PREVALENCE AND FACTORS ASSOCIATED WITH IMMUNIZATION DELAYS AMONG LOW BIRTH WEIGHT INFANTS AT KENYATTA NATIONAL HOSPITAL

A dissertation submitted in partial fulfillment for the award of the degree of Master of Medicine in Pediatrics and Child Health, University of Nairobi.

BY

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DECLARATION

I declare that this dissertation is my original work and has not, to the best of my knowledge, been presented to any other university for the award of degree.

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This dissertation has been submitted with our full approval as supervisors

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APPRECIATION AND DEDICATION

This work is dedicated to my daughter Mueni, for the time she had to endure while I was away for my studies at such a young age, to my husband Syindu for the support and encouragement. I want to acknowledge the dedicated support and mentorship from my supervisors Professors Grace Irimu and Fredrick Were, their vast experience and dedication made this work possible. To the mothers of LBW infants who gave their time to take part in this study, my sincere gratitude.

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LIST OF ABBREVIATIONS

WHO	World Health Organisation
EPI	Expanded Program on Immunization
KEPI	Kenya Expanded Program on Immunization
MoH	Ministry of Health
KDHS	Kenya Demographic and Health Survey
KNH	Kenyatta National Hospital
PEU	Pediatric Emergency Unit
OPD	Out Patient Department
MCH	Maternal and Child Health
NBU	New Born Unit
NOPC	Neonatal Outpatient Clinic
IUGR	Intrauterine Growth Restriction
LBW	Low Birth Weight
VLBW	Very Low Birth Weight
ELBW	Extremely Low Birth Weight
VPD	Vaccine Preventable Diseases
DPT	Diphtheria Pertussis Tetanus
BCG	Bacille-Calmette Guerin
MR	Measles-Rubella
OPV	Oral Polio Vaccine
IPV	Injectable Polio Vaccine
Hib	Hemophilus influenza type b
HBV	Hepatitis B Virus
CHV	Community Health Volunteer

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OPERATIONAL DEFINITION OF TERMS AND PHRASES

Timely vaccination – vaccines given within seven days of the recommended WHO EPI timelines. In this study, these are any vaccine given up to 14 days after the recommended age on the schedule.

Vaccination delay- in this study, these are pentavalent 1, pentavalent 3 and measles vaccines given more than two weeks (14 days) after the recommended timelines (1–3)(see table 2).

Delayed BCG vaccine – this is BCG vaccine administered after the date of discharge of the infants. The Ministry of Health guidelines and WHO both recommend that BCG be administered at discharge from the hospital or at 2000g for the LBW infants whichever comes first (4).

Early vaccination – this is any vaccine administered before the recommended age. For this study any day before the recommended age was considered early.

Low Birth Weight- weight at birth of less than 2500g regardless of gestational age at birth.

Preterm- a live birth that occurs before 37 completed weeks of gestation.

Infant – a child aged less than one year. In this study, these are from one to eleven months of age.

Vaccine – is a biological preparation that improves immunity to a particular disease. In this study, vaccines of interest are Bacille-Calmette Guerin (BCG), Pentavalent 1, Pentavalent 3 and Measles.

KEPI vaccines – BCG, Oral polio vaccine (OPV), injectable polio vaccine (IPV), pneumococcal, rotavirus, pentavalent and measles-rubella.

Pentavalent vaccine - a five-in-one vaccine that provides protection against diphtheria, pertussis, tetanus, hepatitis B and Haemophilus influenza type b (Hib).

ABSTRACT

Background

Globally, 15-20% of all births are low birth weight (LBW) majority in low and middle-income countries. The Kenya Demographic and Health Survey (KDHS) 2014 states that 8% of all births were LBW. LBW infants are at increased risk of vaccine preventable diseases, the biggest cause of childhood morbidity and mortality. WHO recommends that clinically stable premature and LBW infants be vaccinated according to chronological age with the same schedule as the term infants. However, studies have shown that, immunization in LBW infants continues to be delayed putting them at greater risk of preventable diseases. Determining the factors that delay immunization in this vulnerable population would guide in formulating solutions to improve immunization coverage, preventing common childhood diseases and ultimately reducing infant mortality.

Objectives

The primary objective was to determine the proportion of LBW infants with delayed immunization. The secondary objectives were to describe the infants' and maternal characteristics associated with immunization delays.

Study design and methods

This was a hospital based cross-sectional study done at Kenyatta National Hospital (KNH) Pediatric Emergency Unit (PEU), Neonatal Outpatient Clinic (NOPC), Maternal and Child Health (MCH) clinic and the four general pediatric wards. A sample size of 423 mothers with LBW infants (1-11 months) was recruited by consecutive sampling. Data were collected through an interviewer administered pretested structured questionnaire to the mothers of the LBW infants. Additional data on immunization were extracted from Mother & Child Handbook.

Data analysis

Data were analyzed by SPSS version 22.0. Continuous data were expressed using means, standard deviations, medians and interquartile ranges (IQR) and categorical data using proportions. Associations were calculated using Odds Ratio (OR) with the corresponding 95% confidence interval. Pearson-Chi square test was used to test for statistically significant associations.

Results

The prevalence of immunization delay among the LBW infants was 56.7% (95% CI 0.52-0.61). The most delayed vaccine was BCG at 54.6%. Very low birth weight (VLBW) and admission to the NBU were significantly associated with increased odds of immunization delay. Some infants were found to have received their immunization earlier than the recommended age.

Conclusion.

One in two LBW infants experience delay in their immunizations in our setup. BCG is the most delayed vaccine. There is need to adapt and disseminate guidelines for LBW infants' immunization.

CHAPTER 1: INTRODUCTION

The World Health Organisation (WHO) defines low birth weight (LBW) as weight at birth of less than 2500g regardless of the gestational age. Low birth weight can be due to prematurity or intrauterine growth restriction (IUGR). The latter can occur in a term baby. The subsets of LBW are: LBW 1500g-2499g, very low birth weight (VLBW) 1000g- 1499g and extremely low birth weight (ELBW) <999g (5)(6).

Prematurity is defined by WHO as a live birth that occurs before 37 completed weeks of gestation. There are subsets of prematurity: extreme preterm is born before 28 completed weeks of gestation, very preterm is born at 28 – 32 weeks of gestation and moderate to late preterm is born between 32 and 37 weeks of gestation. (7). Prematurity and LBW account for a major cause of morbidity and mortality in the first year of life (5)(8).

Globally, the incidence of LBW is estimated to be about 15-20% (5)(6). South East Asia has the highest incidence at 28%, Sub Saharan Africa at 13% and Eastern and Southern Africa at an estimated 11% (2). These figures however, are estimates since UNICEF notes that nearly half of the worlds' infants are not weighed at birth (2). Other African studies have estimated the prevalence of LBW to be between 15.5% and 22.5% (9)(10). An Ethiopian study found the prevalence to be at 10% while a Pakistani study found 10.6% (11). The Kenya Demographic and Health Survey (KDHS) 2014 estimated LBW in Kenya to be at 8% (12).

Immunization is the most important, efficient and cost-effective public health strategy in primary disease prevention (13)(14). The biggest causes of childhood morbidity and mortality are vaccine preventable diseases (VPD) such as measles, diarrhoea, tuberculosis, pertussis, meningitis and pneumonia (15)(14)(8).

Low birth weight infants are at an increased risk of vaccine preventable diseases due to less transfer of maternal antibodies. The risk is greater in the LBW premature infants who in addition have an immature immune system that makes them even more susceptible to infections (13,14). Vaccination thus becomes even more important in such vulnerable populations and as such timely schedules need to be adhered to.

Studies have shown that preterm infants have an immune response to vaccines that is comparable to term infants (14,16). WHO recommends that medically stable preterm and low birth weight infants be vaccinated based on their chronological age without correcting for birth weight and/or gestational age at birth (10,12). Further, the same dosages of vaccines and the same vaccinating schedule should be maintained for their immunization (4,15).

The WHO policy document on immunization recommends strict adherence to the expanded program on immunization (EPI) schedules and their timelines to allow for adequate development of immune response and to allow the vaccine to be given to the youngest at-risk child before they are exposed to the wild type of the disease-causing organisms (17)(14)(18). Timeliness also ensures development of maximal herd immunity leading to protection even to the ones too young or too ill to be immunised (18,19).

In the immunization policy document, WHO identifies false contraindications as a major contributor to non-vaccination or delaying in completing childhood vaccination schedule (17). Prematurity and small-for-date infants have been recognised to affect immunization coverage in many countries (13).

CHAPTER 2: LITERATURE REVIEW

2.1: Magnitude of Low Birth Weight

Low birth weight (LBW) can be due to prematurity or intrauterine growth restriction (IUGR) (16). IUGR infants may be term but with LBW or may be preterm but also small for age (16). It is estimated that each year, 13 million and 20 million IUGR and LBW infants are born respectively (20).

Globally LBW has been recognized as a major contributor to childhood morbidity and mortality and as such, a decrease by 30% of the LBW births by the year 2025 is one of the WHO set global targets (10)(6). Studies have shown that LBW increased mortality risk 40 times while the VLBW infants were 100-200 times more likely to die than the normal birth weight counterparts (8,10).

Global incidence of LBW has been estimated by UNICEF at 15-20%, South East Asia with the highest at 28% and Sub-Saharan Africa at 13% (1,2). The African prevalence of LBW has been estimated in previous studies to be between 15.5% and 22.5% (5,6). An Ethiopian study to estimate the prevalence of term LBW found it to be at 10% which was comparable to a Pakistani study at 10.6% but different from the findings in India which estimated term LBW to be at 33% (11).

The KDHS report of 2014 estimated that 8% of all reported births were LBW. The report further recognizes birth weight as an important indicator of a child's risk and vulnerability to childhood illnesses and hence their survival (12). There was also regional variation in the LBW rate with the lowest in Nyanza region at 4% while the highest was at 13% in the Coast (8).

2.2: Vaccine preventable diseases among LBW infants

The biggest cause of childhood morbidity and mortality is vaccine preventable diseases (VPDs) such as tuberculosis, pertussis, pneumonia and meningitis. This impact is even greater in lower income and lower-middle income countries like Kenya (14,19). Sepsis and infections including pneumonia and meningitis are still among the leading causes of death among infants (8,10,15). Vaccination is an important, proven, efficient and cost-effective method of reducing the burden of childhood morbidity and mortality (17,19,21).

Premature and low birth weight infants are especially prone to frequent and often life threatening vaccine preventable diseases due to an immature immune system, less transfer of maternal antibodies, concomitant medical conditions and prolonged hospital stay among other reasons (14,19). The availability of advanced care for the premature and the LBW infants even in developing countries has increased their rate of survival. The increased morbidity and mortality of preterm and LBW infants largely due to common childhood infectious diseases whose vaccines are readily available necessitated the need for WHO to recommend that for the medically stable preterm and LBW infants, they should receive their vaccines at the same chronological age as their term counterparts without correcting for gestational age or weight (16,21).

2.3 Routine Immunization in Kenya

The task of ensuring that every person (child or adult) who is at risk receives high quality and effective vaccines is mandated to Kenya Expanded Program on Immunization (KEPI) through National Vaccines and Immunization Program (NVIP) (2). Routine immunizations are available without cost at all government and faith based facilities all over the country. The childhood immunizations are recorded in a Mother & Child Handbook, developed by the Ministry of Health (MoH), which is given without cost to every expectant woman attending ante-natal clinic (ANC).

The MoH has published an immunization guide for health workers which gives information and recommendations concerning handling and administering of vaccines to at risk population (4). However, these guidelines do not give specific recommendations for the LBW infant except for BCG where they recommend vaccination at 2000g or at discharge from the hospital whichever comes first (19).

In the KDHS 2014, it was noted that there is a decline in vaccination coverage with subsequent doses of vaccines (8). The dropout rate for polio 3 and pentavalent 3 was 8% while that for pneumococcal 3 was 9% (8). This data is however not disaggregated to indicate immunization coverage for the LBW infants.

Table 1. Current immunization Schedule in Kenya (22)

Contact	Age of child	Vaccines administered
1	At birth or 1st contact after birth	BCG OPV 0 *
2	6 weeks or 1st contact after 6 weeks of age	Pentavalent 1, OPV 1, pneumococcal 1, rotavirus 1
3	10 weeks or 4 weeks after the 1st doses of pneumococcal, pentavalent, OPV and rotavirus	Pentavalent 2, OPV 2, pneumococcal 2, rotavirus 2
4	14 weeks or 4 weeks after 2nd doses of pneumococcal, pentavalent, OPV and rotavirus	Pentavalent 3, OPV 3, pneumococcal 3 and IPV (injectable polio vaccine)
5	9 months or 1st contact after 9 months of age	Measles-Rubella Yellow fever **
6	18 months	Measles-Rubella

**Yellow fever vaccine is only given in some counties (Baringo and Elgeyo Marakwet and is to be rolled out in West Pokot and Turkana).

* to be given before age 2weeks

- BCG for the LBW infants is given at discharge or at 2000g whichever comes first

2.4: Immunization timing among LBW infants

The WHO policy document on immunization recommends strict adherence to the EPI recommended schedules and their timelines to allow for adequate development of immune response (17). The timelines are also put in place to allow the vaccines to be given to the youngest at-risk child before they are exposed to the wild type of the disease-causing organism (13). Adherence to immunization schedule and timing allows for development of maximal herd immunity which in turn offers protection to even the youngest yet to qualify for vaccination and those whom immunization may be contraindicated (14,19).

A study in the West Coast of the USA to determine the immunization levels among premature and LBW infants and the risk factors for delays found that birth weight <1500g was consistent with lower up-to-date immunization status (23). They studied 11,580 LBW and premature infants enrolled from birth to 24 months and 173,372 term normal birth weight infants as controls (23). The results were analyzed using logistic regression to show the association between patient characteristics and the risk of not being up-to-date for immunization. Up-to-date levels, (the age at which the child was eligible for a vaccine extended up to the end of that period in months) were measured at 2,4,6,15,18 and 24 months. The findings (odds ratio (OR) with 95% CI) at 6 months were, 52-65% (3.47 (1.89-6.36)) of <1500g birth weight were up-to-date for immunization compared to 69-73% (1.47 (0.99-2.17)) of 1500g-2500g and 65-76% (1.00) of normal birth weight infants (23). These findings despite not being statistically significant, show delays in time to immunization especially for the LBW infants.

A retrospective study of a cohort of 135,964 infants, who had more than 2years of military healthcare follow up, was done over a 3-year period 2008-2011 to understand the effect of LBW on immunization after controlling for previously hypothesized mediators. After adjustment for preterm birth, comorbid neonatal conditions, and early childhood patterns of healthcare use, LBW was significantly associated with immunization non-completion in a universal healthcare system (24). The odds of immunization completion were significantly decreased in infants born at LBW (odds ratio [OR], 0.88 [95% confidence interval (CI), 0.79–0.97]), very LBW (OR, 0.61 [95% CI, 0.48–0.77]), or extremely LBW (OR, 0.45 [95% CI, 0.33–0.63 (24). It was proposed that, to increase immunization completion among LBW infants, provider consistency and well child care visits would be important to achieve the target (24).

A study done in Netherlands on Delayed Start of Diphtheria, Tetanus, Acellular Pertussis and Inactivated Polio Vaccination in Preterm and Low Birth Weight Infants included all 883,747 vaccinated children born between 2006-2010. To determine the vaccination age and the proportion of timely vaccinated infants (<70 days), data from national immunization register was used (25). The proportion of timely vaccinated infants was significantly affected by weight and gestation at birth. Timely vaccination was found in, 66%, hazard ratio (HR) with 95% CI of 0.74 (0.66-0.83) for extreme preterm, 76% HR 95% CI 0.89 (0.86-0.92) for preterm and 82% HR 95% CI 0.99 (0.98-1.00) for full term infants which was similar to the results seen by birth weight (25).

In evaluating the timelines of routine immunizations in very preterm infants, an Italian study found that these infants had lower immunization coverage compared to the general population (26). This study included 1196 infants 22-31completed weeks of gestation discharged from critical care unit and followed up to 24 months of age. There was a significant delay in starting immunizations. LBW had an effect on the likelihood to start immunization on time, 87% of

participants received the first dose of DTP–Polio–HBV-Hib by 6 months of age, and 66.7% had their first MMR administered by 18 months (26). DTP–Polio–HBV-Hib timeliness improved with increasing birthweight and paternal employment and decreased with a larger number of siblings in the household (26).

An Indian study of 10,644 infants to assess full immunization at one year and delayed vaccination with DPT1 and DPT 3 among LBW infants found that only 29.7%, OR 0.78 95% CI (0.74-0.82), were fully immunized by age one year (9). Delayed vaccination was seen in 52% and 81% for DPT1 and DPT 3 respectively (5). DPT 1 was further analyzed by gender of the infants to determine the odds of delayed vaccination (9). DPT 3 was analyzed at two points, after 12 weeks of DPT1 and after 18 weeks from birth. At 12 weeks from DPT1, unadjusted OR 1.06 (0.99-1.14) and OR 1.04 (0.97-1.12) when adjusted for other factors such as place of birth, age of mother, infant's gender, wealth quantile, parents' education and occupation (5). At 18 weeks from birth, 95% CI, female infants had OR 0.92 (0.79-1.07) of delayed immunization compared to the male infants (9).

In Ghana, a recent study found a strong dose-response relationship between LBW and not receiving BCG in the neonatal period (p trend <0.0001) (27). This study in a rural Ghanaian health research center enrolled 22,955 infants at 72 hour or less after birth. Infants weighing 1.50– 1.99 kg had 1.6 times higher odds of non-vaccination (AOR 1.64 (1.30-2.08)) while those weighing <1.50 kg had 2.4 times higher odds of non-vaccination (AOR 2.42 (1.50-3.88)) (with 95% CI) compared to non-LBW infants (27). Place of delivery and infant illness did not modify the association between birth weight and vaccination (27). Another Ghanaian study of 22,955 infants assessed the vaccination timing of DTP1 and DTP3 among LBW infants and the associated determinants (28). This study found that, compared to normal birth weight infants, LBW infants had significantly lower DTP1 vaccination rates at 10 weeks (adjusted rate ratio (aRR) 0.58 95%CI (0.43-0.77)) and at 18 weeks (aRR 0.63 95%CI 0.50-0.80) while the 1.5-1.9kgs infants had 25% lower vaccination rates at the same points compared to non-LBW infants (28). DPT3 findings were similar (28).

Two studies done in Chile and in Peru both showed 60-70% delays in receipt of OPV3 and DPT3 (29,30). The Peruvian study, which included a total of 222 infants < 1500g at birth from four hospitals and followed them up every 2 weeks from birth to 12 months of age. They found considerable delay in the time to OPV 1 and Pentavalent 1 with greater delays for infants with even lower birth weights (30). Mean age for Pentavalent 1 and OPV 1 was 4.3 ± 1.4 months for <1000g vs 3.1±1.0 months 1-1.5kg (p<0.001) (30) The same study found that by 7 months only 35% of the infants and by 9 months 81% of the infants had received 3 doses of OPV and pentavalent vaccines (30).

An observational cohort study done in two urban informal settlement in Nairobi Kenya on the effect of LBW on time to BCG vaccination found that 60% of LBW infants received BCG after the 5th week of life (31). This study followed up all infants born within the study area from September 2006 and followed them up every 4 weeks. They analyzed data for 3,6o2 infants among which 229 (6.4%) were LBW (31). Unadjusted time ratio (TR) for infants <2000g at birth was 7.73(5.52,10.82) while those 2000g-2499g had unadjusted TR 1.22(0.98-1.51) to BCG vaccination compared to normal birth weight infants (31).

A Nigerian study, on 512 children 24 months and older, done to evaluate the timelines and completion rates of routine childhood immunizations found that the overall delay in any of the

basic vaccines was 18.9%-65% (1). the overall delay in BCG was 57.8% (given 14 days after birth) with 31.2% receiving the BCG at more than 28 days of age (1). The study also found that 8.1% and 5.8% of the children studied received DTP1 and DTP3 respectively earlier than the recommended age. (1)The deviation from recommended ages of immunization was significant for all the basic vaccines 17.4-45.92 days (p=0.0001) (1). This study, although not specific for LBW infants, shows that there is delays in receipt of vaccines by infants. The same delays in LBW infants would bear more consequences due to their increased vulnerability to VPDs.

These studies have shown that, whether in the high income, lower-middle income or lower income countries, immunization among LBW infants is consistently delayed.

2.5: Factors associated with immunization delays among LBW infants

Many studies have been done on infant and child vaccination. Few studies, especially in developed countries, have been specific to LBW infants. Several factors influence immunization among infants and children in these studies. These factors can be categorized as infant factors, health system factors and parental/family factors.

2.51: Infant factors

Low birth weight has consistently and strongly been associated with delayed start and completion of immunization (9,23–28,31). This finding is consistent in both low-income and high-income countries. The lower the birth weight, the more the delay (9,23,24). The findings in the Indian study found 29.7% of LBW infants, (OR 0.78 95% CI (0.74-0.82)), were fully immunized by the age of one year (9). After adjustment for preterm birth, comorbid neonatal conditions, and early childhood patterns of healthcare use, LBW was significantly associated with immunization non-completion in a universal healthcare system (24). In a Ghanaian study, place of delivery and infant illness did not appear to modify the association between birth weight and vaccination (27).

An observational cohort study done in a poor urban settlement in Nairobi Kenya on the effect of LBW on time to BCG vaccination found that 60% of LBW infants received BCG after more than 5 weeks of life (31). Compared to normal birth weight infants, LBW infants <2000g and those 2000-2499g had time ratio (TR) 7.73 (5.52-10.82) and TR 1.22 (0.98-1.51) respectively (31).

Length of hospital of stay and illness is another factor found to influence immunization among LBW infants. One study found 8-14 days of hospitalization in the 1st month after birth to be significantly associated with up-to-date immunization status (OR 0.27(0.09-0.87)) (23). Children with more well child visits were likely to have been up-to-date in their immunization status (23). In another study, hospitalization and cerebral palsy were found to be associated with immunization delays among premature and LBW infants (26). Prolonged hospital stay especially among VLBW and ELBW due to the complications of prematurity and to enable them gain the desired weight has been linked with delayed start to immunization (32). Tozzi *et al* in an Italian study found that most hospitals do not start immunization for the preterm infants until they are well enough and this will most often coincide with discharge from the hospital (26).

In the Kenyan study, when the effect of gender in association with birth weight and BCG timing was assessed, male LBW infants were shown to receive BCG a day later than the female infants (31). Females infants 2000g-2499g had TR 1.17(0.89,1.54) that is 0.6 times earlier than males who had TR 1.95(1.31,2.90) while those <2000g had female TR 8.82(4.95,15.71) which was

0.97 times earlier than the male infants (19). The other study which analyzed the effect of gender on immunization timing similarly found that there was no statistically significant effect (9).

2.52: Health system driven factors

Appropriately structured and applied health system ensures a high quality immunization program in keeping with the needs of the population.

Studies have reported that factors include; place of delivery, distance to nearest health facility, vaccine stock-outs, health workers' knowledge and practices and false contraindications are associated with immunization delays (17,33,34). Although these studies did not specifically look at LBW infants, the same factors will most likely apply in LBW infants' immunization practices.

Healthcare workers may have insufficient knowledge about safety and effectiveness of vaccines among preterm and LBW infants (18). Fear and adverse events related to vaccination may also contribute to the delays (18,21). No safety concerns have been demonstrated that would warrant delaying administration of immunizations to preterm and LBW infants (14,21,35). It was proposed in a study that there is need to have elaborate universal guidelines on monitoring duration and modalities of monitoring after preterm infant immunization which would go a long way in encouraging start of immunization in a hospital setting (18). A US study found that children with more well child visits were likely to have been up-to-date in their immunization status (23). The study also noted that for VLBW infants, some primary care providers postpone immunization for some infants who have not attained a certain weight like 4.5kg (21). One study concluded that, consistency in the health care provider as well as consistency in child care would be important to increase immunization completion among LBW infants (24).

Mutua *et al* found that BCG immunization was significantly given much earlier among LBW infants born in public health facilities, TR=0.48 (0.44,0.53) compared to those delivered in private health facilities (31). The Ghanaian study found that facility born infants were being vaccinated at an average age of 6 days suggesting that they were not being vaccinated in the facility they were delivered in (27).

2.53: Parental/family factors

The parents or caregivers of a child play an important role in ensuring that a child has access to basic needs which includes healthcare. A Chilean study found that 80% of the reasons given for delaying VLBW infants' immunization were not justified, the primary reasons being lack of parental time and oversight (29). In the childhood immunization studies, it was found that education level, employment status, parity, ANC attendance, marital status, place of delivery and socio economic status were among the major factors influencing immunization practices in children (33,34,36). Maternal education > 12years of schooling was associated with higher odds to full immunization and lower odds of delay in DPT1 in the Indian study OR 5.56 95%CI 4.76-6.50 AOR 2.39 95%CI 1.97-2.91 (9). Lowest wealth quartile OR 0.19 (0.16-0.22), age of mother <20years OR 0.59 (0.51-0.69) and Muslim religion OR 0.24 (0.21-0.28) were found to be significantly associated with lower odds to full immunization and increased risk to delayed time to DPT1 and DPT3 (5).

In the LBW immunization studies, maternal formal education, parental employment and increasing birth weight were found to promote timely vaccination (9,26,27,31). Delays in LBW infants' immunization was found to be associated with lower socioeconomic status, lower

maternal age and education, larger number of siblings, infants with cerebral palsy and a longer distance to the nearest health facility (9,26,28).

Most of the data available is for childhood immunization in general. There are few studies done on LBW immunization and these studies are even fewer in lower income and lower-middle income countries like Kenya.

JUSTIFICATION AND UTILITY

Globally, an estimated 15-20% of all births are LBW with majority occurring in low and middle income countries (1). In Kenya, according to KDHS 2014, 8% of all reported births were LBW (8). Neonatal mortality rate as per KDHS 2014 was 22 per 1000 live births (8). VLBW infants contribute largely to the neonatal mortality as shown in a Kenyan study (37). Vaccination is an important method of reducing childhood morbidity and mortality from vaccine preventable diseases common in childhood (19,21). Global vaccination policy advocates for identifying and targeting groups who are underserved by vaccination to increase equity and uptake. Many local

studies have been done on barriers to immunization in children but there are very few that studied the same specifically in LBW infants.

The few studies available on LBW infants' immunization, even fewer done in our local setup, show delays in immunization of the LBW infants. This is despite the WHO recommendation that medically stable premature and LBW infants be immunized according to chronological age (10,12). Delay in immunization will increase the morbidity of VPD among the LBW infants, increase their mortality and generally contribute to reduction in herd immunity of the total population. This study will add knowledge in the gap on LBW infants' immunization that currently exists in terms of available data. This data will also be helpful to guide policy formulation, decision making and allocation of resources to improve the care of this vulnerable population.

This study aims to determine the factors associated with delays in vaccinating LBW infants. This information will hopefully improve communication about immunization to caregivers and to the health care providers and thus improve immunization practices among LBW infants.

RESEARCH QUESTION

What proportion of LBW infants have delayed immunizations and what are the factors associated with immunization delays among LBW infants at the Kenyatta National Hospital?

STUDY OBJECTIVES

1. Primary objective

To determine the proportion of LBW infants with delayed immunization as per the KEPI schedule

2. Secondary objectives

a. To describe the infants' characteristics associated with immunization delays among LBW infants

b. To describe the maternal characteristics associated with immunization delays among LBW infants

CHAPTER 3: METHODOLOGY

3.1: Study design

This was a hospital based cross-sectional descriptive study.

3.2: Study site

The study was conducted at Kenyatta National Hospital (KNH). This is the largest referral hospital in Kenya, located in Nairobi County. It serves as a teaching hospital for the University of Nairobi School of Medicine and other medical learning institutions. The hospital provides inpatient, outpatient and specialised treatment services. The inpatient facilities have 50 wards with a bed capacity of about 1800 patients. The outpatient facilities include 22 specialised outpatient clinics. The study was carried out at several points in the hospital:

a.) Pediatric Emergency Unit (PEU) which is the outpatient department dedicated to pediatric non-surgical patients and operates every day for 24 hours.

b.) The Maternal and Child Health (MCH) clinic, where the KEPI childhood vaccinations are offered in the facility. It operates weekdays 8am to 1pm. The vaccines are administered by the nurses stationed at the department. On average about 500 children are immunized in a month.

c) The four general Pediatric wards located on level three of the main hospital building. Each ward has a bed capacity of 60 patients. The average number of admissions in a month is about 400 children. Occasionally, not consistently, nurses from MCH come and administer vaccines to the children admitted in the wards.

d.) Neonatal outpatient clinic (NOPC) which takes place every Wednesday 8am to 1pm. Infants discharged from the New Born Unit (NBU) are followed up until the maximum age of one year. It is run by the neonatologists assisted by the registrars who are rotating in the NBU. Each clinic day has approximately 35 patients attending with various conditions that require follow up.

3.3: Study period

The study was carried out between October 2018 and December 2018.

3.4: Study population

LBW (<2500g) infants (1-12 months) with their mothers/caregivers coming for services at the above mentioned points in KNH

Inclusion criteria

LBW infants aged one to eleven months whose mothers/caregivers had given consent to participate in the study.

Exclusion criteria

Mothers with LBW infants who did not consent to participate in the study

Mothers/caregivers who did not have the Mother& Child Handbook/immunization record card as it would have been impossible to confirm the vaccines given and when exactly they were given.

Patients known to have immunosuppressive conditions like severe Human Immunodeficiency Virus (HIV) infection and those on immunosuppressive therapy with severe immunosuppression that would contraindicate administration of live vaccines.(14,22)

3.5: Sample size determination

Fischer's formula was used to calculate the sample size for determination of the proportion of LBW infants with immunization delays

$$n = \frac{Z^2P(1-P)}{d^2}$$

n= 384 infants

Z = standard normal deviate for 95% level of confidence (1.96)

P= estimated at 50%

d= desired level of precision set at 0.05 (5%)

n= estimated sample size

10% of the figure n was added to get the minimum sample size for the study to carter for missing or incomplete data.

A total minimum of 422 LBW infants were thus to be recruited into the study.

N/B the prevalence (p) was estimated at 50% because it gives the largest sample size since there was no study giving a clear prevalence of overall immunization delay specifically among LBW infants.

3.6: Sampling method and recruitment procedure

The study subjects were enrolled using consecutive sampling method until the desired sample size was achieved.

Potential study subjects were identified by visiting the PEU, NOPC, the MCH clinic and the pediatric wards and examining their medical records. Infants who were LBW presenting for service were identified and their mother/caregiver was given an explanation of the study purpose and procedure. Written informed consent using a predesigned consent form was obtained from the mother/caregiver (appendix 3 and 4). Any question, clarification or concerns

were addressed fully. The mothers/caregivers who declined to give consent were excluded from the study.

3.7: Data collection tools and procedure

Data were collected by the principal investigator assisted by trained research assistants. These were registered clinical officers who were trained by the PI during the pilot study and continuously when need arose during the study.

Data collection was done using a structured pre-tested questionnaire (Appendix 5) which was administered by the interviewer to the mothers of the infants who met the inclusion criteria of the study. The interviewer read out the questions and then filled out the responses given by the mothers. The Mother & Child Handbook/immunization record card was also inspected and the required information extracted. This information included birth weight, vaccines administered and the dates of administration. After the interview, the Mother & Child Handbook was marked on the top left corner using an orange-colored sticky note with the unique study id number to ensure the same infant is not sampled and recruited into the study again.

3.8: Data analysis and management

The data were stored and managed using Ms Excel while the analysis was done using SPSS v 22.0. Data were first cleaned, then coded and summarized. Descriptive summary statistics was done followed by univariate then multivariate analysis.

Continuous variables such as age and birth weight were summarized and expressed using means and standard deviations or medians and interquartile ranges (IQR). The proportion of LBW infants with immunization delays was determined and presented as a percentage with the corresponding 95% CI. Immunization delay was determined by the difference between the date of birth and the date of immunization as was recorded in the Mother & Child Handbook. The infant and maternal characteristics were compared between the LBW infants with immunization delays and those without delays. Associations between delays in immunization and maternal and infant characteristics were measured using odds ratio (OR) with the corresponding 95% CI. A p-value of < 0.05 was considered statistically significant. Pearson's Chi-squared test was used to test for independence of associations.

The questionnaires were kept in a lockable cabinet daily after receiving them from the research assistants. The entered data was stored in a password protected computer and these were only accessible to the PI and the biostatistician.

3.10: Study outcomes

The main study outcome was the proportion of LBW infants with immunization delays. Secondary outcomes were the factors associated with immunization delays among LBW infants.

Dependent variables

Time to receipt of the routine vaccines from birth, was determined by the difference between the date of birth and the date of administration of a given vaccine as recorded on the Mother& Child Hand book/immunization card.

1. Age at which BCG was administered to the infant
2. Age of Pentavalent 1 administration to the infant
3. Age at which Pentavalent 3 was administered to the infant
4. Age at which Measles vaccine was administered to the infant

The following table shows the definitions of delay in the above vaccines.

Table 2. Definition of immunization delay in the vaccines being assessed

Vaccine	Age of administration on schedule	Age beyond which was considered delay
BCG	Birth	2 weeks
Pentavalent 1	6 weeks	8 weeks
Pentavalent 3	14 weeks	16 weeks
Measles	9 months	9 months and two weeks

Independent variables

These included the social and demographic characteristics of the infant and caregiver. For example, birth weight, gender, length of hospital stays after birth, major illnesses, (like neonatal jaundice, neonatal sepsis, respiratory distress), birth order, previous hospital admissions and outpatient visits and the reason for the hospital visit, caregiver level of education, religion, marital status, parity, ANC (ante-natal clinic) attendance, socioeconomic status (employment of mother/caregiver).

The infant and maternal/caregiver characteristics was compared between the LBW infants with delays and those without delays.

3.11: Quality assurance procedure

The research assistants were adequately trained on data collection and procedure of handling data prior to the study. The training also involved the research assistants piloting the study tools.

The questionnaire used was pre-tested and standardized. Any questionnaire filled during the study was checked by the principal investigator to ensure completeness and accuracy of information. A standard operating procedure for data collection was developed to ensure the data is collected uniformly. This included verification of information from the Mother & Child Handbook such as birth weight, birth date, vaccines administered and when they were administered.

The mothers/caregivers without the Mother & Child handbook were given a chance to bring the booklet at their next appointment or visit.

A qualified biostatistician was involved to ensure data was entered, managed and analyzed appropriately. Data collection tools were kept under lock and key and the computer used to enter and analyze data was password protected. These tools were only accessible by the PI.

3.12: Ethical consideration

1. Approval was sought from the Kenyatta Hospital (KNH/UON) Ethics Research Committee to collect and analyse data as part of thesis dissertation. (appendix 6)
2. The caregivers were appraised on the importance of the study and they gave an informed written consent before the interview. No gifts or any form of persuasive coercion were offered.
3. The study participants were made aware that participation in the study was entirely voluntary and that they were free to withdraw from the study at any point without any negative consequence.
4. Strict confidentiality was observed throughout the entire study period. No actual names of participants were used.
5. During the course of the study, any unimmunized infant was referred to the immunization clinic after the mother had been explained to the importance of timely immunization.
6. The findings of the study will be availed to KNH to help improve the immunization services offered to LBW infants.
7. The study findings will also be presented to the University of Nairobi (UON) Department of Paediatrics and Child Health Academic Staff and Postgraduate students in fulfilment of the requirements of the Master of Medicine Program.

CHAPTER 4: RESULTS

The findings of the study are presented in this chapter.

4.1: Socio-demographic characteristics of the LBW infants studied

The study involved interviews of mothers to 423 low birth weight (LBW) infants, aged between one and eleven months who were recruited into the study. The median age of the infants was 10 weeks with an interquartile range (IQR) of 6-24 weeks. Of the infants studied, 51.3% were female, 85.8% were LBW (1500g- 2499g) and 66.4% had a history of admission to the NBU immediately after delivery, most (64.7%) being admitted due to prematurity/LBW. The median length of admission was 21 days (IQR 7-30 days). All the infants in the study were delivered in a health facility. Additional characteristics of the infants are shown below in table 3.

Table 3: Socio demographic characteristics of the LBW infants

Variables	Categories	Frequencies (%)
Sex	Male Female	206 (48.7) 217 (51.3)
Birth weight	2000g-2499g 1500g-1999g 1000-1499g <1000g	201 (47.5) 162 (38.3) 54 (13.5) 3 (0.7)
History of admission to the New Born Unit (NBU)*	Yes No	281 (66.4) 142 (33.6)
Reason for NBU admission	Prematurity/ LBW Respiratory distress Neonatal sepsis Others	182 (64.7) 67(23.8) 15 (5.3) 17 (6.2)

* NBU- New Born Unit

4.2: Maternal socio demographic characteristics

Most of the mothers who participated in the study (91.5%) were aged between 20 and 35 years with a median age of 28 years, IQR 25-30 years. During pregnancy, 75.9% had attended at least four ANC visits. Majority (89.6%) of the mothers had attained a secondary school and tertiary level of education. These characteristics are summarised in table 4 below.

Table 4: Maternal socio demographic characteristics

Variable	Categories	Frequencies (%)
Maternal age (years)	< 20 20-35 >35	2 (0.5) 376 (91.5) 33 (8)
Parity	1-3 >3	382 (90.3) 41 (9.7)
Number of ANC visits	<4 >= 4	102 (24.1) 321 (75.9)
Highest level of education achieved	Primary Secondary Tertiary	44 (10.4) 163 (38.5) 215 (51.1)
Employment status	Employed Unemployed	183 (43.3) 240 (56.7)
Religion	Christians Muslims Others	374 (88.4) 21(4.9) 28 (6.6)
Support from CHV* and others	Yes No	39 (9.21) 384 (90.79)

*CHV – Community Health Volunteer

4.3: Vaccination timelines among LBW infants

Delay was any vaccine administered 14 days or more beyond the recommended age. This was for the vaccines administered at six, 14 weeks and the measles at 9 months (see table 1). Pentavalent vaccine was used as a surrogate of the other vaccines (polio, pneumococcal and rotavirus) administered at the same visit.

Although unforeseen, a number of infants were found to have received their vaccines earlier than the recommended age. These findings are summarised in table 5 below.

Out of all the infants with a history of NBU admission, only 17.2% reported to have received a vaccine by the time of discharge from the NBU.

Among the infants studied, 8.75% (37/423) were found to have received BCG and Pentavalent 1 on the same visit.

Table 5: Vaccination timelines among the LBW infants

Variable	Categories	Frequencies (%)	95% CI
BCG n=423	On time **Delayed**	193 (45.6) **230 (54.4)**	40.9-50.4 49.6-59.1
Pentavalent 1 n=340	Early On time **Delayed**	80 (23.5) 210 (61.8) **50 (14.7)**	19.3-28.3 56.5-66.8 11.3-18.9
Pentavalent 3 n=161	Early On time **Delayed**	36 (22.4) 101 (62.7) **24 (14.9)**	16.6-29.4 55.5-69.8 10.2-21.2
Measles n=46	Early On time **Delayed**	2 (4.3) 39 (84.8) **5 (10.9)**	1.2-14.5 71.8-92.4 4.7-23.0

Overall, of the population of the LBW infants studied, the proportion with at least one of the four vaccines of interest delayed was 56.7% (95% CI 0.52-0.61)

4.4: Factors associated with immunization delays among LBW infants

The infant and the maternal factors were analysed to determine their association with immunization delays among LBW infants. The following two tables (6 and 7) presents a summary of this analysis.

Table 6: Univariate analysis of the infant factors associated with immunization delays

Variable	Categories	Delayed	Not delayed	OR (95% CI)	p-value
Sex	Male Female	111 (53.9) 129 (59.4)	95 (46.1) 88 (40.6)	0.8 (0.54 -1.18)	0.248
Birth weight (grams)	>= 1500g <1500g	182 (50.1) 58 (96.7)	181 (49.9) 2 (3.3)	0.04 (0.008-0.14)	**<0.001**
History of admission to NBU	Yes No	230 (81.9) 10 (7.0)	51 (18.1) 132 (93.0)	59.5 (29.2-121.1)	**<0.001**
Reason for admission to NBU*	Prematurity/LBW Others	166 (91.2) 58 (63.7)	16 (8.8) 33 (36.3)	5.9 (3.03 -11.5)	**<0.001**
History of OPD** visits since birth	Yes No	6 (27.3) 234 (58.4)	16 (72.7) 167 (41.6)	0.3 (0.11 -0.78)	**0.004**
Number of siblings	<3 >=3	206 (56.1) 34 (60.7)	161 (43.9) 22 (39.3)	0.8 (0.45 -1.42)	0.519

*NBU- New Born Unit

** OPD- Out Patient Department

Table 7. Univariate analysis of the maternal factors associated with immunization delays among the LBW infants.

Variable	Categories	Delayed	Not delayed	OR (95% CI)	p-value
Parity	1 >=2	67 (57.8) 173 (56.4)	49 (42.2) 134 (43.6)	1.1 (0.71-1.69)	0.794
ANC visits	<4 >=4	80 (78.4) 160 (49.8)	22 (21.6) 161 (50.2)	3.7 (2.2 -6.22)	**<0.001**
Highest level of education achieved	Primary Secondary and beyond	29 (65.9) 211 (55.7)	15 (34.1) 168 (44.3)	1.5(0.78 -2.89)	0.195
Employment status (maternal)	Employed Unemployed	141 (58.8) 99 (54.1)	99 (41.3) 84 (45.9)	1.2(0.81 -1.77)	0.339
Religion	Christians Others	212 (56.7) 28 (57.1)	162 (43.3) 21 (42.9)	1 (0.55 -1.83)	0.951
Support from CHV and others	Yes No	26 (74.3) 209 (55.0)	9 (25.7) 171 (45.0)	2.4 (1.1 -5.26)	**0.028**

The infant and maternal factors with a p-value <0.1 in the univariate analyses were subjected to a multivariate logistic regression model. Chi-square test was used to test for the significance of the associations. Birth weight and history of NBU admission were found to have statistically significant associations with immunization delays. VLBW (<1500g) was associated with higher odds of delayed immunization compared to LBW (>1500g) OR 8.415 (95% CI 1.974-35.862). History of NBU admission largely, OR 51.291 (95% CI 24.42-107.676), increased the odds of delayed immunization albeit with a very wide CI. Male gender, maternal employment and primiparity did not have statistically significant association with delayed immunization. These findings are presented in table 8 below.

Table 8. Multivariate analysis of factors associated with immunization delays among LBW infants

Variables	OR (95% CI)	p-value
Sex Male Female (ref)	0.85 (0.48-1.494)	0.566
Birth weight <1500g >= 1500g (ref)	8.42 (1.974-35.862)	**0.004**
History of NBU admission Yes No (ref)	51.29 (24.42-107.676)	**<0.001**
Maternal occupation Employed Unemployed (ref)	0.72 (0.415-1.358)	0.343
Mother's highest level of education Primary Secondary (ref)	1.51 (0.566-4.040)	0.409
Parity of the mother 1 >=2 (ref)	0.67 (0.361-1.248)	/ 0.208
Religion Christian Others (ref)	1.39 (0.571-3.385)	0.469

4.5: Other factors associated with immunization delays

Out of all the mothers interviewed, 17.02% reported that they had at some point taken their infants for immunization and the vaccine had not been administered. The reasons given for the vaccine denial were that the baby was too small, lacked muscle for injection and that it is required for the baby to be at least 3kg in order to receive the injectable vaccines.

CHAPTER 5: DISCUSSION

The variable age in our study reduced the sample size further for each subsequent vaccine studied. Further, we could not assess for full immunization as was done in most of the other studies.

The mothers who were sampled into our study were above the age of 20yrs (91.5%), had achieved a minimum of a secondary school education (89.6%) and were Christians (88.4%). These could be explained by the study site, a tertiary health facility in the capital city of a country whose population is largely Christian.

The prevalence of immunization delay was found to be 56.7% (95% CI 0.52-0.61) among LBW infants attending KNH. This was similar to an Iranian study that found 42% -67.5% of all infants received vaccines with delay (38) and a Nigerian study that found 18.9%-65% of overall delay in any of the basic EPI vaccines (1). BCG was found to be the most delayed vaccine at 54.4% which was slightly lower than findings in a Kenyan study that found that 60% of LBW infants received BCG after the 5^{th} week of life, a Nigerian study that found BCG delay at 57.8% and a Gambian study that found 63.3% (CI 60.6%-66.1%) delay in the recommended time to receiving a vaccine (1,3,31). The Kenyan study however did not analyse for the duration of admission for the LBW infants if any and only 6.5% of the study population was LBW (31). However, none of these studies were specific for LBW infants. Pentavalent 1 was delayed at 14.7% which was lower than the 52% rates of delay found in an Indian study (9) and 40% rates of delay found in a Ghanaian study (26). The rates of delay for Pentavalent 3 was 14.9% which was considerably lower than the 81% delays for DPT3 found in an Indian study (9). The better performance in the pentavalent vaccine administration could be due to increased confidence among health workers in administration of subsequent vaccines when the child is older and bigger (in terms of both weight and age).

In our study, there was early pentavalent 1 (23.1%) and pentavalent 3 (22.4%) administrations respectively which was much more than the 3% and 0.003% respectively in a study done in Nepal and 8.1% for DTP1 found in a Nigerian study (1,2). While the American Advisory Committee on immunization and the American Academy of Paediatrics (AAP) allow for up to four days before the recommended ages for each vaccine (39), early immunization in our study was any day before the recommended age on the schedule. Expert consultations recommended not a single day earlier to be allowed because the local population receives their vaccines when they are much younger than the American population. The consensus was that rather than administer the vaccine a day or two early, it is better the vaccine be given later by up to seven days after the recommended age. Early administration of vaccines is associated with reduced immune response due to an immature immune system and interference with maternal antibodies for the first doses of the vaccine antigens (39). In this population of LBW infants, receiving vaccines early, especially so for the first antigen (pentavalent 1), does not confer the protection desired when vaccines are administered due to the previously mentioned interference. This means that

these infants remain vulnerable for longer in reality despite having already received the intended vaccine.

WHO recommendations on catch-up immunizations advise that a child be given all the antigens eligible for at any contact with a health facility (17). Only 8.75% of the infants had received BCG and Pentavalent 1 on the same visit. Only 17.2% of the infants studied had reported receiving a vaccine by the time of discharge from the NBU. This is contrary to the Kenyan national guidelines that recommend administration of BCG at discharge from hospital or at 2000g for the LBW infants whichever comes first (4). This finding is comparable to a Ghanaian study that found that the infants were receiving BCG on average at six days after delivery implying referral for immunization rather than immunization at discharge as recommended (28). It is important to note that, WHO recommends that an infant/ child should receive all the vaccines that they qualify for prior to leaving a health facility (17). This recommendation minimizes the events of missed opportunities for immunization.

Low birth weight <1500g was found to be suggestive of a strong association with immunization delays compared to those >1500g, OR 8.42 (95% CI 1.97-35.86). The wide CI in this case can be attributed to our relatively small sample size which was composed of less than 15% of <1500g infants. This finding is however comparable to other larger studies that looked at the effect of birth weight on vaccination timing. A study in USA West Coast found that at 6 months of age, 52-65% of infants <1500g at birth had up-to-date immunization compared to 69-73% up-to-date rates for infants 1500-2500g at birth (23). These findings were consistent with another American study that found reduced odds to immunization completion proportionately to decreasing birth weight for LBW,VLBW and ELBW at 0.88, 0.61 and 0.45 respectively(24). The same effect of birth weight on time to vaccination were seen in Dutch, Italian, Ghanaian and Peruvian studies (9,25–27,30). These studies concluded that decreasing birth weight is the single greatest risk factor associated with immunization delays. LBW infants are admitted to NBU after delivery with longer admission duration required for lower birth weights. This means more delays in initiating immunizations for the infants with the lowest birth weight. WHO recommends that clinically stable premature and LBW infants start immunization with the same schedule as their term counterparts (17). Tozzi *et al* also recommended that for the stable infants, immunization be started while still in the NBU since most neonates are kept in the care units for longer just to gain the desired weight (26).

In our study, 66.4% of the infants had a history of being admitted to the NBU after delivery with 64.7% of them being admitted due to prematurity/LBW. The median length of stay in hospital was 21 days (IQR 7-30 days). In these infants, OR 51.29 (95% CI 24.42-107.68) was suggestive of increased odds of delayed immunization than the infants who were not admitted to NBU after delivery. The smaller sample size in our study was likely responsible for the wide CI recorded. This finding is similar to an American one that found OR 0.27 (95% CI 0.09-0.87) of being up-to-

date for immunization in infants who had 8-14 days of admission in the first month after delivery than the infants who had no or less than seven days of admission (23). However, our study did not analyse the effect of duration of hospital stay on time to immunization because not all infants studied had the discharge summaries available for confirmation. We relied on the mothers' recall for the duration of admission.

The other factors found to be associated with immunization delays among LBW infants in other studies like sex of the infant, mother's age, parity, religion, education level and employment were not found to significantly influence the time to immunization in these infants. Maternal age less than 20 years, less than 12 years of formal schooling, unemployment and Muslim religion were shown to reduce the odds to timely immunization in previous studies (3,9,28).

This large percentage (56.7%) of LBW infants with immunization delay implies that this already vulnerable population is at a continued risk of vaccine preventable diseases and thus contribute to reduced herd immunity. BCG vaccine which was the most delayed vaccine (54.7%) has been shown to have other non-specific beneficial effects in the neonatal period especially for the VLBW infants (40). Delaying this vaccine denies these infants these benefits associated with timely vaccination.

All the infants in the study were delivered in health facilities which means they had an opportunity to receive their BCG before discharge as is recommended in the guidelines (17,22). The delay in BCG vaccination found in this study implies that the health care workers may not be practising as per the immunization recommendations. This is comparable to a Ghanaian study which concluded that infants were receiving BCG vaccine at different facilities than the ones they were delivered in since the vaccine was not being administered at discharge (27).
The finding of smaller proportion of delay in the subsequent vaccines may imply that there was catch up in immunization of these infants. This may be due to greater confidence in the health care workers in immunizing these babies when they become bigger as was reported previously that some health workers postpone immunization until an infant attained a certain weight like 4.5kg (23). In our study, some healthcare workers were postponing immunization for the infants they deemed to be too small.

Health workers' knowledge and practises and false contraindications to immunization have been found to contribute greatly to immunization delays (17,33,34). Although not specific for LBW infants, these reasons can be seen to apply for the LBW infants.

Early administration of vaccines in our study could be due to health care workers not confirming the age of the child from the birth records in the Mother & Child Handbook or the birth records being unavailable/missing for confirmation. The mother may also not be sure of the exact date of birth. The mothers may also be

requesting for early vaccine due to travel or work and their requests are being granted by health care workers who are unaware of the need to strictly adhere to the recommended ages on the immunization schedule.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1: Conclusions

There was a high prevalence of immunization delays among LBW infants in our set-up with BCG being the most commonly delayed vaccine. VLBW, History of NBU admission and the small proportion of infants who received vaccine before discharge from hospital is suggestive that health system or health practitioners' factors may contribute to delay in immunization.

6.2: Recommendations

1. Kenya immunization policy document should give guidance on preterm and LBW immunization which is currently lacking.
2. The mother & child handbook should have the information and schedule for premature and LBW infants' immunization
3. A follow up qualitative study focussing on health system and health care workers factors to explore the reasons for both delayed immunizations among VLBW infants.

6.3: Study limitations

The following were experienced in the course of the study

1. Participation in the study was entirely dependent on the caregiver willingness to be involved in the study thus subject to selection bias
2. The study had a retrospective aspect thus recall bias was difficult to avoid entirely
3. The study population was not stratified in terms of weight thus the study was unable to adequately draw conclusions for each weight category
4. The assumption that what is recorded is what was actually done in terms of the vaccines given
5. Although the infants were studied in KNH, they were not all receiving their vaccines at KNH.

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APPENDICES

Appendix 1. Time Frame

The following is the expected time frame of the study process:

Number	Activity	Estimated Time
1.	Development of Proposal and presentation	January to February 2018
2.	Proposal Submission for ethical approval	June 2018
3.	Data Collection	October to December 2018
4.	Data Analysis	January to February 2019
5.	Thesis Writing	March to April 2019
6.	Poster Presentation	April 2019
7.	Thesis Submission	June 2019

Appendix 2. Study Budget

The following is the estimated cost for the study.

Category	Remarks	Units	Unit Cost	Total (Ksh.)
Proposal Development	Printing drafts	1000 pages	5	5000
	Proposal copies	7 copies	1000	7000
Data Collection	Stationery pack (Pens, paper)	400	50	25000
	Training of the research assistants	2	1000	2000
	Research Assistants	20 weeks	2000 X 2	80000
Data Entry	Data Clerk	1	7000	7000
Data Analysis	Statistician	1	35000	35000
Thesis Write up	Printing drafts	1000 pages	5	5000
	Printing Thesis	10 copies	1500	15000
Contingency fund				5000
Total				**187,000**

Appendix 3. INFORMED CONSENT FORM FOR MOTHERS/CAREGIVERS OF LBW INFANTS AT KNH

Study title: prevalence and factors associated with immunization delays among low birth weight (LBW) infants at KNH.

Patient Study Identification Number: …….

Date: …….

Dear Sir or Madam:

Introduction/purpose:

In collaboration with the University of Nairobi, we are administering a survey to caregivers/mothers accompanied by infants who were LBW. The survey aims to identify the factors associated with immunization delays among LBW infants. To this end, we kindly ask for your participation in helping us complete a questionnaire.

Study procedure:

If you decide to participate, we will ask you questions regarding your baby from birth, birth weight, length of hospital stay after birth, any illnesses, and their immunization status. Specifically, you will be asked if your baby has received vaccines and when and where they were given. And reasons why the vaccines were not given if any are due. We will also ask a few questions about you the caregiver like regarding your age, education level, employment, religion. The whole process will last approximately 25 minutes from consent to the actual interview.

Compensation:

You will receive no compensation for participating in this study. However, your participation allows for the design and implementation of interventions to improve the immunization practices among LBW infants.

Confidentiality:

The information you provide is anonymous and strictly confidential. We will assign a registration number to your questionnaire, and only the person responsible for this study will have access to your personal information.

Potential risks: Questions included in this survey do not present any foreseeable risk. Nevertheless, you may choose to not answer any question that makes you uncomfortable.

Voluntary participation/withdrawal from study: Your participation is entirely voluntary, and you are free to discontinue the interview at any time. Refusing to participate will not affect your ability to continue receiving services in this health care facility.

Person to contact:

If you have any questions or concerns regarding the interview, we are leaving you the contact information of the coordinator of this study.

Dr. Lucy Lyanda

Telephone Number: 0725 219 960

Kenyatta National Hospital Ethics and Research Committee/ University of Nairobi

P.O. BOX 20723-00202, NAIROBI.

Telephone: 7263009

Extension: 44355

Thank you for your participation!

Appendix 4. Consent declaration form

To be completed by the participant

I declare that the study has been explained to me in a manner obvious to me. I understand the nature, method, risks and benefits of the study.

My questions about the study have been answered satisfactorily.

I therefore voluntarily agree to take part in this study while reserving my right to terminate my participation at any time

Date ---------- Signature of participant ----------

Translated declaration

Tamko la mshiriki.

Natangaza kuwa utafiti umeelezewa kwangu kwa njia ya dhahiri kwangu. Ninaelewa asili, mbinu, hatari na faida ya utafiti huu.

Maswali yangu kuhusu utafiti huu yamejibiwa kwa kuridhisha.

Kwa hiyo mimi ninakubali kwa hiari kushiriki katika utafiti huu wakati nikihifadhi haki yangu ya kusitisha ushiriki wangu wakati wowote.

Tarehe ---------- sahihi ya mshiriki ----------

To be completed by the researcher

I declare that I have given both a written and verbal explanation of the study. I have explained the purpose of the study, methods, risks and benefits of the study. I have answered and will continue to answer any questions that may arise about the study. The participant will not suffer any adverse consequences in case of early termination of participation in this study.

Initials of researcher ----------

Date ---------- Signature of the researcher ----------

Appendix 5. QUESTIONNAIRE FOR MOTHER/CAREGIVER OF LBW INFANT

STUDY TITTLE: PREVALENCE AND FACTORS ASSOCIATED WITH IMMUNIZATION DELAY AMONG LBW INFANTS AT KNH

Study Id. ……. Interviewer initials …… Date …….

SECTION 1. INFANT FACTORS

1. Date of birth _____ Birth weight _____grams Gender _____
   Gestation at birth _____ current age _____
   Number of siblings _____ residence _____

2. Was the infant admitted to the New Born Unit (NBU)?
   1.Yes 2. No **If No, proceed to Number 5**

   If yes, how long was the NBU stay? _____

   What was the discharge weight? _____

   Were any vaccines given during the NBU stay?
   1. Yes 2. No

If yes, which vaccines were given? _____

Were you given any advice/instructions concerning immunization at discharge? (which information and who gave the information)

1. Yes 2. No

If yes, specify

3. what was the reason(s) for the NBU admission?

4. Has the infant been readmitted to hospital after discharge from the NBU?
   1. Yes 2. No
      If yes, how many times? _____
      Reason(s) for admission

Proceed to number 6

5. Has the infant had any hospital admissions since birth?
   1. Yes 2. No

If yes, how many times? _____
Reason(s) for admission

If No, proceed to number 6

6. Has the child had any outpatient visits since birth?
   1. Yes 2. No
      If yes, how many? _____
      Reasons for the outpatient hospital visits

7. Does the infant have any known medical conditions?
   1. Delayed milestones (gross motor) 2. Cardiac disease 3. Convulsions 4. Other (specify)

SECTION 2. IMMUNIZATION DATA

1. Which vaccines has the baby received?
   a) Birth – BCG date _____

b.) 6 weeks – Pentavalent 1 date _____

c.) 10 weeks – Pentavalent 2 date _____

d.) 14 weeks - Pentavalent 3 date _____

e.) 9 months - measles date _____

N/B for vaccines due but not given write NOT GIVEN at the space
For vaccines not yet due write N/A

2. Should LBW infants have a different immunization schedule compared to normal birth weight infants?
   1. Yes 2. No 3. I don't know
      Explain

3. Have you ever taken this baby for immunization and it was not administered?

1. Yes 2. No
   If yes, what reasons were you given?

4. Have you been informed when your baby is due for the next vaccine?
   1. Yes 2. No

5. Who is the main decision maker regarding your baby's immunization?
   1. Myself 2. My partner 3. Health care worker
   4. joint decision 5. Other (specify) _____

6. Where do you take your baby for immunization? (verify from immunization card/booklet)
   1. Public health facility 2. Private health facility 3. Other(specify) _____

SECTION 3. FAMILY FACTORS

1. What is the mother's age? _____years

2. What is the highest level of education attained? (include number of years completed)
   1. Primary 3. Tertiary 5. None
   2. Secondary 4. University
3. What religion does the family practice?
   1. Catholic 2. Protestant 3. Muslim 4. Other (specify) _____

4. What is the occupation of the mother?

   _____

5. What is the mother's parity? _____

6. How many times did the mother attend (antenatal clinic) ANC during the pregnancy? (verify from Mother- Child booklet) _____

7. Does the mother have any support from community health workers, peer support group? Specify from whom and the support.