Reasons for delayed pentavalent vaccinations among children aged 12-23 months in Kampala, Uganda

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ABSTRACT

Introduction: Delayed vaccination significantly reduces the proportion of individuals with full immunity against targeted diseases, undermining the goal of achieving herd immunity. Delay also increases the likelihood of missing subsequent doses and dropping out of the schedule. This study examined the reasons for delayed pentavalent vaccinations among children aged 12-23 months in Kampala, Uganda. **Methods:** Selection of 653 study participants into this household survey was done using a three-stage sampling technique. Delayed vaccination was considered if vaccination occurred outside the following time ranges: Pentavalent 1 (4 weeks-2 months), Pentavalent 2 (8 weeks-4 months), and Pentavalent 3(12 weeks-6 months). Data on vaccination status; socio-demographic and attitudinal factors were obtained using an interviewer administered structured questionnaire. Modified Poisson regression analysis was done in STATA version 14.0. **Results:** Overall, 97.4% (636/653) of the children had ever been vaccinated. About 30.7% (95% CI 26.3-33.3) of these had delayed receipt of at least one dose of the pentavalent vaccines. The prevalence of delayed vaccinations was lower if the caretaker had attained secondary school education (APR= 0.52, 95% CI 0.38-0.70); believed in the effectiveness of vaccines (APR= 0.74, 95% CI 0.55-0.99), perceived a higher risk of their child contracting a vaccine-preventable disease (APR= 0.74, 95% CI 0.58-0.94), and if they had trust in the information provided by health workers (APR=0.61, 95% CI 0.43-0.88). The prevalence of delay was higher if the caretaker was not the biological parent of the child (APR=1.82, 95% CI 1.11-3.00) or if they had negative emotions resulting from previous vaccination experiences (APR=1.48, 95% CI 1.15-1.90). **Conclusions:** It is imperative to strengthen initiatives to improve knowledge and understanding of the benefits of age-appropriate vaccination for children among primary caretakers in this setting. This study describes the individuals that could be targeted for such interventions

Introduction

The global under-five mortality rate declined from 93 deaths per 1,000 live births in 1990 to 38 deaths per 1000 live births in 2021[1]. Despite this considerable progress, improving child survival remains a matter of urgent concern. In 2021 alone, about 13,800 under-five deaths occurred every day, an intolerably high number of largely preventable childhood deaths[1]. Regionally, sub-Saharan Africa continues to have the highest rate of under-5 mortality(U5MR) in the world, estimated at 75·8 deaths per 1000 livebirths in 2019[2]. The U5MR in Uganda, as reported by the Uganda Demographic and Health Survey (UDHS), is 40.5 deaths per 1,000 live births[3]. Childhood vaccination is a critical intervention in promoting child survival and averting deaths from vaccine-preventable diseases (VPDs) worldwide[4].

However, despite the immense financial, material and health system investment into vaccination with countries reporting high vaccination coverage[5], several outbreaks of VPDs including pertussis and diphtheria still occur globally with Africa recording the most outbreaks. Globally, diphtheria outbreaks have been reported in various countries including Indonesia[6], Brazil[7]and Nigeria[8]. Outbreaks of pertussis have been reported in Ethiopia[9] with South Africa reporting an increase in pertussis among children under five years in the recent years [10]. A study by Kayina et al found the prevalence of pertussis to be 20% among children at Mulago Hospital in Kampala[11] despite a safe and effective vaccine against pertussis and diphtheria being available.

While crude vaccination coverage is a crucial indicator for general population immunity, ensuring timely and age-appropriate vaccination is equally essential for better vaccination outcomes. Delayed vaccine uptake may significantly reduce the proportion of individuals with full immunity against targeted diseases hence affecting the goal of achieving herd immunity[12].

Delayed administration of vaccines can result in longer periods of susceptibility among children and the presence of a pool of such susceptible children can result in an epidemic[13]. A study by Lutwama and colleagues[14] showed that distinct patterns of T-cell induction occurred when BCG vaccine was given at birth and at 6 weeks of age. Infants who received BCG vaccine at birth had greater frequencies of IFN-γ–expressing CD4+ T cells, compared with infants vaccinated at 6 weeks of age emphasizing the need for timely vaccination. Delayed vaccine uptake may also increase the likelihood of missing subsequent doses and even dropping out prior to completion of the recommended vaccine schedule [15].

Crude vaccination coverage is often used as a measure of program and other health system success. Therefore, research on crude vaccination coverage has been extensive indicating coverage rates of over 90% for the primary series of childhood vaccines [3, 16-18]. However, validity of these vaccinations has been neglected at the global and Ugandan levels[16, 19]. The few studies in Uganda, indicate delays of 26% to 82% for various vaccinations and only a few have considered the pentavalent vaccinations[19, 20]. This wide variation in measurements, the lack of prioritization to prevent delays in vaccinations coupled with the growing concern of increasing reports of diphtheria and pertussis related outbreaks globally[6, 7, 9], indicates imminent epidemics in settings whose health system is ill equipped to handle large numbers of patients with these illnesses[21]. This study examined the reasons for delayed pentavalent vaccinations among children aged 12-23 months in Kampala, Uganda.

Methods

Study design

This community-based cross-sectional study was conducted from November – December 2023 in Kampala Uganda.

Study setting

Kampala is the capital and largest city of Uganda, located in the central region of the country. As Uganda's political, economic, and cultural hub, Kampala plays a crucial role in the nation's health infrastructure as it hosts numerous public and private health centres that serve both local residents and individuals from surrounding regions.

Kawempe Division is a representative of one of the five divisions that make up Kampala District. The division is a poor urban setting with the largest proliferation of slums; low literacy levels; and poor health service delivery indicators compared with the entire Kampala City[22, 23]. Many of the residents in the division are unemployed and difficult to mobilize to participate in community health services like immunization [22]. The Health Management

Information System (HMIS) reports indicate that there were 11 health facilities (both public and private) providing static immunization services in the Kawempe Division from the start of FY 2015/16 but only seven were providing both static and outreach immunization services [22].
Kawempe Division has a population of 338,700 people [23], of whom 16,900 (5%) are infants while 71,400 (21%) are children under five years of age. Health services are provided by a referral hospital (Kawempe National Referral Hospital) which is part of the Mulago National Referral Hospital complex and serves as a specialized facility for maternal and neonatal services; lower-level government health facilities, private for-profit (PFP) and private not-for-profit (PNFP) facilities. The division has a total of 310 health facilities (i.e., 3 government facilities, 12 PNFPs, and 295 PFPs) [24].

Sample size calculation and sampling techniques
The required sample size for this study was 653 child-caretaker pairs using the Kish Leslie single proportion formula with the following assumptions: prevalence of delayed uptake of the pentavalent vaccines estimated at 25.7% according to a previous study done in Kampala[19], 95% confidence interval, a design effect of two to cater for the increase in sampling error[26], and 10% non-response rate.
Child-caretaker pairs were eligible for study inclusion if the caretaker was aged 18 years and above, had a child aged 12-23 months, had a child health card and consented to study participation. Child-caretaker pairs who met the above criteria but were too sick to participate were excluded from the study.
A three-stage sampling technique was used to select study participants. At the first stage, five parishes (administrative unit) were randomly selected from the 19 that constitute Kawempe Division using computer generated random numbers. Probability proportionate to size sampling method was used to determine the number of child-caretaker pairs to interview per parish using UBOS 2016 parish population level estimates for children aged 0-4 years in Kawempe division[23].

At the second stage, five villages (smallest administrative unit) were randomly selected from each of the five parishes using computer generated random numbers. The number of child-caretaker pairs selected for each village was obtained by equally dividing the sample size for each parish into the five selected villages.
At the third stage, a sampling frame for each village was obtained by listing all households in the village through the Local Council (LC) 1 office. Systematic sampling was then used to select households from the sampling frame. The sampling interval was the quotient of the number of households in the village and the number of households to be selected per village. A no replacement sampling technique was used for this study at the household level. For selected households, all eligible child-caretaker pairs that spent the night prior to interview were considered for study participation.

Measurements
Operational definition: In this study**,** delayed vaccine uptake referred to the postponement or lateness in receiving recommended vaccinations according to the WHO-recommended immunization schedule. The WHO recommended timeframes for receipt of the pentavalent vaccines are: Penta 1 (4 weeks-2 months), Penta 2 (8 weeks-4 months), and Penta 3 (12 weeks-6 months). Any vaccine given beyond the provided upper limit for any dose was categorized as delayed.
The primary outcome of this study was delayed pentavalent vaccination; a categorical variable recorded as a binary outcome indicating whether or not a child aged 12-23 months experienced a delay in receipt of any of the three doses of the pentavalent vaccine. Therefore, a child experiencing a delay in administration of any of the three doses of the pentavalent vaccine was categorized as having delayed vaccination. To determine the age at receipt of the pentavalent vaccine, we calculated the duration between the date of birth of the child and the date of receipt of the vaccines which were abstracted from the child health card.

Attitudinal variables: The attitude of the primary caretaker towards child vaccination was assessed using the following statements: i) I generally feel positive about childhood vaccinations ii) I believe vaccines are effective in preventing vaccine-preventable diseases iii) Concerns about side effects can influence my decision to vaccinate my child iv) I consider vaccine-preventable diseases to be serious and life threatening illnesses v) I believe my child is at risk of contracting vaccine-preventable diseases vi) Negative emotions such as fear or anxiety can influence my decision to vaccinate my child.

Responses were scored on a five-point Likert scale. The Cronbach's Alpha for the scale used to measure attitude was 0.70. These categorizations allowed for the analysis of caretakers' attitudes towards childhood vaccination based on their responses to the Likert scale items.

Socio-demographic variables: Additional data were collected on social demographic characteristics such as the age of the child, age of the caretaker, child's birth order, place of birth, education level of the caretaker, occupation of the caretaker, household income, marital status, religion, and distance to the nearest health facility.

Data collection

An interviewer-administered semi-structured questionnaire was used to collect data for this study between November 2023 and December 2023. The questionnaire included data on socio-demographic factors, economic factors, caregiver factors, child's factors, and service-related factors. Six data collectors and two supervisors were recruited and trained for one day. The supervisors followed the process of data collection, checked the data completeness consistency, and communicated with principal investigators on daily basis. The questionnaire was designed, uploaded onto Kobo collect and downloaded onto the smart phones of the data collectors. Information from the child health cards including date of birth, date of vaccination for the three doses of the pentavalent vaccine was also reviewed and abstracted.

Data management and analysis

Data collected was uploaded to the server and downloaded daily to Microsoft Excel 2016 for cleaning and thereafter exported to STATA version 14 for analysis. At data analysis descriptive and inferential statistics were performed. Tables, statements, and graphs were used to present the findings of the analysed data. Bivariate analysis was performed to determine crude associations between the outcome and predictor variables using modified Poisson regression with robust standard errors. At multivariable level, modified Poisson regression analysis with robust standard errors was used to determine factors associated with delayed vaccine uptake. Variables with a p-value<0.2 at bivariate analysis were added using a stepwise approach to the final model to control for the confounding effect. Adjusted prevalence ratios with a 95% confidence interval were used to determine the strength of association between the predictor and outcome variables. Only variables with p-value<0.05 in the final model were considered independent factors associated with delayed vaccine uptake.

Ethical consideration

Ethical approval was obtained from Makerere University School of Public Research and Ethics Committee (MakSPH-REC) and assigned protocol number 313. Permission to conduct the study was obtained from Kawempe Division Health Office and written informed consent was obtained from each study participant before the interview.

Results

We approached and enrolled 653 child-caretaker pairs representing a response rate of 100%. The mean age (standard deviation (SD) of caretakers was 28.5 years (±3.5). More than half (62.3%) of the caretakers had attained at least secondary education, were married (61.3%) and were self/formally employed (74%). The majority (97.5%) of the children were biologically related to the primary caretakers. Slightly over half (51.3%) of the children were males. Over 89.2% of the caretakers reported that their nearest health facility was within a 5km radius. The majority (81.0%) of the study respondents sought vaccination services from a government-owned health facility (Table 1).

Overall, 97.4% (636/653) of the children had ever been vaccinated. About thirty percent (195/636; 30.7%, 95% CI 26.3-33.3) of these had delayed receipt of at least one dose of the pentavalent vaccines. At multivariable analysis, children whose caretakers had attained secondary education had 48% lower prevalence of delayed vaccination compared to children whose caretakers had not attained any formal education [APR 0.52, 95%CI (0.38-0.70), p-value <0.001]. Children who were not biologically related to their caretakers had 82% higher prevalence of delayed vaccination compared to children who were biologically related to their caretakers [APR 1.82, 95%CI (1.11-3.00), p-value 0.018] (Table 2).

The prevalence of delayed vaccination was 26% lower among caretakers that believed in the effectiveness of vaccines compared to those who did not [APR 0.74, 95%CI (0.55-0.99), p-value 0.0042]. The prevalence of delayed vaccination was also 26% lower among caretakers who perceived a higher risk

of their child contracting vaccine-preventable diseases compared to those who didn't [APR 0.74, 95%CI (0.58-0.94), p-value 0.012].

Caretakers who had trust in the information provided by health workers had a 39% lower prevalence of delayed vaccination compared to caretakers who had no trust in the information provided by healthcare workers [APR 0.61, 95%CI (0.43-0.88), p-value 0.007]. The prevalence of delayed vaccination was 48% higher among caretakers who had negative emotions resulting from previous vaccination experiences compared to those who never had such negative emotions [APR 1.48, 95%CI (1.15-1.90), p-value 0.009] (Table 3).

Discussion

The study found a relatively high prevalence of delayed uptake of at least one dose of the pentavalent vaccines overall (30.7%) in Kawempe division. The findings are agreement with findings from other studies conducted in similar settings. A related study in Kampala revealed that about 50% of the children did not receive their vaccines in the recommended timeframe[26]. Other studies conducted in India[27] Ethiopia[28] and Tanzania[291] found the prevalence of delayed vaccination to be between 30-40%. Studies in Saudia Arabia [30] and Gambia[31] found the prevalence of delayed vaccination to be above 50%.

Delayed uptake of the pentavalent vaccines was more common among children not biologically related to their caretakers. This finding is in agreement with findings from a study in Ethiopia which found that the odds of defaulting from full vaccination were three times higher among children whose primary caretakers was a non-biological caregivers compared to the children whose primary caretaker was the biological mothers[32]. This finding can be linked to the idea that biological parents, who typically have a stronger sense of responsibility toward their children's health, might adhere more strictly to vaccination schedules than caretakers who have no biological kinship to the child. Such children should thus be targeted through strengthening interventions that target children at the community level.

There was a significant association between delayed uptake of the pentavalent vaccines and maternal education. Delayed uptake was less common among children whose caretakers had attained secondary-level education and beyond. Studies in Burkina Faso and India found similar results[33-35]. The possible explanation is that formal education often correlates with increased health literacy enabling caretakers to understand the benefits of timely vaccinations.

Caretaker beliefs on vaccine effectiveness, perceptions on susceptibility of children contracting vaccine-preventable diseases, and trust in healthcare information were the attitudinal factors significantly associated with more timely uptake of the pentavalent vaccines of children consistent with findings from studies done in other developing countries [36-40]. This underscores the importance of addressing these attitudinal factors in vaccination campaigns and healthcare interventions aimed at improving vaccination outcomes in the division.

Caretakers who had negative experiences from the past vaccinations, had higher delayed uptake of the pentavalent vaccines for their children which suggests that negative experiences resulting from past vaccination experiences can have a lasting impact on an individual's perception of child vaccination similar to findings from studies in Sweden [41] and Washington [42]. Therefore, negative emotions are pervasive in vaccine hesitancy and must be acknowledged alongside specific predispositions of intended vaccine refusal.

The study however had some limitations, child-caretaker pairs without vaccination cards were excluded from the study so we might have missed children with delayed vaccinations. However, we gathered data on a relatively large sample size and selection into the study was random to minimize the selection bias. The study was conducted in one division of the city so the results may not be generalized to the general population of the country. The design effect of the two used in sample size calculation was assumed and not calculated.

Conclusion

The study emphasizes the significance of improving caretaker beliefs on vaccine effectiveness, perceptions on the susceptibility of children contracting vaccine-preventable diseases, and trust in healthcare information in influencing the timely uptake of the pentavalent vaccines in Kawempe division. The study also highlights the need for addressing past negative experiences from vaccination as a critical factor in promoting the timely uptake of pentavalent vaccines.

The study underscores the influence of caretaker level of education, and biological relationship between the caretaker and child, in promoting timely uptake of the pentavalent vaccines. Initiatives that foster collaboration between healthcare providers, social services, and community organizations to identify and support vulnerable populations, including children with non-biological caretakers should be implemented.

What is already known about the topic

- It is known that delayed vaccine uptake reduces the number of individuals with full immunity against targeted diseases.
- It is also known that delayed vaccine uptake may also increase the likelihood of missing subsequent doses during the first year of life.

What this study adds

- The study highlights the importance of addressing attitudinal factors among care takers during the pentavalent vaccination campaigns and healthcare interventions aimed at improving immunization outcomes

Competing Interest

The authors of this work declare no competing interest

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Availability of data and material

The datasets used and/or analysed during the study are available from the corresponding author upon reasonable request.

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Authors´ contributions

JS, ADM and JNB contributed towards the study design. JS conducted the data analysis and drafting of first version of manuscript. MB contributed towards reviewing the initial drafts of the manuscript. All authors contributed towards data interpretation and critical comments on the first and subsequent drafts of the manuscript. All authors read and approved the final manuscript.

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Table 1: Characteristics of study participants		
Variable	**Frequency (N=653)**	**Percent**
Relationship between child and caregiver		
Biological child	637	97.5
Non-biological child	16	2.5
Sex of the child		
Male	335	51.3
Female	318	48.7
Caregivers' education level		
No formal education	97	14.9
Primary education	199	30.5
Secondary education	288	44.2
Tertiary education	69	10.4
Partners' education level		
No formal education	89	13.7
Primary education	157	24.0
Secondary education	298	45.6
Tertiary education	109	16.7
Marital status		
Single	212	32.4
Married	400	61.3
Widowed	12	1.9
Separated/divorced	29	4.4
Caregivers' employment status (last 7 days)		
Unemployed	170	26.0
Formally employed	227	34.8
Self-employed	256	39.2
Partners' employment status (last 7 days)		

Table 1: Characteristics of study participants		
Variable	**Frequency (N=653)**	**Percent**
Unemployed	25	3.8
Self-employed	210	32.2
Formally employed	418	64.0
Caregivers' age (Years) Mean (SD): 28.5 (±3.5)		
<25	176	27.0
25-34	371	56.8
35-44	93	14.3
≥45	13	1.9
Religion		
Anglican	167	25.6
Catholic	190	29.1
Pentecost	133	20.3
Moslem	120	18.4
Others (SDA, etc.)	43	6.6
Distance to nearest health facility		
0-5kms	582	89.2
>5kms	71	10.8
Ownership of nearest health facility		
Government	529	81.0
Private for profit	95	14.6
Private not for profit	29	4.4
Household monthly income		
<250,000 Ugx	280	42.8
250,000–500,000 Ugx	273	41.8
>500,000 Ugx	100	15.4

Table 2: Socio-demographic factors associated with delayed uptake of the pentavalent vaccines among children aged 12–23 months in Kawempe Division, Kampala at bivariate and multivariable analysis

Variable	Yes (N=195) n (%)	No (N=458) n (%)	CPR	95% CI	p-value	APR	95% CI	p-value
Relationship between the child and caregiver								
Biological child	186 (95.4)	451 (98.4)	ref					
Non-biological child	9 (4.6)	7 (1.6)	1.81	[1.13–2.88]	0.012	1.82	[1.11–3.00]	0.018
Age of caregiver (years)								
<25	60 (30.8)	116 (25.3)	ref			ref		
25–34	115 (59.0)	256 (55.9)	0.93	[0.72–1.21]	0.607	1.02	[0.79–1.32]	0.883
35–44	18 (9.2)	75 (16.4)	0.59	[0.37–0.93]	0.024	0.65	[0.40–1.06]	0.082
≥45	2 (1.0)	11 (2.4)	0.50	[0.14–1.80]	0.290	0.46	[0.17–1.24]	0.124
Caregiver's highest level of education								
No formal education	40 (20.5)	57 (12.4)	ref			ref		
Primary education	69 (35.4)	130 (28.4)	0.84	[0.62–1.14]	0.279	0.75	[0.57–1.01]	0.062
Secondary education	70 (35.9)	218 (47.6)	0.58	[0.43–0.80]	0.001	0.52	[0.38–0.70]	0.000
Tertiary education	16 (8.2)	53 (11.6)	0.58	[0.36–0.94]	0.029	0.54	[0.33–0.87]	0.011
Partner's highest level of education								
No formal education	37 (19.0)	52 (11.4)	ref	Collinear with caregiver education level (excluded)				

Table 2: Socio-demographic factors associated with delayed uptake of the pentavalent vaccines among children aged 12–23 months in Kawempe Division, Kampala at bivariate and multivariable analysis

Variable	Yes (N=195) n (%)	No (N=458) n (%)	CPR	95% CI	p-value	APR	95% CI	p-value
Primary education	52 (26.7)	105 (23.0)	0.82					
Secondary education	78 (40.0)	220 (48.0)	0.62					
Tertiary education	28 (14.4)	81 (17.6)	0.63					
Family monthly income (UGX)								
<250,000	77 (39.5)	203 (44.3)	ref			ref		
250,000–500,000	82 (42.0)	191 (41.7)	1.07	[0.82–1.39]	0.601	1.06	[0.81–1.39]	0.653
>500,000	36 (18.5)	64 (14.0)	1.28	[0.93–1.77]	0.132	1.32	[0.95–1.84]	0.097

Table 3: Attitudinal factors associated with delayed uptake of the pentavalent vaccines among children aged 12–23 months in Kawempe Division, Kampala at bivariate and multivariable analysis

Variable	Yes (N=195) n (%)	No (N=458) n (%)	CPR	95% CI	p-value	APR	95% CI	p-value
I believe that vaccines are effective in preventing VPDs								
No	39 (20.0)	60 (13.1)	ref			ref		
Yes	156 (80.0)	398 (86.9)	0.74	[0.56–0.98]	0.036	0.74	[0.55–0.99]	0.042
Concerns about side effects of vaccines can influence my decision to vaccinate my child								
No	56 (28.7)	179 (39.1)	ref			ref		
Yes	139 (71.3)	279 (60.9)	1.42	[1.09–1.86]	0.009	1.25	[0.92–1.68]	0.143
I believe that diseases vaccines protect against are serious and can have severe health consequences								
No	43 (22.0)	131 (28.6)	ref			ref		
Yes	152 (78.0)	327 (71.4)	1.21	[0.91–1.62]	0.188	1.28	[0.58–1.72]	0.116
I believe that my child is at risk of contracting VPDs								
No	112 (57.4)	207 (45.2)	ref			ref		
Yes	83 (42.6)	251 (54.8)	0.73	[0.58–0.93]	0.011	0.74	[0.58–0.94]	0.012
Negative emotions such as anxiety can influence my decision to vaccinate my child								
No	72 (36.9)	236 (51.5)	ref			ref		
Yes	123 (63.1)	222 (48.5)	1.51	[1.18–1.93]	0.001	1.48	[1.15–1.90]	0.009
I believe that the information health workers provide about vaccination is accurate								
No	23 (11.8)	85 (18.6)	ref			ref		
Yes	172 (88.2)	373 (81.4)	0.63	[0.46–0.88]	0.004	0.61	[0.43–0.88]	0.007