Seroprevalence and Risk Factors Associated with Measles outbreaks among Children in Kwale, Lamu and Narok Counties in Kenya, 2014

Abstract
Background: Measles burden has been on the decline globally since 1980 due to universal use of measles vaccine; with outbreaks reported in Africa, Europe and Asia (2008). Population immunity assessment is key to determining progress towards elimination of measles as advised by World Health Organisation (WHO).

Objectives: This study aimed to determine the sero-prevalence and risk factors associated with measles outbreaks among children aged 9 to 59 months in Kwale, Narok and Lamu Counties of Kenya.

Methods: This was a hospital-based cross-sectional descriptive study in which 453 children were studied. Very ill children were excluded. A structured questionnaire was used to capture participants’ demographics and risk factors. Approximately 50µl of blood were collected, dried blood spots (DBS) prepared and transported to KEMRI laboratory for analyses. DBS were used for detection of measles IgG antibodies using the NOVATEC Immunodiagnostic GMBH (NovaLisa™ ELISA) (Germany). Serology results were correlated with actual vaccination coverage, demographic and risk factors using statistical package (SPSS) version 20. Numbers and percentages of positive, negative and equivocal sera were found, Chi-square used to compare proportions and a 95% confidence interval used to describe limits of percentages. A p-value of less than 0.05 was considered statistically significant.

Results: A total of 453 children were recruited, 233 (51.4%) male and 220 (48.6%) female. 413/453 (91.2%) of guardians were aware about measles vaccines, 40 (8.8%) were not (P < 0.001). 280/413 {(67.8%) 95% CI; 61.3% to 74.3%} received information from health workers while 133/413 {(32.2%) 95% CI; 29.1% to 35.3%} got information from elsewhere (P < 0.001). 408/453 {(90.1%) 95%CI; 81.8% to 98.4%)} were vaccinated, while only 11/453 {(2.4%)} were not vaccinated. 34/453 {(7.5%) 95%CI; 6.9% to 8.1%)} could not ascertain their vaccination status. 346/453 (76.4%) children had vaccination cards, 107 (23.6%) did not (P < 0.001). Overall, 376/453 {(83.0%)} children had protective antibody titres, while 77/453 {(17.0%)} did not (P < 0.001).

Conclusion: A huge number of children did not have protective antibody titres against measles despite the wide vaccine coverage. Vaccination awareness was low with large number of children lacking records. Large scale assessment of measles population immunity and measles vaccine awareness is required in Kenya.

Keywords: Sero-prevalence; Sero-protectively; Herd immunity; Risk factors; Measles; Vaccines

Introduction
Measles is an acute, highly contagious viral disease estimated to cause over 158,000 annual deaths globally by 2011 [1-3]. Measles is highly communicable, with greater than 90% secondary attack rates among susceptible persons [4,5]. In the pre vaccination period, Measles used to be a universal childhood disease with attack rates that went beyond 90%. Consequently, in the 10th...
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Methods

Study sites

The study was conducted in hospitals in three counties Kwale, Lamu and Narok of the republic of Kenya which experienced measles outbreak in the year.

Kwale County: Part of the study was conducted at Msambweni Hospital in Kwale County. Kwale County is located in the southern part of coastal Kenya. To the East is the Indian Ocean beach and borders Tanzania from the south and south western regions. It forms an important portal of entry and exit from Tanzania and the larger southern Africa region. Describe the population dynamics to give a picture of numbers of children. According to the department of vaccines and immunisation of Kenya, as by 25th September 2012, Kwale County had 28 suspected measles cases of which 24 were laboratory confirmed (IgM positive) [9,29]. The county benefited from a measles immunisation programme supplemented with vitamin A given to children aged between 9 and 59 months. This Campaign was conducted between 3rd and 7th November 2012 and covered approximately 73.9% of the target population [12].

Lamu County: Part of the study participants were drawn from King Fahd Hospital in Lamu County. Lamu County is located in the Northern coast of Kenya bordering Indian Ocean to the East, Somalia to the North East and Kilifi County to the South. During the 2011/2012 measles outbreaks Lamu County was one of the five counties in Kenya not to record a confirmed measles case, and the only county to record a single suspected case, the lowest in Kenya [9,10]. Nevertheless, the county benefited from a measles mop-up immunisation programme supplemented with vitamin A given to children aged between 9 and 59 months. This Campaign was conducted between 3rd and 7th November 2012 and covered approximately 92.0% of the target population [12].

Narok County: A part of the study participants were drawn from Narok County. A region found within the Great Rift Valley and is made up of 3 constituencies; Narok North, Kilgoris and Narok South. As by September 2012, Narok county had 441 suspected measles cases of which 45 were laboratory confirmed (IgM positive) and 324 patients were linked to positive cases with only 13 laboratory confirmed negative cases [9,10,29]. According to the department of vaccines and immunisation in Kenya, the county benefited from supplemental measles immunisation programme (mop-up programme) with vitamin A given to children aged between 9 and 59 months. This Campaign was conducted between 17th and 21st September 2012 then repeated between 3rd and 7th November 2012 during the countrywide SIA campaign [12]. Narok district Hospital serves mostly people from Narok North although it houses the county heads of the different health departments. Patients from Kilgoris and Narok South districts also do attend this hospital in considerable large numbers.
Study population

A total of 453 participants were randomly selected approximately on a ratio of (9:7:1) from Narok, Kwale and Lamu Counties respectively and according to the population of children below 5 years in the respective County as per 2009 census. Participants were recruited from selected hospitals from the 3 counties. The study targeted health looking children aged between 9 and 59 months attending the well-being (mother-child health) clinic and whose guardians were willing to enrol them into the study. Grossly ill participants and those whose guardians did not consent were left out. Guardians were given a brief explanation of the study and consented by a clinician (nurse in attendance).

Demographic and risk factors information of participants

An open ended questionnaire was used to collect information on participant's demographics, vaccination history and risk factors associated with measles outbreaks. Data was collected on children age, gender, history of suffering from measles, time when this occurred, vaccination status (any evidence), vaccination frequency, period since last vaccinated and residency. Guardian parameters were also collected including relationship with child, availability of child's vaccination card - antenatal care card (ANC), awareness about the Measles virus, awareness about Measles Vaccines and whether or not they experienced a measles outbreak, the approximate time and approximate number of people affected. This information was collected by a trained community health worker using a serialized standard demographic questionnaire.

Sample collection, preparation and transportation

Up to 200ul of blood was collected from finger or heel prick on to pre labelled standardized filter paper discs (Dry Blood Spot cards - DBS). The blood spots were allowed to air dry for 60 minutes before packaging. A natural formed free flowing drop is generally approximated to contain 0.05 millilitres of blood, our starting volume [30]. Each dried filter paper was individually placed into a sealable plastic bag to prevent possible cross contamination and to protect from dust and moisture. The DBS cards were processed, packaged and then transported to the laboratory to await analysis at room temperature.

Detection of Measles IgG antibody

Dried blood was removed from the filter using a paper punch and placed together in 0.5 ml of phosphate buffered saline (PBS). Specimen disks were then soaked for 30 minutes at ambient temperature. Filters were removed and any remaining liquid squeezed from them using duckbill forceps and added to the soaking liquid. Specimens processed from dried blood are considered to have a practical starting dilution of approximately 1:10. Samples were then analysed using ELISA kit from NOVATEC Immunodiagnostics GmbH (NovoLisa™ ELISA) from Germany and optical density measured with a photometer set at 540nm. The results of the ELISA were calculated using the kit instructions and expressed in Nova Tec Units (NTU). The optical density was measured at 450 nm. All samples with absorbance of more than or equal to the cut-off absorbance (mean negative control + 0.100) were considered positive while samples with absorbance less than the cut-off were considered negative as per manufacturers advice. All reports were captured in a notebook initially, and then fed in to computer spread sheets, cleaned, verified for consistency and excel used to present it in form of charts and tables.

Results and Discussion

Baseline characteristics of study participants

A total of 453 children were studied. Out of these, 210 (45.85%) were from Narok, 185 (41.27%) from Kwale and 58 (12.88%) from Lamu Counties respectively. Out of 453, 223 (48.68%) were female, while 230 (51.31%) were male. 103 (46.18%) were from Narok, 39 (41.7%) from Kwale, while 27 (12.11%) were from Lamu. 107 of 235 (45.53%) men were from Narok, while 46 (40.85%) were from Kwale and 32 (13.62%) from Lamu. In Narok 103 out of 210 (49.05%) were female and 107 out of 210 (50.95%) were male, Kwale 93/185 (49.21%) female and 96/185 (50.79%) male and Lamu 27/58 (45.76%) female and 32/58 (54.24%) male (Tables 1-3), (Figure 1).

Data Analysis and interpretation

Statistical analysis was performed using SPSS version 20. Results from serological surveys were categorised as positive, negative or equivocal per participant. Data on demographics and risk factors was used to give counts, proportions and 95% confidence intervals (CI) for participants. The proportion seropositive was calculated for the general study population in relation to sex, age and risk factor groups with the exact 95% CI of the proportions determined. The number and percentages of positive, negative and equivocal sera were calculated according to age in months, gender and vaccination status and frequency. Our results were interpreted according to the manufacturer's recommendation as negative for titres below 9 NTUs, equivocal for titres between 9 and 11 NTUs, and positive for titres above 11 NTUs. Comparable to the 3rd international standards, 9 NTUs is equated to 120 mill international units per millilitre (mIU/ml) while 11NTUs are equivalent to 220mIU/ml. Thus, negative titres were below 120mIU/ml, equivocal titres were between 120mIU and 220mIU/ml, and positive titres were those found to be above 220mIU/ml which is slightly above the widely accepted measles protective titre of 200 mIU/ml [31-33]. Seroprotectivity was compared with risk factors and associations drawn in terms of odds ratios (OR) and likelyhoodness using chi-square and student t tests. The data from this work was presented in tables, histograms and charts. A p-value of less than 0.05 was considered statistically significant.
### Table 1: Baseline characteristics of study participants: Socio-demographics and associated risk factor attributes.

| Category                  | Kwale     | Lamu     | Narok     | Totals | 95% CI Limits | Lower  | Upper  |
|---------------------------|-----------|----------|-----------|--------|----------------|--------|--------|
| Sex                       |           |          |           |        |                |        |        |
| Male                      | 94 (50.8) | 32 (55.2)| 107 (51) | 233    | 46.7           | 51.4   | 56.1   |
| Female                    | 91 (49.2) | 26 (44.8)| 103 (49) | 220    | 44.1           | 48.6   | 53     |
| Age Group                 |           |          |           |        |                |        |        |
| ≤12                       | 27 (14.6) | 3 (5.2)  | 14 (6.7)  | 44     | 8.9            | 10.6   |        |
| 12-24                     | 65 (35.1) | 12 (20.7)| 60 (28.6) | 137    | 27.5           | 33     |        |
| 24-36                     | 46 (24.9) | 12 (20.7)| 71 (33.8) | 129    | 25.9           | 31.1   |        |
| 36-48                     | 26 (14.1) | 15 (25.9)| 48 (22.9) | 89     | 17.9           | 21.4   |        |
| 48-60                     | 21 (11.4) | 16 (27.6)| 17 (8.1)  | 54     | 10.9           | 13     |        |
| Guardian                  |           |          |           |        |                |        |        |
| Parent                    | 174 (94.1)| 36 (62.1)| 90 (88.1) | 399    | 60             | 94.1   | 96.1   |
| Brother/Sister            | 4 (2.2)   | 2 (3.5)  | 18 (5.3)  | 24     | 4.9            | 5.7    |        |
| Uncle/Aunty               | 4 (2.2)   | 1 (1.7)  | 2 (1.6)   | 7      | 1.5            | 1.6    |        |
| Cousin/Friend             | 3 (1.6)   | 19 (32.8)| 1 (0.5)   | 23     | 4.7            | 5.5    |        |
| Awareness about M vaccines|           |          |           |        |                |        |        |
| Yes                       | 173 (93.5)| 56 (96.6)| 184 (87.6)| 413    | 82.8           | 99.6   |        |
| No                        | 12 (6.5)  | 2 (3.4)  | 26 (12.4)| 40     | 8              | 9.6    |        |
| Source of Information     |           |          |           |        |                |        |        |
| Health worker             | 105 (60.7)| 46 (82.1)| 129 (70.1)| 280    | 61.3           | 74.3   |        |
| Others                    | 68 (39.3) | 10 (17.9)| 55 (29.9)| 133    | 29.1           | 35.3   |        |
| Vaccination Card          |           |          |           |        |                |        |        |
| Yes                       | 152 (82.2)| 45 (77.6)| 149 (71)  | 346    | 69.4           | 83.4   |        |
| No                        | 33 (17.7) | 13 (22.4)| 61 (29.1)| 107    | 21.5           | 25.7   |        |
| Vaccination Status        |           |          |           |        |                |        |        |
| Vaccinated                | 178 (96.2)| 55 (94.8)| 175 (83.3)| 408    | 81.8           | 98.4   |        |
| Not                       | 3 (1.6)   | 2 (3.4)  | 6 (2.9)   | 11     | 2.2            | 2.6    |        |
| Don’t know                | 4 (2.2)   | 1 (1.7)  | 29 (13.8)| 34     | 6.9            | 8.1    |        |
| Vaccination Times         |           |          |           |        |                |        |        |
| Once                      | 167 (90.2)| 36 (62.1)| 151 (71.9)| 354    | 78.4           | 95.1   |        |
| Twice                     | 11 (6)    | 14 (24.1)| 24 (11.4)| 49     | 10.9           | 13.1   |        |
| Thrice                    | 0 (0)     | 5 (5.2)  | 0 (0)     | 5      | 1.2            | 1.3    |        |
| HIV Seropositivity        |           |          |           |        |                |        |        |
| Positive                  | 13 (7)    | 5 (8.6)  | 13 (6.2)  | 31     | 6.8            | 7.4    |        |
| Negative                  | 172 (93)  | 53 (91.4)| 197 (93.8)| 422    | 84.6           | 101.7  |        |
Table 2: Measles sero status by sociodemographic and risk factors.

| Category          | Total | Protected | Not Protected | Borderline |
|-------------------|-------|-----------|---------------|------------|
|                   | n     | n(%)      | n(%)          | n(%)       |
| Overall           | 453   | 376(83.0) | 57(12.6)      | 20(4.4)    |
| Gender            |       |           |               |            |
| Male              | 233   | 197(84.6) | 28(12.0)      | 8(3.4)     |
| Female            | 220   | 179(81.4) | 29(13.2)      | 12(5.5)    |
| Age in Months     |       |           |               |            |
| Below 12          | 44    | 33(75.0)  | 8(18.2)       | 3(6.8)     |
| 12 – 24           | 137   | 118(86.1) | 14(10.2)      | 5(3.7)     |
| 24 – 36           | 129   | 108(83.7) | 16(12.4)      | 5(3.9)     |
| 36 – 48           | 89    | 75(84.3)  | 11(12.4)      | 3(3.4)     |
| 48 – 60           | 54    | 44(81.5)  | 8(14.8)       | 2(3.7)     |
| County            |       |           |               |            |
| Kwale             | 185   | 158(85.4) | 18(9.7)       | 9(4.9)     |
| Narok             | 210   | 168(80.0) | 32(15.2)      | 10(4.8)    |
| Lamu              | 58    | 50(86.2)  | 7(12.1)       | 1(1.7)     |
| Vaccination Status|      |           |               |            |
| Vaccinated        | 408   | 346(84.8) | 46(11.3)      | 16(3.9)    |
| Not vaccinated    | 11    | 2(18.2%)  | 6(54.5)       | 3(27.3)    |
| Don’t know        | 34    | 28(82.4)  | 5(14.7)       | 1(2.9)     |
| Vaccination Frequency |   |           |               |            |
| Ones              | 354   | 298(84.2) | 41(11.6)      | 15(4.2)    |
| Twice             | 49    | 43(87.8)  | 5(10.2)       | 1(2.0)     |
| Thrice            | 5     | 5(100)    | 0             | 0          |
| Awareness about Vaccines | |           |               |            |
| Aware             | 413   | 344(83.3) | 50(12.1)      | 19(4.6)    |
| Not aware         | 40    | 32(80.0)  | 7(17.5)       | 1(2.5)     |
| HIV Seropositivity|      |           |               |            |
| Seropositive      | 31    | 5(16.1)   | 24(77.4)      | 2(6.5)     |
| Seronegative      | 422   | 371(87.9) | 33(7.8)       | 18(4.3)    |

Table 3: Measles Seroprotectivity in relation to associated risk factors.

| Factor           | Examined (n) | Protected (n) | Prevalence (%) | Chi Square | P value | Odds Ratio | 95% CI limits |
|------------------|--------------|---------------|----------------|------------|---------|------------|---------------|
|                  |              |               |                |            |         |            |               |
| Gender           |              |               |                |            |         |            |               |
| Female           | 220          | 179           | 81.4           | 0.814      | 0.367   | 1.253      | 0.767, 2.049  |
| Male             | 233          | 197           | 84.6           |            |         |            |               |
| Vaccination Card |              |               |                |            |         |            |               |
| No               | 107          | 68            | 63.6           | 37.566     | 0       | 4.649      | 2.769, 7.805  |
| Yes              | 346          | 308           | 89             |            |         |            |               |
Seroprevalence and Risk Factors Associated with Measles outbreaks among Children in Kwale, Lamu and Narok Counties in Kenya, 2014

Discussion

This study brings open, a rare glimpse, at least for the first time in to the sero epidemiological profile of Measles-specific IgG antibodies among a sub population of Kenyan children. Our results suggest that the general population sero-immunity among children between 9 to 59 months as in 2014, was 83.0%, well below the acceptable herd immunity threshold (93-95%) necessary to interrupt measles transmission as suggested by several studies [14,19,32]. Comparatively, this is much higher than what another recent (2011) study in Bangui, Central African Republic (CAR) found (57.3 %) on a research conducted in 2008 despite having reached immunization coverage’s of more than 90% in 2006 [34]. Whereas CAR is among the regions poorest countries with Human Development Index (HDI) of 0.352, Kenya is among the medium developing countries, HDI of 0.555 [35]. And this could probably be the attributing factor for the difference in sero-immunity despite having almost the same immunization coverage’s albeit at slightly different times. Among the vaccinated, protection stood at 84.8% whereas among the non-vaccinated protection was at 18.2%. This suggests that vaccination using the McV is very effective as far as protection against measles is concerned considering the significant association between vaccination and protection (Chi-square = 33.672; P < 0.001). Such association has been emphasized by world health organization [19,36,37]. And mentioned in reports from other studies as well [14,20,38]. The odds of being seronegative were higher for residents of Narok County as compared to Kwale or Lamu counties. This could have been attributed to factors such as frequent movements of people, land Scape, and distance from health centers which probably limit access to immunization services or population targeted awareness programmes. This is complimented by the fact that this county had the least proportion of vaccinated individuals when compared to the other two.

Although there was no significant difference in protection between male and female populations (Z= 0.9022, P = 0.36812), the risk of not being protected was higher in females than males (Odds ratio = 1.253, 95% CI; 0.767 - 2.069). There was no significant difference in seroprotectivity between children whose guardians were aware of Measles containing vaccines (McV) and those not aware (Chi-square = 0.28, P = 0.597). Despite there being no significant difference, P > 0.05, the risk of not being protected was higher among children whose parents were not aware about the measles containing vaccine (McV) as compared to children whose parents were aware about the vaccine (80.0% vs 83.3%; Odds ratio = 1.246; CI 0.551 – 2.821). Moreover, children whose guardians had no vaccination cards were less likely to be protected with the specific measles IgG antibodies than those with vaccination cards (61.7% vs 89.6%; Odds ratio = 5.349; 95% CI, 3.178 - 9.003), and, there was a significant difference in seroprotectivity between these two groups (Chi-square = 45.133; P < 0.001). Incidentally, such comparative studies are extremely
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There was a significant difference between the measles IgG seropositivity rate in the region of study when compared against reported vaccination intake (83.0% vs 90.1%; Z = 3.1144, P = 0.00188). Reduced vaccine efficacy could have arisen due to compromised vaccine, poor host characteristics that adversely affected seroconversion rates. This, coupled with the now greatly reduced global exposure rates to circulating wild measles virus may play a significant role. Potential confounding limitations of our study: Subject selection was based on hospital/clinic attendance which could have biased our results, and, levels of protective antibodies may not have been fully and rightly categorized because of the method applied and the diagnostic kit used.

Conclusion

The seroepidemiological study revealed that a huge number of children did not have protective antibody titers against measles despite the wide vaccine coverage. Vaccination awareness was low among the adult study population and large number of children lacked vaccination records.

Recommendations

Measures need to be put in place to monitor efficacy of vaccination programmes, such measures may include automated vaccination records for all children, awareness on importance of vaccination cards and attendance of child health clinics, yearly large-scale serological surveillance. In the meantime, the quality of vaccination activities (routine and supplementary immunization campaigns) must be improved, and population awareness of their importance must be increased. Monitoring routine immunization coverage to assess administrative coverage levels, which are habitually unreliable, and robust methods to monitor and evaluate supplementary immunization activities are needed.

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Conflict of Interest

None expressed.

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