Demographic Pattern and Clinical Characteristics of Patients with Smear-Positive Pulmonary Tuberculosis in Kuwait

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Key Words

Tuberculosis epidemiology · Sputum smear · Hypercalcemia

Abstract

Objective: The aim of this study was to document various clinical factors that are likely to be of help in the control of tuberculosis in Kuwait. **Subjects and Methods:** Details of patients with sputum positive for acid-fast bacilli in the period from January 1998 to December 2000 were collected retrospectively from the case records and population statistics from government sources. The data were then tabulated and analyzed. **Results:** Of the 526 cases, 83.5% were expatriates and 16.5% Kuwaiti; 373 (70.9%) were male. Of the expatriates, 66.7% were from Asia and the Far East, 5.7% were ≥ 60 years. The annual incidence was 8.34 per 100,000 population. The lowest incidence was observed in the Jahrah governorate with an overall incidence of 5 (2.0 among Kuwaitis and 6.4 among expatriates) per 100,000 population. The highest incidence overall (10.2) and among Kuwaitis (4.1) was observed in the Farwaniya governorate, while the highest incidence among expatriates was seen in the Capital governorate (13.4). Radiologically, 94 (19.5%) had minimal, 246 (51.5%) had moderately advanced and 141

(29.3%) far-advanced disease. The majority of the patients (72%) had only + status for AFB in the smear. Hypercalcemia (25.7%), hyponatremia (22.15%) and hyperglycemia (29.9%) were common in the patients. Mean serum albumin was low (28.7 ± 5.5 g/l). Two hundred and forty-seven (47.2%) were declared cured while 116 (22.2%) completed treatment. Comparison between nationals and expatriates showed a significant difference only for age, smoking status, defaulter rate and place of residence. **Conclusion:** The lowest regional incidence was found in the Jahrah governorate. Both biochemical abnormalities and radiologically advanced presentations were common. Disease pattern and response to treatment was purely individual and did not differ with respect to nationality or race.

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Introduction

Tuberculosis (TB) has always been linked to population migration [1–3]. The World Health Organization (WHO) has identified the movement of people from high prevalence to industrialized nations as one of the causes of the current worldwide increase in TB prevalence [4]. Not surprisingly, TB incidence in the United States of

America is highest among recent arrivals to the country [3]. TB surveillance data from England during three different periods indicates that persons originating from the Indian subcontinent provided 35–40% of all notified cases [5–7]. Recent studies have shown that the pattern of adult respiratory diseases in migrants from this region is changing [8].

Kuwait being a country where the immigrant population exceeds the native people, the incidence and prevalence of TB is closely linked to the nature of the immigrants. In 2000, 62% of the estimated population were expatriates [9]. The incidence of pulmonary TB in Kuwait showed a steady decline over the past decades, though with a slight increase since 1989 [10]. The disease characteristics, risk factors, access to health care and outcomes vary from country to country and usually differ locally as well. Hence any control measures have to be designed to meet these needs in a culturally appropriate manner. This report presents a collection of assorted data on smear-positive cases in Kuwait.

Subjects and Methods

Since 1954, the State of Kuwait has had a central TB control unit where every sputum-positive patient is referred to for initiation and continuation of treatment. Nearly all smear-negative cases and a significant number of extra-pulmonary cases are also referred to this unit. In addition to the management of TB cases, the unit is actively involved in the screening of new immigrants for pulmonary TB. All smear-positive cases are generally kept as inpatients until they become non-infectious. The study population consisted of sputum-positive patients registered between January 1998 and December 2000. Smears were routinely prepared from a properly collected early-morning sputum sample and stained for acid-fast bacilli by the standard Ziehl-Neelson technique [11].

Geographically, Kuwait lies at the head of the Arabian Gulf, with an area of approximately 17,818 km². It is bordered in the West and North by Iraq, in the East by the Arabian Gulf and in the South by Saudi Arabia. Kuwait is not evenly populated as a large part is gravelly desert. The population density is 123 persons/km². Most of the population is concentrated in cities near or along the Gulf coast. For administrative purposes, the country is divided into 5 governorates: Al-Assimah (Capital), Al-Farwaniya, Hawalli, Al-Ahmadi and Al-Jahrah, the largest being Al-Jahrah and the smallest Hawalli.

The estimated mid-year population, distribution by nationality and area of residence were collected from the yearly publications of the government [9, 12–14]. The incidence of sputum-positive TB cases in the late 1970s and late 1980s were obtained from the studies of the Ministry of Public Health [14]. The average cumulative annual incidence of smear-positive cases was then calculated for the years 1998, 1999 and 2000, and also estimated for a similar period in the previous two decades, excluding 1990 due to the Gulf War.

Kuwaitis or nationals were defined as those persons having a valid citizenship; expatriates or non-nationals were defined as non-citizens. The extent of the lesions visible on radiology examination was noted by the treating chest physicians on admission, and the lesions were categorized as minimal, moderately advanced and far advanced according to the classification of the National Tuberculosis Association [15]. Lesions were considered to be 'minimal' if they were of slight to moderate density without cavitation and involved a part of one or both lungs, the total extent being less than the volume of lung on one side which was present above the second chondrosternal junction. 'Moderately advanced' lesions were present in one or both lungs, but the total extent did not exceed the following limits: disseminated lesions of slight to moderate density which extended throughout the total volume of one lung, or the equivalent in both lungs; dense and confluent lesions which were limited in extent to one third the volume of one lung; total diameter of cavitation, when present, was less than 4 cm. Lesions more extensive than these were recorded as 'far advanced'. Chest radiographs were not reviewed or reinterpreted for this study. Smears were reported as negative, +, ++, and +++ according to the recommendation of the American Thoracic Society [16]. Patients smoking ≤ 20 cigarettes/day were classified as light and those smoking more as heavy smokers [17]. The definitions of radiological lesions, sputum status and smoking history are established criteria for analyzing incidence of TB [15–17].

Sputum examinations were repeated, whenever available, at the end of 2 and 5 months of therapy. The samples were routinely subjected to culture and drug sensitivity studies.

The treatment of choice was a 6-month regimen with rifampicin, isoniazid, ethambutol and pyrazinamide daily at standard doses for 2 months, followed by isoniazid and rifampicin daily for another 4 months. A few patients received other standard regimens. Second-line drugs were used in some instances. The decision to change regimen was based on drug toxicity, ophthalmological status, other organ damage, drug interactions, sensitivity pattern, or compliance.

Basic smear data and culture results at presentation, smoking history, history of diabetes, drug abuse, alcoholism and radiological presentation were retrospectively collected from the medical records. The outcome, the report of the culture, purified-protein derivative (PPD) reaction size, defaulting, record of drug resistance, the exact nationality of the patient and the area of residence were then noted from the national TB register. The outcome was recorded as cured, completed treatment, death, bacteria positive, defaulting, drug resistant, deported and transferred out as per the usual terminologies of the WHO [18].

The data were then tabulated and analyzed using the Epi Info Version 6 for DOS, (Center for Disease Control, Atlanta, Ga., USA). The significance of differences between groups was determined by either using χ^2 or Fisher's exact test for categorical data and analysis of variance for continuous data. Bartlett's test was used to determine if the variances of the groups were different and, if so, Wilcoxon two-sample test was used as a non-parametric test for continuous variables.

Fig. 1. Incidence of sputum smear-positive cases in Kuwait over the last three decades.

Table 1. Clinical characteristics of Kuwaitis and expatriates with smear-positive pulmonary tuberculosis

Characteristics	Kuwaiti (n = 87)	Expatriates (n = 439)	p value
<i>Demographics</i>			
Age	41.4 ± 17.6	36.4 ± 12.0	0.05
Male:female ratio	2.6:1	2.4:1	0.74
Residence	Hawalli	Farwaniya	<0.01
Smoking (n = 434) ^a	46 (66.7)	171 (47.4)	<0.01
<i>Disease characteristics</i>			
Sputum status	+	+	0.40
Radiology	moderate	moderate	0.49
Drug resistance	1 (1.2)	23 (5.3)	0.15
PPD reaction, mm	15.1 ± 8.0	17.9 ± 5.5	0.08
<i>Biochemistry</i>			
Serum albumin, g/l	27.6 ± 6.0	28.9 ± 5.4	0.06
Serum sodium, mmol/l	137.2 ± 4.9	137.7 ± 4.2	0.53
Serum potassium, mmol/l	4.3 ± 0.6	4.4 ± 0.6	0.08
Corrected calcium, mmol/l	2.5 ± 0.2	2.51 ± 0.2	0.68
Diabetes	24 (27.9)	133 (30.2)	0.71
Hypercalcemia (n = 171) ^a	12 (38.7)	32 (22.8)	0.07
Hyponatremia (n = 292) ^a	21 (27.6)	88 (21.2)	0.21
<i>Outcome</i>			
Cured	51 (58.6)	196 (44.7)	0.25
Completed	18 (20.1)	98 (22.3)	0.25
Defaulting	15 (17.2)	43 (9.8)	0.04
Death	0 (0)	5 (1.1)	1.00

Data are presented as mean ± SD or frequency (%) unless otherwise stated.

^a See text.

Results

During the 3-year period, 1,583 patients were treated for TB; of these 526 (33.2%) had sputum smear-positive status, 289 were smear negative, and 768 were extra-pulmonary cases. The average annual incidence per 100,000 population calculated for the last 3 decades were: 1990s (the present study): 8.34, 1980s: 8.17 and 1970s: 31.67 (fig. 1).

Demographics

Of the 526 sputum-positive smear cases, 87 (16.5%) were Kuwaitis and 439 (83%) expatriates. The majority was male (n = 373, 70.9%), 153 were female, giving a male-to-female ratio of 2.4:1. Mean age was 37.2 ± 13.2 years. The majority of the patients was in the 20- to 59-year-old age group. Nineteen percent of the Kuwaiti and 5.7% of the expatriate patients were above 60 years (table 1). In patients with a known history of smoking, nearly half were current smokers (n = 219, 50.5%), equally distributed among heavy and light smokers (49.1 and 50.9%, respectively).

Based on nationalities, 65.6% of the patients were from Asian and Far East Asian countries (table 2). The majority of the Asian patients were from India (33.7%). There was no significant difference in the proportion of males and females among Kuwaitis and expatriates.

The patients were not evenly distributed. Most cases were from the Farwaniya and Hawalli governorates, the highest incidence per 100,000 was in Farwaniya (10.2;

Fig. 2. Incidence of smear-positive cases and average mid-year population of 1998, 1999 and 2000 among Kuwaitis (K), expatriates (NK) and total population (T) in Kuwait and different governorates.

fig. 2). Highest incidence among Kuwaitis (4.1) and non-Kuwaitis (13.4) was in the Farwaniya and Capital governorates, respectively. The overall lowest incidence (5.0) and the lowest incidence among Kuwaitis (2.0) and expatriates (6.4) were in the Jahrah governorate. Twenty-five (4.8%) patients were prison inmates.

Disease Characteristics

Twenty-four cases were resistant to 1 or more drugs, an incidence of 1.5% per year or 0.37 cases per 100,000 population. The mean PPD size was 17.5 ± 6 mm (table 1). The differences in induration size between nationals and expatriates were not statistically significant.

Most patients, both Kuwaitis and expatriates, had a moderately advanced or far advanced radiological presentation: 94 (19.5%) had minimal, 246 (51.5%) had moderately advanced and 141 (29.3%) far advanced lesions.

Though radiologically advanced disease was the commonest presentation, the majority of the patients (n = 382, 72%) had only + status for acid-fast bacilli in the smear. Fifty-one (9.7%) had +++ smear status. More Kuwaitis than expatriates had +++, whereas expatriates predominated the ++ smear group (table 1), but this difference was not statistically significant.

Table 2. Patients' ethnic origins and nationalities

Groups/nationality	Patients	
	n	%
Arab		
Kuwait	87	16.5
Egypt	28	5.3
Local Arab	19	3.6
Saudi Arabia	14	2.7
Other Arab	26	4.9
Subtotal	174	33.1
Asian		
India	177	33.7
Bangladesh	63	12.0
Pakistan	41	7.8
Philippines	28	5.3
Sri Lanka	13	2.5
Other Asian	23	4.4
Subtotal	345	65.6
Others	5	0.9
Missing	2	0.4
Subtotal	7	1.3
Total	526	100

Biochemistry

The mean corrected calcium was 2.5 ± 0.2 mmol/l. In patients in whom both albumin and calcium were measured ($n = 172$), 25.7% had hypercalcemia with a corrected serum calcium above 2.6 mmol/l. Though mean serum sodium was in the normal range (137.6 ± 4.3 mmol/l), 22.2% had hyponatremia. Both hypercalcemia and hyponatremia were common in the Kuwaiti population. Mean serum albumin was low, 28.7 ± 5.5 g/l. Mean serum potassium was in the normal range, 4.4 ± 0.6 mmol/l. At the time of presentation, 29.9% of the patients had diabetes. Diabetes was more common among expatriates, though the difference was not statistically significant.

Outcome

Outcome was recorded in 523 patients; of these, 247 (47.2%) were declared cured while 116 (22.2%) completed the treatment (without demonstrated cure), giving a treatment success rate of 69.4%. Five (1%) patients died while on chemotherapy and 58 (11%) did not complete therapy. The tendency to default was significantly greater ($p < 0.04$) among Kuwaitis than among expatriates (table 1). Eighty-three (15.9%) expatriates were deported due to various reasons and 10 (1.9%) patients were transferred out to other chemotherapy centers outside the country. Four were smear positive at the end of treatment and classified as treatment failures.

Discussion

WHO estimates that each year more than 8 million new TB cases occur in the world, nearly 95% of these in the developing countries [16]. TB in immigrants from these high-incidence countries poses a threat in many developed countries, including Kuwait, where expatriates make up 62% of the population. Somalis record the highest incidence of TB among any nationalities in Denmark and this rate is comparable to or even higher than the estimated incidence in Somalia [19]. In the USA, people originally from Mexico, the Philippines, Vietnam, India, China, Haiti and South Korea account for approximately two thirds of the TB cases occurring in foreign-born persons [2]. In many parts of the world, the case rates were higher in the population migrating from the Indian sub-continent, and even among the different countries of this region itself the patterns may differ [8]. According to a report from Blackburn, UK, an increased proportion of pulmonary disease was seen in Pakistani and Bangladeshi

patients, while glandular TB was common in Indians [20]. In the present study, no significant difference in age, sex, radiological presentation, sputum status, PPD reaction size, biochemical values, outcome and defaulter rates was observed among patients from India, Pakistan, Bangladesh or Sri Lanka.

The present average annual incidence in Kuwait is 8.34 smear-positive cases per 100,000 but in the late 1970s it was 31.7 (fig. 1). The developing nations report considerably larger incidence rates (India: 35, Sri Lanka: 23, Philippines: 89), whereas the rates from the developed world are much less: USA: 2, UK: 2 [18]. An adequate TB control program, efficient screening techniques and the commitment of dedicated staff all contributed to the decline of TB incidence in Kuwait. However, since 1989 there has been a slight but definite increase in the incidence, which has been attributed mainly to the direct or indirect effects of the Gulf War [9].

The regional variation of incidence observed in this study (fig. 2) could be due to overcrowding and/or population density. The Jahrah governorate with the lowest rates is closer to the northern border and is less densely populated. The annual incidence of TB in expatriates is greater in the Capital governorate, which probably is due to the overcrowding accommodations in the center of the city or to the fact that many would have given their work address while registering in the hospital.

Reports from the neighboring country, Saudi Arabia, show the incidence of sputum smear cases to be 8–15.2 per 100,000 population [18, 21], with a higher incidence among young adults [22]. Compared to these studies, the incidence is lower in Kuwait than in Saudi Arabia, but a higher incidence was observed among the older population. Our findings of an increased incidence among older Kuwaitis could be due to the higher prevalence of TB in the earlier decades.

Radiological presentation was rather severe as most of these patients had advanced disease. A study from Turkey recorded parenchymal infiltrates followed by cavitary disease as common presentations of TB in a large number of patients [23]. Though the usual radiographic findings of upper lobe infiltrates and cavitary disease are reported as the commonest presentations, a relative increase in the frequency of unusual presentations, more pronounced in the elderly, in recent years are also reported [24–26]. Surprisingly, when severe disease was visualized on X-rays, the majority of patients presented with a low per-field bacillary count. This radiological-microbiological disparity is well documented. On many occasions, sputum is smear and culture negative,

even when there are well-marked radiological opacities and symptoms [27].

Only 1.5% of our smear-positive patients grew mycobacteria resistant to one or more drugs, quite low when compared to the alarming worldwide reports of increasing drug resistance, including neighboring Saudi Arabia [22, 28–30]. In an earlier report on drug resistance in Kuwait, primary resistance to isoniazid was seen in 4.3% of Kuwaiti nationals and 6.2% of expatriates [31]. The present finding of low incidence may be due to the fact that we are reporting on smear-positive cases only while excluding the smear-negative, culture-positive cases.

Biochemically, the observed hypercalcemia, low serum albumin and hyponatremia of this study are similar to previous reports [32–41]. Hypercalcemia is well reported in TB patients from countries with abundant sunshine [32–35]. For this study, low albumin could not be attributed to poor nutrition because the rich Kuwaiti population also had low serum albumin. Hyponatremia could be due to the release of an ADH-like substance from the affected tissue [16].

Patients with diabetes mellitus are at a higher risk of developing TB [42, 43]. Abnormal glucose tolerance tests have been reported in pulmonary TB patients [44, 45]. In our patients, a slightly higher prevalence was seen in non-nationals (30.2%) than nationals (27.9%). This probably reflects the pattern of diabetes in this community [46].

The overall treatment success rate of 69.4% obtained in this study is within the range observed in other Arabian Gulf countries of Saudi Arabia (64%), Qatar (74%), Oman (87.9%), and WHO estimates of treatment results

of six consecutive cohorts from 1995 to 1999 (77–81% under directly observed therapy and 54–64% worldwide) [18].

Based on our findings, TB has been contained in Kuwait. Defaulting was noted to be high, especially among nationals. Since the problem of drug resistance is low, adequate chemotherapy, better case-holding techniques and tighter screening schedules can further bring the incidence down. Strict monitoring of immigrants from South East Asia is needed, and biochemical abnormalities have to be looked for in all TB patients. Radiological abnormalities should trigger TB suspicion, as most of our cases were diagnosed rather late into the disease.

Conclusion

The lowest regional incidence of TB was found in the Jahrah governorate. Both biochemical abnormalities and radiologically advanced presentations were common. Disease pattern and response to treatment was purely individual and did not differ with respect to nationality or race.

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