

SUMMARY AND CONCLUSION

For many years, the aerobic Gram-negative diplococcus "Branhamella catarrhalis" was described as a species within the genus Neisseria and was known as Neisseria catarrhalis.

In 1970, this organism was transferred to a new separate genus "Branhamella" named in honor of a distinguished American microbiologist : Sarah Branham.

The new generic name was proposed on the basis of comparison of DNA base content between B. catarrhalis and other Neisseria species. Also, other genetic, biochemical and serologic properties support separate classification of this organism.

In 1984, Bovre reclassified B. catarrhalis as a subgenus of Moraxella. This was based on their similar guanine and cytosine base content of DNA which is 40-45 moles percent.

Reports published during the last decade have changed the earlier commonly held view of B. catarrhalis as merely being a harmless commensal of the upper respiratory tract. A pathogenic role of this bacterium has been suggested in several types of infections including

AOM, maxillary sinusitis, bronchopulmonary infections, laryngitis, meningitis, septicemia, endocarditis and even cellulitis. This suggested pathogenic role has been based on microscopic and pure culture finding only. Serological support for such pathogenic role, however, was limited to few reports.

Although B. catarrhalis was thought to be uniformly susceptible to penicillin, several studies, since 1977, have documented that clinically significant isolates of this bacterium were resistant to penicillin by virtue of their ability to produce beta-lactamase enzyme. The proportion of B. catarrhalis strains elaborating this enzyme seems to be universally increasing since 1980. Some centers are now reporting prevalence rates as high as (87%).

In AOM, which is one of the most common diseases of childhood, earlier reports indicated that B. catarrhalis was found in the middle ear exudate of 4-9% of cases. In recent reports from several centers, after 1980, this figure increased to be as high as 10-27%. Serological studies further supported the pathogenic role of B. catarrhalis in AOM by showing local and systemic antibody responses to this organism in children who had culturable B. catarrhalis in their middle ear fluids of AOM.

The increasing incidence of B. catarrhalis in AOM and the emergence of beta-lactamase-producing strains, prompted us to determine the prevalence of this organism in middle ear fluid of children with AOM in Benha locality. Serological examination for antibodies (agglutinins) to B. catarrhalis was also done to be correlated with its isolation as an evidence for its pathogenic role in such cases. Furthermore, the isolated strains were tested for beta-lactamase production and, then in vitro susceptibility testing of all isolated strains to selected antimicrobial drugs was performed.

Three hundred children (up to 12 years) of varying age and sex, with a diagnosis of AOM were the subject of this study. Patients who received antibiotics within the previous week of their visit or who had had an episode of otitis media during the previous month were excluded from the study.

In bacteriological study of the middle ear fluid of these children, B. catarrhalis was recovered in 18 cases (6%). Twelve (66.7%) out of these 18 isolates were in pure culture while 6 (33.3%) were mixed with other pathogens.

B. catarrhalis together with H. influenzae were found to be the fourth in frequency (6% for each) after

Strept. pyogenes (22%), Staph. aureus (17%) and Strept. pneumoniae (13%). Next to B. catarrhalis in frequency came Proteus species (5.7%), E. coli (4.3%), Pseudomonas aeruginosa (4%), Staph. epidermidis (4%), Diphtheroid (4%) and Klebsiella pneumoniae (3%). The total isolation rate of Gram-negative bacilli was (17%) while no growth was found in 20% of cases. This may represent anaerobic infection, or infection with virus, mycoplasma or chlamydia which we did not look for in this study.

The majority (16 strains : 88.9%) of B. catarrhalis strains isolated in this study were recovered from children below the age of 5 years. In older children (5-12 years) the organism was isolated from only 2 cases (11.1%). This may point to a developed immunity to B. catarrhalis by the age of 5 years.

All cases of AOM with B. catarrhalis in this study had a unilateral disease, and eleven (61%) of them had upper respiratory tract infection while, seven (39%) had lower respiratory tract infections, shortly before the attack of AOM. The difference between these two figures may reflect the importance of upper respiratory tract infections in the etiology of AOM with B. catarrhalis.

Also, the majority of B. catarrhalis strains in this study were isolated during the winter months (10

strains : 55.6%). The rate of isolation declined during spring (2 strains only : 11.1%). No isolate was recovered during summer but, during autumn the rate of isolation rised again (6 strains : 33.3%). This seasonal fluctuation indicates that B. catarrhalis is most prevalent during the cold months of the year. This may be due to high prevalence of respiratory tract infections, especially those of viral etiology which may damage mucous membrane and thereby promote colonisation by B. catarrhalis. In a similar way the absence of isolates in summer may be interpreted as a reflection of the reduced prevalence of respiratory infections at this time.

From the clinical point of view, fourteen out of 18 cases (77.8%) of AOM with B. catarrhalis had whitish mucopurulent discharge, while four cases only (22.2%) had mucopurulent yellowish discharge. In the latter cases B. catarrhalis was mixed with other pathogens. This may indicate that AOM with B. catarrhalis is usually accompanied with whitish mucopurulent ear discharge.

On the other hand, none of the patients with AOM due to B. catarrhalis was acutely ill. Most of the patients had fever $\leq 38^{\circ}\text{C}$ with mild or moderate earache. This may indicate that AOM due to B. catarrhalis is a milder

disease than that associated with other major otitis pathogens.

The results of the serological study in the present work showed a good correlation with the results of isolation and this gave a further support to the pathogenic role of B. catarrhalis in AOM. Antibodies (agglutinins) to B. catarrhalis were found in sera of children from whose middle ear fluid B. catarrhalis had been isolated either alone or with other pathogens. However, an increase in the antibody titers between the acute and convalescent phase sera was observed only in children from whose middle ear fluid B. catarrhalis was isolated in pure culture.

On the other hand, antibodies to B. catarrhalis were also found in control sera of children from whose middle ear fluid bacteria other than B. catarrhalis were isolated. However, there was no change in the antibody titers between the acute and convalescent-phase sera and the overall levels were lower than in the children who had otitis media with pure culture of B. catarrhalis.

It is noteworthy to mention that both the presence and the level of such antibodies were found to depend on the age of the child. In children younger than one year, such antibodies were undetectable in the acute phase sera, but reached reciprocal titer of 40 in, only,

the convalescent phase sera of children who had AOM with pure culture of B. catarrhalis.

Out of the 18 B. catarrhalis strains isolated in this study, 11 strains (61%) were found to be beta lactamase-positive while, 7 strains (39%) were beta lactamase-negative. On the basis of in vitro susceptibility tests and comparison of individual and geometric mean MICs of the antimicrobial drugs included in this study, it was found that: (1) nearly all beta-lactamase-positive strains of B. catarrhalis, in this study, were resistant to penicillin G, ampicillin and amoxycillin while, beta lactamase negative strains were susceptible to them; (2) both beta-lactamase-positive and negative strains of B. catarrhalis in this study were susceptible to amoxycillin-clavulanate, erythromycin, cefotaxime, cephradine and TMP-SMX. These drugs showed a little change in activities against both beta-lactamase-positive and negative strains. So they are considered the most active drugs in vitro; (3) the combination of clavulanic acid with amoxycillin was very effective in vitro.

It is noteworthy to mention that two exceptions were observed in this work regarding the susceptibility of beta-lactamase-positive strains of B. catarrhalis for penicillin G and ampicillin. The first exception

comprises one strain which was susceptible to penicillin G (MIC : 1.56 mg/L) while the second comprises two strains which were susceptible to ampicillin (MIC : 0.2 mg/L). These findings may suggest that beta-lactamase production in B. catarrhalis does not predict the degree of the in vitro sensitivity to beta-lactame antibiotics . The significance of these results for the in vivo susceptibility require more work to be elucidated.