

THE EVALUATION OF THE EPIDEMIOLOGICAL POINT OF VIEW TO THE DEVELOPMENT OF MEASLES VACCINATION IN TIMOR-LESTE.

Carlos Boavida Tilman, Isabel de Jesus Amaral, Acácio Pereira Guterres, Celina Maria Godinho, Urraca Magno Corte Real de Araújo, Alexandre Gentil Corte Real Araújo

**Correspondence:*

Carlos Boavida Tilman

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ABSTRACT

Introduction: The epidemiological changes of rubella measles in Timor-Leste, as well as the existence of outbreaks of the disease or disease in neighboring countries Indonesia, Malaysia and Australia and other regions of the world associated with information and communication. Being the updated epidemiological being peeled and in the point of view always be related to the vaccination status, which make it difficult to take decisions based on the area of vaccination, specially with respect to the optimal ages for administration of measles rubella vaccine1 and rubella 2 measles (VASRP I and VASPR II) in the evaluation of the program. This study deals with the most recent updates regarding the approach of the disease in therapeutic support, epidemiological surveillance and the encouragement of vaccination as the main form of prevention.

Objectives: It intends to evaluate the adequacy of the vaccination strategy against rubella measles in force in Timor-Leste, which concerns the ages for the implementation of VASPR I and VASPR II in order to continue eliminate the disease in the national territory.

Methodology: A study was conducted with 90 newborn son of mothers with different states vaccinated against measles rubella (0 dose, 1 dose and 2 doses) by health professionals. We also studied 90 adolescents/young people who underwent VASPR II at different ages. The data obtained come from two sources of information: history of documented vaccination of questionnaires applied by entrevista and serologic information, was obtained by dosing the titer of antibodies especially antimeasles (ATS IgG) in sera, using the enzymatic immune method ELISA of the *Kit EnzygnostrAnti -measles Virus/IgG* of the manufacturer Siemens.

Discussion: The rate of vaccination coverage of the measles vaccine increased from values of just over 38% in the generation born before 2005, with a single dose of vaccine, to values higher than 95% in the generation born after 2010 in two doses of vaccine. The geometric concentration of ATS IgG in the umbilical cord increased with the increase in the age of the mother (OR=0.092; p=0.001). Newborns born to vaccinated mothers (p<0,001), re-

regardless of the number of doses their mothers received ($p=0.222$). The mean geometric concentration (GGM) of ATS IgG in adolescents and young people decreases with the time elapsed since VASPR II tma ($OR=0.244$; $p=0.0001$).

Conclusion: The ages of vaspr I and VASPR II may have to be altered to adapt to the epidemiological changes that occurred in the late years in Timor-Leste and contribute to the elimination of rubella measles in the national territory (PENSS 2011-2030, cited by Tilman CB, 2022).

KEY WORD: Surveillance, Epidemiological, Measles, Vaccine, Plan, Elimination of Virus.

INTRODUCTION

Measles is a serious and highly contagious disease caused by a virus. Prior to the introduction of the vaccine against the disease, in 1963, and the vaccination of mass populations every 2-3 years were recorded important epidemics of measles, which came to cause approximately 2.6 million deaths per year. The trivalent vaccine against measles, against epidemic parotitis and rubella (VASPR) was introduced in the calendar recommended by the Ministry of Health of Timor-Leste of the National Immunization Program in 2002, implementation of the national vaccination campaign cited by (Tilman CB, 2023). The disease remains a leading cause of death among young children worldwide, although there is a safe and effective vaccine available. Approximately 110,000 people died from measles in 2021 – mostly children under the age of five, most affected in this situation in Timor and almost everyone else. Measles is caused by a virus of the family *Paramyxoviridae* and is usually transmitted through direct contact and through air. The virus infects the respiratory tract and spreads throughout the body. It is a human disease, that is, it does not occur in animals. Accelerated immunization activities have a major impact on reducing measles deaths.

From 2000 to 2021, measles vaccination prevented approximately 21.1 million deaths. The number of deaths from the disease worldwide fell by 80% in the period-

from 545,000 in 2000 to 108,000 in 2020. In some countries, the anticipation with immunization strategies equal to Timor-Leste, the priority age of the initial phase has decreased to 1 year to measure has increased in the proportion of newborn children of immunized mothers. These women will have lower risks clear concentrations of antibody, as they responded in babies born, thus they, less convergences of the same model of antibody or immunity, right after protected of each child (Gonçalves et al at 1998; cited by Tilman CB, 2023). The use of higher vaccination coverage with two dose vaspr for a national strategy for measles eradication and universal elimination is academically significant approved By Theeten et al, 2010; Portugal, 2011; Timor-Leste, 2022). Although Timor-Leste had survived documented cases of measles hidden since 2002, there is a need to amplify epidemiological surveillance of the disease in a short way in neighboring Indonesia and Malaysia, the situation has reached island Timor.

General Objective: to characterize in the evaluation of Timor-Leste under study. It is essential to reduce or eliminate pathologies that can prevent through measles vaccines.

Specific objectives:

1. To know the functioning of the procedures of diagnosis, notification, investigation, classification and laboratory support for the surveillance of suspected cases of measles at different levels of the health system.
2. Assess epidemiological surveillance indicators of the

national measles elimination plan.

3. Identify problems and make concrete recommendations to improve surveillance at different levels of the Timor-Leste health system.

THEORETICAL FRAMEWORK

Measles is an acute infectious viral disease, extremely contagious and quite common in childhood, can evolve with serious complications including encephalitis, pneumonia and death. The current viremia of the infection proves a generalized vasculitis, responsible for the appearance of the various clinical manifestations. This virus is responsible for measles in the human population and affects mostly children, adults and young people. It is very pathogenic and superior to contagious existence in larger human populations and being able to keep in circulation or distribution to cause acute individual infection only once in human life (CDC, 2012; CB Tilman, 2023). If a transmission route occurs directly, by means of nasopharyngeal secretions expelled by coughing, sneezing, speaking or breathing by people infected by the virus or rarely by aerosol in mucous membranes of the upper or conjunctive respiratory tract. The disease has an incubation period of usually 10 days, ranging from 7 to 18 days from the date of exposure to the onset of fever, and about 14 days to the only one of the exanthema. The period of transmissibility begins from four to six days before the exanthema and lasts up to four days after its appearance. An important feature of the measles virus is that it is antagonistically monotypic, despite its phenotypic diversity and the fact that RNA viruses have high mutation rates.

New measles vaccines do not need to be developed to combat evolving virus strains because the neutralizing epitopes of the hemagglutinin protein that confer protection are highly conserved. Consequently, attenuated measles vaccines derived from a single genotype of the virus isolated in the 1950s remain effective worldwide.

Measles is one of the leading causes of morbidity and mortality among children under five years of age, most of all malnourished and those living in developing countries. Morbimortality among children under five years of age, especially malnourished children and those living in developing countries. It is a disease with universal distribution, with seasonal variation. In tropical climates, transmission seems to increase after the rainy season. The endemic-epidemic behavior of measles varies from one site to another, and basically depends on the relationship between the degree of immunity and susceptibility of the population, as well as the circulation of the virus in the area. Between 2000 and 2021, due to wide vaccination coverage, the annual incidence of the disease fell by 83%. But in recent years, cases of measles have been reported in various parts of the world and, according to the World Health Organization (WHO, 2022), the countries of the continents Europe, Africa have recorded the largest number of cases of the disease. Although the incidence of the disease is 1 case per 1 million inhabitants in the United States of America (USA), the importation of cases has reflected in the increase in the number of cases since 2018, especially due to low vaccination rates (CDC, 2018).

Measles can affect most organic systems and is more prevalent in young infants, adults over 20 years of age, pregnant women, and immunocompromised or malnourished people, particularly children with vitamin A deficiency. The diagnosis of measles should follow clinical, laboratory and epidemiological criteria. The most commonly used laboratory diagnosis is the enzyme immune assay (ELISA) for the detected specific IgM antibodies that can be detected in the blood ideally in the acute phase of the disease, being present from 3 days to 4 weeks after the onset of symptoms. The measles virus can also be identified by the RT-PCR technique in samples collected up to the fifth day from the beginning of the rash, preferably in the first three days, through clinical

specimens (blood, urine and nasopharyngeal secretion). The sensitivity and specificity of this technique varies between 85% and 98%. Currently, viral isolation is also made, which aims to establish the genetic pattern of the circulating virus in the country, to differentiate autochthonous cases imported and the wild virus of the vaccine virus.

The elimination of susceptible (non-immunized population) disrupts the transmission chain. At the individual level, the home or hospital isolation of cases decreased the intensity of contagions. It should be avoided, mainly, the attendance to schools or day care centers, groupings and any contact with susceptible people within four days after the beginning of the exanthematic period. As the risk of in-hospital transmission is very high, selective vaccination should be promoted for all patients and professionals in the hospitalization sector of the suspected case of measles or, depending on the situation, of all hospital professionals. Hospitalized patients should undergo aerosol respiratory isolation for up to four days after the onset of the exanthema. With the introduction of the measles vaccine, there was a marked reduction in the incidence of the disease and the circulation of the virus, however, even in areas with high rates of vaccination coverage, outbreaks can still occur.

Epidemiological Surveillance

The main objective is to maintain the elimination of measles through sensitive, active and timely epidemiological surveillance, allowing the immediate identification and notification of any suspected case in the population, with relevant control measures:

1. Notify Immediately (24h) to the General Health Directorate Secretariat (Epidemiological Surveillance) all suspected cases of measles is mandatory for concrete action.
2. It is defined as a suspected case of the measles. Every patient who, regardless of age and vaccination status, has fever and papular rash to the company of one or

more of the following signs and symptoms: cough or runny nose and or conjunctivitis; Every individual the suspect with a history of traveling abroad in the last 30 days, or contact, in the same period, with someone who traveled abroad.

3. Carry out The Blockade Vaccination: The main measure of measles control is vaccination. Timely vaccination block should be carried out no later than 72 hours after notification of the case in order to interrupt the transmission chain. Vaccination block is selective and the triple viral vaccine should be administered according to the documented vaccination status of the case contacts; Contacts from six months to 11 months and 29 days; They should receive a dose of triple viral. This dose is not valid for routine vaccination, and the dose should be scheduled at 12 months, as recommended by the National Immunization Program. Contacts from 12 months to 49 years of age: Must be vaccinated according to the indications of the National Immunization or Vaccination Program according to the schedule (Tilman CB, 2023).

METHODOLOGICAL RESEARCH.

It uses descriptive and analytical method of quantitative approach in the application of research. Population is a collection of individual units, which can be people with one or more characteristics in common, who meet analyze. A study was conducted with 90 newborn children of mothers with different states vaccinated against rubella measles (0 doses, 1 dose and 2 doses) by health professionals. We also studied 90 adolescents/young people who perform VASPR II at different ages. The data obtained come from two sources of information: documented vaccine history; from questionnaires applied by interview and serological information, it was obtained by dosing the titer of antibodies especially anti measles (ATS IgG) in sera, using the enzymatic immune method ELISA of the *Kit Enzygnostr Anti-measles Virus/IgG*,

from the manufacturer Siemens. The sampling technique that was applied in this investigation was the intentional non-probabilistic sampling technique. Data analysis we will investigate or use simple descriptive statistics to the Computer Program SPSS (*Statistical package For the Social Sciences*) and the results presented in research (table 1, 2 & 3).

RESULTS OF DISCUSSION

The result of the questionnaires that were collected, described data and types of respondents different from two study groups in their knowledge of rubella measles vaccination in the coverage result that are presented in the following table:

Table 1. The coverage of immunization Measles Rubella 1 and complete immunization of children aged >1 year, between municipalities, Timor-Leste, January-December 2021.

Municipalities	Target Population (< year1) (Jan-Dec)	Measles Rubella One						Complete immunizations 1 year					
		(1) Number			(%)			Number			(%)		
		M	F	Total	M	F	Total	M	F	Total	M	F	Total
Aileu	1,610	816	832	1648	51	52	102	294	310	604	18	19	38
Ainaro	1,392	776	737	1513	5th 6th	53	109	697	709	1406	50	51	101
Baucau	2,629	1753	1717	3470	67	65	132	1748	1740	3488	66	66	133
Bobonaro	1,972	1047	1027	2074	53	52	105	977	953	1930	50	48	98
Covalima	1,803	974	956	1930	54	53	107	974	956	1930	54	53	107
Dili	9,943	4692	4630	9322	47	47	94	4599	4485	9084	46	45	91
Ermera	3,624	2207	2107	4314	61	58	119	2207	2107	4314	61	58	119
Lautem	1,456	887	768	1655	61	53	114	781	701	1482	54	48	102
Liquiçá	2,140	1156	1193	2349	54	56	110	1159	1177	2336	54	55	109
Manatuto	1,014	644	572	1216	64	56	120	643	573	1216	63	57	120
Manufahi	1,251	621	548	1169	50	44	93	690	604	1294	55	48	103
Oecússi	1,178	704	722	1426	60	61	121	369	333	702	31	28	60
Viqueque	1,894	1119	988	2107	59	52	111	0	0	0	0	0	0
East Timor	31905	17396	16797	34193	55	53	107	15138	14648	29786	47	46	93

Before vaccination, in developed countries measles had its maximum incidence in children aged 5-9 years, where infections occurred mainly at the age of children attending primary school. By the age of 20, 93% of individuals had already been exposed to the measles virus. In the Special Administration Region of Oecússi Ambeno (RAEOA) is 60% according to the introduction of the measles vaccine of the vaccination schedule in the different municipalities of Timor-Leste, the incidence of the disease has changed significantly, both in the number and ages with higher incidence. Above all the municipality of Dili within in the nation capital is 91% the coverage of measles vaccination and, Municipality of Bobonaro reached 98% and Municipality of Aileu is 38% in vaccination coverage of measles and the lowest number of immunizations.

The disease affects the human body through the entry of the virus by respiratory or conjunctival route, which then gives replication of the virus in the lymph nodes, then circulating through the respiratory system through the blood

(primary viremia). Five days after the initial infection the virus migrates to other compartments of the body, where it continues to replicate by infecting the skin, kidneys and bladder (secondary viremia). The incubation period lasts more than 10-11 days, from which the first symptoms of the disease appear, entering the prodromic pathway, which lasts 2-4 days followed by measles disease (Cutts et al, 2013; cited by Tilman CB, 2023).

Table 2. The coverage of immunization Measles Rubela2, among children aged 18 months up to 6 years, between municipalities of Timor-Leste, January-December 2021.

Municipalities	Measles Rubeola 2					
	Number			(%)		
	M	F	Total	M	F	Total
Aileu	956	894	1850	39	36	75
Ainaro	737	733	1470	35	35	69
Baucau	1372	1352	2724	34	34	68
Bobonaro	877	836	1713	29	28	57
Covalima	736	721	1457	27	26	53
Dili	4638	4545	9183	31	30	61
Ermera	2133	1983	4116	39	36	74
Lautem	949	752	1701	43	34	77
Liquiçá	1204	1086	2290	37	33	70
Manatuto	598	538	1136	39	35	73
Manufahi	665	654	1319	34	34	68
Oecússi	766	777	1543	43	43	86
Viqueque	1104	998	2102	38	35	73
East Timor	16735	15869	32604	34	33	67

We analyzed the results obtained in table two (2) indicated above, the coverage of Measles Rubella II vaccination was shown in 2021. In each municipalities of Timor-Leste at municipal levels there are equal in the result of coverage, measles vaccination 2 among other municipalities of high and low. Thus, Baucau and Manufahi equal 68%, Manatuto and Viqueque 73%, highest coverage municipality Lautem 77% and low municipality Suai Covalima 53%. Therefore at the National level is 67% and comparing with the other municipalities in average we can see in the same table (2), according to written data. In the definition of priority is an important stage of strategic planning the health of Timor-Leste indispensable for the implementation of relevant plans and national campaign of measles rubella are fundamental. Second (Imperatory, 2017; cited by Tilman CB, 2023), in the organization of health and priorities should take into account the horizon in the future time of programming in the area of program and main theme in the study of continued research. Based on the results presented in the situation diagnosis, we identified a set of problems that were considered to establish priorities in rapid intervention. The method followed was an adaptation of the implementation model of each municipality in the priority plan and execution of rigor (Tilman CB, 2023). The criteria used were programming horizon of the project of available resources (human and material).

Table 3. Risk of at s igs seronegativity (*odds ratio*) in newborns born to mothers with one and two measles vaccine, due to the different independent variables.

Group 1 dose (n=62) + Group 2 doses (n=90)				
Variables	Simple model		Multivariate	
	OR (CI = 95%)	P value	OR (CI = 95%)	P value
Maternal age	0,85 (0,761 – 0,932)	0,001	0,821 (0,768-0,922)	0,005
Birth Generation				
Before 2011	-	-	-	-
2011 – 2021	0,39 (0,155-0,957)	0,040	-	-
After 2021	Reference			
Mother's schooling				
3rd Cycle of basic education	1,34 (0,41 – 4,42)	0,632		
Full secondary education	0,814 (0,24-2,72)	0,738		
Higher education	Reference			
Parity				
First	1,28 (0,235-4,146)	0,999		
2 ^{to}	1,37 (0,30-8,331)	0,999		
3 ^{to}	Reference			
Gestational age				
Preterm	2,95 (0,97 – 8,75)	0,050		
Termo	Reference			
Baby girl sex				
Female	1,44 (0,58 – 3,82)	0,433		
Male	Reference			
Baby girl weight				
<2500g	4,03 (1,068-15,24)	0,036		
>2500g	Reference			
Vaccination status				
2 dose	2,7 (0,936 – 7,789)	0,066		
1 dose	Reference			
Age 1 takes	0,99 (0,977 – 1,004)	0,157		
Last of vaccination	0,95 (0,894 – 1,012)	0,112		

Thus, the risk of ATS IgS seronegability in newborns born to mothers immunized with only one dose of measles vaccine, due to the different variables predicted and calculated in the practice of vaccine implementation is fundamental in timor-leste health services. In the simple logistic regression model of this group of newborns only maternal age ($OR = 0.80$; $95\% CI: 0.692 - 0.929$; $P=0.003$) and the baby's birth weight ($OR=13.32$; $95\% CI: 0.690-253.4$; $p=0.042$) is related or associated in a statistically significant way to risk and line of seronegatividade ATS IgG, it is thought that the line of seronegatividade ATS IgG decreases with increasing age and increase with decreased weight of the baby at birth see in table three (3). In this group of newborns the final measurement model, multivariate logistic regression does not discriminate any variable with significant statistical weight and capable of influencing the line or risk of

ATS IgG seronegativity, according to the research result in the above reference table cited by (Tilman CB, 2023).

CONCLUSION

Vaccination is the main effective measure of measles control, which is achieved with 95% of the immunized population. Thus, campaigns to reach most of the population are necessary, especially to avoid imported cases and disease control. In this conclusion we will interpret the results in the light of academic literature and current theories in this area of research. We will try or provoke account of the main contributions to understanding in the evaluation of vaccine strategies in the control of the elimination of rubella measles in Timor-Leste, in particular and especially with regard to the age of the first taking of VASPR. The discussion will be made for the

group of newborns by the following titles of analysis: internal validity, external validity of the vaccine study, in concentration of ATS IgG and risk of seronegativity, factors associated with the convergence of ATS IgG and the seronegativity line, we recommend the continuity of this research in the future cited by (Tilman CB, 2023).

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