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Letter to Editor

Bacteriological Pattern of Cystic Fibrosis Patients in a Tertiary Care Centre in Saudi Arabia

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Dear Sir,

Pseudomonas colonization of multi resistant type have contributed significantly to early mortality of cystic fibrosis (CF), which is the most common autosomal recessive disease in Caucasians[1]. In small children, the type of bacteria that are most frequently involved in the lower respiratory tract infection are staphylococcus aureus (staph), Hemophilus influenza (H flue) and later Pseudomonas aeruginosa (Pseud), which is considered the most common bacterial pathogen responsible for severe inflammatory process and chronic lung disease – rarely can be eradicated once CF patients become chronically infected[2]. This inflammation induces a phenotypic shift from non-mucoid to mucoid type by producing alginate biofilm in the endobronchial layer of the respiratory tract[3]. The incidence of CF in Saudi Arabia was reported to be in 4243 children[4]. Epidemiological and genetic data have been described in details in many Gulf countries[5-7], but no microbiological data has been described before in Arabian countries. In this report we present the detailed microbiological data of the largest CF population in the Gulf area and discuss its relation to mortality.

CF patients' records during the period from October 1994 to November 1998 were reviewed. Respiratory culture includes sputum in children who were able to give such sample or nasopharyngeal aspirate in smaller children, are taken routinely on initial diagnosis and every clinic visits thereafter. Follow up ranges from 1-3 month according to clinical condition. A total of ninety-six CF patients were diagnosed. Eighty-one (84%) CF patients are alive, fifteen (16%) died. Fifty (52%) were males and 46 (48%) were females. Age at diagnosis 2.9 ± 3.5 years. The mean follow up period was 3.24 ± 2.8 years with a range of 0.01 – 13.8 years. The most common bacteria grown from the first culture samples were: Pseudomonas aeruginosa (Pseud) in 42 (44%) patients, H. flue in 16 (16.6%), Staph in 15 (15.6%), Streptococcus pneumonia (strept) in 6 (6%), Methicillin resistant staph aureus (MRSA) in 4 (4%), Branhamella Cattarrhales (Branh) in 6 (6%), and Respiratory Syncytial viruses (RSV) in 1 (1%) Table 1.

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Table 1. **Culture results of CF patients (Total 94 patients)**

Organism	1st culture No.(a) (94)	1st culture cultures (%)	Follow up culture No. (b) (84)	Follow up culture (%)
Staphylococcus aureus	15	15	17	16
Hemophilus influenza	16	17	14	13
Pseudomonas aeruginosa	42	44	9	7
Streptococcus pneumonia	6	6	17	16
Methicillin resistant staph.aureus	4	4	6	6
Brnahamella catarrhales	6	6	13	13
Gram –ve rods	3	3	5	5
Gram +ve cocci	3	3	2	2
Virus	1	1	1	1
Other	1	1	13	12

Table 2. **Mortality data in relation to Bacteriological pattern (Total 94 patients)***

Antibiotic	Alive (80)	Dead (14)	P Value
Date of first culture (a)	0.7 ± 2	1.5 ± 3	0.1
Date of first Pseud (b)	1.2 ± 2	1.9 ± 3	0.4
Date of first Mucoid (c)	1.8 ± 3	2.8 ± 2	0.3
Date of R-Genta (d)	1.1 ± 0.7	3.4 ± 2	0.04
No. of resistance to Ampicillin (e)	65	15	0.07
No. of +ve Pseud (f)	47	14	0.01
No. of +ve mucoid Pseud (g)	23	8	0.06
No. of +ve MRSA (h)	3	3	0.02
No. of resistance to Gentamycin (I)	13	9	<0.0001
No. of resistance to Amikacin (j)	3	7	0.0002
No. of resistance to Ceftazidime (k)	3	6	<0.0001
No. of resistance to Ciprofloxacin (L)	1	5	<0.0001
No. of resistance to Piperacillin (m)	4	5	0.0005
No. of resistance to Imipenum (n)	1	2	0.01

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* *= All patient who had culture at last follow up visit*

(a) = All dates in years – Date of first positive culture from the diagnosis

(b) = Date of first positive culture of Pseudomonas aeruginosa

(c) = Date of first positive culture of mucoid Pseudomonas aeruginosa

(d) = Date of development of resistance to Gentamycin from the time of diagnosis

(e) = Number of patients with pseudomonas aeruginoa cultures that are resistant to Ampicillin expressed in number of patients with positive culture/total number of patients in the same category (either alive or dead categories)

(f) and (g)= number of patients with positive Pseudomonas or mucoid Pseudomonas culture/total number of patients in the category

(h) = Number of patients with positive Methicillin resistant staphylococcus aureus

(i) = Number of patients that are resistant to Gentamycin

(j) = Number of patients that resistant to Amikacin

(k) = Number of patients that are resistant to Ceftazidime

(l) = Number of patients that are resistant to Ciprofloxacin

(m) = Number of patients that are resistant to Piperacillin

(n) = Number of patients that are resistant to Imipenum

Follow up culture within 1-6 month of treatment showed doubling the number of Branhamella culture to 13 (13%), and an increase in the number of MRSA cultures to 6 (6%) which may point to cross contaminations between patients seen in the same clinic (Table 1). Development of resistant Pseud. Gentamycin (Genta) had the shortest duration of 2 ± 3 years after diagnosis, Amikacin (Amika) in 3.4 ± 0.1 years, Ceftazidime (Cefta) 3 ± o.1 years, Ciprofloxacin (Cipro) in 3.4 ± 2 years, Piperacillin (Pipera) 4 ± 2 years, Imipenum 4 ± 2 years and Development of resistance of MRSA to antibiotics except Vancomycin (Vanco) was 2 ± 3 years. Factors associated with progressive lung disease and early mortality of CF patients were (Table 2): Date of development of Pseud resistance to Genta (P value=0.04), Date of resistance to Ampicillin (P=0.07), positive (+ve) culture of Pseud. (P=0.01), +ve culture of mucoid Pseud. (P=0.06), +ve MRSA (P=0.02). Other factors contributed to early mortality were: Development of resistance to the following antibiotics: Genta (P=<0.0001), Amika (P=0.0002), Cefta (P=<0.0001), Cipro (P=<0.0001), Pipera (P=0.0005) and Imipenum (P=0.01).

Treatment of Pseud differs from one CF center to another, and many centers only treat it when there is acute pulmonary excerbation[3]. One CF center in Copenhagen[8], has introduced a treatment regimen for chronic Pseud colonization, which was found to improve survival. This treatment regimen consisted of: (A) Elective IV antibiotics treatment for 14 days every 3 month regardless of the clinical condition of the patient. Daily colistin inhalation and oral Ciprofloxacin prophylaxis in between IV courses, (2) group of isolation patients with known Pseud colonization from those without in different wards during admission, different clinics during outpatient visits, during social gathering and during summer or winter camps to prevent cross infection. With this arrangement, they found a decrease in the annual incidence of chronic Pseud colonization from 16% to 2%, and the time of acquisition of first Pseud to development of chronic colonization is approximately one year to almost 4 years[8]. Unfortunately, this arrangement could not be followed in our center due to bed limitation and difficulty in applying group isolation. Our study has shown increase in the number of Pseud colonization even after antibiotic treatment and increase in MRSA and Branhamella colonizations. Our study has also shown early development of multi-resistant Pseud to different antibiotics and significant relation to mortality (Table 2). One hypothesis that explains the development of multi resistant bacteria is the use of long-term continuous Gentamycin nebulization treatment to prevent frequent hospitalization for IV antibiotics, especially for patients, which are coming from a remote area where specialized centers are lacking[9]. Our study has shown significant relationship of MRSA colonization to mortality (P=0.02)[2]. Other factors that may have contributed to mortality but not mentioned in our study are: early diagnosis, weight for height and weight for age. Increase in MRSA and Branhamella colonization during follow up treatment could be explained by cross infection, as our patients are not isolated.

CONCLUSION

Early development of Pseud colonization of multi resistant types have contributed significantly to early mortality. Group isolation should be encouraged in CF centers. Early treatment of chronic Pseud colonization should be adopted to improve survival.

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