A Surveillance Bacteriological Study of Acute Bacterial Rhinosinusitis in Thailand and the Clinical Responses to the Culture-directed Antibiotics

Sanguansak Thanaviratananich MD*, Supinda Chusakul MD**,
Greetha Moungthong MD***, Thongchai Luxameechanporn MD****,
Pongsakorn Tantilipikorn MD*****, Supranee Fooanant MD******,
Songklot Aeumjaturapat MD**, Pipat Sribenjalux MSc*******,
Nadtaya Makachen MD********, Seksun Chainansamit MD*,
Saisawat Chaiyasate MD******, Chaweewan Bunnag MD*****

** Department of Otorhinolaryngology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*
*** Department of Otolaryngology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
**** Department of Otolaryngology, Phramongkutklao College of Medicine, Bangkok, Thailand*
***** Department of Otolaryngology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
****** Department of Otolaryngology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand*
******* Department of Otolaryngology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand*
******** Department of Clinical Microbiology, Faculty of Associated Medical Sciences, Khon Kaen University, Khon Kaen, Thailand*
********* Department of Otolaryngology, Khon Kaen Hospital, Khon Kaen, Thailand*

Objective: *To examine: 1) types of bacteria and antimicrobial sensitivity of commonly used antibiotics for acute bacterial rhinosinusitis (ABRS) in Thailand, 2) the effectiveness of using antibiotics according to antimicrobial sensitivity, and 3) the effectiveness of using antibiotics according to the Thai clinical practice guidelines (CPG) of ABRS.*

Material and Method: *Descriptive & experimental studies were conducted in seven tertiary hospitals in Thailand. The specimens from maxillary sinuses were taken for bacterial cultures either by maxillary sinus tap or endoscopically directed middle meatus swabs in patients with clinically diagnosed ABRS. Antimicrobial sensitivity was performed and antibiotics were prescribed according to the results of antimicrobial sensitivity or the Thai CPG of ABRS.*

Results: *A total of 113 patients were enrolled between August 2006 and April 2007, 104 cases of which were performed for bacteriological study. The incidence of bacterial growth was 60.6% (95% CI 51.0-69.4%). The most common bacteria was H. influenzae (25.0%, 95% CI 16.9-35.3%), followed by S. pneumoniae (14.3%, 95% CI 8.2-23.5%) and S. aureus (9.5%, 95% CI 4.7-17.9%), respectively, whilst M. catarrhalis was found only in 2.4% (95% CI 0.5-7.3%). Eight in 12 S. pneumoniae isolates were tested for the minimal inhibitory concentration of penicillin and found to be penicillin resistant strain in five specimens. Beta-lactamase producing H. influenzae was found in eight out of 20 isolates. H. influenzae had a tendency to be sensitive to amoxicillin/clavulanate, cefuroxime, cefpodoxime, azithromycin, clarithromycin, ofloxacin, levofloxacin and gatifloxacin, whilst S. pneumoniae had a tendency to be sensitive to amoxicillin/clavulanate, cefaclor, ampicillin/sulbactam, cefuroxime, ofloxacin, levofloxacin, gatifloxacin, cefpodoxime, cefixime and cefdinir. The effectiveness of antibiotics prescription according to the Thai CPG of ABRS and antimicrobial sensitivity were comparable, 88.5% (95% CI 69.8-97.6%) and 82.2% (95% CI 67.9-92%), respectively.*

Conclusion: *H. influenzae is found to be the most common bacteria in Thai ABRS, followed by S. pneumoniae and S. aureus. There is a high incidence of beta-lactamase producing H. influenzae and penicillin non-susceptible S. pneumoniae.*

Keywords: *Acute bacterial rhinosinusitis, Bacteriology, Microbiology, Streptococcus pneumoniae, Hemophilus influenzae*

J Med Assoc Thai 2015; 98 (Suppl. 7): S204-S216
Full text. e-Journal: *http://www.jmatonline.com*

Correspondence to:
Thanaviratananich S, Department of Otorhinolaryngology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Phone: +66-43-363565, Fax: +66-43-202490
E-mail: sanguans@kku.ac.th

Acute rhinosinusitis is one of the most common complaints in general practice in children and adults with the estimated incidence of acute bacterial rhinosinusitis (ABRS) around 0.5-2% and 2-10% after viral upper respiratory tract infection[1-3]. A survey in the US found that rhinosinusitis was the fifth most common diagnosis for which antibiotics were prescribed in the US[4].

ABRS causes significant symptoms that have the negative impact on quality of life. It can cause serious complications such as blindness or intracranial complications. The mainstay management of ABRS is the antibiotics and the ideal choice of antibiotics for ABRS depends on the type of bacteria found in the paranasal sinuses and its antimicrobial sensitivity. However, obtaining the secretion/pus from the paranasal sinuses is an invasive procedure and takes time. Therefore, the routine uses of antibiotics for uncomplicated community-acquired ABRS are usually initiated empirically and follow the clinical practice guidelines (CPG). The first Thai CPG for ABRS was developed by the representatives of the Thai Rhinologic Society in corporate with the Royal College of Otolaryngologists Head and Neck Surgeons of Thailand, the Royal College of Pediatricians of Thailand and the Allergy, Asthma & Immunology Society of Thailand and published in the year 2003[5], in which the guidelines adapted the guidelines from the western countries. Although there were at least five studies on the bacteriology and antimicrobial sensitivity of ABRS in Thailand, those studies were conducted only at one centre in different years with small sample sizes[6-10]. This guidelines recommended amoxicillin as the first-line drug for naive cases of community-acquired uncomplicated ABRS in those who have not received antibiotics within the previous six weeks.

Since the surveillance studies of ABRS in Thailand were scarce, the objectives of this present multicenter study were to examine the bacteriology of clinically diagnosed ABRS for both Thai children and adults, antimicrobial sensitivity and the effectiveness of antibiotics prescription according to the culture-directed therapy and the Thai CPG.

Material and Method

This was a prospective multi-centre descriptive study and non-randomized controlled trial conducted between August 2006 and April 2007 at the seven tertiary hospitals in Thailand: outpatient ear, nose & throat (ENT) departments of the Srinagarind Hospital, King Chulalongkorn Memorial Hospital, Phramongkutklao Hospital, Ramathibodi Hospital, Siriraj Hospital, Maharaj Nakhon Chiang Mai Hospital and Khon Kaen Hospital. Patients with suspected ABRS diagnosed by ENT doctors were included. Those who previously underwent nasal/paranasal sinus surgery, had nosocomial infection, were immuno-compromised hosts, received antibiotics within seven days before enrolment, presented with nasal polyps or nasal/paranasal tumors or had odontogenic rhinosinusitis were excluded. Criteria for suspected ABRS in this present study were the presence of nasal obstruction or rhinorrhea or decrease smelling within four weeks in combination with either: 1) the anterior rhinoscopic finding of pus in middle meatus, or 2) swelling mucosa at middle meatus or pus in nasopharynx in combination with abnormal plain film findings of maxillary sinus: total opacity or air-fluid level or mucosal thickening more than 4 mm in children and more than 5 mm in adults.

Bacteriological study

Methods of specimen (pus/secretion) collection from maxillary sinus for bacteriological study were performed through sterile techniques either by maxillary sinus tap (MST) through inferior meatus or endoscopically directed middle meatal swab (EDMMS). The specimens were inserted into the transporting media and sent for the microbiological culture within 30 minutes. Blood agar, chocolate agar, MacConkey agar and glycothiolate were used as media for the aerobic bacteriological culture and were incubated at the temperature between 35°C and 37°C. The cultures were read at 24 to 48 hours. Antimicrobial sensitivity was performed to test the susceptibility of bacteria to amoxicillin, amoxicillin/clavulanate, ampicillin/sulbactam, cefuroxime, cotrimoxazole, clindamycin, clarithromycin, ofloxacin, levofloxacin, gatifloxacin, cefpodoxime, cefaclor, cefixime, cefdnir, and azithromycin. Minimal inhibitory concentrations (MICs) of penicillin, azithromycin and cefuroxime for *S. pneumoniae*, *H. influenzae* and *M. catarrhalis* were determined using a broth micro dilution method. *S. pneumoniae* isolates are considered susceptible to penicillin if MICs were $\leq$0.06 µg/ml, intermediate if MICs were 0.12 to 1 µg/ml, and resistant if MICs were $\geq$2 µg/ml according to NCCLS 2000[11].

Effectiveness study

After the specimen collection, antibiotics were prescribed according to the Thai CPG of ABRS. Amoxicillin, 45-50 mg/kg/day for children and 2 grams

per day for adults, was initially prescribed. High dose amoxicillin, 80-90 mg/kg/day for children and 3 grams per day for adults, was prescribed for the patients who had a history of taking antibiotics within six weeks or aged less than 2 years or were in daycare attendance. In case of having a history of penicillin allergy, cotrimoxazole was prescribed with the dosage of trimethoprim 8 mg/kg for children and 160 mg for adults twice daily. The duration of the antibiotic was 7 days. A follow-up was scheduled at day seventh to assess the clinical responses. The antibiotic was changed according to the culture results. In case of negative bacteriological culture or the antimicrobial sensitivity was not performed, if there was clinically improvement, the same antibiotic was continued. In case of no improvement, amoxicillin/clavulanate was then prescribed. Those who had penicillin allergy, cefuroxime 30 mg/kg/day for children and 500 mg twice daily for adults were prescribed. The antibiotic was prescribed for seven and 14 days for those who did and did not improve, respectively. Second generation antihistamine was prescribed for allergic patients. Pseudoephedrine was given for those with nasal congestion. Compliance was assessed by counting the remaining drugs. The outcome was assessed according to the following criteria: 1) cure: substantially improved of symptoms and signs of ABRS, 2) failure: no change or worsen of ABRS symptoms and signs or needed additional antibiotics, and 3) indeterminate: could not assess the outcomes due to early discontinuation of antibiotics or needed additional antibiotics for other comorbidities unrelated to ABRS.

The following baseline characteristics were recorded: gender, age, duration of symptoms, a history of the prior use of antibiotic within six weeks, and symptoms and a history of chronic non-infective rhinitis. The results of bacteriological culture and antimicrobial sensitivity were collected. The effectiveness outcomes were assessed by the ENT doctors at the end of treatment (14 days of antibiotic treatment). Descriptive statistics were used for nominal outcomes.

This present study was approved by the Khon Kaen University Ethics Committee in human research, the Ethical Review Committee for Research Involving Human Research Subjects, Chulalongkorn University, the Royal Thai Army Medical Department Institutional Review Board, the Ethics committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, the Siriraj Institutional Review Board, Faculty of Medicine, Siriraj Hospital, Faculty of Medicine Research Ethics Committee, Chiang Mai University.

Results

A total of 113 cases, 45 males and 68 females, were enrolled with a mean age of 33.4 years (range 4-74 years). The average duration of ABRS symptoms was 11.7 days (range 2-30 days). Postnasal drip, discolored rhinorrhea, cough and headache were the first four common symptoms (Table 1).

There were 73 cases from the four university-hospitals in Bangkok, whilst 40 cases were from upcountry hospitals (Table 2). Only nine cases were not performed the bacteriological culture. Thus there were 104 cases left for the bacteriological analyses. Fifty-one specimens were collected by MST whilst 53 were performed by endoscopically directed middle meatal swab (EDMMS). Bacteriological cultures revealed positive in 63 cases (60.6%). Most of the specimens collected by MST showed single organism whilst EDMMS showed the same percentage of single organism and mixed organisms, 30.2% (Table 3).

Tables 4-6 show types of bacteria of each site of study and the methods of specimen collection. A total of 84 bacterial isolates were retrieved with *H. influenzae* found to be more common than *S. pneumoniae*, 25.0% versus 14.3%, followed by *S. aureus*, 9.5%. There were eight in 20 specimens of *H. influenzae* produced beta-lactamase. Eight specimens of *S. pneumoniae* were investigated for penicillin resistance, which were positive in six specimens. Table 5 shows that *S.* coagulase -ve were found more common in the EDMMS group than the MST group, seven versus one specimens.

Table 7 demonstrates the MICs of penicillin, cefuroxime and azithromycin against *S. pneumoniae* by using the interpretative criteria proposed by the National Committee for Clinical Laboratory Standards (NCCLS) 2000 at three hospitals. One in four specimens from the Srinagarind hospital showed *S. pneumoniae* resisted to penicillin and cefuroxime whilst one in three specimens resisted to azithromycin. All three specimens from the Ramathibodi hospital were penicillin-resistant *S. pneumoniae*. One specimen of *S. pneumoniae* from the resisted to both penicillin and cefuroxime.

Table 8 demonstrates the antimicrobial sensitivity of commonly used antibiotics against *S. pneumoniae*, *H. influenzae* and *M. catarrhalis*. *H. influenzae* had a tendency to be sensitive to amoxicillin/clavulanate, cefuroxime, azithromycin, clarithromycin, ofloxacin, levofloxacin, gatifloxacin,

Table 1. Demographic data of enrolled participants (113 cases)

Demographic characteristics	n (%)
Gender	
Males	45 (39.8)
Females	68 (60.2)
Mean age (range)	33.4 years (range 4-74 years)
Age ≤12 years	12 cases
Mean duration of symptoms	11.7 days (range 2-30 days)
History of chronic non-infective rhinitis	62 cases (54.9)
Symptoms	
Postnasal drip	97 (85.8)
Purulent rhinorrhea	91 (80.5)
Cough	74 (65.5)
Headache	62 (54.9)
Fever	45 (39.8)
Facial pain	40 (35.4)
Cacosmia	31 (27.4)
Hyposmia	29 (25.7)
Maxillary toothache	21 (18.6)
Nasal stuffiness	16 (14.2)
Anosmia	8 (7.1)
Earache/ear fullness	9 (8)
Numbers of bilateral rhinosinusitis	88 (77.9)
Previous use of antibiotics within 6 weeks	42 (37.2)

cefpodoxime and resistant to amoxicillin, cotrimoxazole, cefaclor, ampicillin/sulbactam, clindamycin. *S. pneumoniae* had a tendency to be sensitive to amoxicillin, amoxicillin/clavulanate, cefaclor, ampicillin/sulbactam, cefuroxime, ofloxacin, levofloxacin, gatifloxacin, cefpodoxime, cefixime, cefdinir and resistant to cotrimoxazole, clindamycin, azithromycin and clarithromycin.

Effectiveness of antibiotic prescription according to the Thai CPG for acute bacterial rhino sinusitis and antimicrobial sensitivity

All 113 patients received antibiotics at the first day of enrolment but there were only 87 cases that were prescribed for antibiotics according to the treatment protocol. Of those 87 cases, 83 cases visited the ENT clinics at the end of the first week. However there were only 75 cases who had antibiotic compliance at least 80%. There were 52% (95% CI 40.2-63.7%) of the 75 cases improved or cured at the end of the first week. Two cases were cured and were not prescribed antibiotics anymore. At the end of the first week, 101 cases were prescribed for antibiotics. However, the doctors complied with the treatment protocol for only 81 cases, 51 cases of which had the results of antimicrobial sensitivity whilst 30 cases were not investigated for antimicrobial sensitivity or the culture results revealed negatively. Among 45 cases who took antibiotics according to antimicrobial sensitivity and had antibiotic compliance at least 80%, 37 cases (82.2%, 95% CI 67.9-92%) were cured at the end of antibiotic treatment. Among 26 cases who had negative bacteriological culture results or were not investigated for antimicrobial sensitivity and were prescribed antibiotic according to the Thai CPG with antibiotic compliance at least 80%, 23 cases were cured (88.5%, 95% CI 69.8-97.6%).

Discussion

This is the first surveillance multi-centre study attempting to determine the bacteriology in suspected cases of ABRS in Thailand. It demonstrates the bacterial growth of ABRS resulting in 60.6% (95% CI: 51.0-69.4%) of all specimens being 84 bacterial isolates. The incidences of positive cultures by MST and EDMMS in this study were similar, 60.8% versus 60.4%. The percentage of positive cultures in this study were similar to previous studies[9,12]. Single organisms were found more than mixed organisms, 43.3% (34.2-52.9%) versus 17.3% (95% CI: 11.2-25.8%) which were

Table 2. Number of participants according to each site of study

Sites of study	n	Number of participants that bacteriological culture was not performed
Srinagarind Hospital*	26	0
King Chulalongkorn Memorial Hospital	26	2
Pramongkutklao Hospital	27	6
Ramathibodi Hospital	11	0
Siriraj Hospital	9	0
Maharaj Nakhon Chiang Mai*	10	1
Khon Kaen Hospital*	4	0
Total	113	9

* = upcountry hospitals

Table 3. Methods for collection of specimens sent for culture vs. culture results & sites of study

Sites of study (n of cases performed)	Positive culture		Single organism		Mixed organisms	
	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Srinagarind Hospital (26)	19 (73.0)	57.0-84.9	18 (69.2)	49.9-83.7	1 (3.8)	0.01-20.5
Maxillary sinus tap (24)	18 (75.0)		17 (70.8)		1 (4.2)	
EDMMS (2)	1 (50.0)		1 (50.0)		0	
King Chulalongkorn Memorial Hospital (24)	13 (54.2)	35.1-72.1	8 (33.3)	17.8-53.4	5 (20.8)	8.8-40.9
Maxillary sinus tap (0)	0	0	0			
EDMMS (24)	13 (54.2)		8 (33.3)		5 (20.8)	
Phramongkutklao Hospital (21)	17 (80.9)	50.6-85.3	8 (38.1)	17.8-53.4	9 (42.8)	21.1-57.4
Maxillary sinus tap (7)	4 (57.2)		3 (42.9)		1 (14.3)	
EDMMS (14)	13 (92.8)		5 (35.7)		8 (57.1)	
Ramathibodi Hospital (11)	7 (63.6)	35.2-85.0	7 (63.6)	35.2-85.0	0	
Maxillary sinus tap (11)	7 (63.6)		7 (63.6)		0	
EDMMS (0)	0		0		0	
Siriraj Hospital (9)	0		0		0	
Maxillary sinus tap (2)	0		0		0	
EDMMS (7)	0		0		0	
Maharaj Nakhon Chiang Mai Hospital (9)	6 (66.7)	35.1-88.3	3 (33.3)	11.7-64.9	3 (33.3)	11.7-64.9
Maxillary sinus tap (4)	1 (25.0)		1 (25.0)		0	
EDMMS (5)	5 (80.0)		2 (40.0)		3 (60.0)	
Khon Kaen Hospital (4)	1 (25.0)	3.4-71.1	1 (25.0)	3.4-71.1	0	
Maxillary sinus tap (3)	1 (33.3)		1 (33.3)		0	
EDMMS (1)	0		0		0	
Total (104)	63 (60.6)	51.0-69.4	45 (43.3)	34.2-52.9	18 (17.3)	11.2-25.8
Maxillary sinus tap (51)	31 (60.8)		29 (56.9)		2 (3.9)	
EDMMS (53)	32 (60.4)		16 (30.2)		16 (30.2)	

EDMMS = endoscopically directed middle meatal swab

similar to other bacteriological studies of ABRS in Thailand[7,8,10]. MST yielded single organism more than mixed organisms, 56.9% versus 3.9% whilst EDMMS yielded the same percentage of single organism and

Table 4. Types of bacteria according to each site of study

Sites of Study	Types of bacteria
Srinagarind Hospital	Single organism 18 cases *H. influenzae* (8 cases) - Beta-lactamase, non typeable 5 cases - Non beta-lactamase, non typeable 2 cases (Not tested for beta-lactamase 1 case) *S. pneumoniae* (4 cases) - Non-PNSSP 2 cases - PNSSP 2 cases Other bacteria (6 cases) - *Klebsiella pneumoniae* 1 case - *Neiserria meningitides* 1 case - *Streptococcus* group D 3 cases - Corynebacterium spp. 1 case Mixed organism 1 case - *Pseudomonas aeruginosa & Klebsiella pneumoniae*
King Chulalongkorn Memorial Hospital	Single organism 8 cases *H. influenzae* (4 cases) - Beta-lactamase, type B 1 case - Non beta-lactamase, non typeable 3 cases Other bacteria (4 cases) - *S. aureus* 1 case - *Pseudomonas* spp. 1 case - *S.* coagulase -ve 2 cases Mixed organisms 5 cases - *M. catarrhalis* (non beta-lactamase) *& S. aureus* 1 case - *H. influenzae* (non beta-lactamase, nontype B) *& S. aureus & P. aeruginosa* 1 case - *H. influenzae* (non beta-lactamase, nontype B) *& enterobacter spp.* 2 cases - *S. pneumoniae (PNSSP) & S. aureus & K. pneumoniae* 1 case
Phramongkutklao Hospital	Single organism 8 cases *H. influenzae* (2 cases) - Non beta-lactamase, non typeable 1 case - Beta-lactamase, type B 1 case *S. pneumoniae* (2 cases) (did not determine MIC but disk test showed sensitive to ampicillin) Other bacteria (4 cases) - *S. aureus 1* case - *S.* coagulase -ve 1 case - *Enterobacter cloacae* 1 case - *P. aeruginosa* 1 case Mixed organism (9 cases) - *S. pneumoniae* (not determine MIC & not perform disk test) & *H. influenzae* (non beta-lactamase, non typeable) *& S. aureus* - *S. pneumoniae* (not determine MIC & not perform disk test) *+ H. influenzae* (non-beta lactamase, non typeable) - *H. influenzae* (non beta-lactamase, non typeable) *+ Enterobacter* spp. - *M. catarrhalis (beta-lactamase) + Pseudomonas* spp. - *Streptooccus* group D-non enterococci *& Streptococcus viridans* - *Klebsiella pneumoniae & Pseudomonas aerugionosa* - *S. aureus + S.* coagulase *+ve- Streptococcus* group D-non enterococci *+ S.* coagulase *-ve- E. coli + S.* coagulase *-ve*

Table 4. cont.

Sites of Study	Types of bacteria
Ramathibodi Hospital	Single organism 7 cases *S. pneumoniae* (3 cases) - PNSSP 3 cases *H. influenzae* (2 cases) - Beta-lactamase, non typeable 1 case - Non beta-lactamase, non typeable 1 case Other bacteria (2 cases) - Enterobacter spp. 1 case - *Strept. viridans* 1 case Mixed organisms 0 case
Maharaj Nakorn Chiang Mai Hospital	Single organism 3 cases - *S.* coagulase *-ve* 1 case - *S. epidermidis* 1 case - *P. aeruginosa* 1 case Mixed organism 3 cases - Alpha *Streptococcus & Proteus & E. coli* - *S.* coagulase *-ve + Pseudomonas spp.* - *S. aureus + S.* coagulase *-ve*
Khon Kaen Hospital	Single organism 1 case *Enterococci* spp.

PNSSP = Penicillin-nonsusceptible *Streptococcus pneumoniae*

mixed organisms (30.2%). One possible reason of the high incidence of mixed organisms found in EDMMS is the contamination of normal flora during specimen collection, for example *Staphylococcus* coagulase negative is found in the EDMMS group more than the MST group, seven versus one specimens. *Corynebacterium* spp. was also found only in the EDMMS group. These two bacteria are the list of normal flora for the middle meatus[13,14].

H. influenzae was the most common bacteria more than *S. pneumoniae*, 25% (95% CI 16.9-35.3%) versus 14.3% (95% CI 8.2-23.5%). There was a high incidence of beta-lactamase producing *H. influenzae* in this present study with the incidence of eight in 20 cases (40%, 95% CI 21.8-61.4%). The results of high incidences of *H. influenzae* and beta-lactamase strain were the same as those in previous studies in Thailand since 1999 (Table 9) with the incidence of *H. influenzae* between 20-72.7%[7-10]. All of them were non tapeable with type B in only one case. A meta-analysis of study of bacteriology in ABRS showed the same incidences of *S. pneumoniae* and *H. influenzae* being 27.2 versus 26.6% per isolate and 32.7 versus 31.6% per patient; *S. aureus*, 9.7% per isolate; and *M. catarrhalis*, 8.2% per isolate being the third and fourth most common bacteria[12]. Our present study demonstrates the incidences of *S. aureus* 9.5% (95% CI: 4.7-17.9%) and *M. catarrhalis* 2.4% (95% CI 1.5-12.0%). *M. catarrhalis* is usually an important cause of upper respiratory tract infections in otherwise healthy children and elderly people[15]. The low incidence of *M. catarrhalis* may be due to participants' age in this present study which most of them were not within the extreme ages.

Nowadays, drug resistant *S. pneumoniae* is another concern for the antibiotic treatment of ABRS. Although there were only eight bacterial isolates tested for the MIC of penicillin against *S. pneumoniae* in this study, we found the penicillin-nonsusceptible *S. pneumoniae* (PNSSP) in five isolates which showed that there was a trend of high incidence of PNSSP in ABRS. We could not compare the incidence of PNSSP with the previous studies in ABRS in Thailand because there were no previous studies. However the incidence of PNSSP from patients with respiratory tract infections in four hospitals in Bangkok was reported to increase from 63% in 2002-2003 to 69% in 2004-2005[16].

A study on antimicrobial sensitivity of commonly used antibiotics is important since it will guide the clinicians to choose appropriate antibiotics for ABRS. Although the antimicrobial sensitivity of commonly used antibiotics against *H. influenzae*, *S. pneumoniae* and *M. catarrhalis* was performed in this

Table 5. Types of bacteria and methods of specimen collection

Types of organism	n	% (95% CI)	MST	EDMMS
H. influenzae	21	25 (16.9-35.3)	10	11
Beta-lactamase positive, non typeable	7			
Beta-lactamase negative, non typeable	12			
Beta-lactamase positive, type B	1			
Not tested for beta-lactamase	1			
S. pneumoniae	12	14.3 (8.2-23.5)	8	4
Non-PNSSP	2			
PNSSP	6			
Not tested	4			
M. catarrhalis	2	2.4 (0.5-7.3)		2
Beta-lactamase negative	1			
Beta-lactamase positive	1			
S. aureus	8	9.5 (4.7-17.9)		8
S. coagulase *+ve*	2	2.3 (0.2-8.8)	1	1
S. coagulase *-ve*	8	9.5 (4.7-17.9)	1	7
S. epidermidis	1	1.2 (0.01-7.1)		1
P. aeruginosa	5	6.0 (2.2-13.5)	2	3
Pseudomonas spp.	3	3.6 (1.2-8.9)		3
K. pneumoniae	4	4.8 (1.5-12.0)	3	1
Enterobacter spp.	4	4.8 (1.5-12.0)	1	3
Alpha-Streptococcus	1	1.2 (0.01-7.1)		1
S. viridans	2	2.3 (0.2-8.8)	2	0
Streptococcus group D	5	6.0 (2.2-13.5)	3	2
Enterobacter cloacae	1	1.2 (0.01-7.1)		1
N. meningitidis	1	1.2 (0.01-7.1)	1	
E. coli	2	2.3 (0.2-8.8)		2
Corynbacterium spp.	1	1.2 (0.01-7.1)		1
Proteus spp.	1	1.2 (0.01-7.1)		1
Total	84	0	32	52

Total n for MST = 51 versus EDMMS = 53

Table 6. Three main pathogens according to each site of study

Sites of Study	*S. pneumoniae* (8)		*H. influenzae* (20)		*M. catarrhalis* (2)	
	Non PNSSP	PNSSP	Beta-lactamase	Non Beta-lactamase	Beta lactamase	Non Beta-lactamase
Srinagarind Hospital (26)	2	2	5	2	0	0
King Chulalongkorn Memorial Hospital (26)	0	1	1	4	1	0
King Mongkutklao Hospital (27)	Not tested	Not tested	1	5	0	1
Ramathibodi Hospital (11)	0	3	1	1	0	0
Maharaj Nakhon Chiang Mai Hospital (10)	0	0	0	0	0	0
Khon Kaen Hospital (4)	0	0	0	0	0	0
Total	2	6	8	12	1	1

PNSSP = Penicillin-Nonsusceptible *Streptococcus pneumoniae*, four specimens of *S. pneumoniae* from King Mongkutklao were not investigate for MIC, one specimen of *H. influenzae* was not investigated for beta-lactamase activity

Table 7. Minimal inhibitory concentration (MIC) of penicillin, cefuroxime and azithromycin against *S. pneumoniae*

Sites of study	MIC of penicillin (microgram/ml)	MIC of cefuroxime (microgram/ml)	MIC of azithromycin (microgram/ml)	Types of antibiotics that *S. pneumoniae* resisted to
Srinagarind Hospital	0.750	0.380	Not done	Penicillin, cefuroxime
	0.094	0.016	0.25	Not resist
	0.094	0.190	16	Azithromycin
	0.006	0.016	0.75	Not resist
King Chulalongkorn Memorial Hospital	1.500	2	Not done	Penicillin, cefuroxime
Ramathibodi Hospital	2	Not done	Not done	Penicillin
	1	Not done	Not done	Penicillin
	2	Not done	Not done	Penicillin

Table 8. Antimicrobial sensitivity of commonly used antibiotics against three main pathogens

Types of antibiotics	*S. pneumoniae* (n = 12)	*H. influenzae* (n = 21)	*M. catarrhalis* (n = 2)
Amoxicillin	S:6 (NT:6)	S:1, I:1, R:9	R:1 (NT:1)
Cotrimoxazole	S:3, I:1, R:3 (NT:5)	S:8, R:3 (NT:9)	S:1 (NT:1)
Amoxicillin/clavulanate	S:3 (NT:9)	S:18, I:1, R:1 (NT:1)	S:1 (NT:1)
Cefaclor	S:3 (NT:9)	S:7, I:2, R:2 (NT:10)	(NT:2)
Ampicillin/sulbactam	S:4 (NT:8)	S:16, R:4 (NT:1)	S:1 (NT:1)
Clindamycin	S:5, R:3 (NT:4)	S:1, I:1, R:3 (NT:16)	(NT:2)
Azithromycin	S:2, R:5 (NT:5)	S:12, I:1 (NT:8)	(NT:2)
Clarithromycin	S:2, R:6 (NT:4)	S:13, I:1, R:1 (NT:6)	(NT:2)
Ofloxacin	S:7 (NT:5)	S:14 (NT:7)	(NT:2)
Levofloxacin	S:8 (NT:4)	S:16 (NT:5)	(NT:2)
Gatifloxacin	S:4 (NT:8)	S:11 (NT:10)	(NT:2)
Cefuroxime	S:4 (NT:8)	S:17, IR:1 (NT:3)	R:1 (NT:1)
Cefpodoxime	S:3 (NT:9)	S:11 (NT:10)	(NT:2)
Cefixime	S:3 (NT:9)	S:2 (NT:19)	(NT:2)
Cefdinir	(NT:12)	S:1 (NT:20)	(NT:2)

S = sensitive; I = intermediate resist; R = resist; NT = not tested

present study, there were only few isolates tested. Therefore the results of the antimicrobial sensitivity could only denote the trend of sensitivity. *H. influenzae* had a tendency to be sensitive to amoxicillin/clavulanate, cefuroxime, azithromycin, clarithromycin, ofloxacin, levofloxacin, gatifloxacin, cefpodoxime, cefixime, cefdinir and resistant to amoxicillin, cotrimoxazole, cefaclor, ampicillin/sulbactam and clindamycin. The antimicrobial sensitivity against *S. pneumoniae* showed a tendency to be sensitive to amoxicillin, amoxicillin/clavulanate, cefaclor, ampicillin/sulbactam, cefuroxime, ofloxacin, levofloxacin, gatifloxacin, cefpodoxime, cefixime, cefdinir and resistant to cotrimoxazole, clindamycin, azithromycin and clarithromycin. The interpretation of the results of antimicrobial sensitivity has to be interpreted with caution. For example, amoxicillin was shown to be sensitive to *S. pneumoniae*, six out of six isolates tested. However other six isolates were not tested and the MIC of penicillin against *S. pneumoniae* showed that there were five out of eight isolates resisted to penicillin.

We also conducted a before-after clinical trial to examine the effectiveness of antibiotic prescription according to the Thai CPG guidelines and antimicrobial sensitivity. The outcomes revealed the cure rate of the group following the Thai CPG was 84.6% (95% CI 65.1-95.6%), whilst the cure rate of the culture directed antibiotics group was 88.5% (95%CI 69.8-97.6%). This finding showed that the effectiveness of antibiotic

Table 9. Previous studies of bacteriological culture in acute rhinosinusitis in Thailand since the year 1986

Authors/sites of study	Year of Study	Participants (Number of cases/ number of sinus aspirates)	Methods of specimen collection	Results	Note
Fooanant et al. / Maharaj Nakorn Chiang Mai[6]	1986-1987	Adults- Acute 6/6	MST	Acute - Growth 5/6 (83.3%) (7 bacterial isolates) - *S. pneumoniae* 4/7(57.1%) - *H. influenzae* 1/7(14.3%)	- Not study beta-lactamase activity of *H. influenzae* - *M. catarrhalis was not found*
Prakunhangsit et al./ Ramathibodi Hospital[7]	1992-1993	Acute rhinosinusitis, age 13- 65 years (40/45)	MST	- Growth 36/45 (80%) (48 bacterial isolates) (aerobe 68.9%, anaerobe 2.2%, aerobe + anaerobe 8.9%) - *H. influenzae* 20/48 (41.7%) - *S. pneumoniae* 5/48 (10.4%) - *Streptococcus* spp. 10/28 (20.8%)	-*M. catarrhalis was not found* - Beta-lactamase producing *H. influenzae* 4/20 (20%)
Kongkaew et al./ Ramathibodi Hospital[8]	1998-1999	Acute & subacute rhinosinusitis, ages 16-65 years (39/47)	MST	Acute & subacute - Growth 74.47% (35/47) (53 bacterial isolates) (aerobe 55.32%, anaerobe 14.89%, aerobe + anaerobe 4.26 %) - *H. influenzae* 11/53 (20.8%) - *S. pneumoniae* 6/53 (11.3%) - *Streptococcus* spp. 9/53 (17.0%)	-*M. catarrhalis was not found* - Beta-lactamase producing *H. influenzae* 8/11 (72.7%) - Not study drug-resistant *S. pneumoniae*
Charoencharsri et al./ Siriraj Hospital[9]	1999-2000	Adults - Acute rhinosinusitis (48/48)	MST	- Growth 64.6% (31/48) (60 bacterial isolates) (aerobes 50%, anaerobes 4.2%, aerobes + anaerobes 10.4%) - *H. influenzae* 34.3% (12/35) - *S. pneumoniae* 17.1% (6/35) - *Streptococcus* spp. 17.1% (6/35)	-Not take antibiotics 48 hours - Beta-lactamase *H. influenzae* 50% -*M. catarrhalis was not found*
Moungthong et al./ Phramongkutklao Hospital[10]	2002-2003	Adults - Acute rhinosinusitis (44/44)	MST	Growth 77.2% (34/44)(44 bacterial isolates)(aerobes 70.4%, anaerobes 2.3%, aerobes + anaerobes 4.5%) - *H. influenzae* 29.5% (13/44) - *S. pneumoniae* 9% (4/44) - *M. catarrhalis* 2.3% (1/44)	Beta-lactamase producing *H. influenzae* 23.1% (3/13)

MST = Maxillary sinus tap

prescription according to the Thai CPG of ABRS and culture-directed were comparable. However, since ABRS can be self-resolved nearly 60-70%, the results of this finding may not be robust due to a small sample size.

The limitation of this study is the small sample size. The sample size of this study was originally estimated based on the incidence of *H. influenzae*, 29.5% from the previous study[10]. So it should be 320 cases. Another limitation is the compliance to the protocol. Not all the isolates of *H. influenzae* and *S. pneumoniae* were tested for beta-lactamase activity, MIC levels of specified antibiotics and antibiotic sensitivity. Although the effectiveness of antibiotic prescription according to the Thai CPG of ABRS and culture-directed antibiotics prescription were comparable, this study was not a randomised controlled trial and there were many cases that lost to follow-up and did not follow the protocol. Thus multi-centre surveillance study of ABRS in Thailand should be further conducted with good clinical practice adherence.

Conclusion

This study showed that *H. influenzae* was the most common bacteria in ABRS, followed by *S. pneumoniae* and *S. aureus*. There was a trend for *H. influenzae* to produce beta-lactamase and *S. pneumoniae* to be resistant to penicillin. EDMMS yielded mixed organisms more than MST, which might be due to contamination of normal flora in the nasal cavities. In case of empirical treatment, antibiotic prescription should follow the evidence-based CPG of ABRS.

What is already known on this topic ?

The most common of bacteria in ABRS in western countries was reported to be *S. pneumoniae*. In contrary the previous studies in Thailand since 1992 have shown that *H. influenzae* was more common. However these studies were conducted only in Bangkok and were single site study with a small sample size.

What this study adds ?

This multi-center surveillance study of ABRS confirms the higher incidences of *H. influenzae* in Thailand than *S. pneumoniae*. There is a trend of high incidence of PNSSP and beta-lactamase producing *H. influenzae*. Antibiotic prescription according to the Thai CPG for ABRS seems to be comparable with culture-directed antibiotic prescription.

Acknowledgement

This study was funded by the Clinical Research Collaboration Network, Thailand and supported by The Center of Cleft Lip-Cleft Palate and Craniofacial Deformities, Khon Kaen University in Association with Tawanchai Project (Tawanchai Cleft Center).

Potential conflicts of interest

None.

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การศึกษาการเฝ้าระวังเชื้อแบคทีเรียในโรคไซนัสอักเสบชนิดเฉียบพลันที่เกิดจากเชื้อแบคทีเรียในประเทศไทยและการตอบสนองทางคลินิกต่อยาต้านจุลชีพตามผลการเพาะเชื้อ

สงวนศักด์ ธนาวิรัตนานิจ, สุพินดา ชูสกุล, กรีฑา ม่วงทอง, ธงชัย ลักษมีจันทร์พร, พงศกร ตันติลีปีกร, สุปราณี ฟูอนันต์, ทรงกลด เอี่ยมจตุรภัทร, นาตยา มาคเชนทร์, พิพัฒน์ ศรีเบญจลักษณ์, เสกสันต์ ชัยนันท์สมิตย์, สายสวาท ไชยเศรษฐ, ฉวีวรรณ บุนนาค

วัตถุประสงค์: เพื่อศึกษา 1) ชนิดของเชื้อแบคทีเรียและความไวของยาต้านจุลชีพที่ใช้บ่อยสำหรับโรคไซนัสอักเสบชนิดเฉียบพลันที่เกิดจาก เชื้อแบคทีเรีย (ABRS) ในประเทศไทย, 2) ศึกษาประสิทธิผลของการใช้ยาต้านจุลชีพตามผลของความไวของยาต้านจุลชีพ, 3) ศึกษาประสิทธิผลของการใช้ยาต้านจุลชีพตามแนวทางการดูแลรักษาโรคไซนัสอักเสบชนิดเฉียบพลันที่เกิดจากเชื้อแบคทีเรียของประเทศไทย

วัสดุและวิธีการ: ทำการศึกษาแบบพรรณาและทดลองในโรงพยาบาลตติยภูมิ 7 แห่งในประเทศไทย ทำการเพาะเชื้อจากไซนัสด้วยการเจาะ maxillary sinus หรือการป้ายบริเวณ middle meatus โดยใช้กล้องส่องจมูกในผู้ป่วยที่วินิจฉัย ทางคลินิกว่าเป็นโรคไซนัสอักเสบชนิดเฉียบพลันที่เกิดจากเชื้อแบคทีเรียทำการทดสอบความไวของยาต้านจุลชีพ และให้ยาต้านจุลชีพตามผลความไวของยาต้านจุลชีพ หรือตามแนวทางการดูแลรักษาโรคไซนัสอักเสบชนิดเฉียบพลันที่เกิดจากเชื้อแบคทีเรียของประเทศไทย

ผลการศึกษา: มีผู้ป่วยเข้าร่วมการศึกษาระหว่างเดือนสิงหาคม พ.ศ. 2549 ถึง เดือนเมษายน พ.ศ. 2550 จำนวน 113 ราย มีผู้ป่วยที่ศึกษาเชื้อแบคทีเรีย 104 ราย พบว่าเพาะเชื้อขึ้น 0.6 (95% CI 51.0-69.4%) เชื้อที่พบมากที่สุดได้แก่ เชื้อ H. influenzae (25.0%, 95% CI 16.9-35.3%) รองลงมาคือ S. pneumoniae (14.3%, 95% CI 8.2-23.5%) และ S. aureus (9.5%, 95% CI 4.7-17.9%) ตามลำดับในขณะที่เชื้อ M. catarrhalis พบเพียง 2.4% (95% CI 0.5-7.3%) เชื้อ S. pneumoniae ได้รับการหาค่า MIC ของยา penicillin 8 จาก 12 ตัวอย่าง พบว่าดื้อต่อยา penicillin 5 ตัวอย่าง พบว่าเชื้อ H. influenzae สร้าง beta-lactamase ทั้งสิ้น 8 ใน 20 ตัวอย่าง เชื้อ H. influenzae มีแนวโน้มที่ไวต่อยา amoxicillin/clavulanate, cefuroxime, cefpodoxime, azithromycin, clarithromycin, ofloxacin, levofloxacin, gatifloxacin ในขณะที่เชื้อ S. pneumoniae มีแนวโน้มไวต่อยา amoxicillin/clavulanate, cefaclor, ampicillin/sulbactam, cefuroxime, ofloxacin, levofloxacin, gatifloxacin, cefpodoxime, cefixime, cefdinir สำหรับประสิทธิผลของการรักษาไซนัสอักเสบโดยการใช้ยาต้านจุลชีพ ตามแนวทางการดูแลผู้ป่วยไซนัสอักเสบชนิดเฉียบพลันในประเทศไทย ได้ผลพอๆ กับการให้ยาต้านจุลชีพตามความไวของยาต้านจุลชีพ, 88.5% (95% CI 69.8-97.6%) และ 82.2% (95% CI 67.9-92%) ตามลำดับ

สรุป: พบเชื้อ H. influenzae มากที่สุดในผู้ป่วยไทยที่เป็นโรคไซนัสอักเสบชนิดเฉียบพลันที่เกิดจากเชื้อแบคทีเรียตามด้วยเชื้อ S. pneumoniae และ S. aureus มีอุบัติการณ์ของ beta-lactamase producing H. influenzae และ penicillin non-susceptible S. pneumoniae สูง