Mucoviscidosis (Cystic Fibrosis of the Pancreas) in Bahrain, Arabian Gulf

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ABSTRACT

We report on 8 proved and 2 probable cases of mucoviscidosis diagnosed in Salmaniya Medical Centre over a period of 62 months. Six of the ten cases were anaemic, 4 were hypoproteinaemic and 2 had anasarca. In all instances there was history of siblings dying in early infancy from pulmonary and gastrointestinal problems. The two probable cases, on whom sweat chloride tests could not be carried out because of non-availability of the test kit at the time, were siblings of our proved cases.

Although cystic fibrosis has been described in all racial and geographical groups, this, the most common of the inheritable diseases of Caucasians, is seldom reported from the East. There is no epidemiological data regarding the incidence of this disease in non-caucasian population. [7] Early deaths, difficulty in the performance of the sweat chloride test by conventional means and perhaps the prevalence of tuberculosis and parasitic infestations to explain the common symptomatology of mucoviscidosis, may account for the under-reporting of this condition from the East. Lack of physician awareness of this disease is another factor in under-diagnosis. [7]

The purpose of this paper is to show that this disease is not as rare as is generally believed. That failure to thrive with or without respiratory problems and that hypoproteinaemia and anaemia, manifesting in the early months of life, may be the earliest presenting features of mucoviscidosis.

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The pilocarpine iontophoresis kit for the sweat chloride test became available to us in 1979. This retrospective study covers the period from July 1979 through to September 1984.

PATIENTS & METHODS:

Records of the 10 patients diagnosed since 1979 were reviewed. In some cases parents were recalled and interviewed for further information.

The following information was recorded from the in-patient charts. Age and symptoms at presentation e.g. respiratory, gastrointestinal, failure to thrive, anaemia and oedema. The family history of consanguinity and of deaths in the siblings was also recorded.

Haemoglobin haematocrit level, G6PD enzyme activity and serum protein levels at presentation were also noted.

Standard haemotological techniques were used for haemoglobin and haematocrit estimation. Because of its high incidence in the population, G6PD enzyme activity is routinely assessed. (Dye Decolourisation Test).

Serum protein estimation was carried out by SMA auto-analyser (Technicon, New York).

Chloride estimation of the sweat was carried out by chloride electrode method, using Model 417 skin-chloride measuring system. (Orion Research Corpn. Cambridge, M.A.). [3 5]

Tryptic activity in stools was assessed by gelatin digestion. [10]

RESULTS

The youngest patient was 42 days old and the oldest 5 months of age at the time of presentation. The mean age at presentation was 3 months. Six of the ten patients were females (Table-I).

TABLE I

CLINICAL FINDINGS AT PRESENTATION

No. Patient	Age	Weight (kg)	Sex	Symptoms	Remarks
1. H.A.H.	3 Months	2.200	F	Respiratory, Marasmus G.I.T.	Parents are distant relatives. Sibling of case No. 8 (S.A.J.H.). Died at the age of 9 months from progressive pulmonary disease and malabsorption. History of 2 siblings dying at 2 months of age.
2. Z.J.A.	3 Months	3.600	M	Respiratory F.T.T.	Parents are first cousins. One sibling died at the age of 5 months from malabsorption and hypoproteinaemia. Brother of patient No. 3 (L.J.A.). Died at the age of 14 months from progressive pulmonary disease.
3. L.J.A.	5 Months	4.650	F	Respiratory F.T.T.	Sister of patient No. 2 (Z.J.A.). Died at the age of 6 months from pulmonary disease.
4. F.H.A.	3½ Months	3.820	F	Anasarca Respiratory G.I.T. F.T.T.	Parents are cousins and both related to the parents of case Nos. 2 & 3. Two siblings died at the age of 4 months and 6 months with G.I.T. problems. Patient is alive and followed by one of us.
5. N.A.H.	2 Months	2.800	F	Respiratory Marasmus	One sibling died at the age of 2 months from unknown cause. Patient died at the age of 12 months from progressive lung disease.
6. H.A.E.	2½ Months	2.800	M	Respiratory F.T.T.	Parents are first cousins. Three siblings died in early infancy from chest and G.I.T. problems. One sibling, case No. 9(M.A.E.) died in the hospital. Patient died at the age of 6 months from progressive lung disease and malabsorption.
7. Z.J.A.H.	2 Months	2.275	F	Respiratory Marasmus	Parents are first cousins. One sibling died at the age of age of 2 months from "Chest problems". Died at one year of age from progressive pulmonary disease and and malabsorption.
8. S.A.J.H.	42 days	2.870	M	Respiratory Anasarca	Brother of case No. 1 (H.A.H.). Died after 1 month from progressive pulmonary disease.
9. M.A.E.	3½ Months	3.00	M	Respiratory F.T.T.	Brother of case No. 6 (H.A.E.). Died from progressive lung disease and malabsorption.
10. R.A.A.	5 Months	5.04	F	Respiratory G.I.T.	Parents are second cousins. Two siblings died at the age of 2-3 months with fever and loose motions. Patient is alive and followed by one of us (IMK)

Respiratory — Respiratory symptoms — cough, dyspnoea.
F.T.T. — Failure to thrive
G.I.T. — Gastro-intestinal symptoms — diarrhoea, vomiting.

TABLE II

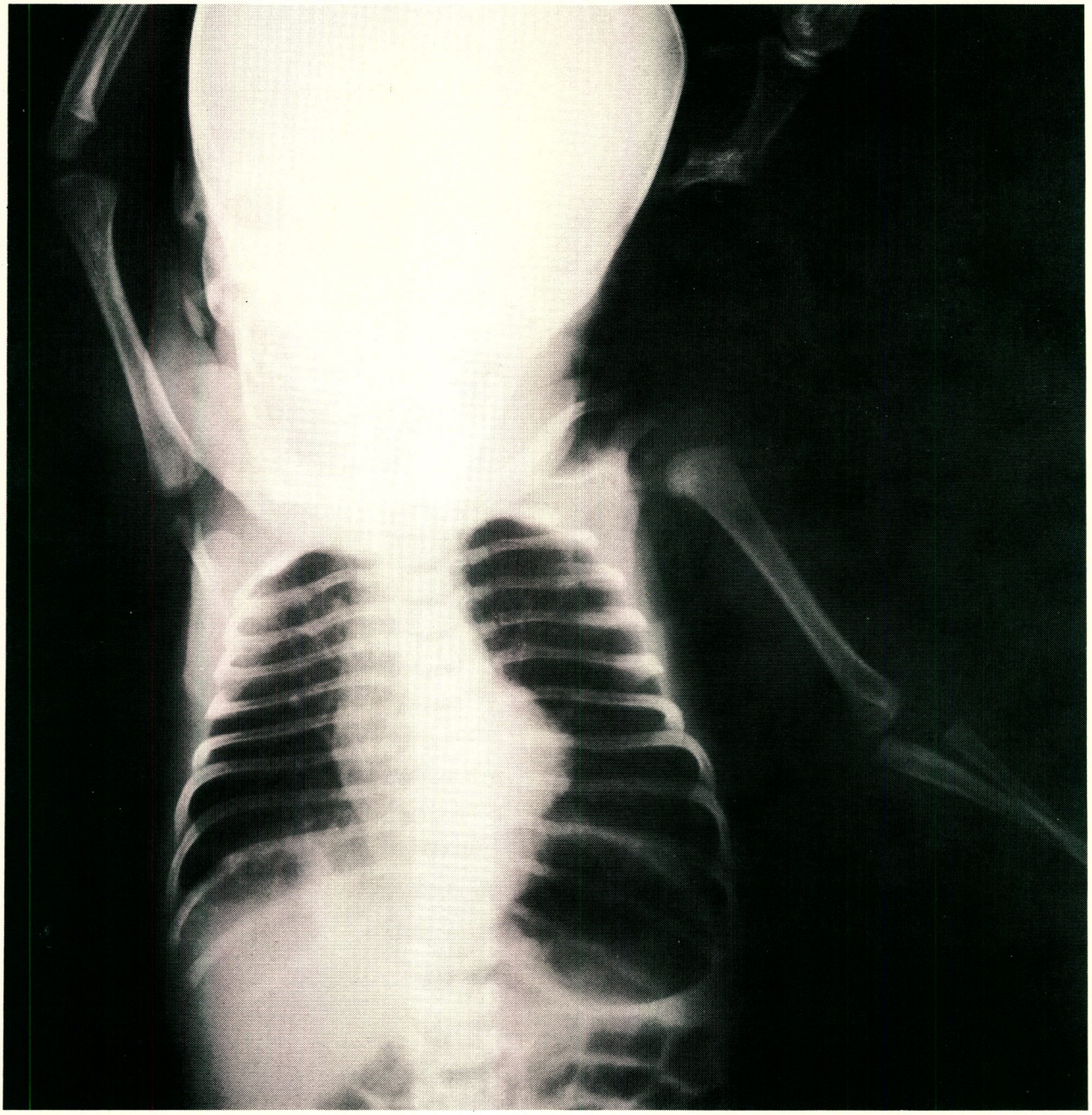
RELEVANT LABORATORY DATA

No. Patient	Haematological	Serum Proteins ALB/GLOB.
1. H.A.H.	Hb-7.4 gms/dl. HCT -24% Retics - 11.4% G6PD activity - normal	not done
2. Z.J.A.	Hb 7.5 gms/dl. HCT 25% Retics -4.5% G6PD activity - reduced Hb electrophoresis -S.A.F.	4.3 gms/dl. Alb 2 gms/dl. Glob. 2.3 gms/dl.
3. L.J.A.	Hb -11 gms/dl. HCT -33% Retics -1% G6PD activity - reduced	6 gms/dl. Alb -3.8 gms/dl. Glob. 2.2. gms/dl.
4. F.H.A.	Hb 7.7 gms/dl. HCT -24% Retics -2% G6PD activity - reduced Hb electrophoresis -S.A.	4.8 gms/dl. Alb. 2.1 gms/dl. Glob. 2.7 gms/dl.
5. NA.H.	Hb -14.8 gms/dl. HCT - 44% G6PD activity - normal Sickling - negative	not done
6. H.A.E.	Hb - 11.5 gms% HCT - 34% G6PD activity - normal Sickling - negative	not done
7. Z.J.A.H.	Hb - 7.4 gms% Hb electrophoresis Retics 2.2% A.F. (F 53%)	4.5 gms/dl. Alb 2.9 gms/dl. Glob. 1.6 gms/dl.
8. S.A.J.H.	Hb 8 gms/dl. HCT - 25% Retics 1.2% G6PD activity - reduced Sickling - negative	5.6 gms/dl. Alb - 2.3 gms/dl. Glob. 2.7 gms/dl.
9. M.A.E.	Hb 8.6 gms/dl. Sickling test - negative	3.5 gms/dl. Alb. 0.6 gms/dl. Glob - 2.9 gms/dl.
10. R.A.A.	Hb 12 gms. dl. HCT - 36% G6PD Activity - normal Sickling - negative	6.7 gms/dl. Alb 3.9 gms-/dl. Glob. 2.8 gms/dl.

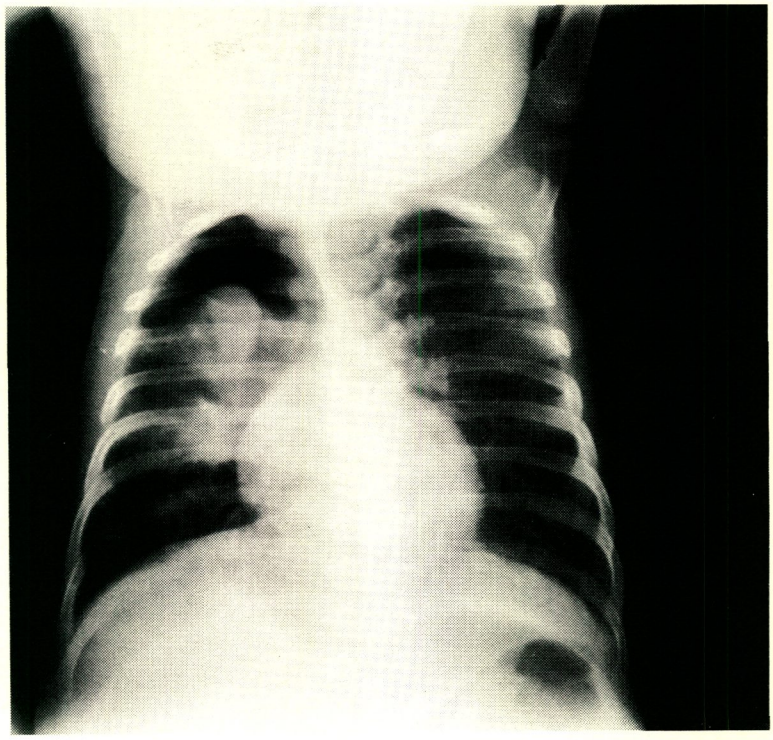
TABLE - III

DIAGNOSTIC STUDIES

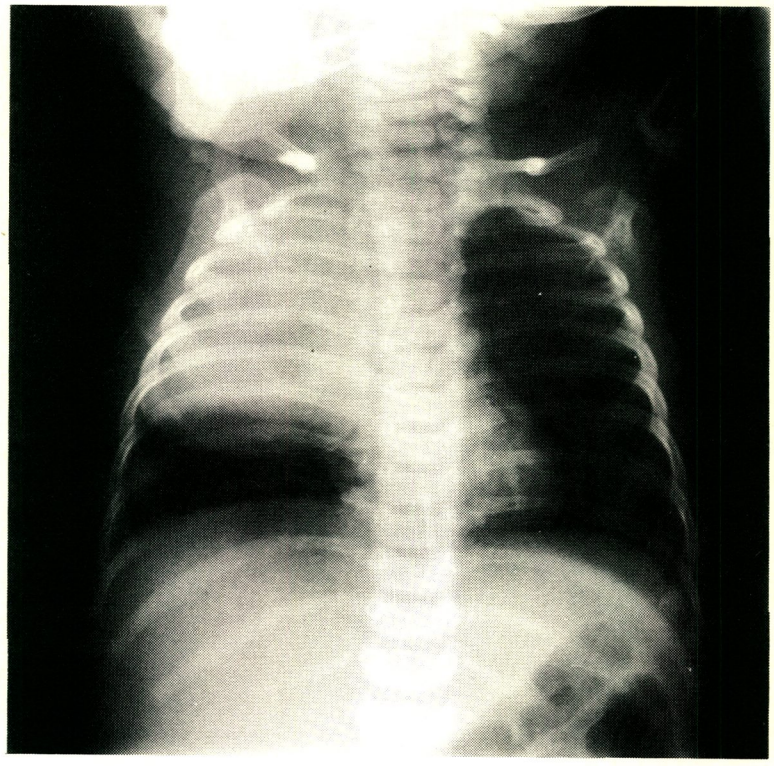
No. Patient	Sweat Chloride Estimation (Normal 60 mmol/L)	Tryptic Activity in Stool (Normal 1/100 dilution)
1. H.A.H.	200mmol/L	Gelatin digestion at less than 1/25 dilution (repeated)
2. Z.J.A.	80mmol/L 100mmol/L 140 mmol/L (M.106)	Gelatin digestion at less than 1/25 dilution (repated)
3. L.J.A.	110mmol/L 120mmol/L 125mmol/L (M.118)	Gelatin digestion at 1/25 dilution (repeated)
4. F.H.A.	90mmol/L 170mmol/L 110mmol/L M 123	Gelatin digestion at 1/50 dilution (repeated)
5. NA.H.	110mmol/L 105mmol/L (M 120)	Gelatin digestion at 1/50 dilution (repeated)
6. H.A.E.	100mmol/L 115mmol/L 104mmol/L (M-109)	Gelatin digestion at less than 1/25 dilution (repeated)
7. Z.J.A.H.	160mmol/L 200mmol/L 70mmol/L (M 143)	Gelatin digestion at less than 1/25 dilution (repeated)
8. S.A.J.H	Not done	Gelatin digestion at less than 1/25 dilution (repeated)
9. M.A.E.	Not done	Gelatin digestion at less than 1/50 dilution (repeated)
10. R.A.A	130mmol/L 140mmol/L 120mmol/L (M-130/L/2)	Gelatin digestion at 1/200 dilution (repeated)



Case No. 8 :
Typical changes in case of Cystic Fibrosis



Case No. 7 : Pneumothorax with consolidation of right apical lobe



Case No. 4 : Massive consolidation of right apical lobe with an area of clearing in the centre.

Respiratory symptoms associated with failure to thrive were the predominant complaints and were present in all the patients. Two patients (NAN & HAE) had cyanosis at presentation.

In two patients anasarca and anaemia was associated with respiratory distress at the time of presentation.

Five patients were the product of consanguinous marriages, there were two brother and sister pairs and two families were closely related by blood.

In six cases there was history of siblings (up to 4) dying in early infancy from gastrointestinal and or "Chest" problems.

Six patients were moderately anaemic with a mean Hb, value of 8 gms/dl. and a range of 7.4 gms/dl. to 8.6 gms/dl. (Table-II). Two of the remaining four had frank cyanosis at presentation. Four of the seven in whom serum proteins were measured were hypoprotienaemic, five had hypoalbuminaemia. Two of the four had pitting oedema. G6PD enzyme activity was reduced in 4 patients out of the 8 cases in whom it was assessed.

Sweat chloride values were consistently and abnormally high in the 8 cases on whom sweat chloride tests could be carried out. In three cases there was wide variation between the lowest (70mmol/L) and the highest (200 mmol/L) sweat chloride values [5] (Table-III). Some of these patients had hypoelectrolytaemia.

Tryptic activity in the stools was reduced consistently in 8 patients. In one patient it was normal (RAA) and in another (SAJH) it was at one point normal but reduced on repeated examination.

The stools of the patients with reduced tryptic activity were noted to be bulky with an offensive odour. The one patient (RAA) with normal tryptic activity in the stool reported with diarrhoea on two occasions.

Hyperinflation and airtrapping with areas of atelectasis was present in 4 cases. Hyperinflation with bronchovascular shadowing and peribronchial inflammatory changes was seen in 3 patients. Collapse consolidation of the right apical lobe was present in 4 cases with associated pneumothorax in one case and consolidation of the left upper lobe was noted in one case.

DISCUSSION:

Since the first report of CF by Salam in 1958, [11] only a few papers regarding the occurrence of the disease in the Middle East have appeared [1 8 9]. The belief that this disease is very rare in this region is still prevalent among the physicians practicing in the Arabian Gulf.

Eight of our ten cases fulfilled the classical clinical trial for the diagnosis of cystic fibrosis, i.e. chronic pulmonary disease, exocrine pancreatic deficiency and abnormally high sweat chlorides. The two patients on whom sweat chloride tests could not be carried out due to non-availability of the test kit, had the typical clinical and radiological features of CF and also they were siblings of our proved cases included in this paper.

Early deaths as well as lack of awareness of the existence of the disease has been suggested as some of the reasons why CF is so rarely seen in the tropics and subtropics. It has been suggested that the tendency to greater loss of electrolytes in CF makes these patients more susceptible to attacks of infantile gastroenteritis which has a high mortality among the underprivileged people in the tropics and subtropics. [7]

Our patients, among themselves, had lost 12 siblings in early infacy from undiagnosed conditions, however all had been suffering from chest and gastrointestinal problems. Three of our patients died by the age of 6 months and the five by 14 months of age. There are two patients still alive.

Failure to thrive and persistent pulmonary symptoms were the most prominent features in our cases and were the main reasons for seeking medical help. CF presenting with oedema, hypoprotienaemia and anaemia is considered unusual or uncommon. Two of our cases had these features and two others had anasarca, anaemia and hypoprotienaemia at presentation. Six of our ten patients were anaemic. Anaemia is explained on the basis of malabsorption. However, Vit. E deficiency resulting from malabsorption could cause haemolysis [6] and this was most probably the cause of anaemia and reticulocytosis in one of our cases (HAH). Mild reticulocytosis was present in one case (ZJA) who had G6PD reduced activity. Recently Congdon et al. have claimed to report the first case of CF with G6PD deficiency [4]. They have also discussed the possibility of increased susceptibility to respiratory infection and consequent pulmonary damage in CF patients with G6PD enzyme deficiency. Four of our cases had G6PD enzyme defi-

ciency which is most probably of the Mediterranean type and widely prevalent in this region. One of these four patients (SAJH) presented with anaemia, respiratory distress and anasarca at the age of 42 days. His reticulocytes count was not elevated. However, inspite of vigorous supportive and antibiotics therapy he died within 3 weeks of presentation. Of the other three one, a girl, is alive and a sibling pair (ZJA and LJA) died but their course did not appear to be any different from those of our cases without G6PD enzyme deficiency.

Severe hypoelectrolytaemia and metabolic alkalosis with cough during an attack of diarrhoea drew our attention to the possibility of CF in one case (RAA). [12]

Unfortunately because of the parents reluctance we were not able to perform autopsy on any of our patients.

It is worth mentioning that all of our patients were diagnosed before the age of six months. Even in countries like Australia and Switzerland with high clinical awareness of the disease, upto 40% of cases are diagnosed after the age of 12 months. [13]

CONCLUSION

We have presented 8 proved and 2 probable cases of CF and we believe that this is the largest number of documented cases so far reported from the Arabian Gulf States.

We would like to suggest that infants presenting with persistent or recurrent pulmonary infections or with failure to thrive or with anaemia and hypoproteinaemia in the early months of life, should alert physicians to the possibility of CF.

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