Transversal Pertussis Sero-Epidemiological Study in Fully Vaccinated Children and Adolescents in Antananarivo, Madagascar, and in Dapaong, Togo

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Abstract

Introduction: African region is thought to contribute to >50% of deadly cases of pertussis worldwide, however surveillance and available data on *Bordetella pertussis* circulation are limited. Currently, pertussis vaccination schedule in most African countries is restricted to a primary immunization consisting of three doses during the first year of life using whole pertussis vaccines for which effectiveness is not known.

Methods: Primary vaccinated children aged 3-15 years were recruited in Antananarivo city and suburban areas, Madagascar, and in Dapaong, Togo. Details on vaccine injections and a capillary serum sample were collected, and anti-pertussis toxin immunoglobulin G (anti-PT IgG) were quantified by ELISA.

Results: Seropositivity rate was 56.9% (588/1033) and 62.2% (565/908) in Antananarivo and Dapaong, respectively. Significantly less children with anti-PT IgG were observed among those aged 3-5 years in Madagascar, seropositivity rate increased thereafter in children older ≥ 6 years old, with substantial sign of recent infection in particular in 6-8 years old children (18.9%; 39/206). In Dapaong, 65.3% (111/170) of the 3-5 years old children were seropositive and frequency did not significantly vary among age groups. Compliance was 89.0% (886/996) and 77.2% (596/772), and children vaccinated at age > 8 weeks represented 33.4% (337/996) and 39.4% (304/772) in Antananarivo and Dapaong, respectively. Compliance was higher among the 3-5 years children in both countries.

Conclusion: *B. pertussis* significantly circulates among vaccinated children in Antananarivo, Madagascar and Dapaong, Togo. Initiating early vaccination should be strengthened and a national surveillance system should be implemented to better characterize the burden of pertussis in those countries.

Keywords: Pertussis; Togo; Madagascar; Whole-cell vaccine; Sero-prevalence

List of abbreviations: PT: Pertussis toxin; IgG: Immunoglobulin G; LMIC: Low and middle-income countries; EPI: Expanded Program on Immunization; HIC: High-income countries; WHO: World Health Organization; wPV: Whole-cell vaccine; ELISA: Enzyme-linked immunosorbent assay; NIBSC: National Institute for Biological Standards and Control; IU: International units; µl: microliters; ml: milliliters; LLOQ: Lower limit of quantitation; IQR: Interquartile range; MDG: Madagascar; TGO: Togo; OR: odds-ratio: wks: weeks; UNICEF: United Nations of International Children's Emergency Fund.

Introduction

Pertussis, also known as whooping cough or the 100-day cough, is a bacterial respiratory illness. It is often considered as a "forgotten disease" as specific vaccines are integrated into national infant immunization schedules since decades, including in low- and middle-income countries (LMIC) with the inception of the Expanded Program on Immunization (EPI) in 1974, which have led to the sharp reduction of cases worldwide. However, due to high contagiousness of its etiological bacteria *Bordetella pertussis*, vaccination coverage >90% is necessary in order to maintain a low incidence. In addition, as for many other vaccines, the vaccine-induced-immunity declines over the years and booster doses are recommended in a lifetime in addition to the vaccination during his infancy [1]. Although severe to deadly illness mainly occurs in infants <3 months of age, pertussis may affect everyone contributing to the circulation of *B. pertussis*. In high-income countries (HIC), where surveillance system is largely implemented, pertussis is still considered as a public health concern due to the difficulty in hindering new cases of severe or deadly cases each year despite the use of effective infant and booster vaccines in children and adolescents. In LMIC, the pertussis epidemiological situation is poorly known due to absence of diagnosis platforms. World Health Organization (WHO) estimated in 2003 about 17.6 million cases of pertussis and about 279 000 fatal cases worldwide, 90% of which were in developing countries [2]. More recently, an updated model from Yeung and colleagues showed that there were 24.1 million pertussis cases and 160 700 deaths from pertussis in children younger than 5 years in 2014, with the African region contributing the largest proportions with 33% of cases and 58% of estimated deaths [3].

It is critical to gather information to inform national public health authorities in African countries, especially as *i.* no booster vaccines are included in EPI, and *ii.* we do not know the effectiveness of, and the duration of protection induced by whole-cell pertussis vaccines (wPVs) currently produced and distributed with the EPI for vaccinating infants during their first year of life. The wPVs are made of chemically or heat-inactivated *B. pertussis* and may suffer from disparities in production processes. Pooled efficacy of those produced in 1980-1990s was close to 80% but significantly varied among the different brands, with efficacy ranging from 46% to 92%. No data exists on currently available wPVs vaccines [1].

A few studies have evidenced the circulation of *B. pertussis* among infants, children, adolescents, and adults and reported outbreaks in several African countries [2,4-8].

Madagascar, an island nation off the east coast of Africa in the Indian Ocean, and Togo, a Western African country, introduced pertussis vaccination through EPI in 1976 and 1980, respectively. Vaccination schedule includes a three-dose immunization at age 6, 10 and 14 weeks using wPVs. While a recent study showed sign of contact of the general population with *B. pertussis* in Madagascar, to our knowledge, no data is available in Togo [6]. Thus, these sero-epidemiological transversal studies were conducted to evaluate serological sign of infection in fully vaccinated (three doses of wPVs) 3-15 years old children and adolescents and compliance with national vaccination schedule. No correlate of protection exists for pertussis, and anti-pertussis

toxin immunoglobulin G (anti-PT IgG) are rapidly lost in the bloodstream. Therefore anti-PT IgG detection at distance of one year from a vaccination is an indirect evidence of contact with *B. pertussis* and thus loss of immunity [9].

Materials and Methods

Study population and design

Children were recruited in schools in Antananarivo, Capital of Madagascar, and in Dapaong, northern Togo. Inclusion criteria were: being aged 3-15 years old and having completed the three injections of pertussis primary vaccination at least a year before sampling date. Presenting a proof of vaccination (i.e. vaccination booklet or diploma) was an additional inclusion criterion in Madagascar. In Togo, the following non-inclusion criteria were applied: having a known hemostasis disorder, or serious acute or chronic illness, or any illness that kept the child from attending the appointment planned for blood collection. Information related to pertussis vaccination history, sex, age, and blood sampling was collected on a standardized questionnaire and data recorded into a computer database. No information related to past or current respiratory illness was collected. A blood sample from the tip of a finger (approximately 200 µl) was collected using a lancet (Becton Dickinson, Sentry 23G) and a serum separating microtainer (Becton Dickinson, reference 365968).

Anti-pertussis toxin serology

Upon collection, blood samples were transferred within 6 hours to the *Unité de Bactériologie Expérimentale* - Institut Pasteur in Madagascar, and the *Centre Hospitalier Regional de Dapaong* in Togo, where serum was collected after a short spinning and then stored at -80°C. In Togo, frozen samples were then shipped to the *Institut National d'Hygiène* in Lomé.

As previously described [10], anti- PT IgG titers were quantified using a commercial purified PT-containing Enzyme-linked immunosorbent assay (ELISA) kit (EUROIMMUN; reference EI 2050-G) [11] and the WHO reference serum available from the National Institute for Biological Standards and Control (NIBSC). All tests had internal negative and positive controls and passed the validity criteria. Results were reported as International Units (IU)/ml. Lower limit of quantitation (LLOQ) was defined as 5 IU/ml. A titer of <5 IU/ ml corresponded to being seronegative and children with anti-PT IgG levels ≥5 IU/ml were considered as seropositive. Anti-PT titers were categorized using 40 IU/ml and 100 IU/ml cut-offs to evidence children who had contact with *B. pertussis* sometime during the past 12 months when [40–100[IU/ml, and 6 months when ≥100 IU/ml [9].

Pertussis immunization schedule

Pertussis vaccination schedule in Madagascar and in Togo include vaccine injections at ages 6, 10, and 14 weeks. Based on WHO recommendation, compliance with national schedule was defined as having received first injection at ≥38 days of life, and the second and third injections 24–70 days after the previous dose.

Statistical analysis

Continuous variables were described using the median, interquartile range (IQR), and comparisons were conducted using two-sided Kruskall-Wallis test. For categorical variables, percentages were estimated, and comparisons were conducted using two-sided chi^2 test. Logistic regression models were used to identify factors associated with compliance and with seropositivity. Statistical analyses were undertaken using Stata software, version 15.1. A 5% alpha risk was considered for statistical tests.

Ethical aspects

After giving the information to the parents/guardians, informed consent of the parents/guardians and the oral assent for children aged >7 years were collected. Only children meeting the inclusion criteria and for whom written and oral consent/assent were obtained participated to the study. The study protocol was reviewed and approved by the Institutional Review Board of *Institut Pasteur*, France (decision number 2016-04/IRB), by the Ethics Committee of Biomedical Research of the Ministry of Public Health of Madagascar (decision number 065-MSANP/CE), and by the *Comité de Bioéthique pour la Recherche en Santé* in Togo (decision number 268/2016/ MSPS/CAB/SGIDPML/CBRS). Authorization for data processing has been obtained from French legal authority (*Commission Nationale Informatique et Liberté*), and pseudonymization was performed assigning a unique code specific to each participant. The ClinicalTrials.gov identifier of the studies is: NCT02983487.

Results

Study population

A total of 1041 and 937 children were recruited in schools in Antananarivo, Madagascar (MDG) and in Dapaong, Togo (TGO), respectively (Figure 1). In Madagascar, children were recruited in 13 primary and 8 secondary schools, located in Antananarivo city and suburban areas, over a period of 4 months (February-May 2018). In Dapaong (TGO), recruitment took place in 7 primary and 3 secondary schools over a period of 3 months (January-March 2017). Several children who did not respond to inclusion criteria or with partial or missing information were subsequently excluded for analyses as detailed in Figure1. Pertussis serology and vaccination timeliness analyses were performed using information from 1033 and 996 children in Antananarivo (MDG; Figure 1A), and 908 and 772 children in Dapaong (TGO; Figure 1B), respectively.

Age groups were defined as 3–5, 6–8, 9–11, and 12–15 years; each group included ≥170 children (Table 1). Information regarding pertussis vaccination was mainly obtained from the child vaccination booklet in Antananarivo (MDG; 97.6%; 1008/1033), and in Dapaong (TGO; 87.6%; 795/908), which provides details on vaccine injection dates. The official confirmation of a complete primary vaccination, but no injection date details, was obtained through the vaccination diploma for a few children in Antananarivo (MDG; 2.4%; 25/1033).

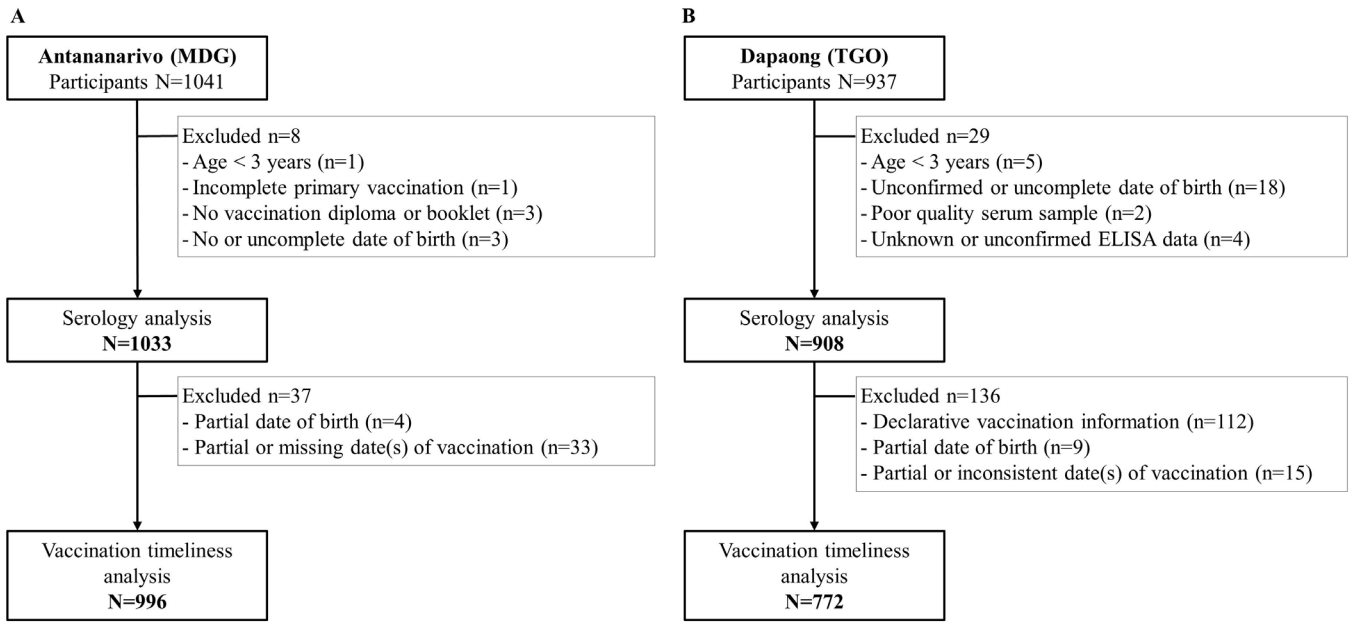

Figure 1: Flow chart of participants in Antananarivo (MDG; A), and Dapaong (TGO; B)

	Antananarivo (MDG)						Dapaong (TGO)					
Age groups	**3-5**	**6-8**	**9-11**	**12-15**	**Total**	**p value**	**3-5**	**6-8**	**9-11**	**12-15**	**Total**	**p value**
N	182 (100)	206 (100)	369 (100)	276 (100)	1033 (100)	-	170 (100)	187 (100)	320 (100)	231 (100)	908 (100)	-
Gender						0.196						0.010
Boys	**97 (53.3)**	112 (54.4)	172 (46.6)	131 (47.5)	512 (49.6)		94 (55.3)	84 (44.9)	157 (49.1)	90 (39.1)	425 (46.9)*	
Girls	**85 (46.7)**	94 (45.6)	197 (53.4)	145 (52.5)	521 (50.4)							
Origin of pertussis vaccination history						<0.001						0.539
Declarative	-	-	-	-	-		16 (9.4)	23 (12.3)	40 (12.5)	33 (14.3)	112 (12.3)*	
Vaccination diploma	2 (1.1)	15 (7.3)	7 (1.9)	1 (0.4)	25 (2.4)		-	-	-	-	-	
Vaccination booklet	180 (98.9)	191 (92.7)	362 (98.1)	275 (99.6)	1008 (97.6)		154 (90.6)	163 (87.2)	280 (87.5)	198 (85.7)	795 (87.6)**	

** 1 child with no information regarding sex*

*** 1 child with no information on origin of pertussis vaccination history*

Table 1: Distribution of the study population recruited in Antananarivo, MDG (left), and in Dapaong, TGO (right) shown by age groups. Results are shown as n (%)

Anti-pertussis toxin serology

At the time of the studies, the shortest timespan since last pertussis vaccine injection was 2.7 years in Antananarivo (MDG), and 2.3 years in Dapaong (TGO). The global seropositivity rate was 56.9% (588/1033) in Antananarivo (MDG), and 62.2% (565/908) in Dapaong, (TGO; Table 2 and Figure 2). In Antananarivo (MDG), seropositivity rate varied from 45.6% (83/182) to 63.0% (174/276) among the age groups, and significant increase in antibody titers was observed in children 6 years old or older, with respect to 3-5 years old children. The 6-8 years old age group included the highest frequency of children exhibiting serological sign of a recent infection with 10.2% (21/206) and 8.7% (18/206) of children having anti-PT titers [40-100] and ≥100 IU/ml, respectively. In Dapaong (TGO), seropositivity rate was the lowest (56.3%; 180/320) in the 9-11 years old age group, and reached 70.1% (162/231) in the 12-15 years old age group. Rate of children exhibiting serological sign of recent infection was similar across the age groups and totalized 11.7% (106/908) and 2.1% (19/908) of children having anti-PT titers [40-100] and ≥100 IU/ml, respectively. Neither sex nor availability of the vaccination booklet was associated to seropositivity.

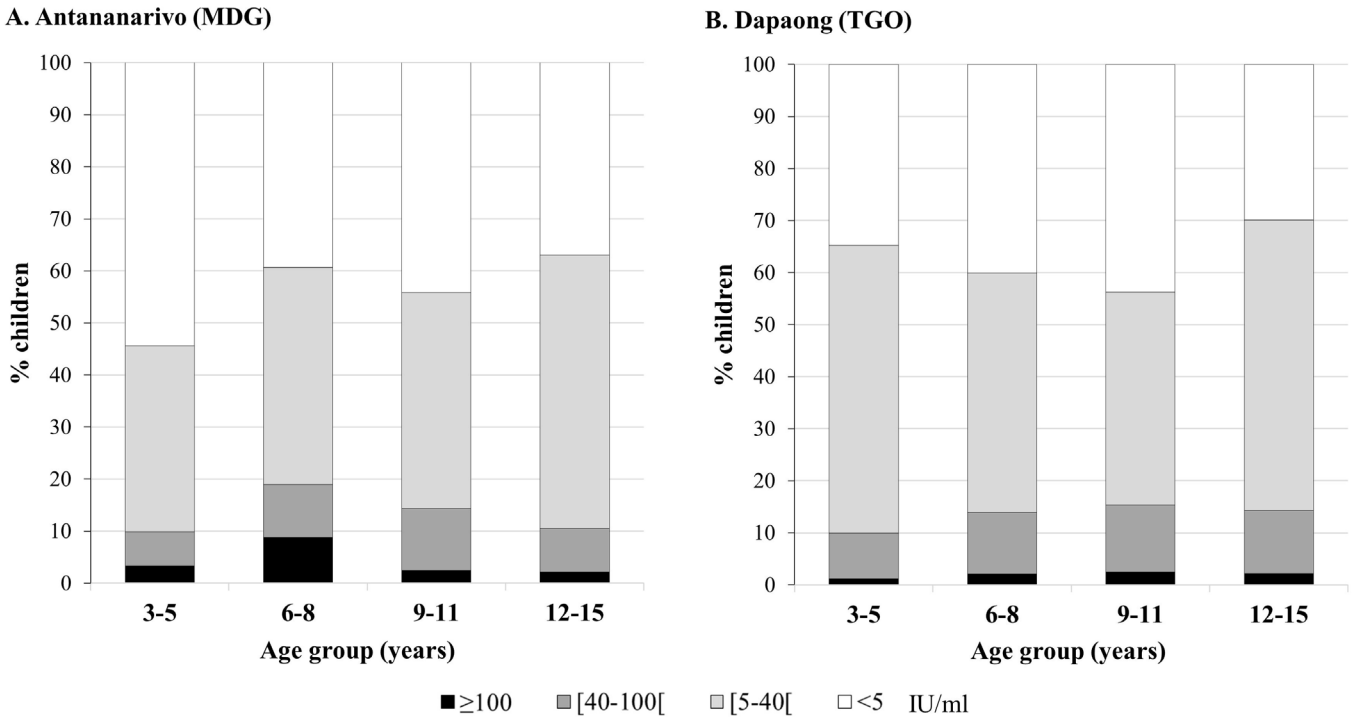

Figure 2: Distribution of anti-PT IgG titers by age groups. Proportions of children exhibiting <5, [5-40, [40-100] and ≥100 IU/ml in Antananarivo (MDG; A), and in Dapaong (TGO; B) are represented by age groups

		Antananarivo (MDG)				Dapaong (TGO)			
			Children with anti-PT IgG titers ≥ 5 IU/ml				Children with anti-PT IgG titers ≥ 5 IU/ml		
		N	**n (%)**	**OR (95% CI)**	***p* value**	**N**	**n (%)**	**OR (95% CI)**	***p* value**
Total		1033	588 (56.9)	-	-	908	565 (62.2)	-	-
Age group (years)									
	3-5	182	83 (45.6)	1	*ref*	170	111 (65.3)	1	*ref*
	6-8	206	125 (60.7)	1.8 (1.2-2.8)	***0.003***	187	112 (59.9)	0.8 (0.5-1.2)	*0.293*
	9-11	369	206 (55.8)	1.5 (1.1-2.2)	***0.024***	320	180 (56.3)	0.7 (0.5-1.0)	*0.053*
	12-15	276	174 (63.0)	2.0 (1.4-3.0)	***<0.001***	231	162 (70.1)	1.2 (0.8-1.9)	*0.305*
Gender									
	Boys	512	299 (58.4)	1	*ref*	425*	254 (59.8)	1	*ref*
	Girls	521	289 (55.5)	0.9 (0.7-1.1)	*0.342*	482*	310 (64.3)	1.2 (0.9-1.6)	*0.159*
Origin of pertussis vaccination history									
	Declarative	-				112**	77 (68.8)	1	*ref*
	Vaccination booklet	-				795**	487 (61.3)	0.7 (0.5-1.1)	*0.127*

** 1 child with no information regarding sex in Togo*

*** 1 child with no information on origin of pertussis vaccination history*

Significant p values are presented in bold.

Table 2: Analysis of pertussis seropositivity according to age groups and other factors in Antananarivo (MDG; left), and in Dapaong (TGO; right)

Vaccination timeliness

Due to the lack of vaccination booklet, or incomplete dates of birth or of vaccine injections, assessment of vaccination timeliness was performed on the data from 996 and 772 children, in Antananarivo (MDG) and Dapaong (TGO), respectively.

Median age at each vaccine dose is presented in Table 3. Overall, median age for each dose was older than recommended in both countries. The rate of children who initiated the vaccination at age >8 weeks was 33.4% in Antananarivo (MDG) and 39.4% in Dapaong (TGO). On the other hand, 1.8% and 3.4% of children received their third vaccine dose at age >12 months old in Antananarivo (MDG) and Dapaong (TGO), respectively. Compliance with national vaccination recommendation was 89.0% (886/960) and 77.2 % (596/772) in Antananarivo (MDG) and Dapaong (TGO), respectively (Figure 3). Vaccine timeliness was found to be significantly associated to the age groups, with children aged 3-5 years showing a better compliance with the recommendations in both countries (Table 3). While girls were significantly more compliant as compared to boys in Antananarivo (MDG), pertussis seropositivity was not associated to vaccine timeliness in both study populations.

		Antananarivo (MDG) - N=996			**Dapaong (TGO) - N=772**		
Age at injection (wks)		**median (IQR)**			**median (IQR)**		
Dose 1		7.3 (6.6-8.9)			7.4 (6.6-9.7)		
Dose 2		12.4 (11.4-14.4)			13.0 (11.6-16.0)		
Dose 3		17.6 (16.3-20.0)			18.7 (16.4-23.4)		
Initiation of primary vaccination at age >8 wks		**n (%)**	**OR (95% CI)**	***p* value**	**n (%)**	**OR (95% CI)**	***p* value**
Total		337 (33.4)	-	-	304 (39.4)	-	-
Age group	3-5	49 (27.4)	1	*ref*	52 (34.2)	1	*ref*
	6-8	62 (33.0)	1.3 (0.8-2.0)	*0.243*	49 (30.3)	0.8 (0.5-1.3)	*0.453*
	9-11	128 (35.9)	1.5 (1.0-2.2)	*0.050*	106 (39.7)	1.3 (0.8-1.9)	*0.265*
	12-15	98 (36.0)	1.5 (1.0-2.3)	*0.056*	97 (50.8)	2.0 (1.3-3.1)	*0.002*
Sex	Boys	162 (32.3)	1	*ref*	147 (41.2)	1	*ref*
	Girls	175 (35.4)	1.1 (0.9-1.5)	*0.314*	157 (37.8)	0.9 (0.7-1.2)	*0.343*
Anti-PT IgG titers	<5 IU/ml	155 (36.4)	1	*ref*	110 (36.8)	1	*ref*
	≥5 IU/ml	182 (31.9)	0.8 (0.6-1.1)	*0.142*	194 (41.0)	1.2 (0.9-1.6)	*0.242*
Timeliness for entire primary vaccination		**n (%)**	**OR (95% CI)**	***p* value**	***n (%)***	**OR (95% CI)**	***p* value**
Total		886 (89.0)	-	-	596 (77.2)	-	-
Age group	3-5	169 (94.4)	1	*ref*	134 (88.2)	1	*ref*
	6-8	166 (88.3)	0.4 (0.2-1.0)	*0.042*	134 (82.7)	0.6 (0.3-1.2)	*0.175*
	9-11	310 (86.8)	0.4 (0.2-0.8)	*0.009*	204 (76.4)	0.4 (0.2-0.8)	*0.004*
	12-15	241 (88.6)	0.5 (0.2-1.0)	*0.040*	124 (64.9)	0.3 (0.1-0.4)	*<0.001*
Sex	Boys	432 (86.2)	1	*ref*	275 (77.0)	1	*ref*
	Girls	454 (91.7)	1.8 (1.2-2.7)	*0.006*	321 (77.4)	1.0 (0.7-1.4)	*0.916*
Anti-PT IgG titers	<5 IU/ml	383 (89.9)	1	*ref*	230 (76.9)	1	*ref*
	≥5 IU/ml	503 (88.3)	0.8 (0.6-1.3)	*0.409*	366 (77.4)	1.0 (0.7-1.4)	*0.883*

Table 3: Age at pertussis vaccination and factors associated to vaccination timeliness in Antananarivo (MDG; left), and in Dapaong (TGO; right). *Wks: weeks*

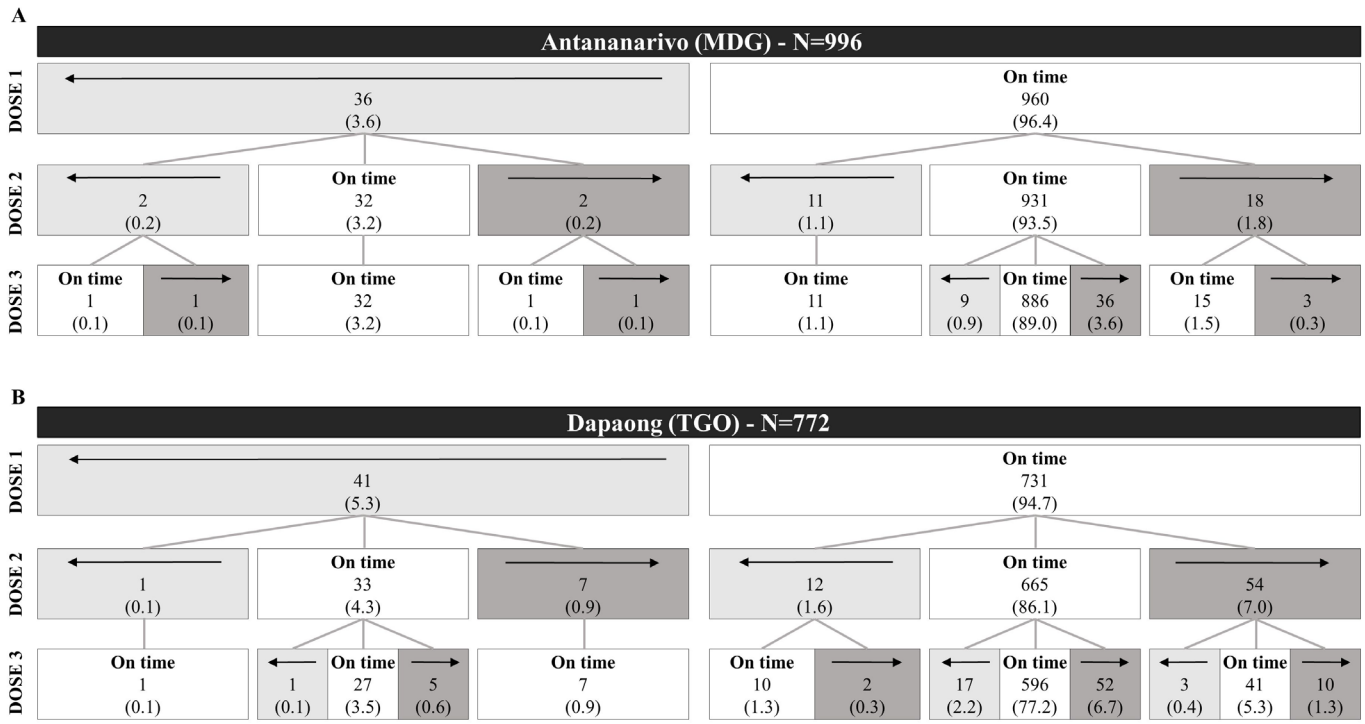

Figure 3: Compliance with national recommendations for pertussis immunization. Numbers and proportions of children who received early (light grey), on time (white), and late (dark grey) pertussis vaccine as compared with national recommendations are presented for each dose in Antananarivo, Antananarivo (MDG; upper panel A) and in Dapaong (TGO; lower panel B). Intervals in between the first and second, and second and third doses are shown with respect to compliance with the first and second dose, respectively. Results are shown as n (%)

Discussions

The present sero-epidemiological studies are novel in addressing the circulation of *B. pertussis* in fully vaccinated children in Madagascar and in Togo**.** The approach using indirect diagnosis applied in these studies is particularly interesting in LMIC settings as *i)* it is easy to implement on a large scale, and *ii)* there is no booster vaccine that may interfere with infection-induced anti-PT IgG detected by ELISA. It allows, not only to diagnose recent infection and address immune responses to vaccines, but also evaluate immunity in populations. These studies, focusing on vaccinated 3-15 years old children and adolescents, evidenced the circulation of *B. pertussis* in Antananarivo, Madagascar, and in Dapaong, Togo, with recent cases occurring, thus suggesting insufficient immune protection at least 3 years from the primary vaccination. Details on vaccination history also highlighted delay in implementing early vaccination, although it appeared to have improved in recent years.

The trend in seropositivity rates observed across the age groups in Antananarivo (MDG) was similar to what we observed in Cambodia, where the same study was run and where the same pertussis immunization schedule is applied [10]. There was a significant increase in frequency of seropositive children among those aged 6 years and older with respect to the 3-5 years age group, anti-PT titers being the highest among the 6-8 years old age group. However, in Antananarivo (MDG), rates were higher with roughly 10% increase for each age category with respect to what was observed in Cambodia, and there were more recent infection cases detected, reaching 18.9% of the 6-8 years old children. By contrast, seropositivity rate in Dapaong (TGO) was as high as 65.3% in the 3-5 age group, with no significant variation among older children. Global seropositivity rates were 56.9% and 62.2% in Antananarivo (MDG) and in Dapaong (TGO), respectively, while it was 47.0% in Cambodia. However, comparison of global seropositivity is difficult since incidence rate varies across the years in a given country. Indeed, pertussis is an endemic disease with 3-5 years cyclic increase of incidence, depending on rate of susceptible individuals. This is linked to demographic differences and different vaccine coverage [12]. With the scarce surveillance in Madagascar and Togo, it is not

possible to determine whether the study was run during a period of low or high circulation of *B. pertussis*. WHO monitoring system reports that annual number of cases ranged from 0 to 350 in Madagascar, and from 10 to 180 in Togo in the past 15 years, including several years for which no data is available for both countries [13,14]. Serological evidence of recent cases occurring in both Antananarivo (MDG) and Dapaong (TGO) in all age groups was found in these studies. Loss of vaccine-induced immunity was well described with wPVs in historical and more recent studies, including in African settings [15-17]. This observation, also true when acellular pertussis vaccines are used, have lead the health authorities to recommend several booster doses including in toddlers and preschool children [1]. Study results are not surprising given the insufficient coverage recorded in these two countries, and vaccination schedule restricted the primary vaccination in newborns. Indeed, despite the improvement in the beginning of the 2000s, vaccine coverage remains below the 90% goal of WHO Global Vaccine Action Plan in both countries. Estimates given by the United Nations of International Children's Emergency Fund (UNICEF) and the WHO show that coverage for third dose of wPV was less than 60% in 2000 in Madagascar; it slightly increased thereafter ranging from 70% to 80% [18]. Similarly, coverage was 64% in Togo in 2000, and then has stayed to approximately 80% since 2005 [19].

The success of the immunization program and population-level immunity is determined by the national coverage, but also by the ability of delivering the three doses within a narrow time window to provide early and adequate protection, and the quality of the wPVs [20]. In Antananarivo (MDG), timeliness of vaccination, in particular intervals in between two doses, was as high as 89.0%. However, >30% of Malagasy children failed to initiate their pertussis vaccination program at ≤8 weeks of age, which is a WHO recommendation [1]. Similar observation was found in a recent large analysis studying coverage in six districts in Madagascar [21]. Of note, this delay in initiating the vaccination program was significantly lower among the youngest children, which suggest an improvement of the national vaccination campaign. In Dapaong (TGO), compliance was not as high, with 77.2% of children who were vaccinated following the national recommendations; delay in administering doses 2 and 3 concerned 7 and 8% of the children, respectively. In addition, 39.4% of the children started the vaccination program at age >8 weeks of age. Similarly to what was observed in Antananarivo (MDG), the youngest children (3-8 years old) represented those who most frequently received their first dose at ≤ 8 weeks of age.

In absence of booster doses, vaccinees become more susceptible for infection and disease as time goes by, and contribute to maintain circulation that may be critical for the very young and unvaccinated children. This delay is also highly dependent on the quality of wPVs that are currently available, which is unknown. Studies on wPVs used in the past have evidenced high variability in immunogenicity, efficacy, effectiveness among the products [22]. This lack of data of contemporary vaccines is a concern that is added to the fact that wPVs distributed in LMICs are often acquired from different vaccine producer's year-to-year.

In this research, the same study protocol was applied in two very different regions of the African continent. On one hand, recruitment took place in Antananarivo (city and suburban areas), which is Madagascar's main city with as very high population density that reached 1.9 million inhabitants in 2018. On the other hand, the study was implemented in Dapaong, the main city of the Savanes region in Northern Togo. Its population was estimated to be 69,900 in 2020. In addition, recruitment of children took place over two different periods, at approximately one-year interval. While the sero-epidemiological results cannot be compared, they spotlight pertussis as a public health concerned that demands a better surveillance in Madagascar and Togo, in order to determine the most adapted health strategy to adopt.

Conclusions

The present results showed that *B. pertussis* substantially circulates among Malagasy and Togolese children vaccinated during infancy, with increasing contact from 6 years old in Antananarivo but at a steady rate in Dapaong. Further efforts are necessary to initiate vaccination schedule as early as 6 weeks of age, and timeliness of vaccination should be improved in Dapaong. These data are local evidence of the need for improving pertussis surveillance in Madagascar and Togo. The presence of a platform for laboratory diagnosis is critical to estimate the burden of the disease and to rapidly confirm the diagnosis to clinicians to eventually adapt the antibiotic therapy. The results also support the extension of the vaccination program with boosters.

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Authors' contributions

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Investigation: AH, BMNL, AKM
Laboratory analysis: LR, AKK, SLR
Supervision: FT, AH, BMNL, JMC, GN, NG
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Formal analysis: GN, NG, FT
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