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Prevalence and Antimicrobial Susceptibility Pattern of *Streptococcus pneumoniae* at General Hospital in the Central Region of Japan from December 2013 to February 2014

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Abstract

Streptococcus pneumonia **infection is important cause of morbidity and mortality. This study was conducted to find out the prevalence and antimicrobial susceptibility pattern of *Streptococcus pneumoniae* isolates at general hospitalin the central region of Japan from December 2013 to February 2014. *Streptococcus pneumoniae* was identified by standard laboratory procedure. Antimicrobial susceptibility testing was performed by micro dilution assay according to CLSI recommendation. One hundred fifty-three *Streptococcus pneumoniae* were isolated among which 80 (52.2%) were males and 73 (47.8%) were females. Nasal discharge (134%/87.6%) contributed more than other biological materials. The age incidence of (0 - 1) years, (1 - 10) years, (11 - 40) years, (41 - 60) years and >60 years age groups were 26 (17.0%), 110 (71.9%), 3 (2.0%), 10 (6.5%), and 4 (2.6%) respectively. Positive samples were received mostly from the pediatrics (137%/89.5%), respiratory medicine (12%/7.8%) and lowest from gastroenterology (1%/0.6%) and neurology (1/ 0.6%) department. Vancomycin and rifampicin were the most active antibiotics with 100% susceptibility rates. The next best were levofloxacin, penicillin G and ceftriaxone. Our study revealed that 82 *Streptococcus pneumonia* isolates had multidrug resistant ability (53.6%). *Streptococcus pneumoniae* infection spreads among community easily and inappropriate use of antibiotics contributes to their resistance. Continuous antimicrobial susceptible surveys are essential to guide policy on the adequate use of antibiotics to reduce the morbidity and mortality and reduce the emergency of antimicrobial resistance.**

Keywords

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1. Introduction

Streptococcus pneumoniae is one of the most common bacteria causing pneumonia, meningitis, bacteremia and many other infections, and continues to be an important cause of morbidity and mortality in the world [1].

Globally, an estimated 1.6 million people including 1 million children less than 5 years old die of invasive pneumonia disease annually [2]. Its clinical burden is concentrated among the very old and very young [2]. Despite this high toll, the vast majority of *Streptococcus pneumoniae* are found in asymptomatic nasopharyngeal carriage, the prevalence of which varies by age and region [3]. The carriage state is responsible for transmission, and is the stage of *Streptococcus pneumoniae* life history at which interventions such as antibiotics and vaccines exert their selective pressure [4].

The present study was conducted to find out the recent prevalence and antimicrobial susceptibility pattern of *Streptococcus pneumoniae* isolates at general hospital in the central of Japan. Our result would be useful in establishing empiric therapy guidelines and to contribute to larger more extensive surveillance study.

2. Materials and Methods

2.1. Strains and Clinical Data Collection

A total of 153 *Streptococcus pneumoniae* were obtained from various clinical specimens at Daido Hospital from December 2013 to February 2014. Daido Hospital is a 404-bed private general hospital in the central region of Japan. We used medical records appended to clinical species for the analysis of clinical feature at Daido Hospital. We considered several isolates from the same region of the same patient as one isolate per one patient for the analysis in this study. All streptococcal isolates were identified by standard conventional biochemical methods or the VITEK2 system (bioMérieux, Durham NC, USA). Our experimental design was approved by the ethics committee at Daido hospital.

2.2. Antimicrobial Susceptibility Analysis

Streptococcus pneumoniae isolates were examined for 15 antibiotic susceptibilities as follows; PCG, penicillin G; AMPC, amoxicillin; CTX, cefotaxime; CTRX, ceftriaxone; IPM, imipenem; MEPM, meropenem; LVFX, levofloxacin; OFLX, ofloxacin; CAM, clarithromycin; EM, erythromycin; VCM, vancomycin; TC, tetracycline; CP, chloramphenicol; RFP, rifampicin, ST, Trimethoprim-sulfamethoxazole. Minimal inhibitory concentration (MICs) were determined at clinical laboratory in Daido Hospital using broth micro dilution methodology with the VITEK2 system. MICs were calculated as MIC_{90} (MIC causing inhibition of 90% of isolates). Percentage susceptibilities were calculated based on Clinical Laboratory Standard Institute (CLSI) break point [5]. We used two separate interpretive breakpoints for meningeal and non-meningeal isolates to define penicillin. Multidrug resistance (MDR) was defined as non-susceptibility to more than any three antimicrobial agents [6].

2.3. Statistical Analysis of the Data

We conducted the statistical analysis with the chi-squared test or Fisher's exact test when appropriate. Differences were considered significant when p was <0.05.

3. Results

One hundred fifty-three *Streptococcus pneumoniae* were isolated among which 80 (52.2%) were from male patient and 73 (47.8%) were from females. Nasal discharge 134 (87.6%) [male-69, female-65], sputum 15 (9.7%) [male-9, female-6], tonsil 2(1.3%) [male-1, female-1], pharyngeal mucus 1(0.7%) [male-1, female-1], and blood 1 (0.7%) [male-1, female-1] were the source of *Streptococcus pneumoniae* isolates (**Table 1**). There was no significant difference between male and female.

The age incidence among 0 - 1 years age group was 26 (17%) [male-17, female-9], among 1 - 10 years age group, 110 (71.9%) [male-52, female-58] ($p < 0.05$), among 11 - 40 years age group, 3 (1.7%) [male-2, female-1], in 41-60 years it was 10 (6.5%) [male-8, female-2] and in >60 years age group it was 4 (2.6%) [male-2, female-2] (**Table 2**). There was no significant difference between male and female.

Most of the *Streptococcus pneumoniae* isolates were from the pediatrics (137/89.5%) [male-69, female-68] followed by respiratory medicine (12/7.8%) [male-9, Female-3], general medicine (2/1.3%) [male-1, female-1]

and lowest from gastroenterology (1/0.6%) [male-0, female-1], and neurology department (1/0.6%) [male-1, female-0] (**Table 3**). There was no significant difference between male and female.

The results of antimicrobial susceptibility of *Streptococcus pneumoniae* isolates to various antibiotics tested in this study are shown in **Table 4**. Vancomycin and rifampicin were the most active antibiotics with 100%.

Table 1. Biological material wise distribution of *Streptococcus pneumoniae* isolates.

biological material	nasal discharge	sputum	tonsil	pharyngeal mucus	blood
male	69	9	1	0	1
female	65	6	1	1	0
total	134	15	2	1	1

Table 2. Age wise distribution of *Streptococcus pneumoniae* isolates.

age groups	(0 - 1) years	(1 - 10) years	(11 - 40) years	(41 - 60) years	>60 years
male	17	52	1	8	2
female	9	58	2	2	2
total	26	110	3	10	4

Table 3. Clinical department wise distribution of *Streptococcus pneumoniae* isolates.

clinical department	pediatrics	respiratory medicine	general medicine	gastroenterology	neurology
male	69	9	1	0	1
female	68	3	1	1	0
total	137	12	2	1	1

Table 4. Antimicrobial susceptibility of *Streptococcus pneumoniae* isolates.

antimicrobial agents	MIC90 (mg/mL)	range	% susceptibility
PCG	2	$\leq$0.06 - 4	97.4
AMPC	2	$\leq$0.06 - 4	92.8
CTX	1	$\leq$0.06 - 4<	93.5
CTRX	1	$\leq$0.06 - 4<	96.1
IPM	0.25	<0.03 - 0.5	74.5
MEPM	1	$\leq$0.06 - 0.12	73.9
LVFX	2	$\leq$0.5 - 8$\leq$	98.7
OFLX	4	$\leq$1 - 8$\leq$	88.9
CAM	1$\leq$	$\leq$0.25 - 1$\leq$	6.5
EM	1$\leq$	$\leq$0.25 - 1$\leq$	7.2
VCM	$\leq$1	$\leq$1	100.0
TC	16$\leq$	$\leq$1 - 16$\leq$	8.5
CP	16	$\leq$2 - 32$\leq$	87.6
RFP	$\leq$0.25	$\leq$0.25	100.0
ST	20	$\leq$10 - 80	79.7

susceptibility rates. The next best antibiotics with over 95% susceptibility rates were levofloxacin (98.7%), penicillin G (97.4%), and ceftriaxone (96.1%). Significant resistant were observed in tetracycline (8.5%), erythromycin (7.2%), clarithromycin (6.5%).

Our study revealed that 82 *Streptococcus pneumoniae* isolates had multidrug resistant ability (53.6%). The most common pattern of MDR was resistant to clarithromycin, tetracycline, and imipenem (25.5%), followed by resistant to clarithromycin, tetracycline, and trimethoprim - sulfamethoxazole (16.3%). Most *Streptococcus pneumoniae* isolates with MDR were resistant to at least one of the macrolides tested.

4. Discussion

In this study, we described the characteristics of *Streptococcus pneumonia* isolates from December 2013 to February 2014 at general hospital in the central region of Japan.

With respect to gender group, *Streptococcus pneumoniae* were isolated more from female patients than male patients. Although previous report showed that the number of male patient was significant greater than that of female patient [7], our study showed the male to female ratio was about 1.1 time and there was no significant differences among gender.

We clarified *Streptococcus pneumoniae* with age distribution. The present study reveals the prevalence of *Streptococcus pneumonia* more in extremes of age group as seen in 0 - 1 years age group, it is 17%, increasing to 71.9% in 1 - 10 years age group, diminishing to 2% in 11 - 40 years age group, again increasing to 6.5% in 41% - 60 years age group and finally diminished to 2.6% in more than 60 years age group. Although young patients under 10 years frequently caused *Streptcococcus pneumoniae* infection, the large numbers of *Streptcococcus pneumoniae* were not isolated from over 60 years age patients in our study. Previous report showed that high incidence of pneumonia in children and elder people in different parts of world [7] [8]. It is suggested to decrease immunity in the extremes of age groups.

In the analysis of clinical departments, we found that department where most patients with *Streptococcus pneumoniae* were detected was pediatrics. *Streptococcus pneumoniae* infection, especially acute pharyngitis and tonsillitis, was usually popular as pediatric diseases [1].

The disease burden of *Streptococcus pneumoniae* infections has increased due to widespread emergence of antimicrobial resistance in many countries from 1990's [2]. Previous studies documented very high prevalence rates of beta-lactam and macrolide resistance in *Streptococcus pneumoniae* in Asian countries [2] [9]-[13]. Particularly, macroride resistance has remarkably increased in many Asian countries, where over 70% of clinical isolates were fully resistant [2] [9] [12] [13]. Antimicrobial susceptible analysis of *Streptococcus pneumoniae* revealed that macrolide was no longer effective against these bacteria because macrolide resistant rates of *Streptococcus pneumoniae* were more than 90%. Recently Clarithromycin and Azithromycin, which we call new macrolide, have been used frequently against respiratory tract infectious disease. Thus, we need further antimicrobial surveillance to prevent the spread of new macroride resistant *Streptococcus pneumoniae*.

Streptococcus pneumoniae also had tetracycline - resistant pattern. This result implies that Streptococcus possesses the same pathogenic island including both macrolide and tetracycline resistant genes [4]. We found a low prevalence of penicillin resistance in non-meningeal isolates according to the revised CLSI breakpoints for resistance to parenteral penicillin, although penicillin MICs have increased in some countries such as China and India compared with past investigation [9]. Most of the non-meningeal isolates from Asian countries were susceptible to parenteral penicillin, a finding consistent with other study worldwide (<7%) [2] [9] [13]. As the emergence of penicillin resistant *Streptococcus pneumoniae* is low, our result showed that the prevalence of imipenem non-susceptibility was not low in Japan. We need to focus on the carbapenem susceptible pattern in *Streptococcus pneumonia* hereafter. The overall rates of resistance to fluoroquinolone in *Streptococcus pneumoniae* remained low in most countries including Japan [2] [9] [13]. Thus, given the popular use of respiratory fluoroquinlone in clinical practice, the emergency of these strains highly resistant to fluoroquinolone could be a concern in the future in the treatment of *Streptococcus pneumoniae* pneumonia. In addition, MDR *Streptococcus pneumonia* was also very prevalent in Asian countries (59.3%), particularly in China (83.3%), Vietnam (75.5%), South Korea (63.9%), Hong Kong (62.2%), and Taiwan (59.7%) [9]. From our result, multi drug resistance was 53.6% in Japan. But this rate in Japan was much higher than those in other parts world such as 9% to 24% in North America and 0% to 43% in Europe [2] [9] [14]. The emergence of MDR *Streptococcus pneumonia* including macrolide, tetracycline, and carbapenem resistant strains will raise the serious problem in Asian coun-

tries including Japan [13] [15].

5. Conclusions

Incidence of *Streptococcus pneumoniae* infection is increasing worldwide affecting the children and aged adult population which may lead to severe invasive infection by dissemination to other organs of the body if not treated adequately. The indiscriminate and inadvertent use of antibiotics has led to the emergence of multidrug resistance among commonly used antibiotics.

Our investigation aims to guide medical officer on appropriate use of antibiotics. This aim is not only to reduce the morbidity and mortality in the patients but also to control the emergence and spread of resistance among *Streptococcus pneumoniae*. Continuous surveillance of the use of antibiotics helps in preserving the effectiveness of antibiotics. The results from our study strongly emphasize the need for continuous epidemiological monitoring of antibiotic resistant.

Acknowledgements

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