SESSION 3: EPIDEMIOLOGY AND CONTROL OF HUMAN VIRAL INFECTIONS

Chair: ***Dr. Wallace Bulimo.***

Organizer: ***Dr. Clayton Onyango.***

ORAL PRESENTATIONS

1. **Household transmission of respiratory syncytial virus: Who acquires infection from whom?**

Munywoki PK[1], Koech DC[1], Kibirige, NA[1], Cane PA[2], Medley GF[3], Nokes DJ[1, 3]

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Background: Respiratory syncytial virus (RSV) is a major cause of childhood acute respiratory infection (ARI) worldwide. Studies from Kilifi District show that around 1-2% of infants are admitted to hospital with RSV associated severe pneumonia each year. A promising live attenuated vaccine is currently undergoing clinical trials. The potential usefulness of such a vaccine and information on how best it can be implemented requires a better understanding of the spread of the virus within the community. Data are scarce on who acquires infection from whom (WAIFW) in order to realistically evaluate the impact of different population-based vaccination strategies.

Objectives: To estimate the rates of infection and recovery of RSV and other respiratory viruses by age groups within households, and define and quantify the WAIFW matrix.

Methods: This is a prospective household-based study involving about 50 households with a child born after the preceding RSV epidemic and with at least one elder sibling(<13 years). Nasal samples were taken every 3-4 days from all the household members, irrespective of symptoms, for 26 weeks (while the RSV epidemic persisted). Oral fluid was collected once-a-week. Clinical data were also collected in every home and/or clinic visit.

Results: We recruited 56 households and followed them during the 2009/10 RSV season though 9 households withdrew (outmigration (2), dislike nasal swab (4), unknown (3)). The cohort had 294(53%) females and 31% were school-going. Overall, 19,816 home visits were made yielding 16,284(82%) and 9,226 (93%) nasal and oral samples, respectively. In 3624 (18%) of the home visits the participants had ARI symptoms (runny/blocked nose and/or cough and/or difficulty in breathing). The frequency of respiratory viruses in 572 randomly selected samples from children with ARI episodes compared with 450 samples from asymptomatic individuals was 27.6% vs 3.6% (rhinovirus), 12.2% vs 3.8% (RSV), 12.4% vs 1.6% (adenovirus), 7.6% vs 3.2% (coronavirus), and 3.8% vs 0% (parainfluenza virus). . Screening of further nasal samples using real time PCR is in progress.

Conclusion: Rhinovirus and RSV A/B were the most prevalent viruses. Preliminary analysis of the detailed multiple infection data is promising in identifying transmission patterns within the households.

2. **Title: Who should be targeted for RSV vaccination?**

Kinyanjui T.M[1], Cane P.A[2], Nokes D.J[1,3], Medley G.F[3]

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Background: Respiratory Syncytial Virus (RSV) is a major cause of lower respiratory tract infections in infants, and there is no licensed vaccine. The highest burden of severe disease is on children less than six months old. However, candidate vaccines are poorly tolerated or insufficiently immunogenic in the target 1-

3 month age group, and thus there is merit in exploring other vaccination strategies outside of this age group.

Objectives:
1.Identify the most important parameters explaining the variability observed in the model outcome
2.Identify the optimal age of vaccination

Methods: We developed a realistic age structured (RAS) model capturing the most important epidemiological aspects of RSV. The model was parameterized using data from a rural coastal population in Kenya. The effect of homogeneous versus age-dependent mixing patterns was explored. We assessed the impact of vaccination on the disease burden (defined as the steady state ratio of incidence of hospitalised cases after and before introducing vaccine) by introducing routine vaccination to all ages sequentially between birth and 14 months. Uncertainty analysis was done using Latin Hypercube Sampling method and sensitivity analysis presented using Partial Rank Correlation Coefficient (PRCC).Results: The RAS model was capable of capturing the age-specific disease and epidemic nature of RSV in the specified population. We found optimal reduction in disease by routinely vaccinating children 4 months of age; 80% coverage is sufficient to reduce the burden of disease by 90% assuming a homogeneous mixing population. Further delay in delivery up to 6 and 9 months continued to provide significant benefit e.g. vaccinating at 75% coverage prevents in excess of 80% of RSV associated hospitalizations, with substantial indirect effects from reduced virus circulation. Duration of RSV specific maternal antibody was identified as the most important parameter in explaining the variability observed in the model prediction.

Conclusions: The magnitude of impact of RSV vaccination even when delayed to 6 - 9 months of age potentially offers highly effective disease prevention with current vaccine candidates. Vaccine efficacy trials in older children may be warranted where the disease burden justifies. Further investigation needs to concentrate on (a) protective effect and duration of maternal antibody and (b) the factors influencing the indirect effects of vaccination on virus circulation.

5. **The genetic relationship between the infecting and re-infecting respiratory syncytial virus strains isolated from young children at Coastal Kenya**

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Background: It is been suggested that the occurrence of respiratory syncytial virus (RSV) repeat infections may be in part due to antigenic variation in its surface glycoproteins, but data to support this notion are limited.

Methods: We recruited 635 children from birth between 2002 and 2003, and observed them for acute respiratory symptoms through three RSV epidemics. 83 repeat RSV infections were diagnosed by immunofluorescence test on nasal washings. During the talk I will present the RSV group re-infection patterns and the analysis of the nucleotide and amino acid sequence data of the attachment (G) protein gene of strains from 54 paired infections.

Results: In summary, five of the 54 cases appeared to be persistent infections lasting for up to seven weeks. Of the 49 remaining cases, 29 were of the heterologous group while 20 were of the homologous group. All the homologous group re-infections were of a heterologous genotype except four. Three of these four had amino acid changes within the sequenced region of the G gene. All the confirmed re-infections occurred in separate epidemics except two.

Conclusion: Our data supports the hypothesis that RSV re-infections in nature are usually with a genetically different strain.

SESSION 3: POSTER PRESENTATIONS

1. **Contact Mixing Patterns Among School-Going Children.**

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Background : Schools provide an important setting for the spread of infectious diseases in the community. No data exists on respiratory related contact patterns in developing countries. Contact data stratified by age groups, is being used in modeling the spread of respiratory infections, in particular emerging viruses pandemic influenza.

Objectives: The study aimed to determine the contact patterns among school children that are relevant for the spread of respiratory infections. We aim to quantify students' contact rates both within and out of school setting, during the school term and vacation. To demonstrate the use of contact diaries in defining transmission patterns within schools in a developing country setting.

Methodology: 7 public schools (6 primary 1 secondary) in a rural coastal location were selected. 630 students were enrolled in the study. Self completed diaries were kept by students above the aged 11years and above (Median [IQR]age:16 [13-18]) on randomly selected days both during the vacation and school term. A contact was defined as type 1(conversation) or type 2(physical contact). A contact questionnaire was also administered. The analyses used multilevel modeling to determine the effects of clustering in the contacts by the students.

Results: Variations in contacts exist between the different times – school term and vacation. Majority of the contacts that occur at schools are of type 1 contacts. A lot of mixing occurs outside home during the vacation periods. The number of contacts made decreases with the increasing age. Female students had significantly higher contacts than male students. Fewer contacts recorded on weekend days though not significant. Diary studies in the developing country setting are feasible and should be explored further.

Conclusion: Comparative contact rates for school term and vacation times will be of use in predictive modeling of the impact of school closures on respiratory virus transmission e.g. preventing the spread of emergent influenza.

3. **Who-Contacts-Whom - assessment through diary and electronic methods.**

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Background: Determining the social contacts and mixing patterns of a population is crucial in understanding the transmission of pathogens that spread via close or direct physical contact. Previously, data on age, frequency, location and duration of contacts has been collected through retrospective and prospective paper diaries. Used mainly in the developed world, these methods face serious challenges, with the greatest being recall bias. In the developing world, other challenges such as acceptability and illiteracy abound. To overcome these hurdles, various suggestions such as using shadow persons, verification questionnaires and more recently, electronic devices, have been suggested. We propose the use of a combination of paper diaries and Radio Frequency and Identification (RFID) tags and Global

Positioning Systems (GPS) loggers to collect this data in the community and within the household setting.

Objectives: The main objective is to estimate the age-specific rates of contacts. We first aim to determine the feasibility of using paper diaries and electronic tags for data collection, and then assess the variability within and between the data collected using both methods. Finally, we will investigate the age, space and time distribution and variation of contact patterns.

Methodology: Participants will fill in diaries with details of their contacts in the community, while similar data will be collected in the household using the electronic devices in a feasibility study. Focus group discussions will also be held to get the participants' views on the acceptability of the methods for future studies.

Expected results: The age-specific rates of contact will be used to create predictive models for control and preventive strategies against respiratory infections. The focus group discussions on feasibility and acceptability will guide future projects on the best method to use for data collection.