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SENSITIVITY PATTERN OF STREPTOCOCCUS PNEUMONIAE AMONG PRE-SCHOOL CHILDHOOD CARRIERS

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Summary

Streptococcus pneumoniae (*S.pneumoniae*) is the most common bacterial cause of pneumonia, meningitis and otitis media, with the highest incidence among young children and the elderly.
S.pneumoniae was once considered to be routinely susceptible to penicillin, but since the mid-1980s the incidence of resistance to penicillin and other microbiological agents had been increasing. Resistant strains have been reported from all over the world.
To optimise the empirical regimens and initial therapy for pneumococcal infections, clinical health-care providers must be informed about the prevalence and pattern of drug resistance among the isolates in their communities. No such data is available for the Malaysian population.
The aim of this study was to determine the sensitivity pattern of *S.pneumoniae* in carriers among pre-school children.
Nasopharyngeal and oropharyngeal swabs were collected from children of 1 month to 6 years of age. *S.pneumoniae* organisms were identified according to the standard procedures. All isolates were tested for penicillin resistance with a 1-μg oxacillin disk by the Kirby-Bauer disk diffusion methods.
A total of 502 (nasopharynx 355, oropharynx 147) specimens were obtained from kindergarten students, inpatients and paediatric clinics over a period of one year. Thirty seven carriers were detected: 36 from nasopharynx and 1 from oropharynx swabs. The children with age between 4 to 6 years, had the highest carriage rate (10.43%). The carriage rate was higher in children who: (1) were institutionalised (2) have 2-4 siblings (3) are malnourished (4) live in urban area. All isolates, except one, were sensitive to penicillin. The resistant isolate was sensitive to cephalosporin group of antibiotics.
Overall about 10% of the pre-school children were carriers.
S.pneumoniae was isolated significantly more often ($p<0.001$) from the nasopharynx than from the oropharynx and 2.7% of the organosms in carrier children were resistant to penicillin.

In conclusion in Kota Bharu use of penicillin as an empirical and initial therapy for pneumococcal infection can be continued, however a close monitoring for the sensitivity of this organism is recommended.

Key Words

Streptococcus pneumoniae, Penicillin resistance, Prevalence, Pre-school children.

SENSITIVITY PATTERN OF

STREPTOCOCCUS PNEUMONIAE

AMONG PRE-SCHOOL CHILDHOOD CARRIERS

INTRODUCTION

Streptococcus pneumoniae (*S.pneumoniae* or pneumococcus) is the most common bacterial cause of pneumonia and meningitis in children and adults[1]. It is also the most common bacterial aetiology of acute otitis media, causing 30-50% of episodes [2]. In the United States, every year an estimated 6 million cases of otitis media 500,000 cases of pneumonia and over 6000 cases of meningitis are caused by this organism [3,4], with the highest incidence among young children and the elderly [5,6].

S.pneumoniae normally resides in the pharynx of healthy people. The rate of colonisation is high in young children in institutions, ranging from 25-50%. Most children are colonised at sometime during the first year of life [7,8].

S.pneumoniae was once considered to be routinely susceptible to penicillin, but since the mid-1980s the incidence of resistance to penicillin and other antimicrobial agents has been increasing [9,10]. Resistant strains have been identified in many countries including South Africa, New Guinea, US, Australia, Canada, Israel, Poland, Hungary and Romania. Pneumococccal penicillin resistance has also been reported in the Middle and the Far East, although data are scant from most Asian countries [11]. In Pakistan 14.3% of healthy carriers of *S.pneumoniae* had penicillin-resistant strains [12].

Resistant pneumococcal strains can spread readily in communities [13,14] and may increase the public health impact of *S.pneumoniae* infections because of increased morbidity and reduced effectiveness of antimicrobial treatment. Of special concern is resistance to extended-spectrum cephalosporins, which are often used as empirical therapy for meningitis [15].

To optimise the empirical regimens and initial therapy for pneumococcal infections, clinical health-care providers must be informed about the prevalence and patterns of drug resistance among the isolates in their communities.

No such data is available for the Malaysian population. We conducted an investigation to determine the prevalence of carriage of drug resistant *S.pneumoniae* among children in our community.

It has become generally accepted that strains of pneumococci with MICs of less than or equal to 0.06 μg/mL of penicillin are regarded as susceptible, whereas strains with MICs of 0.12 to 1.0 μg/mL of penicillin are relatively resistant or intermediate and strains with MICs of greater than or equal to 2.0 μg/mL are highly resistant [16,17].

The objectives of the present study were :

- To find out the prevalence of penicillin-resistant *S.pneumoniae* in pre-school children in Kota Bharu.
- To determine the antibiotic susceptibility of penicillin-resistant strains of *S.pneumoniae*.

METHODS

We cultured nasopharyngeal (NP) and oropharyngeal (OP) swabs of 502 children, 1-96 months of age, attending kindergarten schools in and around Kota Bharu, Kelantan, Malaysia and also from patients admitted to paediatric wards or attending paediatric outpatient clinics of Hospital Universit Sains Malaysia who were not acutely ill.

A written permission was obtained from the administrators of the kindergarten schools and also from the parents/guardians to culture secretions from the upper airways of their children. The parents were interviewed and a questionnaire with social and demographic information was filled by a research nurse. Questions included: age , race, the number of siblings, place of residence and history of any medication. Children were examined by a paediatrician to assess their nutritional status (based on modified Wellcome classification of protein-energy malnutrition) and to find out any concomitant or underlying illness.

Children with a history of receiving antibiotics within 2 weeks prior to collection of samples were excluded from the study.

The OP swab was taken with a cotton-tipped wooden applicator from the posterior wall and tonsillar areas of the oropharynx. Each applicator was then immediately placed into the Stuart's transport medium and sent to the bacteriology laboratory for inoculation on blood agar plates, within 4-6 hours after collection. This routine was followed for the first 147 specimens. Another 355 specimens were collected from the nasopharynx using a cotton tipped flexible metal applicator. Swabs were inserted into the subject's posterior nasopharynx, rotated slowly for approximately 30 seconds, removed and inoculated immediately onto blood agar plates, and incubated at 37°C for 24-48 hours in a 3-12% CO_2-enriched atmosphere. Organisms were identified and confirmed as *S.pneumoniae* by using standard diagnostic microbiological techniques [18]. Penicillin sensitivity was performed by the disc diffusion method [19] using Mueller- Hinton agar containing 5% lysed human blood and 1% vitox (Oxid). A 1-µg oxacillin disk (breakpoint, 20 mm) was used [20,21,22] for this purpose. Data were entered into and analysed with EpiInfo Version 6.02®(CDC, Atlanta and World Health Organisation).

Carriage rate was defined as the percentage of swabs found to be positive for *S.pneumoniae*.

RESULTS

A total of 502 specimens (355 from nasopharynx and 147 from oropharynx) were collected over a period of one year (March 1995 to February 1996).

The epidemiological data of the 502 children studied is presented in Table I.

The study population mainly comprised of healthy (80.28%), well nourished (66.73%) children from urban area (83.07%).

Almost equal number of specimens were obtained from kindergarten schools (39.44%), paediatric clinics (31.07%) and paediatric wards (29.48%).

The majority of the children came from two age groups : less than 2 years (45.42%) and from 4 to 6 years (36.25%). The children were mainly Malay (68.92%) followed by Chinese (23.90%), Indians (4.58%) and others (2.60%).

Among the 502 children included in the study 60 had upper or lower respiratory tract infection, 20 had acute gastro-enteritis, 19 had developmental delay and the rest of them were healthy subjects.

Thirty seven carriers were detected: 36 from nasopharynx and 1 from oropharynx (Table II). The carriage rate detected by nasopharyngeal swabs was considerably higher (10.14%) than by oropharyngeal sampling (0.7%) ($p<0.001$) (Fig. I)

The carriage rate in children attending the kindergarten schools was 9.59 % whereas in others it was 5.92%, with a male to female ratio of 1.64:1.

Among the carriers, 16 had 3-4 siblings, 15 had 1-2 , 4 had 5 or more and only 2 carriers did not have any siblings (Fig II), 7.67% of them came from the urban and 5.88% from the rural area (Fig. III).

The carriage rate was higher (9.58%) in underweight children as compared to well nourished children (6.26%) (Fig IV).

Carriage rate in Malays was 6.35%, in Chinese 9.16%, in Indians 13.04% and others 7.70% (Fig. V).

Of the 37 carriers, 14 were up to 2 years of age (carriage rate 6.14%), 4 were between 3 and 4 years of age (carriage rate 4.34%%) and 19 were above 4 years of age (carriage rate 10.43%) (Fig VI).

If nasopharyngeal swabs were analysed separately, the carriage rate in Malay children in kindergarten schools was 11.36% (5/44) as compared to 10.05% (17/169) in children at home. Chinese children (all from the kindergarten schools) had a carriage rate of 10.86% (10/92).

Out of 37 isolates only one organism was found to be resistant to penicillin. This organism was sensitive to erythromycin and cephalosporin group of antibiotics.

DISCUSSION

As sensitive and rapid diagnostic tests are not available, most pneumococcal infections are treated empirically. Until recently, penicillin and related drugs have been the treatment of choice. However because of the emergence of drug-resistant *S. pneumoniae*, decisions regarding the management of infections caused by this pathogen have become increasingly complicated [20].

Upper respiratory tract (URT) carriage studies are important in monitoring the patterns of resistance to antimicrobial agents [12]. Surveillance for drug-resistant pneumococci in respiratory secretions obtained by nasopharyngeal swab may provide useful information on the prevalence of drug-resistant strains causing invasive disease [23].

The overall carriage rate of about 10% in our study was comparable to carriage rate of 10.8% in Chinese children in Hong Kong but significantly less than 55.7% in Vietnamese children reported in the same study [8]. The high carriage rate in Vietnamese children in Hong Kong was attributed to extreme overcrowding in this community.

In our study the carriage rate detected by nasopharyngeal swabs (10.14%) was significantly higher than by oropharyngeal swabbing

(0.7%) ($p<0.001$). Similar findings were reported in other studies. Maria et al reported that in all age groups *S.pneumoniae* was isolated significantly more often from the nasal site than from the oropharyngeal site [24]. In our study the possibility of sampling or laboratory error needs to be considered as a cause of very low carriage rate in OP swabs. Although the same staff was involved for both types of sample, but for OP swab, a transport medium before culture was used whereas NP swab was directly cultured on the blood agar and then transported to laboratory.

The significant difference between the NP and OP carriage of *S.pneumoniae* indicated the paramount importance of the choice of the swabbing site.

The majority of the children studied were Malay, healthy, well nourished, from urban area, and mainly came from 2 age groups: less than 2 years and 4 to 6 years of age.

The carriage rate increased with the increasing age and number of siblings. Carriage rate was higher in children (1) attending kindergarten schools compared to those staying at home, (2) with poor nutritional status compared to those with normal nutrition (3) from urban than from rural areas (4) having 2 to 4 siblings.

The increase in carriage rate with age, with increased number of siblings and the high rate in kindergarten schools and in urban children is most likely due to overcrowding and increased exposure in these children.

Sung et al [8] showed that having a smaller household area per person or having more than 2 siblings were both associated with higher carriage rates of *S.pneumoniae*.

The carriage rate among the Indian and Chinese children was higher than Malay children, which was probably due to the fact that almost all of the Chinese and Indian children were sampled from those attending kindergarten schools, whereas the majority (81.8%) of Malay children were not attending these schools or were sampled elsewhere.

The carriage rate was higher in poorly-nourished (9.58%) as compared to well-nourished children (6.26%). This difference could be due to several reasons. The secretary IgA in nasopharyngeal secretions which prevents the adherence of micro-organisms to the upper respiratory tract could be different both in quantity and quality in poorly nourished children and may increase or prolong the rate of colonisation.

The age of first acquisition of pneumococcus in infants has been reported to range from 4 days to 18 months [25]. In our study the carriage rate was higher (6.14%) in the first 2 years of life than in those aged 3-4 years. It increased again in those aged 5-6 years (10.43%), perhaps because most of those studied in this age group were attending kindergarten schools.

Only one of the 37 isolates was found to be resistant to penicillin. This organism was sensitive to other antibiotics including erthromycin and cephalosporins. This particular child had recently came back after visiting his relatives in Thailand. His other siblings were not carriers and a repeat culture after 2 weeks was negative.

The prevalence of penicillin-resistant pneumococci was lower (2.7%) in our population than in most previous reports. This could be due to a number of reasons: (1) the majority of previous reports showing higher incidence were conducted in children suffering from upper or lower respiratory tract infection or otitis media. (2) the incidence of penicillin-resistant pneumococcus is higher in children who have repeatedly received antibiotics [23,,26,27,28,29]. Both these risk factors were missing in our study population.

The prevalence of penicillin-resistant pneumococcus varies from nation to nation and within the same nation in different locations and at different times of the year [30]. The information collected in one community cannot be applied to another community or to the same community all the time. Therefore there is a need to have constant surveillance and careful evaluation of the antibiotic sensitivity of the pneumococcus, especially in patients with invasive disease such as meningitis and those not responding to treatment with penicillin.

At least four strategies may play a role in preventing morbidity and mortality associated with infection with drug resistant *S.pneumoniae* (DRSP).

(1) Comprehensive surveillance for DRSP can play an important role for this purpose. This includes the screening of invasive pneumococcal isolates for resistance to penicillin and other drugs that are likely to be used in treating these cases [22].

(2) Optimal management strategies must be determined for infections with DRSP. In areas with high rates of pneumococcal resistance to

extended spectrum cephalosporins, empirical therapy with vancomycin in addition to an extended spectrum cephalosporin should be considered for cases of meningitis potentially caused by *S.pneumoniae* until the results of culture and susceptibility testing are available.

(3) Because infection with DRSP is probably facilitated by increasing exposure to antimicrobial agents [20] strategies for their rational use should be promoted.

(4) Persons aged 2 years or older who are at increased risk for serious pneumococcal infection and all persons aged more than 65 years should receive 23-valent pneumococcal capsular polysaccharide vaccine [31]. Although children less than 2 years old are at increased risk for serious drug-resistant pneumococcal disease, pneumococcal vaccines are not immunogenic in this population; pneumococcal protein-conjugate vaccines are being evaluated for use in this age group.

The emergence of DRPS indicates the need to reassess the efficacy of prophylactic antimicrobial drug regimens for otitis media and to develop new antimicrobial drugs for treatment of drug-resistant infection.

CONCLUSION

Overall about 10% of the pre-school children were carriers of *S.pneumoniae*. Pneumococcus was isolated significantly more often ($p<0.001$) from the nasopharnyx than from oropharynx. Although resistance of *S.pneumoniae* to penicillin in carrier pre-school is negligible (2.7%), constant surveillance and regular monitoring for resistance are needed.

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TABLE I

Demographical Features of 502 Pre-school Children

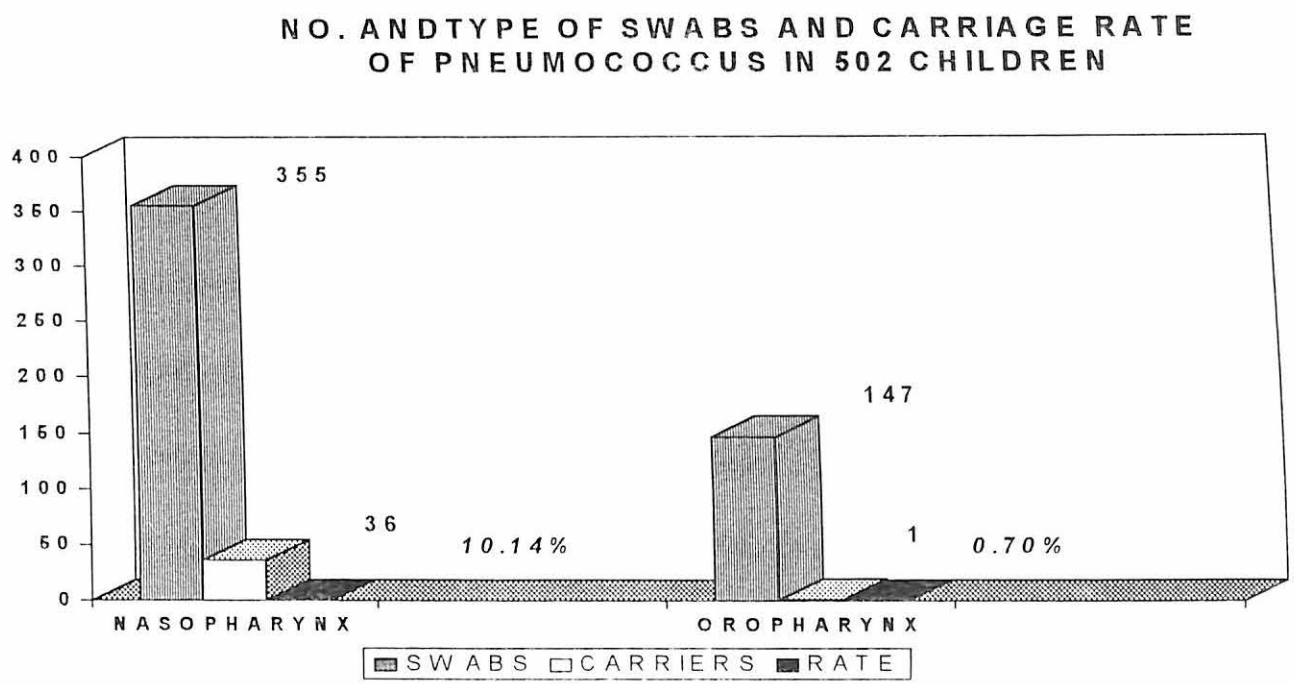
	Malays	Chinese	Indians	Others	Total
	346	120	23	13	502
AGE (mo)					
1 - ≤24	213	14	1	0	228
>24 - ≤48	63	19	5	5	92
>48 ≤72	70	87	17	8	182
GENDER					
Male	196	67	13	9	285
Female	150	53	10	4	217
PLACE					
School	63	102	21	12	198
Clinics	145	11	0	0	156
Wards	138	7	2	1	148
RESIDENCE					
Urban	267	115	23	12	417
Rural	79	5	0	1	85
NUTRITION					
Good	198	105	20	12	335
Poor	148	15	3	1	167
SIBLINGS					
0	24	3	1	0	28
1-2	132	65	14	8	219
3-4	87	49	8	4	148
>4	103	3	0	1	107

TABLE II

Demographical Features of 37 Carriers of Streptococcus pneumoniae Among Pre-school Children

	Malays	Chinese	Indians	Others	
Total	22	11	3	1	37
AGE (mo)					
1 - ≤24	13	1	0	0	14
>24 - ≤48	3	0	1	0	4
>48 ≤72	6	10	2	1	19
GENDER					
Male	13	7	2	1	23
Female	9	4	1	0	14
PLACE					
School	5	10	3	1	19
Clinics	12	0	0	0	12
Wards	5	1	0	0	6
RESIDENCE					
Urban	17	11	3	1	32
Rural	5	0	0	0	5
NUTRITION					
Good	11	8	1	1	21
Poor	11	3	2	0	16
SIBLINGS					
0	2	0	0	0	2
1-2	8	7	0	0	15
3-4	9	3	3	1	16
>4	3	1	0	0	4

FIGURE I



NO. ANDTYPE OF SWABS AND CARRIAGE RATE
OF PNEUMOCOCCUS IN 502 CHILDREN
400
350
300
250
200
150
100
50
0
355
36
10.14%
147
1
0.70%
NASOPHARYNX
OROPHARYNX
SWABS
CARRIERS
RATE

FIGURE II

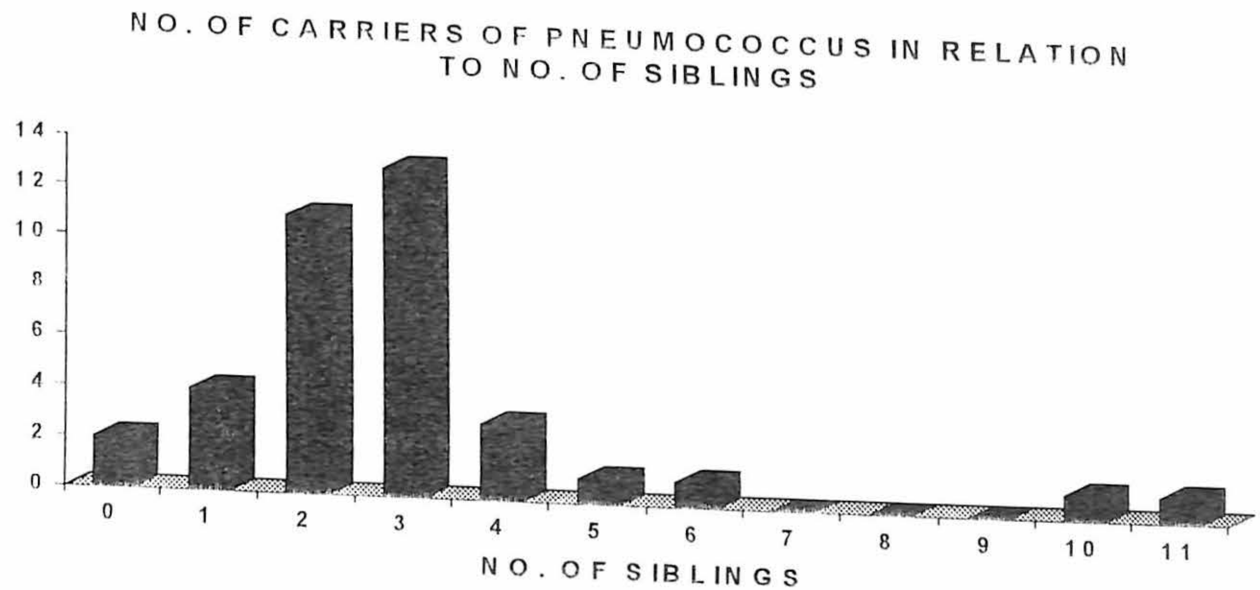
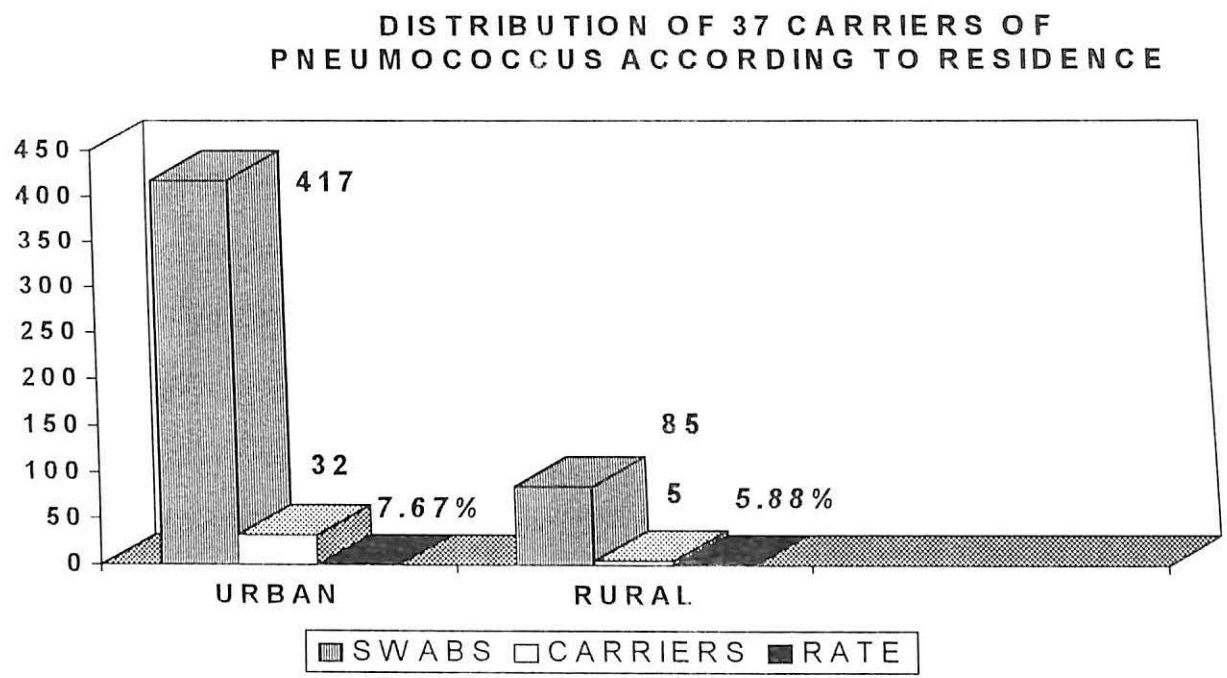

NO. OF CARRIERS OF PNEUMOCOCCUS IN RELATION TO NO. OF SIBLINGS
14
12
10
8
6
4
2
0
0
1
2
3
4
5
6
7
8
9
10
11
NO. OF SIBLINGS

FIGURE III



DISTRIBUTION OF 37 CARRIERS OF PNEUMOCOCCUS ACCORDING TO RESIDENCE
450
400
350
300
250
200
150
100
50
0
417
32
7.67%
85
5
5.88%
URBAN
RURAL
SWABS
CARRIERS
RATE

FIGURE IV

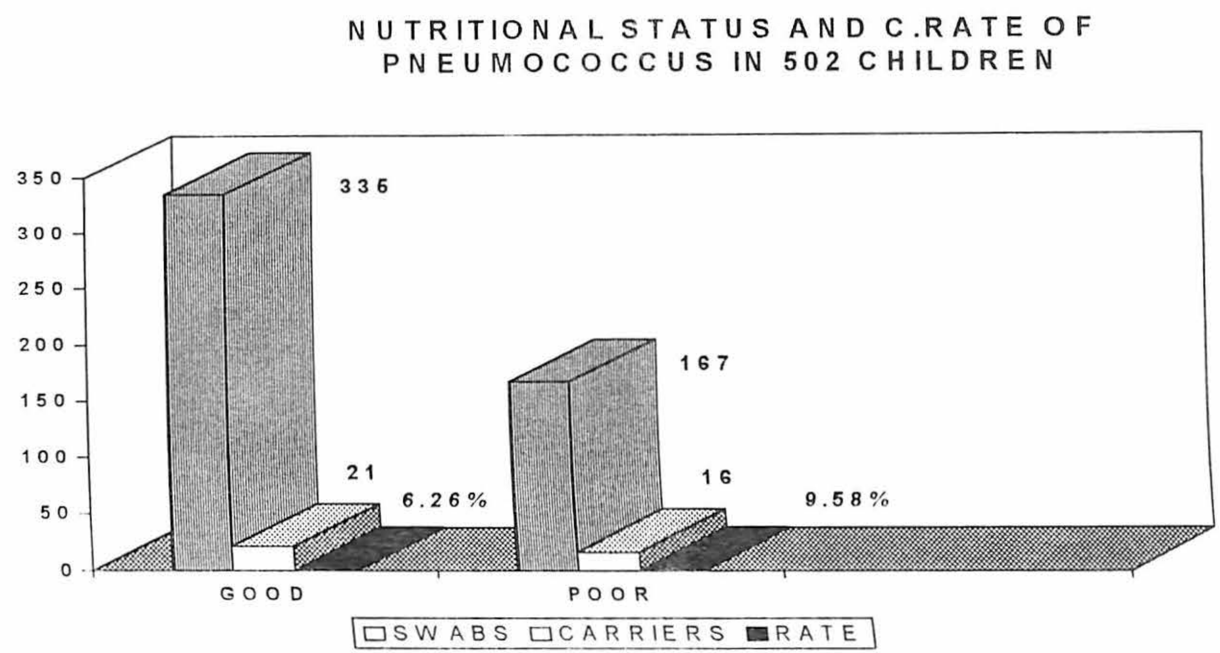

NUTRITIONAL STATUS AND C.RATE OF PNEUMOCOCCUS IN 502 CHILDREN
350
300
250
200
150
100
50
0
335
21
6.26%
167
16
9.58%
GOOD
POOR
SWABS
CARRIERS
RATE

FIGURE V

NO. AND CARRIAGE RATE OF PNEUMOCOCCUS ACCORDING TO RACE IN 502 CHILDREN

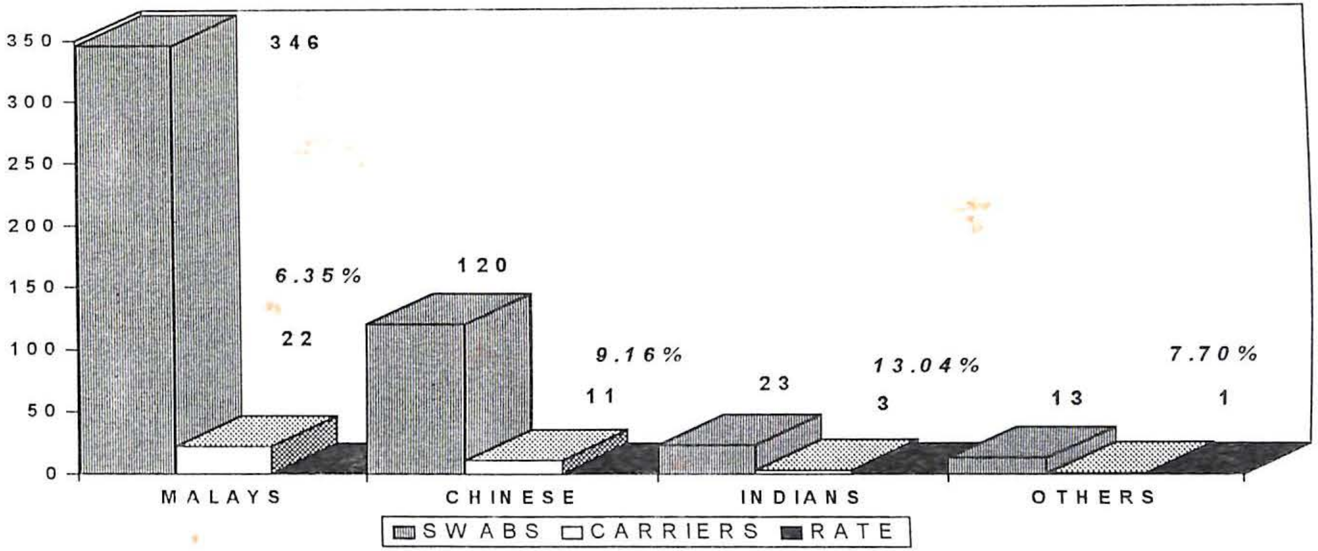
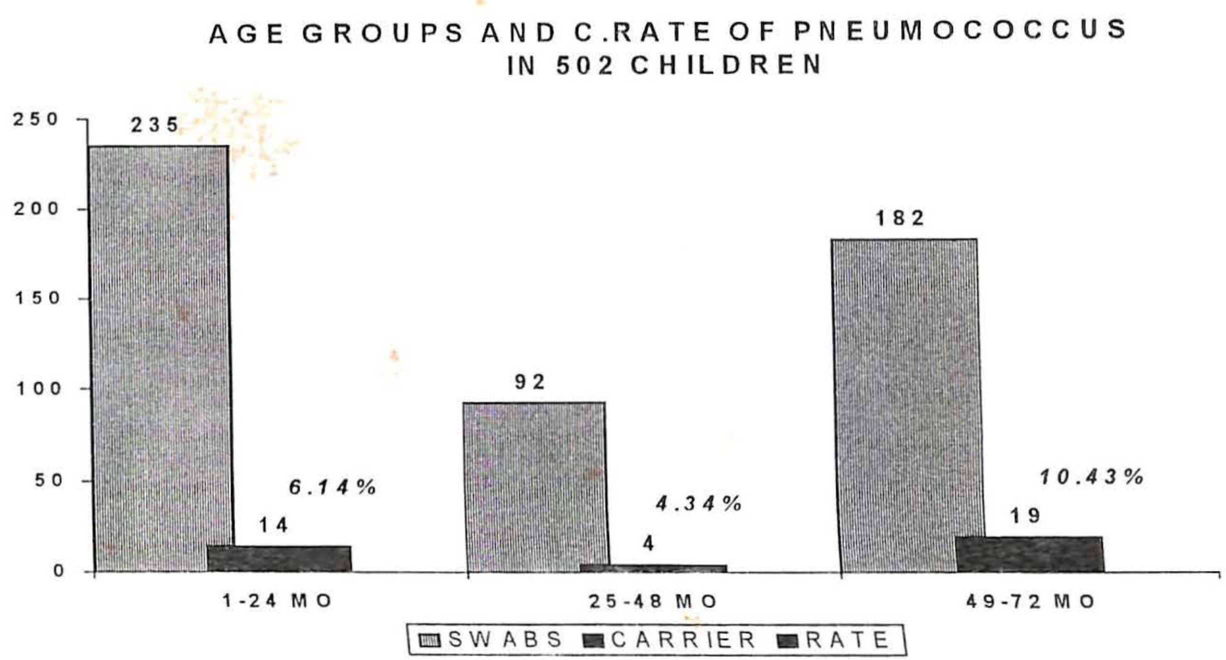


FIGURE VI


AGE GROUPS AND C.RATE OF PNEUMOCOCCUS
IN 502 CHILDREN
250
200
150
100
50
0
235
14
6.14%
92
4
4.34%
182
19
10.43%
1-24 MO
25-48 MO
49-72 MO
SWABS
CARRIER
RATE