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NASOPHARYNGEAL *STREPTOCOCCUS PNEUMONIAE* AMONG UNDER-FIVE YEAR OLD CHILDREN AT THE MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA
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ABSTRACT

Objectives: **To determine the prevalence, risk factors and antibiotic sensitivity of *streptococcus pneumoniae* carried in the upper respiratory tract of children.**
Design: **A cross-sectional study on consecutive clients.**
Setting: **Maternal Child Health Clinic (MCH) at Moi Teaching and Referral Hospital (MTRH) in western Kenya.**
Subjects: **Seventy eight of children attending Maternal Child Health Clinic between March 10th 2003 and July 11th 2003.**
Main outcome measures: **Upper airway carriage status, ventilation, housing, age, illness, sensitivity patterns.**
Results: **Fifty six percent were boys; the median age was six months (range 1-42 months). *Streptococcus pneumoniae* carriage rate was in 28 (35.9%) cases. Fifty two percent of *S. pneumoniae* were resistant to penicillin, *25%* to ampicillin and 78% to cotrimoxazole. There was significant association between the type of floor with pneumococcal carriage (p = 0.009) with people living in earth floor houses being five times more likely to be pneumococcal carriers as compared to those living in cement floor houses.**
Conclusions: **A significant resistance of *S. pneumoniae* to penicillin, ampicillin and cotrimoxazole was found. Earth floored houses may increase susceptibility to upper airway *S. pneumoniae* carriage.**
Recommendation: **Similar studies should be conducted in other parts of Kenya in order to learn about susceptibility patterns and associated risk factors, including floor type, in the country and tailor better treatment regimens.**

INTRODUCTION

Streptococcus pneumoniae (S. pneumoniae) is an important cause of morbidity and mortality in children worldwide. Its main reservoir is the nasopharynx from where the organisms can enter the blood stream to cause invasive infections, spread to adjacent mucosal tissues or be transmitted by direct contact through aerosols to other individuals.

Many individuals in a population are colonised by this organism at any given time in their life (1-3). Before three years of age children harbor the organism more than adults and are more likely to use antibiotics (4-6). The prevalence in a population of upper respiratory tract (URT) carriage of *S. pneumoniae* increases under circumstances that facilitate person to person transmission such as day care centres, schools, barracks etc.

Information of URT pneumococcal carriage is important in order to evaluate the prevalence of this important pathogen, for monitoring its resistance patterns to antimicrobial agents and for measuring the efficacy of vaccines used for prevention of infections caused by *S. pneumoniae.* Resistance of *S. pneumoniae* to antimicrobial agents which was first reported in the mid 1960's (7,8) is increasing worldwide and has an enormous impact on clinicians, microbiologists, drug manufacturers and public health authorities (9-12).

Infants and young children more often than adults carry antibiotic-resistant strains of *S. pneumoniae* (13). In the past, this bacterium has been highly susceptible to penicillin which was the drug of choice for benign and life-threatening infections caused by the organism. In the last three decades, however, increasing resistance of pneumococci to beta-lactam and other antibiotics has been reported from many countries including USA, Canada, France, Spain, Israel and Taiwan (14-18) causing a growing therapeutic dilemma. This phenomenon is related to an extensive use of antibiotics and the selection pressure they exert on bacterial strains of the naso-pharynx.

The Eldoret region of Kenya has a multi-ethnic population, majority of who live in a rural setting. Children in this region, like the rest of the country, are eligible to routine vaccination against TB, poliomyelitis, diphtheria, pertussis, tetanus, measles and recently hepatitis B and *haemophilus influenzae* type b.

In a study done by Menge *et al* (19) it was found that among the most common causes of morbidity and mortality were pneumonia, malaria, neonatal sepsis and malnutrition. These findings emphasize the importance of the assessment of pneumococcal URT carriage rates in infants and young children and of the antibiotic sensitivity profile. Such data in this area and in Kenya has not been published before, and in view of the current state of antibiotic utilisation, it can help clinicians to better rationalise the use of first-line drugs for conditions commonly seen in the health facilities including pneumonia, otitis media and sepsis. It can also be useful for policy makers in better planning and understanding of trends of *S. pneumoniae* carriage and resistance patterns.

The primary objective of this study was to determine the rate of upper respiratory tract carriage of *S. pneumoniae* and its antibiotic susceptibility patterns in children attending the Maternal Child Health (MCH) clinic at Moi Teaching and Referral Hospital in Eldoret, Kenya. The secondary objective was to determine risk factors associated with *S. pneumoniae* carriage.

MATERIALS AND METHODS

Study site and target population: The research was conducted in the Eldoret area in western Kenya. The children recruited were attending the MCH clinic at the Moi Teaching and Referral Hospital (MTRH).

The MTRH, MCH is an out patient clinic that operates from Monday to Friday serving between 20-70 children daily. Its routine functions include monitoring of infants and young children's growth, immunisation, nutritional advice, and management of simple ailments. Each child pays Ksh 20 (US$ 0.25) for the service provided.

The study population derived from Eldoret municipality and outlying towns, centres and villages. The population therefore was a blend of people staying both in urban and rural areas. Any child less than five years whose guardian gave consent for participation was included in the study.

Study design: The study was cross sectional and conducted during the rainy season on children seen at the MCH clinic on two days in a week whose mothers gave consent.

Sample size: This was limited to the 78 patients due to the number of bottles of transport media available to the researchers then.

Data collection: A questionnaire was administered to the parents or guardians for the collection of information including socio-economic status, nutritional status, prior antibiotic use in child and family members, breast-feeding, immunisation, housing and ventilation. Ventilation was described as good if the percentage window area was estimated to be more than 15% of the floor surface area, fair if 10-15%, and poor if < 9%.

Procedure for specimen collection and culturing: Specimens were collected by trained personnel from the nasopharynx by gentle insertion of a flexible swab stick with Dacron-tipped flexible-wire swabs through the child nostrils until resistance was found and in a single 30-second motion. The swabs were inoculated into modified Stewart transport medium (Transwab MW173 Transport Medium; Medical Wire and Equipment) and were brought to the microbiology laboratory of the MTRH. Swabs were cultured on Trypticase soy agar plates containing 5% sheep blood and 5 micgr of gentamicin sulphate per ml to isolate PN. Plates were incubated at 35 to 37ºC in a 5% CO_2 for 18-24 hours.

S. pneumoniae organisms were identified by their alpha haemolytic colony morphology, gram stain and susceptibility to the optochin disc. Once identified, the organisms were sub-cultured and stored at –80ºC in transport medium.

Antibiotic susceptibility was performed by the disk diffusion method of Bauer and Kirby, according to the Clinical and Laboratory Standards Institute recommendations (20). Isolates exhibiting resistance to three drug classes or more were defined as multidrug resistant. The antibiotic tested were: penicillin, ampicillin, cotrimazole, chloramphenicol, methicillin, erythromycin, minocyclin, lincomycin.

Statistics: Data were analyzed using the Statistical Package for Social Sciences (SPSS) and SAS Institute version 9.1.

Summary statistics such as mean, median, mode and range were used to describe both the response and the explanatory variables.

Frequency tables were used to summarise information on categorical variables. The tables indicate in terms of percentages or absolute values how much each category contributes to the variables. Cross tabulations were also used to express the relationship between categorical variables. These enabled us to study the association amongst a set of categorical variables. For continuous data student T-test was used to compare means. For categorical variables the Chi square test was used to investigate whether there was any significant association. In cases where 90% of the cells had scores less than five the Fisher's exact test was used to check for any association.

The Kruskal Wallis nonparametric test was used to compare independent samples. For ordinal categorical independent samples the Jonckheere Terpstra test, which is a nonparametric test for ordered differences among classes, was used.

RESULTS

Baseline characteristics (Table 1): Seventy eight children were enrolled during the rainy season between March and July 2003 and their parents or guardians interviewed. The child's mother was the major source of information (96%).

Forty three (55.8%) of the children were female and 34 (44.2%) male. The median age was six months (range 1-42 months). Twenty nine children (37.6%) had a current medical condition at interview with the predominant diagnosis being pneumonia (eight cases) followed by upper respiratory infection (URTI). The prevalence of URTI in household was 23.7%, but only in 11.7% of the households was somebody reported to be receiving an antibiotic. No relationship between antibiotics treatment during the previous two months and resistance patterns was found.

Parents' occupation: The majority of fathers were professional (37.2%) and skilled worker ((26.9%) with 10% unemployed. Among the women, the majority were unemployed (46.2%) with a large number listed as "housewives" among the category "other".

Housing and ventilation: Twenty six (33.3%) families reported living in mud walls houses, 19 (24.3%) in brick walls houses and 27 (34.6%) in stone / block walls house. Forty eight families (62%) lived in houses consisting of two rooms or less and 30 (38.5%) had three or more rooms. Fifty eight (74%) had a cement floor in their houses whereas 20 (26%) had earth floor.

Ventilation was described as good if the percentage window area was estimated to be more than 15% of the floor surface area, fair if 10-15%, and poor if < 9%. It was listed as "good" in 29 (38%) of the houses, "fair" in 43 (56%) and poor in five (6%).

Culture results: Out of 78 samples, 63 (81%) yielded significant growth. Twenty eight (35.9%) yielded *S. pneumonia*, 13 (16.7%) *Streptococcus viridans*, 11 (14.1%) *Staphylococcus aureus* and 11 (14.1%) others. Of interest are only two isolates of *Haemophilus influenza.*

Of the eight children with pneumonia three (37.5%) had *S. pneumoniae*, two had no growth, one had *Staphylococcus aureus*, another one had *Micrococci* and the remaining one had *Viridans streptococcus*.

Susceptibility patterns (Table 2): Fifty two percent of *S. pneumoniae* isolates were resistant to penicillin, *25%* to ampicillin and 78% to co-trimoxazole. *S. pneumoniae* isolates were less resistant to chloramphenicol (4%) and no resistant isolate to erythromycin, minocycline and lincomycine was found.

Relationship of pneumococcal carriage to living conditions and age categories: Simple logistic regression models indicated that type of floor, ventilation and age categories were associated with pneumococcal carriage status (P<0.10). These variables were incorporated in a multiple logistic regression. Based on the multiple logistic regression model the only variable with a significant association with pneumococcal carriage status was the type of floor (odds ratio 0.199, Confidence interval: 0.059-0.670, p = 0.009). People living in earth floor houses were found to be five times more likely to be pneumococcal carriers as compared to those living in a cement floor house.

We further looked for an association between overcrowding, type of floor and *S. pneumoniae* carriage. For the assessment of overcrowding three family size categories were evaluated: less than three persons, four to five persons, more than five persons. An association was found between overcrowding and type of floor (p = 0.063) based on a type three analysis. The analysis was comparing families with more than five children compared with that with less than three persons (odds ratio = 0.652, Confidence interval: 0.204-2.086, p = 0.3046) and one with four to five persons compared to that with less than three (Odds ratio = 0.13, Confidence interval: 0.024-0.714, p = 0.0218). However there was no association between the type of floor and the number of persons per room.

Table 1

Basic characteristics: children with positive carriage S. pneumoniae versus children with negative nasopharyngeal carriage

			Positive (n = 28)		Negative (n = 49)		
	No.	(%)	No.	(%)	No.	(%)	
Gender: Female	43	56	17	61	26	53	0.5153
Informant							
Mother	71	96	26	93	45	98	0.5529
Other	4	4	2	6	1	2	
URTI in family							
Yes	18	24	3	11	15	31	0.0556
No	58	76	24	89	34	69	
Anybody in family on antibiotics							
Yes	9	12	4	15	5	10	0.7119
No	68	88	23	85	45	90	
Housing							
Stone / Block wall	27	35	9	32	17	34	
Brick wall	19	25	16	57	30	60	0.8689
Mud wall	26	33	3	11	3	6	
Number of rooms							
One roomed	25	32	10	36	15	30	
Two roomed	23	30	8	28	15	30	0.7550
> Three roomed	30	38	10	36	20	40	
Floor type							
Cement floor	58	74	17	61	41	82	0.0389
Earth floor	20	26	11	39	9	18	
Ventilation							
Good	29	38	13	48	16	32	0.3407

Table 2

Resistance patterns of streptococcus pneumoniae isolates from children

Antibiotic	No.	Resistant		Intermediate		Susceptible	
		No.	(%)	No.	(%)	No.	(%)
Penicillin	25	13	52	2	8	10	40
Ampicillin	28	7	25	7	25	14	50
Erythromycin	27	0	0	0	0	27	100
Co-trimoxazole	27	21	78	1	4	5	18
Chloramphenicol	27	1	4	3	11	23	85
Methicillin	23	1	4	8	35	14	61
Minocycline	25	0	0	2	8	23	92
Lincomycine	25	0	0	2	8	23	92

DISCUSSION

In this study we found 36% *S. pneumoniae* nasopharyngeal carriage rate. It was resistant to a variety of commonly used antibiotics: penicillin (52%), ampicillin (25%), co-trimoxazole (78%), whereas a high sensitivity rate was found to erythromycin, chloramphenicol, lincomycin and methicillin.

Respiratory infections contribute significantly to child mortality worldwide, worse so in Africa (21). The *S. pneumoniae* carriage rate that we reported is similar to that reported in other African countries (1-3). The worrisome high resistance of *S. pneumoniae* to commonly used antibiotics that we found is similar to other reports worldwide (7-12,14-18), and to a report from Kilifi district in Kenya (22). Our local penicillin resistance is however much higher than reported from New Zealand (10.9%), Canada (10%), Mexico (9.1%) and United States (5.1%) (7-12,14-18).

Antibiotic use in African countries has tended to be indiscriminate and may have given rise to resistance to many of the commonly used antibiotics. Majority of health care facilities use antibiotics that have been in the Ministry of Health's' drug list for decades without any reassessment of the sensitivity patterns that definitely change with time. MTRH still largely depends on the Governments drug list. Antibiotics that have shown resistance in our report are cheap and readily available (also, as over the counter drugs), therefore contributing to drug pressure and subsequent resistance. *S. pneumoniae* is still sensitive to erythromycin, lincomycin, methicillin and chloramphenicol, as described also in other studies (7-12,14-18).

Local antibiotic surveillance programmes, like the one we present are crucial for policy makers and should be done in other districts of Kenya since substantial regional variation between countries with higher levels of penicillin resistance has been already reported (16,17).

Penicillin resistant *S. pneumoniae* has both an economic and clinical impact. The uncontrolled use of antibiotics has an impact on the high resistance rate of different micro-organisms.

We also found an increased colonisation of the upper airway by S. *pneumoniae* in children who lived in earth floored houses. The association to the type of floor might be a proxy to poor socio-economic status, overcrowding or ventilation.

This could be due to the difficulties of cleaning such houses and getting rid of any particles with the bacteria. Additionally, cleaning of such houses is accompanied by sprinkling of water to reduce the dust and the associated dampness may contribute to easier transmission as the room dries. Our data generated an association (though weak) between earth floored houses to over-crowding, in itself a known risk factor for *S. pneumoniae* carriage (23). It would seem then, that staying in cement-floored houses would reduce carriage of *S. pneumoniae*. This finding needs to be further investigated due to the implications of such an intervention, both culturally and financially.

Of the 38% children who had current medical problems, 45% had either URTI or pneumonia, making the findings of this study even more relevant.

The study had limitations. Since children who were recruited came from different socio-economic background and due to a relatively small number of isolates, stratification of the results should be regarded cautiously. The study had limited numbers due to limited funding, hence not allowing for more robust and conclusive interpretation of results.

In conclusion, the prevalence of S. *pneumoniae* carriage is similar to what is found in other countries, including developed countries. There is a high rate of resistance to commonly used first line drugs like penicillin and co-trimoxazole. Living in earth floor houses seems to contribute to higher pneumococcal nasopharyngeal carriage rates.

We recommend that similar studies should be conducted in other parts of Kenya in order to learn about susceptibility patterns and associated risk factors, including floor type, in the country and tailor better treatment regimens.

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