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Risk factors of infant mortality in rural The Gambia: a retrospective cohort study

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ABSTRACT

Objective The main objective was to assess the risk factors for infant mortality among children living in the Health and Demographic Surveillance System (HDSS) in Farafenni, The Gambia. Our secondary objective was to assess these risks separately in the neonatal and postneonatal (>28 days) period.

Design Retrospective cohort study.

Setting HDSS in an urban centre and surrounding area in The Gambia.

Patients 7365 infants (47% female) born between 2014 and 2018, of which 126 (1.71%) died in the first year.

Main outcome measures Infant mortality.

Results Risk factors for mortality were death of any sibling (HR 2.78, 95% CI 1.54 to 5.00), having a twin (HR 1.96, 95% CI 1.01 to 3.80), being born in the harvest season (HR 1.55, 95% CI 1.07 to 2.24), living in a rural village (HR 4.34, 95% CI 2.03 to 9.29) and longer distance to the nearest village with a public health centre (HR 1.33, 95% CI 1.11 to 1.59). In addition, no breast feeding (HR 10.73, 95% CI 6.83 to 16.86) and no BCG vaccination in the first week of life (HR 3.47, 95% CI 1.07 to 11.24) were associated with infant mortality. Similar risk factors were found in the neonatal and postneonatal periods.

Conclusion Most risk factors associated with infant mortality (neonatal and postneonatal) are not easily modifiable at the individual level and would require programmatic approaches to target vulnerable infants and facilitate access to health services.

What is known about the subject

⇒ In 2018, there were approximately 4 million infant deaths worldwide, with one-third of them occurring in West and Central Africa.
⇒ Multiple risk factors have been associated with infant, neonatal (0–28 days) and postneonatal (29–365 days) mortality. However, substantial heterogeneity exists across regions and within countries.
⇒ In The Gambia, infant mortality rate is 39 deaths per 1000 live births, far higher than the target set in the Sustainable Development Goals.

What this study adds

⇒ In The Gambia, sibling death, twins, season of birth, rural setting, distance to a health centre, breast feeding and early vaccination were associated with infant mortality.
⇒ Similar risk factors were found in the neonatal and postneonatal periods.
⇒ Most risk factors for infant mortality are not modifiable at the individual level, requiring programmatic approaches targeting vulnerable infants and facilitating access to health services.

INTRODUCTION

In 2018, there were approximately 4 million infant deaths worldwide, with one-third of them occurring in West and Central Africa, whose infant mortality rates are estimated at 64 deaths per 1000 live births, about half of them during the first 28 days of life.[1]

Multiple risk factors have been associated with infant (first year), neonatal (0–28 days) and postneonatal (29–365 days) mortality, including fertility behaviour, nutritional status, feeding, maternal and child health status, use of health services and environmental and socioeconomic factors.[2] However, substantial heterogeneity exists across regions and within countries[3] and both risk factors and mortality rates can be highly heterogeneous when comparing rural and urban settings.[4]

In The Gambia, the infant mortality ratio was estimated at 39 deaths per 1000 live births, with most deaths occurring during the neonatal period (26 deaths per 1000 live births in 2018), far higher than the 12 deaths per 1000 live births set in the Sustainable Development Goals.[1 5]

The primary healthcare in The Gambia is based on a community-based health delivery system, where each village with a population of 400 or more identifies a village health worker and a traditional birth attendant for training, who then deliver primary healthcare to their village of responsibility.[6] Secondary healthcare is provided by around

7 main government-run/private health centres and 12 smaller centres, each providing inpatient and out-patient treatment. Tertiary healthcare is provided by four main referral hospitals. The estimated gross national income per capita was estimated in 2011 to be at US$635, although about 45% of the resident population earned less than US$150 per year.[6] Knowing the main risk factors of infant mortality is essential to identify suitable strategies to decrease infant deaths. We analysed data of the ongoing Health and Demographic Surveillance System (HDSS) in Farafenni area to identify the main risk factors for infant mortality also stratified as neonatal and postneonatal mortality.

METHODS

Study area

The study area is situated in the North Bank Region and covers Farafenni town, its peri-urban area (5 km) and 42 surrounding villages. The HDSS follows a population of over 50 000 people, mostly Muslim and subsistence farmers. There is one regional hospital in Farafenni town and 17 public health centres (PHCs) in the surrounding villages. Between 1998 and 2007, about half of all deaths (all ages) were caused by infectious diseases, including pneumonia (14%), malaria (13%) and pulmonary tuberculosis (10%). In infants, the main causes of death were acute respiratory infections (including pneumonia, 28%), neonatal causes (21%), malaria (16%) and diarrhoeal diseases (10%).[7]

Demographic surveillance system

The Farafenni HDSS was established in 1981, initially covering the villages surrounding Farafenni town and then expanded in 1989 to Farafenni town and its peri-urban villages. Demographic events and residency status have been regularly (since 1989, every 4 months) and uninterruptedly (except for a 13-month period between February 2008 and March 2009) collected for almost 40 years by trained field workers.[6]

Study population

For this study, all children in the Farafenni HDSS area born between 1 January 2014 and 31 December 2017 were included. The period was chosen because many variables related to birth (eg, place of birth, mode of delivery and birth weight) were systematically collected only since 2014 and were not available for most of the infants born before this date. Infants born outside of the study area but who migrated into it before their first birthday were included in the analysis (using the date of immigration as starting time). Infants with unreliable date of birth were excluded from the analysis.

Statistical analysis

Infant mortality, that is, deaths during the first year of life, is the primary outcome; risk factors for neonatal (0–28 days) and postneonatal (29–365 days) mortality were analysed separately as well. The reasons for this approach are (1) risk factors between first month of life and postnatal period may differ and (2) data collected retrospectively for neonatal deaths may be less accurate.

The potential explanatory variables of interest include demographic and epidemiological characteristics of the infant, pregnancy and delivery, the family and the environment, as well as significant events (tables 1–4). Some of these explanatory variables could change over the observation period, such as where they lived (urban/peri-urban or rural area and if the village has a PHC), characteristics of the household head (sex, age and education level) and the vital status of family members (deaths of mother, father and older sibling). To ensure that these covariates remained constant within episodes, we prepared our database splitting episodes at the time any of these covariates changed.

Vaccination with BCG vaccine within the first week of life was taken as a proxy for health-seeking behaviour.

The time at risk was defined as the amount of time that the infant spent in the study area between their birth and their death, their first birthday or 1 January 2018 (whichever came first).

We used multivariable Cox proportional hazards models (accounting for clustering of siblings by mothers using robust standard errors) to examine the association between potential risk factors and mortality. Variables with p values<0.20 at the univariable level were included in each multivariable model. For the model assessing infant mortality, any variable selected in either the neonatal or postneonatal model was included. Variables with >20% missing values were described and analysed at the univariable level but excluded from the multivariable models. We considered that living in a rural or urban setting could modify the association of mortality for other variables and therefore assessed this potential interaction in each of the multivariable models. No further interactions were explored.

We found that ‘spacing to previous sibling’ and ‘birth order’ were highly correlated, as all first-borns had no elder siblings. The former was removed from the analyses to avoid collinearity in the multivariable model, as we considered birth order easier to interpret. Nevertheless, the effects of removing birth order were explored in sensitivity analyses. Similarly, as ‘distance to nearest village with PHC’ and ‘PHC in the village’ were highly correlated, the latter was excluded from the multivariable analyses as the former is more informative; the effects of this exclusion were explored in the sensitivity analyses. The effect of excluding early neonatal deaths (first week of life) was also explored as several variables were not relevant for this period.

Finally, we also planned to use multiple imputation for missing values. However, the multiple imputation models for missing data did not converge for most of the risk factors considered and, on the few occasions the models converged, there was no substantial change on the overall

Table 1 Characteristics of included infants born between 2014 and 2018 in the Farafenni Health and Demographics Surveillance System and their association with mortality in each of the three periods considered (neonatal, ≤28 days; postneonatal, 28–365 days and first year, 0–365 days)

	Died in ≤28 days	Died in >28–365 days	Died in 0–365 days	Alive at 365 days	Total
Subjects	64/7131 (0.90%)	62/7152 (0.87%)	126/7365 (1.71%)	7239/7365 (98.29%)	7365
Infant characteristics					
Sex	p=0.739	p=0.251	p=0.287		
Male	32 (50.79%)	28 (45.16%)	60 (48%)	3801 (52.92%)	3861 (52.83%)
Female	31 (49.21%)	34 (54.84%)	65 (52%)	3382 (47.08%)	3447 (47.17%)
Missing	1	0	1	56	57
Year of birth	p=0.719	p=0.535	p=0.880		
2014	19 (29.69%)	17 (27.42%)	36 (28.57%)	1938 (26.77%)	1974 (26.8%)
2015	16 (25.00%)	21 (33.87%)	37 (29.37%)	1809 (24.99%)	1846 (25.06%)
2016	15 (23.44%)	13 (20.97%)	28 (22.22%)	1716 (23.7%)	1744 (23.68%)
2017	14 (21.88%)	11 (17.74%)	25 (19.84%)	1776 (24.53%)	1801 (24.45%)
Ethnic group*	p=NA	p=0.642	p=0.755		
Wollof	29 (45.31%)	32 (51.61%)	61 (48.41%)	3333 (46.07%)	3394 (46.11%)
Mandinka	19 (29.69%)	11 (17.74%)	30 (23.81%)	1852 (25.6%)	1882 (25.57%)
Fula	16 (25%)	16 (25.81%)	32 (25.4%)	1731 (23.93%)	1763 (23.95%)
Other	0 (0%)	3 (4.84%)	3 (2.38%)	318 (4.4%)	321 (4.36%)
Missing	0	0	0	5	5
BCG vaccination in first week†	p=NA	p=0.569	p=0.058‡		
Yes	0 (0%)	3 (4.84%)	3 (2.38%)	522 (7.21%)	525 (7.13%)
No	64 (100%)	59 (95.16%)	123 (97.62%)	6717 (92.79%)	6840 (92.87%)

Row percentages do not add up to 100% because the sample size is slightly different for each group. P values are for the univariable analysis (Cox regression) of each risk factor on mortality in each time period (values<0.05 are bolded).
*Ethnicity was self-reported.
†Proxy for health-seeking behaviour.
‡This variable was included in the multivariable model, as p<0.20.

results. We therefore present the results of the original data (without imputed values).

All analyses were performed using Stata V.14.[8]

There was no patient or public involvement during the development of this research.

RESULTS

Overall mortality

There were 7365 infants born between 1 January 2014 and 1 January 2018 and 126 (1.71%) of them died during this period. Half of deaths (n=64, 50.8%) occurred in the first 28 days of life, mostly during the first week (n=39, 60.9% of neonatal deaths) (figure 1). This is reflected in figure 2, which shows when mortality occurred within the neonatal and postneonatal period using the Nelson-Aalen cumulative hazard function.

Univariable analysis on mortality

The univariable analyses showed that death of any sibling, multiple pregnancy, season of birth, setting (urban or rural), place of birth (hospital, health centre/clinic or someone's home), breastfeeding history, spacing to previous sibling and education level of the father were associated with infant mortality.

In addition, birth order was associated only with neonatal mortality while mode of delivery and increased distance to the health facility were associated only with postneonatal mortality (tables 1–4).

Multivariable analysis on mortality

In the multivariable analysis, death of any sibling (HR 2.78, 95% CI 1.54 to 5.00), multiple pregnancy (HR 1.96, 95% CI 1.01 to 3.80), lack of breast feeding (HR 10.73, 95% CI 6.83 to 16.86), BCG vaccination in the first week (HR 3.47, 95% CI 1.07 to 11.24), being born in the dry season (HR 1.55, 95% CI 1.07 to 2.24) and in a rural area (HR 4.34, 95% CI 2.03 to 9.29) and longer distances from the nearest village with PHC (HR 1.33, 95% CI 1.11 to 1.59) were associated with infant mortality (table 5).

In the neonatal period, risk of death increased with death of any sibling (HR 2.60, 95% CI 1.19 to 5.71), lack of breast feeding (HR 23.60, 95% CI 13.73 to 40.56) and being born in a rural area (HR 3.70, 95% CI 1.57 to 8.70) and the risk decreased for

Table 2 Pregnancy-related and delivery-related variables of included infants born between 2014 and 2018 in the Farafenni Health and Demographics Surveillance System and their association with mortality in each of the three periods considered (neonatal, ≤28 days; postneonatal, 28–365 days and first year, 0–365 days)

	Died in ≤28 days	Died in >28–365 days	Died in 0–365 days	Alive at 365 days	Total
Subjects	64/7131 (0.90%)	62/7152 (0.87%)	126/7365 (1.71%)	7239/7365 (98.29%)	7365
Pregnancy-related and delivery-related variables					
Any IPTP	p=NA	p=0.740	p=0.313		
No	0 (0%)	1 (1.61%)	1 (0.79%)	144 (2.07%)	145 (2.05%)
Yes	64 (100%)	61 (98.39%)	125 (99.21%)	6812 (97.93%)	6937 (97.95%)
Missing	0	0	0	283	283
Season of birth	p=0.335	**p=0.042**	**p=0.035**		
Hungry (July to December)	28 (43.75%)	21 (33.87%)	49 (38.89%)	3645 (50.35%)	3694 (50.16%)
Harvest (January to June)	36 (56.25%)	41 (66.13%)	77 (61.11%)	3594 (49.65%)	3671 (49.84%)
Place of birth	**p=0.009**	p=0.590	**p=0.017**		
Hospital	21 (32.81%)	28 (45.16%)	49 (38.89%)	3130 (45.02%)	3179 (44.91%)
Health centre/clinic	25 (39.06%)	16 (25.81%)	41 (32.54%)	1548 (22.27%)	1589 (22.45%)
Someone's home	18 (28.13%)	18 (29.03%)	36 (28.57%)	2274 (32.71%)	2310 (32.64%)
Missing	0	0	0	287	287
Mode of delivery	p=0.794	**p=0.026**	p=0.065*		
Vaginal	60 (96.77%)	57 (91.94%)	117 (94.35%)	6775 (97.41%)	6892 (97.36%)
Caesarean section	2 (3.23%)	5 (8.06%)	7 (5.65%)	180 (2.59%)	187 (2.64%)
Missing	2	0	2	284	286
Birth weight	**Num: p<0.001† Cat: p<0.001†**	**Num: p<0.001† Cat: p=0.016†**	**Num: p<0.001† Cat: p<0.001†**		
Median (IQR)	2.6 kg (1.8–3.2)	2.8 kg (2.5–3)	2.8 kg (2.1–3.13)	3 kg (2.7–3.3)	3 kg (2.7–3.3)
>2500 g	22 (62.86%)	30 (76.92%)	52 (70.27%)	4079 (91.27%)	4131 (90.93%)
<2500 g	13 (37.14%)	9 (23.08%)	22 (29.73%)	390 (8.73%)	412 (9.07%)
Missing; born in hospital: 11%; health centre: 7%; someone's home: 73%	29	23	52	2770	2822
Breast feeding	**p<0.001**	**p<0.001**	**p<0.001**		
Yes	34 (54.84%)	54 (87.1%)	88 (70.97%)	6656 (96.32%)	6744 (95.88%)
No	28 (45.16%)	8 (12.9%)	36 (29.03%)	254 (3.68%)	290 (4.12%)
Missing	2	0	2	329	331

Row percentages do not add up to 100% because the sample size is slightly different for each group. P values are for the univariable analysis (Cox regression) of each risk factor on mortality in each time period (values<0.05 are bolded). Bolded p values indicate statistical significance.
*This variable was included in the multivariable model, as p<0.20.
†This variable was not included in the multivariable model, despite having a significant association with the outcome at the univariable level, because of the high number of missing values.
cat, categorical variable; IPTP, intermittent preventive therapy during pregnancy; num, numerical variable.

second, third or fourth born infants (HR 0.47, 95% CI 0.23 to 0.99) (table 5).

After the neonatal period, the risk of death increased with death of any sibling (HR 2.26, 95% CI 1.17 to 4.37), multiple pregnancy (HR 2.39, 95% CI 1.05 to 5.44), no breast feeding (HR 3.34, 95% CI 1.53 to 7.29), being born during the harvest season (HR 1.83, 95% CI 1.08 to 3.10) and distance to the nearest village with PHC (HR 1.18, 95% CI 1.01 to 1.39) (table 5).

When testing for interactions, setting reduced the association between distance to the nearest village with a PHC and death, but only in the model for the first year of life (online supplemental tables 1 and 2).

Sensitivity analyses

Comparing the models of infant and the postneonatal mortality, risk factors were mostly similar. However, BCG vaccination in the first week and setting (as well as its interaction with distance to nearest village with PHC) were significantly associated with infant mortality, but not in the postneonatal period.

When we excluded the 39 infants who died in the first 7 days (31% of all deaths)—period in which

Table 3 Family characteristics of included infants born between 2014 and 2018 in the Farafenni Health and Demographics Surveillance System and their association with mortality in each of the three periods considered (neonatal, ≤28 days; postneonatal, 28–365 days and first year, 0–365 days)

	Died in ≤28 days	Died in >28–365 days	Died in 0–365 days	Alive at 365 days	Total
Subjects	64/7131 (0.90%)	62/7152 (0.87%)	126/7365 (1.71%)	7239/7365 (98.29%)	7365
Family characteristics					
Age of mother at birth of infant (years)	Num: p=0.839 Cat: p=0.135*	Num: p=0.977 Cat: p=NA	Num: p=0.872 Cat: p=0.885		
Median (IQR)	27 years (27–33)	26 years(24–30.75)	26 years (23–33)	27 years (22–32)	27 years (22–32)
<18	6 (9.52%)	0 (0%)	6 (4.88%)	318 (4.59%)	324 (4.6%)
18–35	47 (74.60%)	52 (86.67%)	99 (80.49%)	5703 (82.32%)	5802 (82.29%)
36+	10 (15.87%)	8 (13.33%)	18 (14.63%)	907 (13.09%)	925 (13.12%)
Missing	1	2	3	311	314
Age of father at birth of child (years)	Num: p=0.943 Cat: p=0.954	Num: p=0.857 Cat: p=0.910	Num: p=0.955 Cat: p=0.915		
Median (IQR)	40 years (33–48)	40 years (33–49)	40 years(33–48.5)	40 years (33–47)	40 years (33–48)
<41	27 (52.94%)	25 (54.35%)	52 (53.61%)	2816 (53.17%)	2868 (53.18%)
41+	24 (47.06%)	21 (45.65%)	45 (46.39%)	2480 (46.83%)	2525 (46.82%)
Missing	13	16	29	1943	1972
Age of household head (at start of each episode)†	Num: p=0.480 Cat: p=0.699	Num: p=0.516 Cat: p=0.446	Num: p=0.904 Cat: p=0.796		
Median (IQR)	52 years (44–63)	52 years(41.75–63.25)	52 years (43–63)	53 years (44–63)	53 years (44–63)
20–40	0.18 (11.93%)	4.84 (20.15%)	6.02 (19.92%)	952.16 (18%)	958.18 (18.01%)
41+	1.33 (88.07%)	19.19 (79.85%)	24.2 (80.08%)	4338.67 (82%)	4362.87 (81.99%)
Missing	0	0.54	0.55	902.75	903.3
Spacing to previous sibling	**p<0.001‡**	p=NA	**p<0.001‡**		
<18 months	1 (1.56%)	0 (0%)	1 (0.81%)	101 (1.46%)	102 (1.45%)
18–36 months	23 (35.94%)	24 (40.00%)	47 (37.9%)	3191 (46.03%)	3238 (45.89%)
>36 months	14 (21.88%)	23 (38.33%)	37 (29.84%)	2013 (29.04%)	2050 (29.05%)
Died before index birth	8 (12.50%)	2 (3.33%)	10 (8.06%)	148 (2.14%)	158 (2.24%)
No elder sibling	18 (28.13%)	11 (18.33%)	29 (23.39%)	1479 (21.34%)	1508 (21.37%)
Missing	0	2	2	307	309
Birth order	**p=0.017**	p=0.890	p=0.136*		
First	18 (28.13%)	11 (18.33%)	29 (23.39%)	1479 (21.31%)	1508 (21.34%)
Second, third or fourth	18 (28.13%)	28 (46.67%)	46 (37.1%)	3205 (46.17%)	3251 (46.02%)
Fifth or higher	28 (43.75%)	21 (35.00%)	49 (39.52%)	2257 (32.52%)	2306 (32.64%)
Missing	0	2	2	298	300
Singleton/multiple pregnancy	p=0.059*	**p=0.020**	**p=0.003**		
Singleton pregnancy	56 (87.50%)	52 (86.67%)	108 (87.1%)	6548 (94.34%)	6656 (94.21%)
Multiple pregnancy	8 (12.50%)	8 (13.33%)	16 (12.9%)	393 (5.66%)	409 (5.79%)
Missing	0	2	2	298	300
Education level of mother	p=0.224	p=0.724	p=0.220		
None, other, vocation	5 (9.09%)	8 (15.69%)	13 (12.26%)	883 (15.52%)	896 (15.46%)
Religious (Quranic education)	32 (58.18%)	25 (49.02%)	57 (53.77%)	2463 (43.3%)	2520 (43.49%)
Lower basic/primary	2 (3.64%)	1 (1.96%)	3 (2.83%)	311 (5.47%)	314 (5.42%)

Continued

Table 3 Continued

	Died in ≤28 days	Died in >28–365 days	Died in 0–365 days	Alive at 365 days	Total
Upper basic, junior secondary, senior secondary, madaras, college or university	16 (29.09%)	17 (33.33%)	33 (31.13%)	2031 (35.71%)	2064 (35.62%)
Missing	9	11	20	1551	1571
Education level of father	**p=0.007**§	p=0.150	**p=0.005**§		
None, other, vocation	2 (4.00%)	2 (5.26%)	4 (4.55%)	409 (8.81%)	413 (8.73%)
Religious (Quranic education)	34 (68.00%)	30 (78.95%)	64 (72.73%)	2715 (58.5%)	2779 (58.77%)
Lower basic/primary	6 (12.00%)	1 (2.63%)	7 (7.95%)	174 (3.75%)	181 (3.83%)
Upper basic, junior secondary, senior secondary, madaras, college or university	8 (16.00%)	5 (13.16%)	13 (14.77%)	1343 (28.94%)	1356 (28.67%)
Missing	14	24	38	2598	2636
Education level of household head†	p=0.144§	p=0.865	p=0.217		
None, other, vocation	0.1 (6.53%)	0.79 (3.73%)	1.12 (4.16%)	396.2 (8.04%)	397.33 (8.01%)
Religious (Quranic education)	1.21 (80.22%)	16.36 (76.76%)	20.64 (76.54%)	3341.16 (67.77%)	3361.8 (67.81%)
Lower basic/primary	0.02 (1.45%)	0.24 (1.1%)	0.33 (1.24%)	114.33 (2.32%)	114.67 (2.31%)
Upper basic, junior secondary, senior secondary, madaras, college or university	0.18 (11.8%)	3.92 (18.41%)	4.87 (18.06%)	1078.76 (21.88%)	1083.63 (21.86%)
Missing	0.01	3.26	3.81	1263.12	1266.93
Sex of household head†	p=0.956	p=0.252	p=0.390		
Male	1.32 (86.98%)	22.94 (95.47%)	28.7 (94.98%)	4771.02 (90.15%)	4799.72 (90.17%)
Female	0.2 (13.02%)	1.09 (4.53%)	1.52 (5.02%)	521.45 (9.85%)	522.97 (9.83%)
Missing	0	0.54	0.55	901.11	901.66

Row percentages do not add up to 100% because the sample size is slightly different for each group. P values are for the univariable analysis (Cox regression) of each risk factor on mortality in each time period (values <0.05 are bolded). Bolded p values indicate statistical significance.
*This variable was included in the multivariable model, as p<0.20.
†Time-varying variable. Categories described in person-years (%).
‡This variable was not included in the multivariable model, despite having a significant association with the outcome at the univariable level, because it was highly correlated with 'birth order'. It was included in the sensitivity analyses, though.
§This variable was not included in the multivariable model, despite having a significant association with the outcome at the univariable level, because of the high number of missing values.
cat, categorical variable; num, numerical variable.

vaccination might not have taken place—in the overall model absence of BCG vaccination in the first week, twin pregnancy and the interaction term between setting and distance to the nearest village with PHC had similar HR, but wider CIs covering the null effect (table 5, online supplemental table 3).

The remaining sensitivity analyses, choosing different variables of the collinear pairs, yielded no significant changes in the multivariable models or only minimal ones (table 5, online supplemental tables 4 and 5).

Multiple imputation models for missing data did not converge for most of the risk factors considered; on the few occasions the models converged, there was no substantial change on the overall results.

DISCUSSION

Half of infant deaths occurred in the first month of life, mainly during the first week. Several factors associated with infant mortality were non-modifiable factors such as multiple pregnancy, being born during the harvest season or being born in a rural village. Death of a sibling was also associated with infant mortality, indicating the clustering of neonatal deaths in this population. Other risk factors were no BCG vaccination in the first week of life, no breast feeding and distance to nearest village with a PHC.

As mentioned above, our data show a clustering of deaths, as infants with a deceased sibling were at an increased risk of dying. Such effect has also been detected in other cohorts in sub-Saharan Africa,[9 10] probably reflecting family-specific factors such as nutrition and lifestyle features.[9] In Kenya,

Table 4 Significant events and environment characteristics of included infants born between 2014 and 2018 in the Farafenni Health and Demographics Surveillance System and their association with mortality in each of the three periods considered (neonatal, ≤28 days; postneonatal, 28–365 days and first year, 0–365 days)

	Died in ≤28 days	Died in >28–365 days	Died in 0–365 days	Alive at 365 days	Total
Subjects	64/7131 (0.90%)	62/7152 (0.87%)	126/7365 (1.71%)	7239/7365 (98.29%)	7365
Environment characteristics					
Setting*	**p<0.001**	p=0.494	**p<0.001**		
Urban and peri-urban	0.43 (28.52%)	13.42 (54.59%)	16.3 (52.98%)	3642.31 (58.81%)	3658.61 (58.78%)
Rural	1.08 (71.48%)	11.16 (45.41%)	14.47 (47.02%)	2551.27 (41.19%)	2565.74 (41.22%)
Village has public health centre (PHC)*	p=0.078†	p=0.538	p=0.085†		
No	0.48 (31.59%)	3.43 (13.96%)	4.75 (15.45%)	928.28 (14.99%)	933.04 (14.99%)
Yes	1.04 (68.41%)	21.14 (86.04%)	26.02 (84.55%)	5265.3 (85.01%)	5291.32 (85.01%)
Distance to nearest village with PHC	p=0.144‡	**p=0.047**	p=0.924		
Median (IQR)	0.5 km (0–1.5)	1.5 km (0–3)	1 km (0–2.75)	1 km (0–2)	1 km (0–2)
Significant events					
Mother's death*	p=NA	p=NA	p=NA		
No	1.52 (100%)	23.7 (100%)	29.82 (100%)	5992.35 (99.97%)	6022.17 (99.97%)
Yes	0 (0%)	0 (0%)	0 (0%)	2.08 (0.03%)	2.08 (0.03%)
Missing	0	0.87	0.95	199.15	200.1
Father's death*	p=NA	p=NA	p=NA		
Alive	1.14 (100%)	18.97 (97.25%)	23.57 (97.46%)	4627.92 (99.11%)	4651.48 (99.1%)
Died before birth	0 (0%)	0.54 (2.75%)	0.61 (2.54%)	35.26 (0.76%)	35.88 (0.76%)
Died in first 30 days/year	0 (0%)	0 (0%)	6.59	6.25 (0.13%)	6.25 (0.13%)
Missing	0.37	5.07	23.57 (97.46%)	1524.16	1530.74
Any sibling died (any time)	**p<0.001**	**p=0.015**	**p<0.001**		
No	46 (71.88%)	47 (78.33%)	93 (75%)	6203 (89.37%)	6296 (89.12%)
Yes	18 (28.13%)	13 (21.67%)	31 (25%)	738 (10.63%)	769 (10.88%)
Missing	0	2	2	298	300
Older sibling's death*	p=0.945	p=NA	p=0.551		
<18 months older sibling	0.05 (3.61%)	0 (0%)	0.05 (0.18%)	85.71 (1.43%)	85.77 (1.43%)
No older sibling, died before birth or >18 months older	1.46 (96.39%)	23.7 (100%)	29.76 (99.82%)	5900 (98.57%)	5929.77 (98.57%)
Missing	0	0.87	0.95	207.87	208.82
Moved during first year	p=NA	p=0.571	p=0.524		
No	64 (100%)	61 (98.39%)	125 (99.21%)	6925 (96.15%)	7050 (96.21%)
Yes	0 (0%)	1 (1.61%)	1 (0.79%)	277 (3.85%)	278 (3.79%)
Missing	0	0	0	37	37

Row percentages do not add up to 100% because the sample size is slightly different for each group. P values are for the univariable analysis (Cox regression) of each risk factor on mortality in each time period (values<0.05 are bolded). Bolded p values indicate statistical significance.
*Time-varying variable. Categories described in person-years (%).
†This variable was not included in the multivariable model, despite being associated (p<0.20) with the outcome at the univariable level, because it was highly correlated with 'distance to nearest village with PHC'. It was included in the sensitivity analyses, though.
‡This variable was included in the multivariable model, as p<0.20.
cat, categorical variable; NA, not applicable; num, numerical variable.

for example, slightly over 1% of the families accounted for up to 18% of neonatal deaths, while in Burkina Faso, the death of the older sibling was associated with a risk increase of almost 50%.[9 10]

Living in a rural village was associated with higher risk of dying during the first year of life. Such an association was not found in other African cohorts in Kenya and Zimbabwe.[11 12] Furthermore, a study of 18 African countries found that initial statistical differences between living in urban or rural areas disappeared after adjusting for demographic and socioeconomic variables such as parental occupation, water source and wealth.[4] The authors of that study suggested that, rather than the place of residence itself, it is the access to services and economic opportunities that might affect child survival. In our cohort, distances to the nearest village with a PHC were small (third quartile=2 km) and the city defining the urban population is not particularly large. Therefore, such a difference between urban and rural areas was unexpected after adjusting for the remaining covariates. However, given our limited

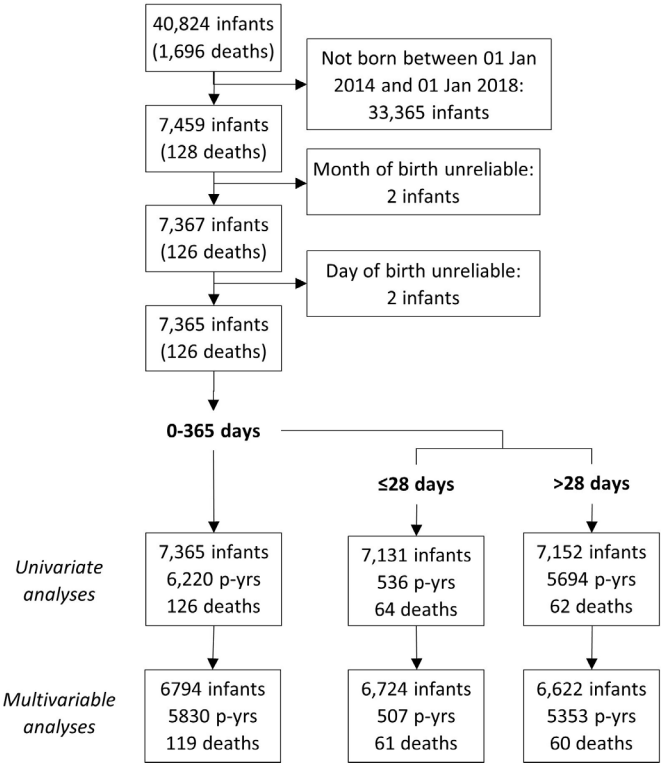

Figure 1 Flow chart of the number of infants and deaths at each stage of the study.

capacity to adjust for socioeconomic factors, there may still be residual confounding that may explain the observed association.

In West Africa, the rainy season coincides with food shortage and an increase of malaria and other infectious diseases. Therefore, higher infant mortality during this period would be expected and has been described in Burkina Faso.[9] This was not observed in Farafenni and confirms the finding of an earlier study carried out in a different, rural region of The Gambia (Upper River Division, between 1989 and 1993), in which no association

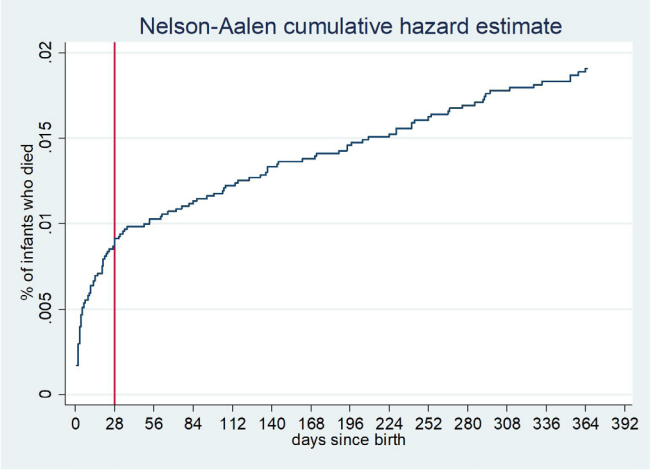

Figure 2 Cumulative hazard function of infants who died during the first year of life in the Farafenni Health and Demographics Surveillance System in the years 2014–2017.

between season of birth and postneonatal mortality was found.[13] Furthermore, being born in the 'hungry season' (July to December), which corresponds to the rainy season and the malaria transmission season, seems to have a protective effect. While the absence of association of the previous study could be explained by the low prevalence of malaria in The Gambia, it would not explain an inversion of the expected risk. Alternatively, the food shortage in the 'hungry season' might not affect the infants directly if they are breastfed but could affect them indirectly if the breastfeeding pattern of the mothers is modified by the season. Another potential explanation could be that mothers may be too busy in the fields to constantly feed the baby or because hard physical work depletes her milk supply.

Twins have been identified as being at an increased risk of dying before the first birthday, both in The Gambia[14] and in other sub-Saharan African countries,[9 12] with the risk in twins about double the risk of singletons (similar to our results). The increased risk of early death can not only be linked to complications at birth and early life, including low birth weight, but also to cultural beliefs which can influence growth patterns and gender-biased care.[9 14–17] The information required to identify the cause of death in our cohort was not available.

Other factors associated with increased mortality include no breast feeding and no BCG vaccination within the first week of life. Breast feeding is almost general in The Gambia. Due to the nature of the study, it was not possible to determine directionality and the strong association described could be explained by reverse causation, with children born with difficulties or from sick mothers being less likely to be breastfed.

In The Gambia, vaccine coverage at birth and the neonatal period is low,[18] as vaccination offer takes place outside of the delivery and postnatal ward and women take back the children for vaccination after the naming ceremony that occurs 1 week after birth. BCG vaccination in the first week can therefore be interpreted as a proxy for health-seeking behaviour or good health from both mothers and babies, which could explain the observed association.

Our study has several limitations. First, recall bias is an important structural limitation of HDSS data and may have influenced the classification of outcomes and exposure variables. Since data are collected every 4 months, this can disproportionally affect early deaths. Therefore, the quality of the information may vary according to the endpoint. Furthermore, given Gambian's reluctance to speak about deceased members of their family, the number of neonatal deaths captured by the HDSS, especially those taking place in the early neonatal period, is probably higher, potentially introducing bias. However, when we excluded this initial neonatal period in sensitivity analyses (first 7 days) the results did not change substantially, suggesting that the data from the first week did not substantially bias the results. Another limitation is the retrospective design which did not allow us to check the quality of the variables included in the analysis. For example, distances to the nearest village with a PHC was not originally collected and

Table 5 Results (HRs) of the multivariable Cox proportional hazard models for neonatal, postneonatal and infant mortality in the Farafenni Health and Demographics Surveillance System in the years 2014–2017

	0–≤28 days		>28–365 days		0–365 days	
Variable	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**
Age of mother at birth						
<18	ref				ref	
18–35	0.66 (0.26 to 1.69)	0.383			1.04 (0.44 to 2.49)	0.93
36+	0.48 (0.14 to 1.68)	0.250			0.85 (0.29 to 2.49)	0.77
Death of any sibling						
No	ref		ref		ref	
Yes	2.60 (1.19 to 5.71)	**0.017***	2.26 (1.17 to 4.37)	**0.015**	2.78 (1.54 to 5.00)	**<0.01**
Birth order						
First born	ref				ref	
Second, third or fourth	0.47 (0.23 to 0.99)	**0.046**			0.70 (0.41 to 1.17)	0.17
Fifth or higher	0.82 (0.38 to 1.76)	0.610			0.71 (0.41 to 1.24)	0.23
Singleton/multiple pregnancy						
Singleton	ref		ref		ref	
Multiple pregnancy	2.07 (0.83 to 5.18)	0.118	2.39 (1.05 to 5.44)	**0.037**	1.96 (1.01 to 3.80)	**0.05**†
Season of birth						
Hungry (July to December)			ref		ref	
Harvest (January to June)			1.83 (1.08 to 3.10)	**0.026**	1.55 (1.07 to 2.24)	**0.02**
Place of birth						
Hospital	ref				ref	
Health centre/clinic	1.01 (0.43 to 2.38)	0.978			1.00 (0.52 to 1.94)	0.99
Someone's home	0.64 (0.28 to 1.46)	0.292			0.68 (0.37 to 1.23)	0.20
Mode of delivery						
Vaginal birth			ref		ref	
Caesarean section			2.56 (0.90 to 7.33)	0.080	1.33 (0.47 to 3.78)	0.59
Breast feeding						
Yes	ref		ref		ref	
No	23.60 (13.73 to 40.56)	**<0.001**	3.34 (1.53 to 7.29)	**0.003**	10.73 (6.83 to 16.86)	**<0.01**
BCG vaccination in first week						
Yes					ref	
No					3.47 (1.07 to 11.24)	**0.04**†
Setting						
Urban and peri-urban	ref				ref	
Rural	3.70 (1.57 to 8.70)	**0.003**			4.34 (2.03 to 9.29)	**<0.01**‡
Distance to nearest PHC	0.96 (0.78 to 1.19)	0.735	1.18 (1.01 to 1.39)	**0.043**	1.33 (1.11 to 1.59)	**<0.01**
Setting×distance to nearest PHC interaction						
Urban and peri-urban					ref	
Rural					0.7	**0.01**†

Univariate analyses for these variables are presented in tables 1–4. P values<0.05 are bolded.
*When we removed the variable 'birth order' from the model instead of 'spacing to previous sibling', this variable was no longer statistically significant.
†This variable was not statistically significant if we excluded infants who died in the first 7 days.
‡When we removed the variable 'distance to nearest PHC' from the model instead of 'PHC', this variable was no longer statistically significant.
PHC, public health centre.

we had to calculate approximate values using the centre of the participant's village as the starting point instead of the actual household's position. These inaccuracies could have had an impact, considering the range of distances in our sample (0–4 km only). We used BCG vaccination within the first week of life as proxy for health-seeking behaviour and should therefore be interpreted with caution, as discussed above. Another limitation was the large amount of missing data for some variables (some as important as birth weight), which we were unable to impute and, therefore, were excluded from the multivariable models.

Finally, while our analyses describe the associations between risk factors and infant mortality, more in-depth studies would be required to better understand why these

associations exist and how the different risk factors are inter-related.

CONCLUSION

Although in our analysis we found several variables associated with infant mortality (both neonatal and postneonatal), most of the risk factors described are not easily modifiable at the individual level. Programmatic approaches such as improving access to health services in rural areas, as well as targeting particularly vulnerable infants such as twins and infants unable to breastfeed, could have a substantial impact on neonatal and infant mortality in this region and could contribute to reach the Sustainable Development Goals in The Gambia.

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Contributors AJ and AR conceived the study. AJ, AR, NIM and UD designed the study. PCS and PG lead and supervised data collection. AJ analysed the data under the supervision of NIM and AR and wrote the manuscript. All authors contributed to the interpretation of the results and writing of the manuscript.

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Data availability statement Data may be obtained from a third party and are not publicly available. The clinical data has been collected following provision of informed consent under the prerequisite of strict participant confidentiality. Qualified researchers may request access with the Gambia Government/MRC Joint Ethics Committee. The review process and release of data will be facilitated by MRC Unit The Gambia (http://www.mrc.gm/) through the Head of Governance at MRCG Dr Elizabeth Batchilly (Elizabeth.Batchilly@lshtm.ac.uk). Access will not be unduly restricted.

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REFERENCES

1 UNICEF W. Levels and trends in child mortality: report 2019. *Estim Dev UN Inter-Agency Group Child Mortal Estim N Y United Nation's Child Fund* 2011.
2 Rutstein SO. Factors associated with trends in infant and child mortality in developing countries during the 1990s. *Bull World Health Organ* 2000;78:1256–70.
3 Sartorius BKD, Sartorius K. Global infant mortality trends and attributable determinants – an ecological study using data from 192 countries for the period 1990–2011. *Popul Health Metr* 2014;12:29.
4 Bocquier P, Madise NJ, Zulu EM. Is there an urban advantage in child survival in sub-Saharan Africa? Evidence from 18 countries in the 1990s. *Demography* 2011;48:531–58.
5 Rosa W, ed. *Transforming our World: the 2030 agenda for sustainable development. In: a new era in global health*. New York, NY: Springer Publishing Company, 2017.
6 Jasseh M, Gomez P, Greenwood BM, *et al*. Health & Demographic Surveillance System Profile: Farafenni Health and Demographic Surveillance System in The Gambia. *Int J Epidemiol* 2015;44:837–47.
7 Jasseh M, Howie SRC, Gomez P, *et al*. Disease-specific mortality burdens in a rural Gambian population using verbal autopsy, 1998-2007. *Glob Health Action* 2014;7:25598.
8 College Station TSL. StataCorp. 2015. Stata statistical software: release 14 2015.
9 Becher H, Müller O, Jahn A, *et al*. Risk factors of infant and child mortality in rural Burkina Faso. *Bull World Health Organ* 2004;82:265–73.
10 Omariba DWR, Beaujot R, Rajulton F. Determinants of infant and child mortality in Kenya: an analysis controlling for frailty effects. *Popul Res Policy Rev* 2007;26:299–321.
11 Mustafa HE, Odimegwu C. Socioeconomic determinants of infant mortality in Kenya: analysis of Kenya DHS 2003. *J Humanit Soc Sci* 2008;2:1934–722.
12 Kembo J, van Ginneken JK. Determinants of infant and child mortality in Zimbabwe: results of multivariate hazard analysis. *Demogr Res* 2009;21:367–84.
13 Jaffar S, Leach A, Greenwood A. Season of birth is not associated with delayed childhood mortality in upper river division, the Gambia. *Trop Med Int Health*.
14 Miyahara R, Jasseh M, Mackenzie GA, *et al*. The large contribution of twins to neonatal and post-neonatal mortality in the Gambia, a 5-year prospective study. *BMC Pediatr* 2016;16:39.
15 Parker JD, Schoendorf KC, Kiely JL. A comparison of recent trends in infant mortality among twins and singletons. *Paediatr Perinat Epidemiol* 2001;15:12–18.
16 Bjerregaard-Andersen M, Lund N, Jepsen FS, *et al*. A prospective study of twinning and perinatal mortality in urban Guinea-Bissau. *BMC Pregnancy Childbirth* 2012;12:140.
17 Asindi AA, Young M, Etuk I, *et al*. Brutality to twins in south-eastern Nigeria: what is the existing situation? *West Afr J Med* 1993;12:148–52.
18 Miyahara R, Jasseh M, Gomez P, *et al*. Barriers to timely administration of birth dose vaccines in the Gambia, West Africa. *Vaccine* 2016;34:3335–41.