Curvilinear pattern of pulmonary tuberculosis among migrant workers entering Kuwait: 1997-2006

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Abstract

**Background:** There is paucity of published data on the pattern of tuberculosis among immigrants entering Middle Eastern countries. The objectives of this study were to use routine health surveillance data to i) to estimate the prevalence of pulmonary tuberculosis to migrant workers to Kuwait and ii) to determine the occurrence of any time trends in the proportions of pulmonary tuberculosis positive workers over the study period.

**Methods:** Monthly aggregates of number tested and pulmonary tuberculosis positive diagnosis results obtained from routine health examinations of migrants from tuberculosis high-prevalence countries conducted between January 1, 1997 and December 31, 2006, were analysed using time series methods.

**Results:** Overall prevalence (per 100,000) of pulmonary tuberculosis positive migrants was 198 (4608/2328582). Year-specific tuberculosis positive (per 100,000) cases consistently declined from 456 (95% CI: 424 - 490) in 1997 to 124 (95% CI: 110 - 140) in 2002 before showing a steady increase till 2006. The second-order polynomial regression model revealed significant ($P < 0.001$) initial decline followed by a significant ($P < 0.001$) increasing trend thereafter in monthly proportions of tuberculosis positive migrants.

**Conclusion:** The significant increasing trend in tuberculosis cases towards the end of the study period, underscore the need to maintain the current policy of screening of migrants from tuberculosis endemic countries using improved diagnostic protocol combined with treatment, to ensure that the risk of local *M. tuberculosis* transmission is minimized.
KEYWORDS: pulmonary tuberculosis, prevalence, time series analysis, migrant workers, Kuwait

Background

Tuberculosis remains one of the leading infectious causes of death globally, killing nearly 2 million people a year [1]. Sub-Saharan Africa has the highest incidence rate (290 per 100000), but the most populous countries of Asia have the largest numbers of cases and together account for more than half the global burden [2]. Tuberculosis control programmes can achieve a high level of treatment success and are associated with a decline in reported burden of disease [3-6]. However, for the past two decades, a levelling off or a reverse trend in tuberculosis notifications has been reported from many developed countries [7-8]. This disturbed declining trend has been attributed, in part, to the spread of human immunodeficiency virus (HIV); homelessness, deterioration of living conditions and health care delivery, increased drug abuse, immigration from tuberculosis high to low prevalence countries [7,9]. Nonetheless, reasons for this phenomenon are complex, differ from one country to another, and have not been entirely elucidated [10].

Kuwait is an oil rich country with an estimated population of 3 million, of which 60% are non-Kuwaiti nationals, most of whom are from South-East Asia. Tuberculosis incidence in Kuwait showed a steady decline from 1965 to 1989. However, from 1989 to 1999, there was a slight increase in the tuberculosis incidence both among nationals and non-nationals suggestive of Mycobacterium tuberculosis transmission from non-nationals to nationals, perhaps through intimate close contact, since a large proportion of expatriates
from South-East Asian countries live and work in Kuwaiti homes as domestic workers [11]. This reversal of the observed tuberculosis trend in Kuwait may be explained partly by the concomitant increase in the proportion of migrant workers from high tuberculosis prevalence countries following first Gulf War in 1990 [12]. Furthermore, disruption of tuberculosis control program due to Gulf war in 1990 also may have contributed to this reversal of tuberculosis trend in Kuwait [11].

The epidemiologic importance of migration from tuberculosis high to low incidence countries has been recognized for several years; the main countermeasure has been implementation of screening programs for immigrants at the time of arrival [13, 14]. But it not clear that to what an extent the increased immigration from high-incidence countries contributes to an increased risk of tuberculosis in host community of low-incidence countries.15 Elsewhere immigrants from high-incidence countries to developed and Middle Eastern countries reportedly have high prevalence of tuberculosis [16, 17], but there is paucity of published data on the prevalence of tuberculosis in migrant workers to Kuwait. Here, we take advantage of the routine screening of migrant workers for tuberculosis, upon arrival in Kuwait from tuberculosis-endemic regions, to do a first large-scale quantification of the tuberculosis status of this work population. Specifically, the cumulated data on the results of tuberculosis testing of these workers over the past ten years gave us an opportunity in this study not only to undertake 1) the estimation of the prevalence of tuberculosis in this population of workers, but also to 2) ascertain if any significant time trend or changes had occurred in the
prevalence of tuberculosis among these workers during the recent past.

Methods

Data source
Monthly aggregates of test results for pulmonary tuberculosis among migrant workers entered in Kuwait between January 1, 1997 and December 31, 2006 were available for this study. These immigrant workers predominantly come from India (31%), Bangladesh (14%), Sri-Lankan (14%), Egypt (12%), Indonesia (9%), Philippine (5%), Pakistan (5%) and 10% from other countries including those from African counties such as Tanzania, Mali, Gambia, Sudan (12%) [18, 19]. Routine consensual medical examination procedures are conducted on these workers upon their arrival by Ports & Borders Health Division of the Ministry of Health, Kuwait. For the diagnosis of TB, migrants were screened by the serial application of various tests. For each migrant chest radiograph was taken. In the presence of any suspicious lesion in the lungs, confirmatory TB diagnosis was made by sputum smear examination for acid fast bacilli (AFB) using Ziehl Neelsen technique and bacterial culture. Subsequently, migrant worker was classified as a TB case if sputum smear and/ or bacterial culture was positive for AFB or negative otherwise [20].

Statistical methods
The monthly aggregates of daily number of migrant workers tested and number of pulmonary tuberculosis positive were used to generate the monthly series of proportions of pulmonary tuberculosis positive (per 100,000) workers over a period of 120 months from January 1, 1997 to December 31, 2006.
These monthly proportions (per 100,000) of pulmonary tuberculosis positive workers were used for all further analyses unless stated otherwise. Overall and year-specific prevalences (per 100,000) along with their 95% confidence interval (CI) were calculated.

**Time series analysis**

We employed standard time series methods to assess and model the presence of statistically significant long term trends in the data [21]. Trend estimation or detection was done by first de-seasonalizing the series using the moving average smoothing method. We smoothed the data by taking a 13-point (months) moving average filter (Figure 1). Predictive modelling of the trend was then performed following the removal of seasonal effects by initially fitting a locally weighted (Lowess) scatterplot smoother (with bandwidth 0.3) to explore the form of the long-term trend in the relationship between time (months) and monthly proportions of pulmonary positive cases [22]. Examination of the results from this exercise suggested the existence of a possible curvilinear temporal trend (Figure 2), and therefore a polynomial regression model was fitted to the deseasonalized data to model the observed monthly proportions of tuberculosis positive cases with respect to “time”, and a quadratic term of time (i.e. time^2). The goodness- of-fit of the final model was evaluated via residual analysis by plotting residuals against fitted values and also versus the time variable [23].
Results

Descriptive statistics
During the study period of 120 months from January 1, 1997 to December 31, 2006, 2328582 migrant workers from pulmonary tuberculosis high prevalence countries were included in this analysis. Overall prevalence (per 100,000) of pulmonary tuberculosis positive migrant workers was 198 (4608/2328582). Total yearly pulmonary tuberculosis positive (per 100,000) cases consistently declined from 456 (95% CI: 424 - 490) in 1997 to 124 (95% CI: 110 - 140) in 2002 before it showed a yearly increase up to 184 (95% CI: 171-199) and 183 (95% CI: 169-197) cases in 2005 and 2006 respectively (Table 1; Figure 3).

Polynomial regression model
Overall second-order polynomial regression model with time as the single predictor was significant ($F$-statistic = 961; $p < 0.001$) (Table 2). The polynomial terms in the model were also statistically significant ($p < 0.001$), and the point estimates ($\pm$ standard errors) were $\hat{\beta}_0 = 524.684$ ($\pm$ 7.853), $\hat{\beta}_1 = -10.657$ ($\pm$ 0.294), $\hat{\beta}_2 = 0.070$ ($\pm$ 0.002). The monthly series of proportions of pulmonary tuberculosis positive migrant workers revealed significant ($P < 0.001$) initial decline followed by a significant ($P < 0.001$) increasing trend thereafter during 120 months of the study period (Figure 4). The two terms in model together explained about 95% variation in the monthly proportions of tuberculosis positive migrant workers (coefficient of determination: $R^2 = 0.948$). The predicted monthly proportions of tuberculosis positive cases ranged from 119 to 514 with mean ($\pm$ SD) of 220 $\pm$ 107. The plot of observed verses predicted monthly proportions showed adequate fit of the model.
Residual analysis to evaluate the aptness of the model suggested that quadratic response function is a good-fit.

**Discussion**

To our knowledge, this study constitutes one of the largest ever investigations conducted anywhere in the world for estimating and assessing the role of tuberculosis burden in migrant workers as a potential source of infection to low tuberculosis incidence regions. This topic is not only of particular relevance to countries, such as Kuwait and the other Middle Eastern countries, which attract a large number of migrant workers from tuberculosis endemic areas, but also, the results of this study clearly underline the substantial potential of migrants to serve as sources of new infection in low burden areas. In Kuwait, we found that the overall prevalence (per 100,000) of tuberculosis positive migrant workers was 198 (4608/2328582) or 0.198% during the entire 10-year study period. Almost a similar magnitude of prevalence of tuberculosis has been reported in high burden counties in South Asia [24, 25]. Also, it has been shown elsewhere, that the risk of tuberculosis among immigrants mirrors the tuberculosis prevalence in their country of origin [26, 27]. The longitudinal data series based on a 10 year period of observations also uniquely allowed an investigation of the temporal epidemiology of tuberculosis in workers migrating to the country. This has also specifically enabled us to establish that the tuberculosis risk from migrant workers to the country has reduced dramatically over the past decade, such that the tuberculosis infection prevalence in the cohort of workers recruited in 2002 was only around 0.124% (275/221566) in contrast to a peak of 0.456%
(737/161682) observed in counterparts in 1997 (Table 1). However, a reversal of trend of significantly increased prevalence occurred in the following years. These results highlight that migrant workers may pose a risk although currently small for the establishment of *M. tuberculosis* transmission in Kuwait, but also underscore the value of routine health screening of workers as an effective tool to quantify and track changes in this risk over time.

Indeed, although featuring an initial steady decline, our analysis of long-term trend in the data using time series methods revealed the occurrence of an interesting curvilinear pattern in the prevalence of tuberculosis in migrant workers over the 10-year study period. Proportions of tuberculosis positive workers showed an initial decline between 1997 and 2002 and a subsequent steady increase to the present time. The observed initial downward trend in the proportions of tuberculosis positive workers in this study appears to corroborate previous findings of decreasing prevalence of tuberculosis during the same period in immigrants from India, Asia and sub-Saharan Africa to Canada [28]. This decline in the proportions of tuberculosis positive migrant workers over 1997 to 2002 could reflect the effective implementation of WHO-recommended DOTS (Directly Observed Therapy, Short-course) strategy during the same period by the public health authorities of respective endemic countries of origin of these workers [29]. If found to be true, this suggests that sustained DOTS intervention in affected areas over several years could by reducing transmission in those areas contributed significantly in minimizing the risk of exporting *M. tuberculosis* infection into Kuwait and perhaps to other countries in the region. Alternatively, this decline may simply indicate that
more workers from a different socio-economic background with lower \( M. \) 
tuberculosis infection risk were being enlisted in Kuwait during that period. We do not have sufficient data at present to investigate this likely change in population characteristics. Nonetheless, whatever the reason for this decline, the slight but significant increase in the tuberculosis positive proportions of migrant workers towards the end of the time series (2005-2006) is consistent with contemporary reports of increased global tuberculosis caseloads [30, 31]. A longer period of observation is however required to confirm this small trend of a significantly increased prevalence at the end of time series. Nonetheless this trend of tuberculosis caseloads is expected to grow further during next few years as recent evidence suggests [32]. This piece of results clearly underscores the need for maintaining the current health screening of these workers to ensure that incidence of \( M. \) tuberculosi s infection is not on the increase again. In particular, the need for surveillance is indicated if this increase reflects the outcome of a shift in the health priority of public authorities in the endemic countries resulting in the slow down of tuberculosis control efforts.

Some limitations of this study should be considered while interpreting the results. First, as only few variables of interest were available for longitudinal analysis, we are unable to evaluate the roles of potential host factors, e.g. age, gender, in influencing the observed changes in the prevalence of tuberculosis. Second, the non-availability of information on exact locations of tuberculosis positive workers within their countries of origin precluded any spatial or location-based analysis in this study. Finally, some worker might be
incubating the infection and/or at early stage of the disease and escaped. It is therefore, likely that the estimated proportions of tuberculosis positive migrant workers may have been somewhat underestimated in this study.

Nonetheless, this work has highlighted how routine screening procedures may provide an effective public health surveillance tool to quantify and track the tuberculosis burden of migrant workers into Kuwait. Indeed our analysis of the available longitudinal screening data on tuberculosis has shown not only that the incidence of tuberculosis may be declining in these workers thus reducing the risk they pose to the local community in the host country but also that tuberculosis control in endemic countries may be a contributory factor and indeed should be maintained to keep the incidence *M. tuberculosis* infection declining. The final conclusion of specific significance to Kuwaiti and other Gulf country public health authorities from this study is that the data, particularly either the levelling or slight rise in tuberculosis in these workers towards the end of the study period, suggest that there is a need to maintain the current policy of screening migrant workers from tuberculosis endemic countries, perhaps using improved diagnostic techniques or even through screening combined with treatment, to ensure that the risk of local transmission of *M. tuberculosis* infection is minimized.

**Acknowledgements:**

The cooperation of the staff of Ports and Borders Health Division, Ministry of Health in data compilation is gratefully acknowledged. The study was funded by Kuwait University research grant no. MC 01/05.
Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

SA conceived, design, analyzed and interpreted data and drafted the
manuscript.  HGHM supervised data collection and reviewed the manuscript.
Both the authors have read and approved the final manuscript.

References


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Table 1. Distribution of pulmonary tuberculosis positive proportions (100,000) of migrant workers in Kuwait: 1997-2006.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total tested</th>
<th>No. positive</th>
<th>No. positive (per 100,000)</th>
<th>95% confidence limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>161682</td>
<td>737</td>
<td>456</td>
<td>424 – 490</td>
</tr>
<tr>
<td>1999</td>
<td>177129</td>
<td>523</td>
<td>295</td>
<td>271 – 322</td>
</tr>
<tr>
<td>2000</td>
<td>130984</td>
<td>261</td>
<td>199</td>
<td>176 – 225</td>
</tr>
<tr>
<td>2001</td>
<td>178472</td>
<td>225</td>
<td>126</td>
<td>111 – 144</td>
</tr>
<tr>
<td>2002</td>
<td>221566</td>
<td>275</td>
<td>124</td>
<td>110 – 140</td>
</tr>
<tr>
<td>2003</td>
<td>254608</td>
<td>334</td>
<td>131</td>
<td>118 – 146</td>
</tr>
<tr>
<td>2004</td>
<td>327216</td>
<td>436</td>
<td>133</td>
<td>123 – 144</td>
</tr>
<tr>
<td>2005</td>
<td>356983</td>
<td>657</td>
<td>184</td>
<td>171 – 199</td>
</tr>
<tr>
<td>2006</td>
<td>356616</td>
<td>652</td>
<td>183</td>
<td>169 – 197</td>
</tr>
<tr>
<td>Total</td>
<td>2328582</td>
<td>4608</td>
<td>198</td>
<td>192 – 204</td>
</tr>
</tbody>
</table>
Table 2. Polynomial regression model of the deseasonalized monthly proportions (per 100,000) of pulmonary tuberculosis positive migrant workers in Kuwait, 1997-2006.

<table>
<thead>
<tr>
<th>Linear and quadratic terms</th>
<th>Un-standardized partial regression coefficients</th>
<th>t-statistic</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time ($\hat{\beta}_1$)</td>
<td>Estimate = -10.657, SE = 0.294</td>
<td>36.25</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time$^2$ ($\hat{\beta}_2$)</td>
<td>Estimate = 0.070, SE = 0.002</td>
<td>29.78</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Constant ($\hat{\beta}_0$)</td>
<td>Estimate = 524.684, SE = 7.853</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SE = standard error
Coefficient of determination ($R^2$) = 0.948
F-statistic for overall significance of the model = 961; $P < 0.001$
Figure 1. Distribution of proportions of pulmonary tuberculosis positive (per 100,000) migrant workers in Kuwait: 1997-2006.

Figure 2. Lowess smoother (bandwidth 0.3) showing trend in de-seasonalized data on pulmonary tuberculosis positive (per 100,000) migrant workers in Kuwait; 1997-2006.
Figure 3. Yearly distribution of pulmonary tuberculosis positive (per 100,000) migrant workers in Kuwait 1997-2006.

Figure 4. Polynomial regression model fitted to deseasonalized data on pulmonary tuberculosis positive cases of migrant workers in Kuwait 1997-2006.