Biomedical Research 2018; 29 (5): 1008-1013

ISSN 0970-938X
www.biomedres.info

The characteristics of bacterial pathogens in 15000 cases of children with respiratory tract infection in Eastern area.

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Abstract

Objective: To understand the characteristics of bacterial pathogens in children with respiratory tract infection.

Methods: The clinical data of 15000 cases of children admitted to Children's Hospital because of respiratory tract infection for consecutive 9 years from November 2005 to October 2014 were collected for retrospective analysis.

Results: In 15000 cases of sputum specimens of children with respiratory tract infection, the first bacterial pathogens were *Streptococcus pneumonia* (12.79%). In different years, different seasons, different ages of children with bacterial, the differences of detection rate had statistical significance (P<0.01). The rate of 3 y old~ group was the highest, ≥ 5 y old group was the lowest, and the difference was statistically significant (χ^2=92.83, P<0.001). In summer it was the highest, and autumn the lowest, the difference of which was statistically significant (χ^2=22.18, P<0.001). The positive rate of sputum bacterial culture in children who didn't receive antibiotics use before admission was higher than those who received antibacterial drugs (P<0.01).

Conclusion: *Streptococcus pneumoniae* is the most common bacterial pathogens that cause respiratory tract infection of children, followed by *Haemophilus influenzae* and *Moraxelle catarrhalis*. The detection rate of bacterial pathogens varies in different years and seasons and children of different ages. The course of the disease before admission and the course of antibiotic use outside hospital had an effect on the positive detection rate of bacteria.

Keywords: Respiratory tract infection, Bacteria, Pathogens, Children.

Accepted on December 1, 2017

Introduction

In worldwide, respiratory infection is one of the most common pediatric diseases, and according to the statistics of WHO, respiratory tract infection is the second leading cause of death at the age of under 5, followed by premature birth. In developed countries, the main pathogens was virus, while in developing countries it's mainly bacteria [1,2]. It is pointed out by the guidelines for the management of community-acquired pneumonia in children in 2013 that the common pathogens which cause community-acquired pneumonia in children are bacteria, viruses, mycoplasma, chlamydia, in addition, fungi and protozoa [3]. Among them, the bacteria mainly include *Streptococcus pneumoniae* (SP), *Haemophilus influenzae* (HI), *Staphylococcus aureus* (SA), *Moraxelle catarrhalis* (MC), *Escherichia coli* (*E. coli*), *Klebsiella pneumoniae* (KPN) and so on.

Common bacteria that cause hospital acquired pneumonia are *E. coli*, KPN, *Pseudomonas aeruginosa* (*Pseudomonas aeruginosa* PA), Bauman Acinetobacter (*Acinetobacter baumannii*, AB) in gram negative bacilli and SA, SP, *Enterococcus faecalis* and *Enterococcus faecium* of *Enterococcus* in gram positive cocci [4]. In 2000, Toikka et al. [5] reported that in 126 cases of children with pneumonia, 54% were bacterial infection. The results of a study in Finland showed that 85% of children with lower respiratory tract infection could have clear etiological diagnosis, and bacterial infection rate was 53% [6]. Domestic reports indicated that the positive detection rate of bacteria in children with respiratory tract infection was 18.30%~56.82% [7-11]. Therefore, bacterial infection is an important pathogen of respiratory tract infection, and its detection rate is affected by geographical environment, season, age, disease constitution, antimicrobial use, drug resistance and other factors [12,13]. Brad et al. also reported that bacteriological diagnosis and antibiotic resistance surveillance are indispensable in the effective management of Lower Respiratory Tract Infections (LRTIs) [14]. Through the analysis on bacterial etiology of children with community-acquired respiratory tract infection admitted to Children's Hospital for consecutive 9 y, this study is to understand the epidemiological characteristics of bacterial etiology in children with respiratory tract infection in this local area.

Data and Methods

Research subjects

15000 cases of children admitted to Children's Hospital because of respiratory tract infection from November 2005 to October 2014 were collected as research subjects. According to the season the groups were divided into four groups: 4023 cases of spring group (2~4 months), 3717 cases of summer group (5~7 months), 3498 cases of autumn group (8~10 months), and 3762 cases of winter group (November to January of next year). There were 4772 cases of children with the use of antibiotics outside hospital to divide three groups, including 2928 cases of antibiotic use time outside hospital ≤ 3 d, 1280 cases of 4~7 d, and 564 cases of >7 d. There were total of 11370 cases that had course related data in medical history, according to the course of disease outside hospital to divide three groups: 10674 cases of <1 month group, 559 cases of 1~3 months group, 137 cases of >3 months group.

Collection of sputum samples

The sputum was collected at the admission of 24 h, and the aseptic suction tube was inserted into the child's nasal cavity of 7~8 cm until under the pharynx, 1~2 ml secretions induced to be absorbed were placed in a sterile saline test tube and submitted within half an hour. The collected sputum specimens were first smeared and examined by microscopy, and squamous cells<10/low magnification view, white blood cells>25/low magnification view were regarded as qualified, and the unqualified were re-collected or discarded.

Detection of sputum samples

The 1 ml sputum was added into 75 µL phlegm digestive juice (including two sulfur threonic sugar 0.1 g, muriate 0.02 g, sodium chloride 0.78 g, disodium hydrogen phosphate 0.112 g, monopotassium phosphate 0.02 g), after 0.5 h incubation in 35°C incubator, the sputum was taken out with a sterile inoculation ring, and were inoculated in Columbia blood agar plates and chocolate plates, then put into an incubator containing 5%~8% CO_2 for 18~24 h incubation. According to the characteristics of colony on the culture medium, gram staining, microscope observation, biochemical reaction and other methods, the bacteria were identified.

Statistical analysis

SPSS17.0 statistical software packet was used for statistical processing and analysis, count data were expressed by the number of cases and the percentage (%), χ^2 test, trend χ^2 test was adopted for comparison between groups, and the comparison of the rates among multi groups was compared by the Chi square method. P<0.05 was believed as statistically significant difference.

Result

The male: female ratio was 1.67:1. The youngest child was 29 d, and the oldest 15 y and 10 months, including 4578 cases of <6 months, 2594 cases of 6 months~, 2610 cases of 1 y old~, 1271 cases of 2 y old~, 2246 cases of 3 y old~, and 1701 cases of ≥5 y old.

The total bacterial detection rate in 9 y

In 15000 cases of samples, 3950 cases had positive bacteria test, and the positive rate was 26.32%. Among them, the mixed infection rate of two or more than two was 2.33% (350/15000). A total of 4286 strains were detected, and the detection rate of SP was the highest, followed by HI, MC, SA, *E. coli*, KPN. In 350 cases of mixed infection, the top 3 were: SP merged with HI 21.7% (76/350), SP merged with MC 12.0% (42/350), and HI merged with MC 5.7% (20/350).

The bacterial detection situation in each season

The bacterial detection rate of each season as spring, summer, autumn winter were in turn 26.93% (1083/4023), 27.51% (1022/3717), 23.28% (814/3498), 27.34% (1028/3762). In summer it was the highest, and autumn the lowest, the difference of which was statistically significant (χ^2=22.18, P<0.001). The detection rates of SP, HI in the two seasons of spring and summer were both higher; the detection rates of SP, SA in autumn were higher; the detection rates of SP, MC in winter were higher. For single bacteria, the detection rates of SP in four seasons were all higher than that of other bacteria, and the highest was in winter and the lowest in spring; the highest detection rate of HI was in spring and the lowest in autumn; the highest detection rate of MC was in winter and the lowest in autumn; detection rate of *E. coli* in spring was the highest, the lowest in summer; the highest detection rate of PA was in autumn, and the lowest in winter; in the summer AB detection rate was the highest, and the lowest in winter; the difference in detection rate of SA, KPN in the four seasons was not significant (Table 1).

Detection situation of bacteria in different age groups

The bacterial detection rates in all ages such as <6 months, 6 months~, 1 y old~, 2 y old ~, 3 y old~, ≥ 5 y old were respectively 27.95% (1278/4578), 27.83% (722/2594), 27.20% (710/2610), 20.22% (257/1271), 29.21% (656/2246), 19.05% (324/1701), of which the rate of 3 y old~ group was the highest, ≥ 5 y old group was the lowest, and the difference was statistically significant (χ^2=92.83, P<0.001).

The influence of antibiotics use before admission on bacterial detection

Among the 15000 cases of children, 5721 cases had related data whether antibiotics were used before admission, including 4772 cases (83.41%) with antibiotics use before admission. The bacteria detection in sputum culture of children without antibiotics use before admission was 33.29% (316/949), which was higher than that of the children with antibiotics use, accounting for 20.93% (999/4772) (P<0.001). The use course of antibiotics before admission also had impact on the composition of bacteria: the difference in the detection rate of SA in the three groups such as use course ≤ 3 d, 4~7 d, >7 d was statistically significant (P<0.05). Among them, the detection rate of AB in 4~7 d group was higher than that of ≤3d group, the difference of which was statistically significant. Under the condition of same use course of antibiotics, the positive detection rates of SP in the groups with different use courses of antibacterial drugs were all the highest (Table 2).

The influence of disease course before admission on bacterial detection situation

11370 children with course related data before admission collected were analysed, showing that the positive rate of bacteria in sputum culture of children in 3 groups such as course outside hospital <1 month group, 1~3 months group, >3 months group were respectively 29.47% (3146/10674), 34.35% (192/559). 33.58% (46/137), the difference of which was statistically significant (χ^2=7.00, P=0.03). The positive rate of sputum culture in 1~3 months group was higher than that in <1 month group, the difference of which was statistically significant.

The disease course outside hospital also affected the composition of detected bacteria: in disease course outside hospital <1 month group, 1~3 months group, >3 months group, the difference in detection rate of SP, MC and AB was statistically significant (P<0.05). Among them, the detection rates of SP and MC in disease duration 1~3 months group were higher than that of disease duration<1 month group; detection rate of AB in disease duration>3 months group was higher than that of <1 month group; under the condition of same disease course before admission, the positive detection rates of SP were all higher than that of other bacteria (Table 3).

***Table 1.** The detection situation of 8 common bacteria in different seasons (case (%)).*

Bacterial species	Spring (n=4023)	Summer (n=3717)	Autumn (n=3498)	Winter (n=3762)	χ^2 value	P value
SP	434 (10.74)	473 (12.70)	404 (11.52)	613 (16.25)	60.49	<0.001
HI	324 (8.06)	262 (7.05)	67 (1.92)	100 (2.66)	224.48	<0.001
MC	123 (3.06)	100 (2.69)	77 (2.20)	137 (3.64)	14.29	<0.001
SA	108 (2.69)	95 (2.56)	88 (2.52)	72 (1.91)	5.69	0.13
E. coli	63 (1.57)	29 (0.78)	44 (1.26)	53 (1.41)	10.58	0.014
KPN	38 (0.95)	36 (0.97)	43 (1.23)	42 (1.12)	1.88	0.60
PA	23 (0.57)	33 (0.89)	54 (1.54)	21 (0.56)	26.7	<0.001
AB	20 (0.50)	38 (1.02)	23 (0.66)	8 (0.21)	21.71	<0.001
χ^2 value	1208.47	1350.50	1113.15	2160.30		
P value	<0.001	<0.001	<0.001	<0.001		

Note: SP: *Streptococcus pneumoniae*; HI: *Haemophilus influenzae*; MC: *Moraxelle catarrhalis*; SA: *Staphylococcus aureus*; *E. coli*: *Escherichia coli*; KPN: *Klebsiella pneumoniae*; PA: *Pseudomonas aeruginosa*; AB: Bauman *Acinetobacter*.

***Table 2.** The detection situation of 8 common bacteria in different use courses of antibiotic (case (%)).*

Bacterial species	≤ 3 d (n=2928)	4~7 d (n=1280)	>7 d (n=564)	χ^2 value	P value
SP	375 (12.81)	177 (13.83)	84 (14.89)	2.16	0.34
HI	142 (4.85)	62 (4.84)	23 (4.08)	0.65	0.72
MC	83 (2.83)	22 (1.72)	13 (2.30)	4.67	0.09
SA	96 (3.28)	16 (1.25) a	7 (1.24) a	19.20	<0.001
E. coli	33 (1.13)	16 (1.25)	13 (2.30)	5.15	0.08
KPN	31 (1.06)	8 (0.63)	5 (0.89)	1.84	0.39
PA	24 (0.82)	13 (1.02)	9 (1.60)	3.03	0.22
AB	1 (0.03)	7 (0.55) a	2 (0.35)	11.85	0.001
χ^2 value	1080.73	606.45	267.72		
P value	<0.001	<0.001	<0.001		

Note: [a]showed that compared with ≤ 3 d group, P<0.0125 (chi square segmentation method was used for comparison among multi groups, the test level was adjust to 0.0125). SP: *Streptococcus pneumoniae*; HI: *Haemophilus influenzae*; MC: *Moraxelle catarrhalis*; SA: *Staphylococcus aureus*; *E. coli*: *Escherichia coli*; KPN: *Klebsiella pneumoniae*; PA: *Pseudomonas aeruginosa*; AB: Bauman *Acinetobacter*.

***Table 3.** The detection situation of 8 common bacteria in different disease courses (cases (%)).*

Bacterial species	<1 month (n=10674)	1~3 months (n=559)	>3 months (n=137)	χ^2 value	P value
SP	1352 (12.67)	95 (16.99)[a]	24 (17.52)	11.42	0.003
HI	564 (5.28)	21 (3.76)	8 (5.84)	2.62	0.27

MC	364 (3.41)	43 (7.69)[a]	9 (6.57)	30.97	<0.001
SA	331 (3.10)	13 (2.33)	1 (0.73)	3.27	0.19
E. coli	145 (1.36)	7 (1.25)	0	1.30	0.58
KPN	123 (1.15)	7 (1.25)	1 (0.73)	0.11	0.95
PA	131 (1.23)	10 (1.79)	2 (1.46)	1.82	0.35
AB	61 (0.57)	5 (0.89)	3 (2.19)[a]	5.97	0.047
χ^2 value	3421.55	277.42	78.08		
P value	<0.001	<0.001	<0.001		

Note: a showed that compared with <1 month group, P<0.0125 (chi square segmentation method was used for comparison among multi groups, the test level was adjust to 0.0125). SP: *Streptococcus pneumoniae*; HI: *Haemophilus influenzae*; MC: *Moraxelle catarrhalis*; SA: *Staphylococcus aureus*; *E. coli*: *Escherichia coli*; KPN: *Klebsiella pneumoniae*; PA: *Pseudomonas aeruginosa*; AB: Bauman *Acinetobacter*.

Conclusion

The surveillance of sputum bacterial etiology in children with respiratory tract infection admitted to the department of respiration in children's hospital for consecutive 9 y was carried out, a total of 15000 specimens were collected, including 3950 cases of positive specimens in sputum culture, and the total positive rate was 26.32%, lower than 28.63% in Guangxi, 56.82% in Guangzhou, 35.38% in Sanya, 28.10% in Shandong, but higher than 18.30% in Hunan [7-10,15-19], indicating that in various regions, the detection rate of respiratory tract bacterial pathogen had differences.

This study suggested that in the total rate of bacteria in the four seasons such as spring, summer, autumn and winter, the highest detection rate was in summer and the lowest in autumn, indicating that the season had a certain influence on the detection rate of bacteria in children with respiratory tract infections. In the four seasons of spring, summer, autumn and winter, detection rate of SP was the top one, and the highest detection rate was in winter and the lowest in spring, which were consistent with the reports from Cai et al. [16] and Huang et al. [20]. The detection rate of *E. coli* was highest in spring and lowest in summer; the detection rate of PA was highest in autumn and lowest in winter; the detection rate of AB was highest in summer and lowest in winter, suggesting that the distribution and kind of pathogenic bacteria in children with respiratory tract infection in different seasons were different. The detection rate of bacteria in children with respiratory tract infection at different ages is also different. In each age group of <6 months, 6 months~, 1 y old~, 2 y old~, 3 y old~ and ≥ 5 y old, the positive detection rate of bacterial was the highest in 3 y old~ group, followed by 6 months group, <6 months group, and the lowest in ≥ 5 y old group, which showed a significant difference. As a result, the probability of bacterial infection in children under 1 y old and 3~5 y old were the highest, which was related to respiratory and systemic specific and nonspecific immune dysfunction in children of this age group. In addition, children of 3~5 y old are in the nursery period, the susceptible environment of kindergartens and immune function which have not been well developed yet cause it prone to bacterial infection of respiratory tract. In all age groups, detection rate of SP come first, especially in the age group 3~5 y old, it was the highest and the lowest in <6 months group, which were basically consistent with the reports from Cai et al. [19] and Sun et al. [21-23]. Previous reports have suggested that HI and *E. coli* infections are mainly seen in children under 1 y old [20,23,24]. This study showed that HI was detected in all age groups with high incidence in 6 months~ group, followed by 1 y old group and <6 months group, and *E. coli*, SA, KPN, PA, AB had high incidence in <6 months group. All of the above bacteria were more common in hospital acquired infections, and the results of this study showed that under 1 years old, especially in <6 months group, it's more common, which may be related to more susceptible to infection due to the immature development of specific and non-specific immune function of this age group in the early stage of life, and inappropriate adaptation to the external environment. Thus, the work of strengthening the health of children and prevention of infection in this age group is particularly important, and when it is found in clinic that respiratory infections occur in children of this age group, especially severe infection, antimicrobial agents may be considered for the above bacteria.

Previous reports have confirmed that the detection rate of SA in 3~7 d course of antibiotic use outside hospital is obviously higher, and the detection rate of SP in <3 d course of antibiotic use outside hospital is obviously higher [13]. The data in this study showed that, detection rate of sputum bacterial culture in children without antibiotics use before admission (33.29%) was higher than those with antibiotics use (20.93%). There are two possibilities for this result, one is the treatment of antibiotics before admission produces effective containment of bacterial infectious diseases, in addition, it may be due to the use of antibiotics to some extent causes bacterial culture difficulties, resulting in false negative. The detection rate of SA in use course of antibiotics ≤ 3 d group (3.28%) was higher than that in more than 3 d group, which was inconsistent with the above reported [13], but it was consistent with the report of Sun et al. [23] in this research group, which might have something to do with different ages of the study. The detection rate of AB in group of antibiotic use course 4~7 d before admission was higher than that of less than 3d group, suggesting that for different bacteria, rational antibiotic treatment course of outpatient may be more effective to decrease the infection rate of respiratory tract, meanwhile, it may also partly explain why AB is mostly multi resistant bacteria.

This study also showed that the difference in positive detection rate of sputum culture bacteria in disease course outside hospital<1 month group, 1~3 months group, >3 months group was statistically significant. The course of disease also affected the composition of bacteria: in children of disease course 1~3 months, the detection rate of SP and MC was higher than that in <1 month group; the detection rate of AB in children of disease course >3 months was higher than that in <1 months group. The above results suggested that the positive detection rates of SP, MC and AB showed an increase trend with the prolongation of the disease duration; the differences in the detection rates of different bacterial species in different disease course groups were considered to be related to the biological characteristics of bacteria, the use of antibiotics before admission and secondary infection. The specific reasons still need further study.

In conclusion, *Streptococcus pneumoniae* is the most common bacterial pathogens that cause respiratory tract infection of children, followed by *Haemophilus influenzae* and *Moraxelle catarrhalis*. The detection rate of bacterial pathogens varies in different years and seasons and children of different ages. The course of the disease before admission and the course of antibiotic use outside hospital had an effect on the positive detection rate of bacteria.

Limitations

Several limitations of this study should be considered. Firstly, this research was a cross-sectional study, further studies are needed to unravel this. Secondly, the sample size is not big enough. However, the study setting is a modern, high level comprehensive medical institution with sophisticated clinical diagnosis facilities and medical record management. Thus, the data used can be deemed reliable.

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