

Clinical Characteristics of Vaginal Discharge Associated *Streptococcus pyogenes* at General Japanese Hospital

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Abstract

Streptococcus pyogenes (*S. pyogenes*) is popular pathogen caused various infectious disease. This study was conducted to find out the recent clinical characteristics of *S. pyogenes* isolates from vaginal discharge at Japanese hospital. *S. pyogenes* was identified by standard laboratory procedure. Antimicrobial susceptibility testing was performed by microdilution assay according to CLSI recommendation. Total 61 *S. pyogenes* were isolated from vaginal discharge. The major age incidence among 0 - 10 years age group was 14 (23%), among 21 - 30 years age group, 7 (11.5%), among 31 - 40 years age group, 13 (21.3%), among 51 - 60 years age group, 8 (13.1%), and among 61 - 70 years age group, 11 (18%). The numbers of ciprofloxacin and clarithromycin no-susceptible *S. pyogenes* from 0 - 10, 31 - 40, and 61-70 years age group were higher than those from other groups. The numbers of clindamycin and minocycline no susceptible *S. pyogenes* from 0 - 10, and 21 - 40 years age group were higher than those from other group. Furthermore, our study revealed that clarithromycin was completely ineffective in 21 - 30 years age group ($p < 0.05$). As the numbers of under and not less than 13 year age group were 15, and 46, respectively, the number of adult cases was higher than the number of child cases. Clarithromycin no-susceptible rate was highest and minocycline no-susceptible rate was lowest in both group. There was no significant difference of antimicrobial susceptible trends between under and not less than 13 year age groups. Our study suggests the need for continuous epidemiological surveillance of vaginal discharge associated *S. pyogenes* because the trend of infectious disease epidemiology is always changing drastically.

Keywords

Streptococcus pyogenes, Susceptibility, Antimicrobial Resistance, Vaginal Discharge, Clarithromycin

1. Introduction

Bacterial vaginosis is the most prevalent cause of vaginal discharge in reproductive age women [1], is present in ~30% of women in the United States [2] and is characterized by vaginal colonization with anaerobic bacterial species and a loss of normal lactobacilli. The clinical presentation of Bacterial vaginosis is characterized by an odorous discharge or no symptoms at all, without the redness, swelling or pain typical of inflammation. However, at the mucosal level, this condition has a significant pro-inflammatory impact that is associated with some miserable clinical outcomes [3]. Bacterial vaginosis is known to be common vaginal infection worldwide [4]. It is associated with important public health issues, such as preterm labor and the acquisition and transmission of sexually transmitted infections [5] [6].

Streptococcus pyogenes (*S. pyogenes*) is a gram-positive bacterium that infects the tonsils and pharynx. It is responsible for rheumatic fever, glomerulonephritis, and streptococcal toxic shock-like syndrome [7]. Although the pathogenesis of *S. pyogenes* has not been unclear, many virulent proteins are considered to be causative factors.

Although group B streptococci have been described as common members of the vaginal flora, vaginal colonization with *S. pyogenes* has been reported infrequently. Because of recent concern over the increasing incidence of severe, invasive *S. pyogenes* infections including vaginosis-induced streptococcal toxic shock-like syndrome [8], questions have been raised regarding the value of vaginitis for *S. pyogenes* [9].

The present study was conducted to find out the recent clinical characteristics of *S. pyogenes* isolates from vaginal discharge at general hospital in the central of Japan.

2. Materials and Methods

2.1. Strains and Clinical Data

A total of 61 *S. pyogenes* was obtained from vaginal discharge at Daido Hospital between 2009 and 2017. 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 streptococcus 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

S. pyogenes isolates were examined for 10 antibiotic susceptibilities as follows AMPC; amoxicillin, CTM; cefotiam, CAZ; ceftazidime, CTRX; ceftriaxone, FOM; fosfomycin, MEPM; meropenem, CAM; clarithromycin, CLDM; clindamycin, MINO; minocycline, CPMX; ciprofloxacin. Minimal inhibitory concentrations (MICs) were determined at clinical laboratory in Daido Hospital using broth microdilution methodology with the VITEK2 system. Evaluation of susceptibilities was calculated based on Clinical Laboratory Standard Institute (CLSI) breakpoint [10].

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

First of all, we evaluated that all *S. pyogenes* isolates were beta hemolysis in this study. Next, we compared the differences among age. Furthermore we compared the differences between under and not less than 13 years age group in this study. **Figure 1** demonstrated the comparative analysis of *S. pyogenes* among age. Sixty-one *S. pyogenes* were isolated from vaginal discharge. The age incidence among 0 - 10 years age group was 14 (23%), among 11 - 20 years age group, 1 (1.6%), among 21 - 30 years age group, 7 (11.5%), among 31 - 40 years age group, 13 (21.3%), among 41 - 50 years age group, 5 (8.2%), among 51 - 60 years age group, 8 (13.1%), among 61 - 70 years age group, 11 (18%), among 71 - 80 years age group, 1 (1.6%), and among 81 - 90 years age group, 1 (1.6%). Next, we investigated the relationship between age distribution and ciprofloxacin susceptibility of *S. pyogenes*. The numbers of ciprofloxacin no-susceptible *S. pyogenes* from 0 - 10, 31 - 40, and 61 - 70 years age group were higher than those from other groups (**Figure 2**). As we investigated the relationship between age distribution and clarithromycin susceptibility of *S. pyogenes*, the numbers of clarithromycin no-susceptible *S. pyogenes* from 0 - 10, 21 - 40, and 61 - 70 years age group were higher than those from other groups in **Figure 3**. Especially, all *S. pyogenes* from 21 - 30 years age group had clarithromycin no-susceptible ability ($p < 0.05$). **Figure 4** showed that the numbers of clindamycin no-susceptible *S. pyogenes* from 0 - 10, and 21 - 40 years age group were higher than those from other group with regard to the relationship between age distribution and clindamycin susceptibility of *S. pyogenes*. **Figure 5** revealed that the numbers of minocycline no-susceptible *S. pyogenes* from 0 - 10, and 21 - 40 years age group were higher than those from other group. This antimicrobial pattern of

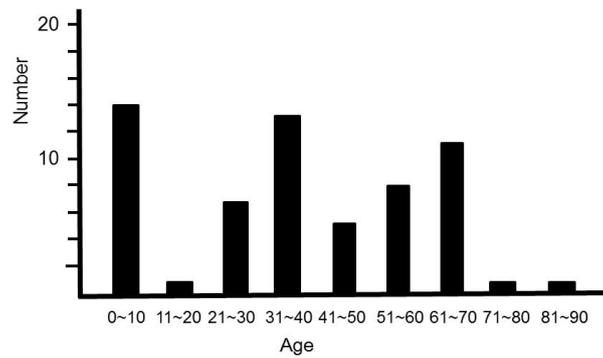


Figure 1. Age distribution of *Streptococcus pyogenes* isolates.

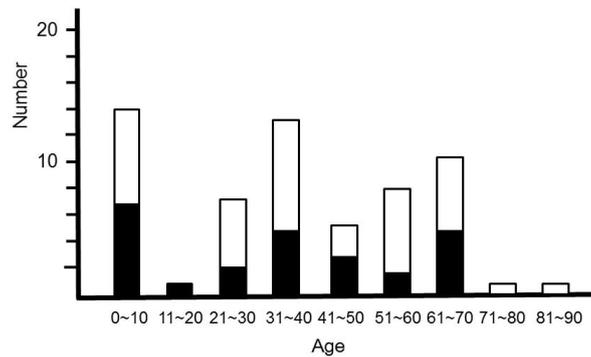


Figure 2. Ciprofloxacin susceptibility of *Streptococcus pyogenes* isolates. Black box: no-susceptible, white box: susceptible.

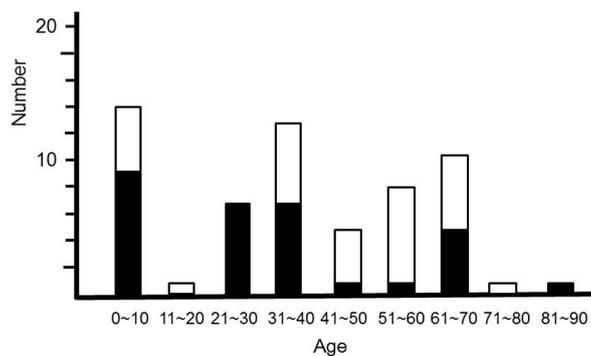


Figure 3. Clarithromycin susceptibility of *Streptococcus pyogenes* isolates. Black box: no-susceptible, white box: susceptible.

minocycline no-susceptible *S. pyogenes* was same as those of clarithromycin no-susceptible *S. pyogenes*. As other antibiotics were the most active antibiotics with 100% susceptible rates, we did not perform further analysis about these antibiotics. Furthermore, we analyzed the differences of four antimicrobial susceptible patterns (CPFX, CAM, CLDM, and MINO) both under and not less than 13 years age group. As the numbers of under and not less than 13 years age group were 15, and 46, respectively, the number of adult cases was higher than the number of child cases. The results of antimicrobial susceptible patterns of

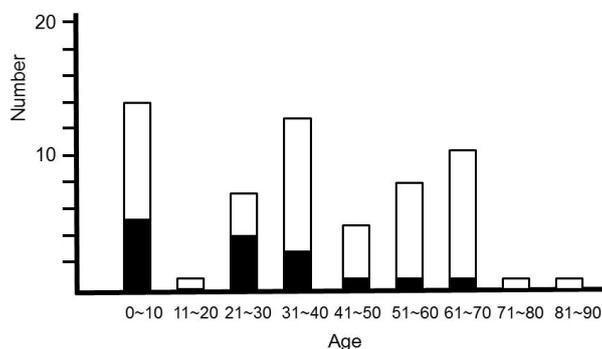


Figure 4. Clindamycin susceptibility of *Streptococcus pyogenes* isolates. Black box: no-susceptible, white box: susceptible.

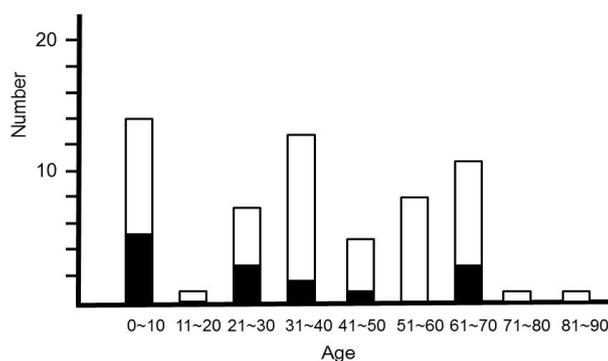


Figure 5. Minocycline susceptibility of *Streptococcus pyogenes* isolates. Black box: no-susceptible, white box: susceptible.

S. pyogenes isolates to four antibiotics tested in under 13 year's age group were shown in **Figure 6**. Clarithromycin no-susceptible rate was highest.

Both clindamycin and minocycline no-susceptible rate were same. **Figure 7** demonstrated that clarithromycin no-susceptible rate was highest in not less than 13 years age group. Minocycline no-susceptible rate was lowest. There was no difference of antimicrobial susceptible trends between under and not less than 13 years age group.

4. Discussion

In this study, we described the characteristics of *S. pyogenes* isolates from vaginal discharge at general hospital in the central of Japan.

The present study revealed that the numbers of vaginal discharge-related *S. pyogenes* isolated from 0 - 10 years' children were most popular. However, the numbers of *S. pyogenes* isolated from 31 - 40 and 61 - 70 years' adult were also high.

In the analysis of antimicrobial susceptibility, the rate of ciprofloxacin and clindamycin no-susceptible *S. pyogenes* was similar in 0 - 10, 31 - 40, and 61 - 70 years' patients. However, especially, we found that clarithromycin was completely antimicrobial ineffective in 21 - 30 years' patients. Macrolide including clarithromycin is popular for treatment of several infectious diseases in Japan

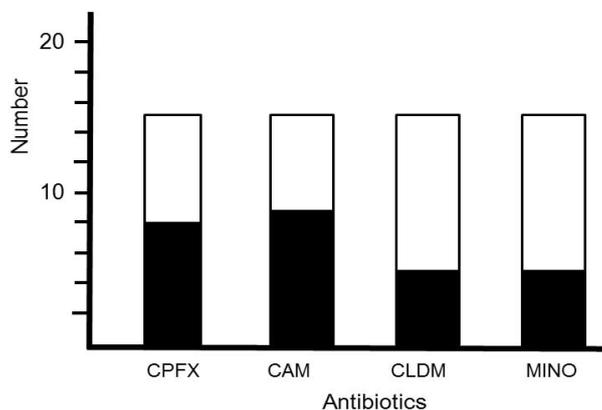


Figure 6. Four antimicrobial susceptibility of *Streptococcus pyogenes* isolates from under 13 years age group patients. Black box: no-susceptible, white box: susceptible. CPFX: ciprofloxacin, CAM: clarithromycin, CLDM: clindamycin, MINO: minocycline.

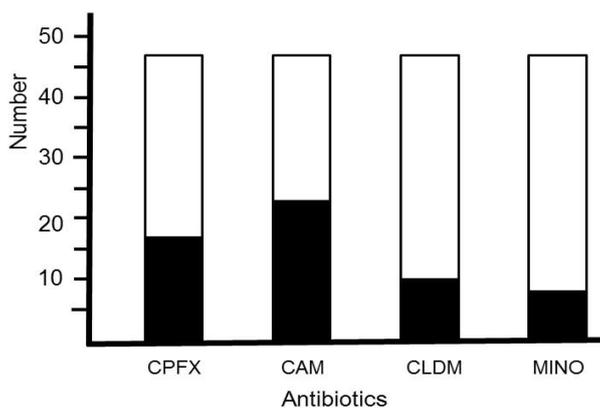


Figure 7. Four antimicrobial susceptibility of *Streptococcus pyogenes* isolates from not less than 13 years age group patients. Black box: no susceptible, white box: susceptible. CPFX: ciprofloxacin, CAM: clarithromycin, CLDM: clindamycin, MINO: minocycline.

[11]. Furthermore, low dose macrolide therapy is also popular for treatment of chronic disease [12] [13]. Our result suggested that inadequate usage of macrolide may increase the macrolide no-susceptible bacteria.

The comparative analysis between under and not less than 13 years age group demonstrated that ciprofloxacin and clarithromycin were less effective in *S. pyogenes* from about a half of under 13 years' patients. Even though *S. pyogenes* from a quarter of under 13 year's patients had clindamycin and minocycline no susceptibility, careful management must be taken in selecting antibacterial drugs for treatment of bacterial vaginosis. We found the numbers of bacteria from not less than 13 years' patients were about three times as same as those from under 13 years' patients. Streptococcal vaginosis was thought to be a disease that a child of 13 years old or less used to be [14] [15]. But recently we should change

the perception that streptococcal vaginosis is also a disease that is an adult disease.

Further epidemiological analysis is needed for the clarification of several problems about vaginal discharge-associated *S. pyogenes* because the trend of infectious disease epidemiology is always changing drastically.

5. Conclusion

Our results showed that *S. pyogenes*-caused vaginosis was not children's illness, but an illness of adults, and that the prevalence of drug-resistant bacteria was also high. The results from our study strongly suggest the need for continuous epidemiological surveillance of *S. pyogenes* isolated from vaginal discharge.

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