariable model, shortness of breath (aOR = 21.6; $p < 0.001$), cyanosis (aOR = 5.45; $p = 0.006$), fitting (aOR = 14.2; $p = 0.027$), and post-tussive vomiting (aOR = 136.0; $p = 0.004$) were independent predictors of death. Male sex was protective (aOR = 0.23; $p = 0.008$). Age, citizenship, and vaccination status were not statistically significant after adjustment. The model demonstrated good fit (Hosmer–Lemeshow $p = 0.807$; Nagelkerke $R^2 = 0.471$).

Conclusion: Pertussis mortality in Sabah remains high and is driven primarily by severe clinical manifestations, with additional influence from demographic and structural factors. Strengthening early clinical recognition, improving referral and intensive care capacity, and expanding preventive strategies particularly maternal vaccination and equitable immunisation for non-Malaysian populations are critical to reducing preventable deaths.

KEYWORDS:
Pertussis; whooping cough; mortality; risk factors; Sabah

INTRODUCTION

Pertussis, or whooping cough, is a highly contagious respiratory disease caused by *Bordetella pertussis*. Despite the availability of effective vaccines, it remains a major cause of infant morbidity and mortality worldwide. The World Health Organization (WHO) estimates more than 150,000 cases annually, with the greatest burden in low- and middle-income countries.[1] The global resurgence of pertussis has been attributed to waning immunity, suboptimal vaccine effectiveness, and gaps in immunisation coverage.[2,3]

In Malaysia, pertussis is a notifiable disease under the Prevention and Control of Infectious Diseases Act 1988. Although the National Immunisation Programme has achieved high coverage, cyclical outbreaks persist, particularly among infants too young to be vaccinated.[4] The COVID-19 pandemic further disrupted immunisation services, leading to delayed or missed childhood doses and increased susceptibility to outbreaks.[3,5]

Sabah, a state in East Malaysia, has recorded the highest national burden of pertussis in recent years, with major peaks in 2019 and 2023.[6] Most deaths occurred in infants under six months, consistent with global evidence that young infants are the most vulnerable.[7] Non-Malaysian populations are disproportionately affected, reflecting inequities in healthcare access and vaccination coverage.[8] Antenatal pertussis vaccination provides passive immunity to newborns and has been shown to reduce infant morbidity and mortality.[9] In Malaysia, this strategy was only introduced in 2024, leaving previous cohorts dependent on herd immunity and infant vaccination.[10]

Despite descriptive reports and outbreak investigations, limited studies have examined the determinants of pertussis mortality in Sabah. Existing evidence largely derives from high-income countries, where health systems differ significantly. Understanding local demographic, vaccination, and clinical determinants is essential to guide targeted interventions and reduce preventable deaths. Therefore, this study aimed to identify factors associated with pertussis mortality using all confirmed cases reported in Sabah between January 2023 and December 2024.

MATERIALS AND METHODS

This study was conducted in Sabah, a Malaysian state in northern Borneo with an estimated 3.4 million residents in 2022, distributed across 27 districts. Sabah shares extensive land and maritime borders contributing to its unique demographic and healthcare challenges. Pertussis is a

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notifiable disease, whereby all suspected cases are reported via the Communicable Disease Control Information System (CDCIS) to district health offices for investigation and surveiilance.

We performed a retrospective registry-based study of confirmed pertussis cases notified to CDCIS between 1st January 2023 and 31st December 2024. The study comprised descriptive and analytical epidemiology to identify factors associated with pertussis mortality. Data was extracted from CDCIS and linked investigation forms completed by district health teams. All confirmed cases with a documented outcome (alive or death) were included. Data completeness was assessed prior to analysis. Any missing or inconsistent variables identified in the CDCIS registry were cross-checked against the original case investigation forms maintained by district health offices. After verification, all variables included in the final analysis were complete, and no imputation was required. Informed consent was waived for this study.

A confirmed pertussis case was defined based on laboratory confirmation and/or epidemiological linkage. Pertussis deaths were defined as cases verified by the attending hospital or district health office and recorded as such in CDCIS. The primary outcome was pertussis status (alive or death). Independent variables included sociodemographic (age, gender and citizenship), vaccination status (complete, incomplete, or ineligible) and clinical features (shortness of breath (SOB), cyanosis, seizures, post-tussive vomiting, cough, fever, and runny nose)

Categorical variables were summarised as frequencies and percentages, and continuous variables as min, max and median (interquartile range). Simple logistic regression was first used to estimate crude odds ratios (cOR) and 95% confidence intervals (CI) for each independent variable. Variables with a p-value < 0.25 in bivariable analysis were considered for entry into the multiple logistic regression model.[11] The final multiple logistic regression model included these predictors, and results were presented as adjusted odds ratios (aOR) with 95% CI. Selection of variables for multiple logistic regression model was made by forward, backward and stepwise elimination. Confounder was further assessed using a ≥10% change-in-estimate rule with interaction terms were explored, and model diagnostics included variance inflation factors (VIF) for multicollinearity, the Hosmer–Lemeshow test for calibration. All analyses were performed using RStudio (version 2025.05.1, Build 513; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Epidemiological distribution

Figure 1 illustrates the weekly distribution of pertussis cases and deaths during the study period. Between January 2023 and December 2024, a total of 287 confirmed pertussis cases were reported. Of these, 35 deaths (12.2%) were recorded. Peaks in case notifications were observed between epidemiology weeks (EW) 10 and 27 of 2023, during which both incidence and mortality were highest. In 2024, reported cases declined substantially, although sporadic deaths continued to occur until EW 45.

Descriptive characteristics of pertussis cases

Table I summarises the sociodemographic, vaccination, and clinical characteristics of pertussis cases by outcome. In terms of age, 45.8% occurred in infants younger than 2 months, followed by those aged 2–<18 months (37.1%). Children aged ≥18 months accounted for only 17.1% of deaths. Females represented a larger proportion of deaths (68.6%) compared with survivors (52.4%). With respect to citizenship, non-Malaysian children comprised many deaths (80.0%), whereas Malaysians and non-Malaysians were more evenly distributed among survivors (49.6% vs 50.4%). Vaccination status showed 88.6% of deaths occurred among ineligible or unvaccinated infants, compared with 73.8% of survivors. In contrast, only 8.6% of deaths were reported among fully vaccinated children, compared with 25.0% of survivors.

Several clinical features distinguished deaths from survivors. SOB was the most prominent, affecting 68.6% of deaths compared with only 12.3% of survivors. Cyanosis was also more frequent among deaths (22.9% vs 7.1%), while seizures was reported in 8.6% of deaths compared with only 0.8% of survivors. Fever occurred in both groups but was slightly higher among deaths (71.4% vs 63.9%). In contrast, cough was present in all cases (100%), reflecting its role as a hallmark symptom, and thus did not differentiate between outcomes. Runny nose and post-tussive vomiting were uncommon overall and did not show meaningful differences between deaths and survivors.

Descriptive statistics of numerical variables

Table II presents the distribution of continuous variables stratified by outcome. The median age at diagnosis among deaths was 0.19 years (IQR 0.11–0.44), which was lower than that of survivors (0.29 years; IQR 0.15–2.29), reflecting the higher vulnerability of very young infants.

The duration of cough before diagnosis was shorter among deaths (median 4 days; IQR 2.0–7.0) compared with survivors (median 6 days; IQR 3.0–11.3), suggesting that children who died tended to present earlier in the disease course, possibly due to rapid progression of severe symptoms.

For logistical factors, the median distance of the cases' residence from the nearest government hospital was shorter among deaths (6.5 km; IQR 3.1–17.4) compared with survivors (10.2 km; IQR 6.0–23.6). Similarly, the median distance to the nearest government clinic was 3.0 km (IQR 1.3–7.1) among deaths and 3.8 km (IQR 1.9–8.1) among survivors. These findings indicate that proximity to healthcare facilities did not necessarily protect against fatal outcomes, and deaths still occurred even among those living nearer to hospitals and clinics.

Factors associated with pertussis mortality: Simple logistic regression

Table III presents the results of the simple logistic regression analysis examining factors associated with pertussis mortality in Sabah between 2023 and 2024. Among continuous variables, age and duration of cough before diagnosis was associated with mortality. Each additional year of age slightly reduced the odds of death (OR=0.78; 95% CI 0.60–1.02; p=0.072), while each additional day of cough prior

Table I: Descriptive analysis statistical results

Mortality	Yes (n, %) 35 (12.2)	No (n, %) 252 (87.8)	Total (n, %) 287 (100)
Age			
<2 months	16 (45.8)	75 (29.8)	91(31.7)
2-<18 months	13 (37.1)	102 (40.4)	115(40.1)
>18 months	6 (17.1)	75 (29.8)	81(28.2)
Gender			
Male11 (31.4)	120 (47.6)	131 (45.6)	
Female	24 (68.6)	132 (52.4)	156 (54.4)
Citizenship			
Non-Malaysian	28(80.0)	127 (50.4)	155 (54.0)
Malaysian	7 (20.0)	125 (49.6)	132 (46.0)
Vaccination status			
Ineligible/unvaccinated	31 (88.6)	186 (73.8)	217 (75.6)
Incomplete	1 (2.8)	3 (1.2)	4 (1.4)
Complete	3 (8.6)	63 (25.0)	66 (23.0)
Clinical symptoms			
Cough			
Yes	35 (100)	252 (100)	287 (100)
Cyanosis			
Yes	8 (22.9)	18 (7.1)	26 (9.1)
No	27 (77.1)	234 (92.9)	261 (90.9)
Shortness of breath			
Yes	24 (68.6)	31 (12.3)	55 (19.2)
No	11 (31.4)	221 (87.7)	232 (80.8)
Seizures			
Yes	3 (8.6)	2 (0.8)	5 (1.7)
No	32 (91.4)	250 (99.2)	282 (98.3)
Fever			
Yes	25 (71.4)	161 (63.9)	186(64.8)
No	10 (28.6)	91 (36.1)	101(35.2)
Runny nose			
Yes	0 (0.0)	5 (2.0)	5 (1.7)
No	35 (100)	247 (98.0)	282 (98.3)
Post-tussive Vomiting			
Yes	1 (2.9)	1 (0.4)	2 (0.7)
No	34 (97.1)	251 (99.6)	285 (99.3)

Table II: Descriptive statistics for numerical variable

Mortality	Yes (n=35)		No (n=252)		Total(n=287)	
variable	Min-Max	Median (IQR)	Min-Max	Median (IQR)	Min-Max	Median (IQR)
Age (year)	0.05-3.92	0.19 (0.11-0.44)	0.02-75	0.29 (0.15-2.29)	0.02-75	0.267 (0.15-2.03)
Duration of cough before diagnosis (day)	0-21	4 (2.00-7.00)	0-40	6 (3.00-11.25)	0-40	6 (3.0-10.5)
Distance of cases from nearby government hospital (km)	0.6-111.0	6.5 (3.10-17.40)	0.3-137.0	10.15 (6.0-23.6)	0.3-137	9.9 (5.65-23.6)
Distance of cases from nearby government clinic (km)	0.2-35.8	3 (1.25-7.05)	0.2-54	3.75 (1.87-8.10)	0.2-54	3.7 (1.55-8.05)

IQR: Inter quartile range (Q1-Q3)

to diagnosis decreased the odds of death by 8% (OR=0.92; 95% CI 0.86–0.99; p=0.018). In contrast, distance to the nearest hospital and government clinic were not significantly associated with mortality (p=0.874 and p=0.697, respectively).

Regarding categorical variables, infants aged <2 months had higher odds of death compared with those aged ≥18 months (OR=2.67; 95% CI 0.99–7.19; p=0.052), although this finding was not statistically significant. Male had lower odds of death compared with females (OR=0.50; 95% CI 0.24–1.07; p=0.076). Non-Malaysian children had nearly fourfold higher odds of death compared with Malaysians (OR=3.94; 95% CI 1.66–9.34; p=0.002).

For vaccination status, ineligible or unvaccinated infants had a significantly greater risk of death compared with fully vaccinated children (OR=3.50; 95% CI 1.03–11.84; p=0.044).

Clinical features strongly associated with mortality included cyanosis, SOB, and seizures. Cases presenting with cyanosis had almost fourfold higher odds of death (OR=3.85; 95% CI 1.53–9.70; p=0.004), those with SOB had 15-fold higher odds (OR = 15.55; 95% CI 6.94–34.84; p<0.001), and those with seizures had 12-fold higher odds of death (OR=11.72; 95% CI 1.89–72.81; p=0.008). Fever, runny nose, and post-tussive vomiting were not significantly associated with death.

Table III: Simple logistic regression of factors associated with pertussis death

Variable	Simple Logistic Regression	
	Crude OR (95% CI)	p-value
Age (year)	0.78 (0.6,1.02)	0.072**
Duration of cough before diagnosis (day)	0.92 (0.86,0.99)	0.018**
Distance of cases from nearby government hospital (km)	1.00 (0.99, 1.01)	0.874
Distance of cases from nearby government clinic (km)	0.99 (0.96, 1.06)	0.697
Age		
<2 months	2.67 (0.99,7.19)	0.052**
2-<18 months	1.59 (0.58,4.38)	0.367
>18 months	1	
Gender		
Male	0.5 (0.24, 1.07)	0.076**
Female	1	
Citizenship		
Non-Malaysian	3.94 (1.66,9.34)	0.002**
Malaysian	1	
Vaccination status		
Ineligible/unvaccinated	3.5 (1.03,11.84)	0.044**
Incomplete	7 (0.55,88.96)	0.134 **
Complete	1	
Clinical symptoms		
Cyanosis		
Yes	3.85 (1.53,9.7)	0.004**
No	1	
Shortness of breath		
Yes	15.55 (6.94,34.84)	<0.001**
No	1	
Seizures		
Yes	11.72 (1.89,72.81)	0.008**
No	1	
Fever		
Yes	1.41 (0.65,3.07)	0.383
No	1	
Runny nose		
Yes	0 (0,Inf)	0.989
No	1	
Post-tussive Vomiting		
Yes	7.38 (0.45,120.78)	0.161**
No	1	

**p-value of < 0.25: include in multiple logistic variable

Variables with p<0.25 were selected for inclusion in the multiple logistic regression model. The following variables were selected for the multiple logistic regression model: age, duration of cough before diagnosis, gender, citizenship, vaccination status, cyanosis, SOB, seizures, and post-tussive vomiting.

Factors associated with pertussis mortality: Multiple logistic regression

Table IV shows the multiple logistic regression analysis of factors associated with pertussis mortality. Shortness of breath (SOB) was the strongest predictor, where affected cases had 21.6-fold higher odds of death compared with those without SOB (aOR=21.6; 95% CI 8.05–65.4; p<0.001). Cyanosis was also associated with mortality (aOR=5.45; 95% CI 1.59–18.4; p=0.006). Likewise, seizures increased the odds of death more than fourteen-fold (aOR=14.2; 95% CI 1.43–180.0; p=0.027), while post-tussive vomiting, was associated with markedly elevated odds of death (aOR=136.0; 95% CI 3.69–5289; p=0.004), although this estimate should be interpreted cautiously due to the very small number of death cases and wide confidence interval.

Among demographic factors, male was significantly protective, with males showing 77% lower odds of death compared with females (aOR=0.23; 95% CI 0.07–0.64; p=0.008). Citizenship and vaccination status were not statistically significant after adjustment, although non-Malaysian children still had approximately threefold higher odds of death (aOR=2.90; 95% CI 0.88–11.0; p=0.094). Similarly, age was not a significant predictor, despite higher crude mortality among infants aged < 2 months.

The final model demonstrated good overall fit (Hosmer–Lemeshow p=0.807) and explained 47.1% of the variation in mortality (Nagelkerke R^2=0.471). No multicollinearity was detected. After adjustment for potential confounders, several clinical features remained significant predictors of death. Gender, vaccination status, and citizenship were identified as confounders: gender mainly confounded the associations of citizenship, vomiting, and seizures; vaccination status confounded the effects of citizenship, cyanosis, vomiting, and seizures; and citizenship strongly confounded the relationships between vaccination status, gender, and young age.

Table IV: Multivariable logistic regression of factors associated with pertussis death

Variable	Multiple Logistic Regression	
	Adjusted OR (95% CI)	p-value
Age		
<2 months	2.15(0.59, 8.68)	0.3
2-<18 months	0.53(0.14, 2.08)	0.3
>18 months	1	
Gender		
Male	0.23(0.07, 0.64)	0.008*
Female	1	
Citizenship		
Non-Malaysian	2.90(0.88, 11.0)	0.094
Malaysian	1	
Vaccination status		
Ineligible/unvaccinated	0.72(0.13, 4.54)	0.7
Incomplete	1.54(0.05, 37.0)	0.8
Complete	1	
Clinical symptoms		
Cyanosis		
Yes	5.45(1.59, 18.4)	0.006*
No	1	
Shortness of breath		
Yes	21.6(8.05, 65.4)	<0.001*
No	1	
Seizures		
Yes	14.2(1.43, 180)	0.027*
No	1	
Post-tussive Vomiting		
Yes	136(3.69, 5,289)	0.004*
No	1	

*p-value <0.05: significant level
AIC: 153.5. No multicollinearity among the variables was detected in the final model. Nagelkerke's R-squared: 47.1%. Hosmer-Lemeshow Goodness-of-Fit Test: 0.807.
Gender, vaccination status, and citizenship were identified as confounders. Gender confounded the effects of citizenship, post-tussive vomiting, and seizures. Vaccination status confounded the associations of citizenship, cyanosis, post-tussive vomiting, and seizures. Citizenship strongly confounded the relationship between vaccination status, gender, seizures, and young age.

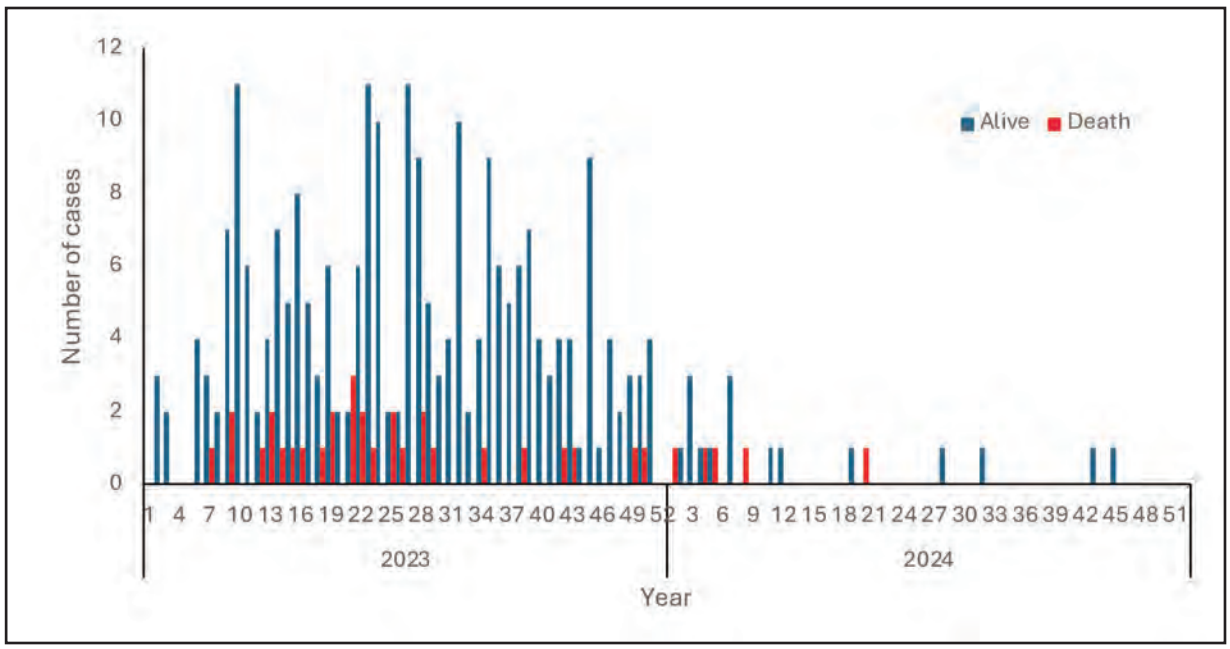

Fig. 1: Distribution of pertussis cases and mortality cases in Sabah according epidemiology week (EW) from 2023 until 2024

DISCUSSION

This study analysed all confirmed pertussis cases reported in Sabah between 2023 and 2024 and identified several factors associated with mortality. The overall case fatality rate (CFR) was 12.2%, which is substantially higher than CFRs reported in many high-income settings, where deaths are typically below 1% due to strong immunisation coverage and intensive care support.[1,2] These findings demonstrate the persistent burden of pertussis mortality in Sabah, consistent with global evidence showing that low- and middle-income countries continue to face disproportionate risk.[3]

Globally, there has been a resurgence of pertussis in recent years, driven by waning immunity, suboptimal vaccination uptake, and disruptions to immunisation programmes during the COVID-19 pandemic.[12] The pandemic disrupted routine childhood immunisation services worldwide, including in Malaysia, leading to delayed or missed vaccinations and altered health-seeking behaviours due to fear of COVID-19 exposure.[13] Similar to other regions, Sabah reported vaccination coverage below the 95% threshold required for herd immunity, contributing to increased pertussis susceptibility during and immediately after the pandemic years.[14]

Malaysia's National Immunisation Programme schedules pertussis vaccination via the hexavalent combination vaccine (diphtheria, tetanus, pertussis, polio, hepatitis B, and *Haemophilus influenzae* type b) administered at 2, 3, 5, and 18 months.[4] In recognition of inequities faced by non-Malaysian children, the Ministry of Health issued an exemption for polio vaccination fee in 2022, granting free hexavalent vaccination for all non-Malaysian children under seven years old.[15] These initiatives, combined with catch-up campaigns, contributed to the decline in pertussis incidence observed in 2024 following the 2023 epidemic peak.

In the present study, female infants had higher mortality compared with males. The adjusted model showed that males had significantly lower odds of death (aOR=0.23; 95% CI 0.07–0.64; p=0.008). Although evidence on sex differences in pertussis outcomes is limited, biological differences in immune regulation may contribute to this observation. Females typically develop stronger immune responses to infections and vaccination, influenced by hormonal and genetic factors.[16,17] However, stronger immune activation during severe respiratory illness may also increase inflammation and tissue damage. The observed protective association among males may reflect statistical variability due to the relatively small number of deaths. Further research in larger populations is needed to better understand this association.

Severe clinical symptoms particularly SOB, cyanosis, seizures, and post-tussive vomiting were strong predictors of death. These clinical features should not be interpreted as independent causal determinants of mortality, but rather as markers of advanced disease severity. Symptoms such as shortness of breath, cyanosis, and seizures likely reflect underlying respiratory compromise and systemic hypoxia preceding fatal outcomes. Thus, they function primarily as prognostic indicators for triage and escalation of care rather than primary etiological risk factors.[18,19]

In contrast, age, vaccination status and citizenship were not statistically significant after adjustment, although nearly half of the deaths occurred in infants younger than two months and most fatalities were among those ineligible or unvaccinated. This pattern reflects the influence of both biological vulnerability and structural inequities. Young infants remain immunologically immature and rely on maternal or herd immunity for protection. Global studies consistently show that under vaccinated infants, especially in lower-income settings, face the highest risk of severe disease and death.[9,20] In Sabah, the relationship between these factors is further shaped by contextual issues such as healthcare access, vaccination opportunities, and social determinants of health.[21,22] The association of citizenship and vaccination effects after adjustment may also reflect residual confounding from unmeasured structural variables not captured in surveillance data.

The persistence of high mortality despite proximity to health facilities suggests that delayed recognition and initiation of critical care, rather than geographic access alone, may underlie many deaths. Similar challenges have been observed in other low- and middle-income countries, where structural barriers such as transport limitations, healthcare costs, and fear of discrimination may impede timely care.[9,22]

Several limitations should be considered when interpreting these findings. The retrospective study design limits causal inference, while the CDCIS registry does not capture important variables such as socioeconomic status, household crowding, parental education, maternal vaccination history, healthcare access barriers, care-seeking delays, and underlying co-morbidities. The absence of these variables may have introduced residual confounding, particularly regarding the associations involving citizenship and vaccination status after adjustment. In addition, the relatively small number of deaths reduced statistical power and contributed to wide confidence intervals for some estimates, particularly post-tussive vomiting, where sparse data may have led to model instability and overestimation of effect size. Furthermore, the two-year study period may not fully capture the cyclical epidemic patterns characteristic of pertussis, limiting long-term trend interpretation and generalisability.

Despite these limitations, the use of comprehensive CDCIS surveillance data allowed complete case capture across Sabah and strengthened the validity of the findings. By combining descriptive and multivariable analyses, this study identified important clinical and sociodemographic predictors of pertussis mortality in a high-burden setting. Overall, pertussis mortality in Sabah reflects the combined effects of clinical severity, biological vulnerability, and structural inequities, underscoring the need for targeted interventions to strengthen early diagnosis, equitable vaccination access, and critical care management.

CONCLUSION

In conclusion, pertussis mortality in Sabah remains high, driven by both clinical severity and sociodemographic inequities. Policy responses must address both clinical management (early recognition, referral, and intensive

support) and prevention (strengthening immunisation) which has shown strong protective effects in other countries.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

ETHICS STATEMENT

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