International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Vaccine-Specific Aspects Associated with the Abandonment of Early Childhood Vaccination in the City of Kisangani, Dr Congo

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Abstract
In Kisangani, the dropout rate of 17.5% among children aged 12 to 23 months is higher than the threshold of less than 10% tolerated by the WHO, despite the free availability of vaccines. This study aims to analyze vaccine-specific aspects in order to identify predictors associated with vaccine dropout among children aged 12 to 23 months. A cross-sectional observational study was conducted from October 25, 2022 to February 25, 2023 among mothers of 336 children aged 12 to 23 months in Kisangani. A pre-tested and administered questionnaire was used for data collection based on three-stage cluster sampling. Analyses were performed on STATA 13 using stepwise logistic regression with a threshold of 0.05. A total of 336 children aged 12 to 23 months from 5 health zones in the city of Kisangani were included in the analysis. We observed a 37.5% prevalence of early childhood vaccination drop-out in Kisangani. After adjustment by multivariate logistic regression, the following determinants were significantly associated with drop-out from early childhood vaccination : preference for vaccine administration mode, refusal of a vaccine during a mass campaign, delay in vaccinating when a new vaccine is introduced, lack of confidence in vaccinators who go door-to-door, preference of vaccination site, presence of adverse events following immunization and poor reception by health professionals. Thus, the results of this study can help planners, policy-makers and decision-makers to focus on both individuals and the communities in which they live.

Keywords : Immunization, vaccine, vaccine hesitancy, early childhood, Kisangani

1.Introduction

Vaccination is recognized as one of the most effective and cost-effective public health interventions. In particular, it has led to the eradication of smallpox, reduced the global incidence of poliomyelitis by over 99% and neonatal tetanus by 94%, and dramatically reduced morbidity, disability,

mortality and complications from infectious diseases [1,2]. Advances in vaccination have prevented around 2.5 million deaths each year, and ensured that vaccinated children enjoy healthy growth [3].

However, despite this progress, disparities in immunization coverage persist between countries and within national territories, so that reaching unvaccinated or insufficiently vaccinated children remains a challenge. As a result, vaccine-preventable diseases (VPDs) are still a major cause of morbidity and mortality in children under five [3].

In response to this situation, the World Health Assembly has declared the decade 2011-2020 the "decade of immunization" to ensure universal access to vaccines. The Global Vaccine Action Plan aims, among other things, to achieve national coverage of 90% and at least 80% in every district for all vaccines included in national programs, and to introduce one or more new or underused vaccines in low-income countries [1, 3,4].

Worldwide, coverage for the third dose of the combined diphtheria-tetanus-pertussis (DTP) vaccine and for the measles vaccine (VAR), in children under one year of age, was 86% and 85% respectively in 2014. In addition, 18.7 million children have not received the full three-dose series of DPT, of whom 11.5 million have not received the first dose of this vaccine. For nearly five years, a third of the world's countries have not achieved 90% national coverage with DTP3, and an estimated 20.6 million children were not vaccinated against measles in 2014 [4 - 6].

As a result, more than 50% of pre-school mortality was due to diseases preventable by existing vaccines. In 2018, the World Health Organization (WHO) estimated that 5.6 million children under the age of five died ; this translates into 15,000 deaths every day. With proven strategies, vaccines can be accessible to even the hardest-to-reach and most vulnerable populations [7,8].

Despite the medical importance of vaccines in eliminating potentially fatal infectious diseases, the WHO has reported that 19.5 million infants are partially or unvaccinated. There is clear evidence that unvaccinated or undervaccinated children are at high risk of developing diseases, a condition that can result in the re-emergence of nearly eradicated killer diseases [9]. Moreover, during an epidemic, all unvaccinated children and their families may be quarantined and even excluded from certain areas. Similarly, unvaccinated or partially vaccinated children may also be legally excluded from certain schools and after-school programs [8]. All these events, as highlighted by Jit et al, ultimately have additional negative economic implications at household, community and national level. This is because vaccine-preventable diseases can be recurrent and severe, while exerting pressure on household economies, overall health spending and healthcare programs [7].

In sub-Saharan Africa, the under-five mortality rate remains the highest in the world, with one-fifth of 13-year-olds dying before their fifth birthday ; this is 5 times higher than in high-income countries. Sub-Saharan Africa and Central and South Asia accounted for more than 80% of the 5.3 million under-five deaths in 2018, despite representing only 52% of the world's under-five population. More than half of all under-five deaths are due to diseases that can be prevented with simple, affordable interventions from the Expanded Program on Immunization. Strengthening the health system to offer all children such interventions will save many young lives [7,8].

Among the ten countries in the world with around 11.4 million (61%) unimmunized or inadequately immunized children are five low- and middle-income African countries : Nigeria, Ethiopia, Democratic Republic of Congo (DRC), Uganda and South Africa [5,6].

The Democratic Republic of Congo has made progress in reducing under-five mortality from 158 to 104 per 1,000 live births in 2007 and 2013 respectively [11], and to 70 per 1,000 live births in 2017[10].

Despite this progress, the situation remains worrying when compared to the global situation and the achievement of the third sustainable development goal. This excess mortality among children is largely attributable to vaccine-preventable diseases [11].

In 2013, estimates of immunization coverage based on information from the vaccination record showed that only 41% of children aged 12 to 23 months were fully vaccinated before the age of 12 months in the DRC. When information provided by the mother is taken into account, this percentage rises to 45%. The report recorded disparities in vaccination coverage between rural (42%) and urban (53%) areas, and between the country's provinces [12].

In addition, the MICS 2017 - 2018 study showed 35% vaccination coverage among fully vaccinated children aged 12 to 23 months. This overall figure conceals significant disparities at provincial level. With 71% of children fully vaccinated, North Kivu recorded the best immunization coverage, followed by Kinshasa where 68% of children received all EPI vaccines. On the other hand, Kasaï Oriental, Équateur and the former Orientale province recorded the lowest vaccination coverage, at 37%, 33% and 30% respectively [11,12].

As a result, the DRC still has one of the highest neonatal mortality rates in the world (30%), and 1.8 million children do not receive all the necessary vaccinations every year. According to UNICEF, only 35% of children between the ages of 12 and 23 months in the DRC are fully vaccinated before their first birthday, so the risk is high. Of all the vaccine-preventable diseases, the country has experienced major epidemics of measles, polio and yellow fever in recent years [13].

Numerous epidemiological studies conducted in low-income countries, including the DRC, have identified several barriers to childhood immunization, including factors at the individual, household and community levels. For example, at the individual level, Shrivastwa et al reported that child gender, birth rank and age influence vaccination status [14]. At household level, paternal education [15], maternal characteristics, household income, health care utilization, distance from health facilities, religion, and source of information [16] were significantly associated with children's immunization status. At community level, geographic region and place of residence, communities with high illiteracy rates, socioeconomically disadvantaged communities, communities with higher institutional delivery rates and maternal prenatal care were associated with children's immunization status [17,18].

In Tshopo province, the drop-out rate of 17.6% in 2021 is higher than the threshold of minus 10% tolerated by the WHO [2]. This is indicative of the weakness of the vaccination program's effective management. Indeed, the results of the vaccination coverage survey showed that 25.7% of mothers do not have a vaccination card. With regard to BCG and VAR, the survey showed vaccination coverage of 19.7% and 43.2% respectively, based on the vaccination card and the mother's declaration. Only 11.3% of children were fully vaccinated for all 13 antigens. The proportion of children who received no vaccine rose from 24.6% in 2020 to 44.3% in 2021[11]. As a result, the number of children affected by the measles epidemic rose from 2,626 cases and 66 deaths in 2022 to 7,693 cases and 196 deaths in week 20 of 2023[19].

Despite the availability and free supply of vaccines, many children miss out on the various strategies put in place to reach them, notably the "Reach Every Zone" approach as the basic strategy for implementing routine immunization activities, fixed, advanced and mobile strategies, intensified immunization activities, supplementary immunization activities and African Immunization Week activities. Missed vaccination opportunities are high [20 - 22]; they limit the catch-up of children who

have missed their appointment. As a result, vaccine-preventable diseases remain a concern, and children under five remain susceptible to epidemics.

Generally speaking, there are two reasons for the frequency of vaccine-preventable diseases : low vaccination coverage and the fact that the immunity conferred by the vaccine declines, so that by adolescence, some children no longer possess protective antibodies [23]. With regard to lack of vaccination coverage or completeness, the vaccination schedule and fear of side effects were the main reasons for lack of information cited by mothers of children interviewed in 2021 in the 23 health zones of Tshopo. Other reasons were also reported, but with a low proportion : ignorance of the need for vaccination, ignorance of the need to return for the next dose, unknown vaccination site and misconceptions about contraindications [11].

In Kisangani, the vaccination drop-out rate was reported by all urban health zones. In June 2020, the Lubunga, Tshopo and Kabondo health zones had not achieved BCG coverage of at least 85%. On average, BCG and VAR coverage was 57.3% and 30.9% respectively.

According to the 2021 vaccine coverage survey, the Kabondo health zone recorded a Penta1 dropout rate of 48%, Lubunga 53.9%, Makiso - Kisangani 47.3%, Mangobo 20.1% and Tshopo 53.3%. The proportion of children who have not received a single dose of vaccine is highest in the Kabondo health zone (35.2%), Lubunga (35.5%), Makiso-Kisangani (32.6%) and Tshopo (40.2%), with an average of 32% for the city of Kisangani. With regard to the drop-out rate for children aged 12 to 23 months, three health zones have rates higher than WHO standards, namely the Lubunga health zone (20.9%), Makiso-Kisangani (20.8%) and Tshopo (29%), i.e. an average of 17.5% for the city of Kisangani [11]. And yet, recent studies have shown that vaccination services are better used in urban areas [7]. This suggests that the proportion of children actually protected by immunization activities remains low. This leads to recurrent epidemics with high case-fatality rates due to vaccine-preventable diseases. The number of children affected by the measles epidemic in the city of Kisangani rose from 675 cases and 1 death in 2022 to 2,381 cases and 13 deaths in week 20 of 2023 [19].

As immunization services are relatively accessible geographically in urban areas, immunization activities are essentially based on a passive strategy, dependent on the demand and consumption of services by users [24,25]. In this context, service utilization can only be maximized when "individuals and communities understand the value of vaccines and demand vaccination as a right and responsibility" [26]. However, the vaccine-specific aspects underlying mothers' motivations to use vaccination services have not been sufficiently explored by previous studies. And those that have studied the case of the city of Kisangani are rare.

To address this shortcoming, we initiated this study to analyze vaccine-specific aspects associated with vaccine dropout among children aged 12 to 23 months in the city of Kisangani, in order to contribute further to the reduction of infant and child morbidity and mortality due to vaccine-preventable diseases. Specifically, the aim was to :

- Determine the prevalence of early childhood vaccination drop-out in Kisangani
- Identify vaccine-specific aspects of vaccine dropout among children aged 12 to 23 months in Kisangani.

2. Materials and methods

Study setting

This study was carried out in the city of Kisangani, with 5 health zones and 88 health areas. It covers an area of 1,910 km2 and a total population estimated at 1,247,628 in 2023. The target population of children aged 12 to 23 months is 43,606.

Inclusion criteria : This study included children living in Kisangani, aged 12 to 23 months during the survey period, whose mothers agreed to answer our survey questionnaire.

Non-inclusion criteria :

- All children residing in Kisangani, aged less than 12 months or more than 23 completed months during the survey period.
- All children residing in Kisangani, aged between 12 and 23 months during the survey period, whose mothers did not consent to answer our survey questionnaire.

Exclusion criteria : Children residing in Kisangani, aged between 12 and 23 months during the survey period, whose mothers abruptly interrupt the interview for reasons of personal convenience.

Study design

We conducted a cross-sectional analytical observational study from October 25, 2022 to February 18, 2023, administering a pre-tested structured questionnaire to 366 mothers of children aged 12 to 23 months in the city of Kisangani (5 health zones), selected from 88 health areas.

Sampling

To obtain representative data for the health zones in the city of Kisangani, three-stage probability cluster sampling was carried out. As all five health zones were involved, and within each health zone, all health areas were also concerned, the study used as sampling frame the list drawn from the National Health Information System database, which lists all health zones in Tshopo province with their health areas. This sampling frame was obtained using DHIS2 software from the Tshopo Provincial Health Division.

In the survey approach, each health zone was considered as a study area. There were as many surveys as there were health zones, i.e. 5 separate surveys. Within each health zone, the health areas formed clusters. The primary sampling unit was the cluster.

Sampling was carried out at three levels :

- 1st stage : in each health area, two clusters were selected by simple random draw with discount based on the exhaustive list of health areas ;
- 2nd stage : in each selected health area, 30% of avenues/neighborhoods were selected by simple random draw based on the exhaustive list of avenues/neighborhoods ;
- 3rd stage : in each health area, the selected avenues/neighborhoods formed the sampling frame. A systematic draw of households proportional to the number of children aged 12 to 23 months was carried out on the basis of a plot survey drawn up by the interviewers.

Data relating to the avenues/neighborhoods of the health areas were collected from the head nurses of the health areas. These service providers have annually updated lists of all neighborhoods/

avenues or streets in each health area. The random samples for the secondary sampling units were drawn from these lists.

Sample size estimation

The sample size was estimated according to the WHO procedure for calculating cluster sample sizes. Taking into account an average drop-out rate of 17.5% obtained during the 2021 immunization coverage survey in the city of Kisangani, a confidence coefficient of 1.96 for a confidence level of 95%, a degree of precision of 5%, a cluster effect of 1.5 and 1% non-responses, the minimum sample size was estimated at 336 children aged 12 to 23 months.

Data collection tools and techniques

Using a pre-tested structured questionnaire, mothers were questioned about vaccine-specific aspects related to the abandonment of early childhood vaccination. The information collected concerned vaccine safety, the risk/benefit ratio, delay in vaccination when a new vaccine was introduced, preference for the method of vaccine administration and delivery, fear of pain or needles during vaccination, refusal of vaccination during mass campaigns, compliance with the vaccination calendar, the mother's occupation as an obstacle to vaccination, poor reception, lack of confidence in the door-to-door strategy and the presence of adverse post-immunization events.

The BCG and VAR vaccines received by the child were obtained from the vaccination card or from the child's vaccination history as reported by the mother.

Variable definitions

Early childhood vaccination drop-out is the dependent variable. It refers to the situation of a child who has had at least one contact with vaccination services and who has not completed the full series of six contacts before his or her first birthday. In our study, this refers to children aged 12 to 23 months who received BCG and did not receive VAR. It was measured by BCG vaccine status, VAR and vaccination refusal.

The independent variables were specific aspects of vaccines or vaccination likely to influence vaccine refusal in children aged 12 to 23 months : the risk/benefit ratio or safety of vaccines, the introduction of a new vaccine, the mode of administration, the mode of delivery, the vaccination schedule, costs and the role of health professionals.

Data analysis

Data were entered into an Excel database and analyzed using STATA 13 software. Data-entry checks enabled us to minimize errors. We used contingency tables and Pearson's Chi-square test to determine the links between the dependent and independent variables. The strength of associations was estimated using raw ORs, while any probability value below 5% was considered statistically significant. To account for potential confounding factors, we used the logistic regression model, including variables that showed a significant association at the 5% threshold in bivariate analysis using a stepwise degressive approach. The first was a univariate analysis using logistic regression, which enabled us to obtain 95% confidence intervals and p-values for each of these variables. The variables with a p-value < 0.05 were all entered into a multivariate logistic regression model to control for confounding factors and determine independent predictors of early childhood vaccination dropout. A p-value < 0.05 and an adjusted odds ratio (AOR) with its 95% confidence interval not containing 1.00 was considered significant. The variable with the

highest non-significant p-value ($p > 0.05$) in model n was taken out of the model, resulting in model n-1 and so on until all variables in model n-x had a p-value < 0.05.

Ethical considerations

The ethical considerations of the research were respected. The research project protocol and questionnaire were approved by the supervisory team and the ethics committee of the Faculty of Medicine and Pharmacy of the University of Kisangani. The survey was conducted in accordance with their requirements.

Mothers with children aged 12 to 23 months were interviewed individually in their households. The researcher, after introducing himself and explaining the purpose of the study, gave a brief overview of the survey, explaining what they had to do as informants. They were informed that their participation was not compulsory. In addition, the questionnaire had to be completed anonymously, and each respondent was identified by a code. Verbal consent was obtained each time, and willingness to complete the questionnaire was considered another form of tacit consent. Data confidentiality, voluntary participation and the possibility of withdrawing from the study at any time without prejudice were observed.

3. Results

Prevalence of vaccination dropout

This study showed that 11.1% and 17.6% of children had not received BCG and VAR respectively. On the other hand, 48.5% of children had no vaccination card, while 37.5% had been refused a vaccine by their mother.

Table 1 : Prevalence of vaccination dropout among children aged 12 to 23 months in Kisangani in 2022 (n=336)

Variables	Categories	Staff	%
BCG vaccine			
	Yes	299	88.9
	No	37	**11.1**
VAR vaccine			
	Yes	277	82.4
	No	59	**17.6**
Immunization card			
	view	173	51.5
	not seen	163	**48.5**
Vaccination refusal			
	Yes	126	**37.5**
	No	210	62.5

Specific aspects of vaccines and immunization

For 15.8% of mothers surveyed, vaccines are not safe for their children. The latter experienced a delay in vaccination because of a new vaccine that had just been introduced (31.3%). In the opinion of the mothers surveyed, there is a mode of vaccination that the mother can refuse for her child (44.1%), while 26.8% preferred to vaccinate their children at school or church. The refusal to vaccinate children during the mass campaign and the fear of pain or needles during vaccine administration were respectively

affirmed by 39.9% and 48.8% of the mothers surveyed. Agreeing to vaccinate the youngest child was not asserted by 15.8% of mothers, while 41.1% saw a disadvantage in taking time off work to make sure their child was vaccinated. This has already happened to 44.1% of mothers who have experienced a lack of respect from health professionals. Door-to-door vaccinators are not trusted by 25.6% of mothers, while 44.9% have experienced adverse events following immunization of their children.

Bivariate analysis

The following vaccine-specific aspects were significantly associated with BCG vaccination, VAR and vaccine refusal in the bivariate analysis : vaccine safety, introduction of a new vaccine, vaccination mode, refusal to vaccinate during the mass campaign and cadet vaccination. Vaccination site preference and the presence of post-immunization adverse events were significantly associated with BCG vaccination and vaccination refusal. In contrast, lack of trust in door-to-door vaccinators showed a significant association with VAR vaccination and vaccine refusal. Fear of pain or needles during vaccine administration and poor reception by health professionals, as well as the mother's occupation as a handicap to her child's vaccination, were significantly associated with refusal of vaccination and VAR respectively.

Multivariate analysis using simple logistic regression

The analyses concerned the independent variables significantly associated with vaccine discontinuation in the bivariate analyses ($p < 0.05$). In view of these, the following vaccine-specific aspects showed a significant association with vaccination drop-out : introduction of a new vaccine, vaccination mode, vaccination site preference, refusal to vaccinate during a mass campaign, poor reception by healthcare professionals, presence of MAPI (adverse events following immunization) during vaccination, and distrust of vaccinators who go door-to-door. A non-significant association was found for vaccine safety.

Multivariate analysis using multiple logistic regression

After adjustment, the following factors remained associated with dropping out of vaccination in children aged 12 to 23 months : preference for vaccine administration method, refusal of a vaccine during the mass campaign, delay in vaccinating when a new vaccine is introduced, lack of confidence in vaccinators who go door-to-door, preference for vaccination site, presence of MAPI and poor reception by health professionals. The following determinants lost their association with vaccine dropout, notably vaccine safety, fear of pain or needles, cadet vaccination and mother's occupation as an obstacle to vaccination.

Table 2 : Multivariate logistic regression of specific aspects associated with dropping out of early childhood vaccination in Kisangani

Variables	**BCG**		**VAR**		**Refusing vaccination**	
	p	ORa[$IC_{95\%}$]	p	ORa[$IC_{95\%}$]	p	ORa[$IC_{95\%}$]
New vaccine	0.00	**2.9**[1.4-6.1]	0.02	**2.1**[1.1-3.9]	0.03	**1.8**[1.1-3.2]
Vaccination mode	-	1	0.06	1.9[0.9-3.7]	0.00	**4.1**[2.2-7.7]
Site preference	0.04	**2.1**[1.1-4.4]	-	1	-	1
Mass campaign	0.04	**2.1**[1.1-4.6]	-	1	0.00	**3.6**[2.0-6.3]

Poor reception	-	1	-	1	0.03	**1.9**[1.1-3.4]
MAPI*	-	1	-	1	0.01	**2.0**[1.1-3.6]
Door-to-door strategy	-	1	0.00	**2.8**[1.5-5.4]	-	1

* Adverse events post - immunization

Children whose mothers have a preference about how vaccines are administered are 4 times more likely to drop out than those who have no choice. The same applies to those who refuse the vaccine during the mass campaign. The probability of a child dropping out of vaccination is almost 3 times higher when a new vaccine is introduced and the door-to-door strategy is used. This probability is almost 2 times higher for children of mothers who abandon vaccination because of the choice of vaccination site, the presence of adverse events post - immunization and poor reception by health professionals.

4. Discussion

Prevalence of vaccination drop-out

The early childhood vaccination dropout prevalence of 37.5% obtained in this study (Table 1) is higher than that observed by Gebeyehu and colleagues. In a systematic review and meta-analysis of childhood vaccine dropout in sub-Saharan Africa, they noted that Ghana showed the lowest prevalence of vaccine dropout (11.13%) and Nigeria 33.59%. For community and institutional studies, the figures were 39% and 13.7% respectively. Thus, in sub-Saharan Africa, the combined frequency of vaccine non-use is 21% [27]. Study setting, time interval and sample size may be factors contributing to this variation.

Compared with BCG and VAR (Table 1), the results of this research are clearly superior to those of a study carried out in India [28], which found that drop-out rates for BCG and VAR were 8%. This may be due to differences in sample size, study participant composition, health system architecture and policy. For example, the total sample size of the previous study was 550, but the current study had 336 participants. The time lag between studies may also provide an explanation for this disparity.

Determinants specific to vaccines and vaccination

Introduction of a new vaccine

The introduction of a new vaccine results in 31.3% of children not completing the immunization schedule in Kisangani (Table 2).

Prior to the 21st century, vaccination programs were generally recognized as one of the most cost-effective public health interventions, and the arrival of new vaccines was almost always welcomed by public health decision-makers and clinicians [29,30]. In recent years, however, we have seen an increase in the number of new vaccines licensed and marketed. In the USA, the number of vaccines included in the state-funded immunization program for children from birth to 18 years of age more than tripled between 1990 and 2012. The increase in the number of vaccines has led to differences in the addition of new vaccines to regular programs or the use of different vaccination schedules. Some have argued that differences in vaccination schedules and programs adopted in different countries, or even in different jurisdictions within the same country, may increase individuals' negative perceptions of the appropriateness of certain vaccines or vaccine schedules [31,32].

In order to achieve high vaccination coverage, some countries have introduced laws requiring children to be vaccinated before entering school. Policies that make vaccination compulsory have always been controversial [33]. However, it seems that opposition to compulsory vaccination is growing, as shown, for example, by the increase in exemption rates in the USA. The results of a population-wide

survey in the USA showed that over 10% of parents were opposed to compulsory vaccination. Unsurprisingly, parents who disapprove of compulsory vaccination are much more likely to have negative views about the safety of vaccines and their usefulness in protecting their child's health [34].

In 2018, interviews conducted in a tertiary care center with 150 mothers of children aged 1-5 years revealed that suspicion of new vaccines (61.4%), concern about adverse reactions (90.7%) and the perception that vaccines are not necessary for uncommon diseases (85.3%) were linked to hesitant behavior, as measured by the vaccine confidence index [35].

Mode of administration

Mothers' refusal to vaccinate is 4.1 times more likely to be justified by a preference for the method of vaccine administration (Table 2).

In this respect, the majority of mothers prefer the oral route of vaccine administration to the injectable route. This result concurs with that of Renukunda et al. who state that the oral route is the most desirable and accepted by patients, since over 60% of marketed small-molecule drugs are administered orally [36]. Ependja et al. found a similar result for Yahisuli. In their study of Yahisuli parents' behavior towards early childhood vaccination, the authors found that the majority of parents preferred the oral route because it had no side effects (64.3%). Ease of administration was also favored by 31.4% of parents surveyed [37].

As far as the route of administration is concerned, each vaccine is unique in its presentation and mode of administration (injection or oral). Injection is preferred in certain cultures, while the oral route is, depending on the case, appreciated for its ease and analogy with food, or disparaged for its banality. Scarification can also easily be seen as a disturbing marking of the body. The vaccinator's personality, social status, ethnicity, gender, etc. may also come into play [37].

Taddio et al. and Davitt et al. have noted that oral vaccines have the ability to improve distribution over traditional injections due to their ease of administration, which allows self-administration of oral formulations. Self-administration is ideal for the rapid, large-scale distribution of vaccines, as it minimizes the need for skilled healthcare personnel [38,39]. This could further reduce the cost of immunization programs, since training and mobilizing healthcare personnel can account for up to 25% of the cost of introducing a new vaccine. In addition, needle-free administration would eliminate needlestick injuries, which affect around 5% of healthcare workers each year and expose them to blood-borne infectious diseases such as HIV/AIDS and hepatitis [40].

From a regulatory point of view, oral vaccines could enable more cost-effective production, since they do not require the extensive purification needed for injectable formulations. Parenteral injections require :

- Aseptic technique during synthesis and manufacturing,
- Equipment and training of nursing staff for optimal administration,
- and appropriate use of sterile needles [41].

In addition, the use of these traditional techniques generates an enormous amount of biohazardous waste, which the majority of developing countries simply do not have the infrastructure to handle properly. All these factors increase the cost of vaccinations, which can significantly affect access in emerging regions [40].

Although extremely rare, attenuated pathogens can revert to a pathogenic form and cause disease. For example, live oral poliovirus vaccine (OPV) has not been administered in the USA since 2000, due to

the risk of vaccine-associated paralytic poliomyelitis and the availability of a safer alternative in the form of an inactivated injectable vaccine [40].

Mode of delivery

Vaccination dropout in children aged 12 to 23 months is 3.6 times more associated with refusal to vaccinate during mass campaigns (Table 2). In this respect, Pakistan has historically reported a higher number of incidents of vaccine refusal during mass vaccination campaigns and vaccine supplementation activities [42 - 44].

Of the 230 parents or guardians interviewed by Asif Khaliq et al, there were 141 (61.3%) who refused routine vaccines to their children and 89 (38.7%) refused it during the mass campaign or supplementary vaccine activities. Reasons for not vaccinating among the first category of parents included cost, vaccine side effects and contraindications, rumors and alternative medicine. However, distance to clinics, reduced clinic hours, the influence of community or religious leaders and lack of trust in government were mainly reported by potential refusers. Both actual refusals (routine vaccination) and potential refusals (mass campaign) indicated that the new vaccines are not safe for their children's health. [45]. Other previous studies also support the notion that a lack of confidence in the preventive efficacy of vaccines and a fear of adverse vaccine reactions are major contributors to vaccine refusal [46 - 48].

Role of healthcare professionals

Reluctance to vaccinate among healthcare staff in Europe has been reported in numerous studies [49,50] and is a real cause for concern, since the role of healthcare staff is known to be paramount in teaching vaccine acceptance [51].

It should be noted, however, that scientific knowledge is not the only skill identified for influencing vaccine-related behavior. One study found that healthcare providers are often insufficiently trained to manage difficult conversations with reluctant parents, and identified this lack of preparation as an inhibiting factor in recommending vaccination [52].

The results of a study of doctors in Switzerland showed that almost 5% of doctors (non-paediatricians) refused or delayed MMR or DPT vaccinations for their own children [53].

Finally, several studies carried out in Europe have confirmed the key role played by healthcare workers in modifying knowledge, personal beliefs and vaccination choices in the general population [54 - 56].

In this regard, this study revealed that poor reception, lack of confidence in the door-to-door strategy and the presence of adverse events post - immunization were significantly associated with dropout from early childhood immunization in Kisangani (Table 2).

Powelson et al. found that many caregivers interviewed about the determinants of vaccination dropout in Mozambique began the process of immunizing children highly motivated, and some also described having had positive experiences in health facilities. However, others were dissatisfied with their experiences at the point of service delivery due to vaccine stock-outs, long waiting times and inconsistent health facility schedules. Caregivers of partially vaccinated children also described being frustrated by interactions with disengaged health workers. After expending considerable effort to reach the health facility, some caregivers interviewed arrived to find that health workers were late or busy talking on the phone ; this caused them to lose confidence in the health system and lose their motivation to vaccinate. They feared that health workers would scold them and send them home if they went out of schedule after

missing doses, didn't bathe their child before the visit, or forgot to bring their vaccination booklet [57 - 59].

This study showed that children of mothers who don't trust the door-to-door strategy are 3 times more likely to drop out of the immunization schedule than those of mothers who do (Table 2). This result is contrary to that found by Miguel Pugliese-Garcia et al. in Zambia and other researchers. To improve access to immunization, respondents supported initiatives such as mobile campaigns, door-to-door and weekend delivery, addressing well-known barriers to access including long working hours, remoteness from health facilities and the limited physical mobility of some community members [60 - 62]. These initiatives align with evidence that outreach services increase childhood immunization coverage by reducing the distance between a household and a vaccine supply point in low-income, peri-urban areas [60].

In a study of the social mobilization campaign to combat vaccine reluctance in the Sargodha and Khushab districts of Pakistan, Malik et al showed that door-to-door visiting was considered by 88.9% of vaccinators to be one of the best strategies for raising awareness of vaccine reluctance among community members [63].

Regarding post immunization adverse events (MAPI), it was observed that 44.9% of mothers experienced adverse events after vaccination of their children (Table 2). These results corroborate those obtained by Kouassi et al in 2017 in the Bondoukou commune. The authors found that a history of IPD was significantly associated with vaccine dropout in children aged 0 to 11 months (ORa = 67.64; CI95% [22.45 - 302.27]). Of the mothers surveyed, almost 42% had received MAPI for their children [64].

For their part, Joshi et al. emphasized that assessing the value and risk of vaccines is an important aspect of the perception of any vaccine. Therefore, it is vital to maintain and use the national vaccine adverse event surveillance program to establish evidence of vaccine safety and to assure the public that ongoing monitoring is in place to help assess any suspected safety issues [65].

Powelson et al. conducted a study on the determinants of vaccine dropout among children under 2 years of age in the Zambézia province of Mozambique. These authors observed that concerns about side-effects, exacerbated by the "accumulation" of vaccines, lead to vaccine hesitancy, notably : fear of vaccine "accumulation", lack of information about side-effects and the vaccine schedule, and the perception of side-effects as an abnormal situation. The latter is exacerbated when the child has to receive too many vaccines simultaneously, for example in the case of catch-up administration [57 - 56].

A survey exploring the reasons for vaccine refusal among parents and caregivers of children under the age of two in Pakistan showed that around 60% of parents refused routine and mass campaign vaccination because of fever (64.8%) and injection site pain (57.4%) as common MAPI. Inflammation (59.1%), allergic reactions (21.7%), hospitalization (22.6%), disability (12.6%) and death (7.8%) were also reported by parents or guardians [45].

Study limitations

The results of this study are not without limitations. The lack of cooperation from certain households, the unavailability of mothers due to the survey schedule and the difficulty of translating the questionnaire into Lingala or Swahili, with the risk of distorting its content, were observed in this work.

Qualitative analysis was not included in this study. Further work is therefore needed, both to fill in the gaps in this study and to monitor this complex phenomenon as it evolves over time. This should enable

public health authorities to design appropriate policies to address the unresolved determinants of vaccine dropout in Kisangani, for better vaccine acceptance.

An additional limitation is that this study was conducted during the COVID-19 pandemic and its mediatized corollaries on its various vaccines. This may also have biased our findings on drop-out during non-pandemic periods.

Despite these limitations, this study shows that dropping out of early childhood immunization is complex, with mothers facing different combinations of obstacles during their child's immunization journey. However, they in no way detract from the scientific value of this work, which for the first time in Kisangani tested the WHO expert advisory working group's standard questionnaire on immunization. These results can be generalized to other cities in developing countries.

5. Conclusion

This study has enabled us to analyze the determinants of early childhood vaccination dropout and identify its main influences linked to specific aspects of vaccines in the city of Kisangani, in order to provide verifiable information on the phenomenon to members of the scientific community. Many vaccines are currently under development. As such, it's not just a question of increasing adherence to existing vaccines, but also of convincing people of the benefits of vaccination so that these new vaccines are fully accepted. We need to make sure that mothers understand that vaccination is a preventive measure that only makes sense if as many children as possible in the target population are vaccinated. The abandonment of vaccination is not negligible in Kisangani, because of its consequences on vaccination status, morbidity, mortality and the outbreak of epidemics. It should be investigated in greater depth in the future, along with its determinants, through quantitative and qualitative studies at national level. Understanding today's mothers means convincing tomorrow's mothers. Mothers' choices and attitudes will shape the vaccination coverage of the next generation, and influence their children's attitudes to vaccination.

The results of the analysis revealed a significant association between abandonment of early childhood vaccination and specific aspects of vaccines such as the introduction of a new vaccine, the mode of vaccination, the choice of vaccination site, refusal to vaccinate during the mass campaign and the role of health professionals.

The results of this study highlighted the need for innovative strategies based on a holistic approach to overcome the obstacles to early childhood vaccination in Kisangani.

Funding : This study did not receive specific funding from any public, commercial or non-profit agency.

Authors' contributions and responsibilities : All authors attest to compliance with the criteria of the International Committee of Medical Journal Editors (ICMJE) with regard to their contribution to the article. All authors contributed to the conduct of this research and to the drafting of the manuscript. They have all read and approved the final version.

Declaration of links of interest : The authors declare that they have no links of interest.

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