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EC MICROBIOLOGY
Research Article

Tuberculosis Trends in the Kingdom of Bahrain, Twelve Years Experience with the Implementation of Selective BCG Vaccination Strategy

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Received: September 11, 2017; **Published:** September 20, 2017

Abstract

Objective: Evaluate the trend of tuberculosis (TB) in the kingdom Bahrain over the 12 years period (2005 - 2016) with emphasis on miliary and meningeal form among pediatrics population to detect any adverse trend in the disease after implementation of selective BCG vaccination policy in the kingdom since 2003.

Methods: Retrospective review of TB surveillance data from public health directorate in ministry of health (MOH) with further analysis of miliary and meningeal TB cases in pediatrics over the study period.

Results: There was a total of 2,997 reported TB cases during the period (2005 - 2016); 81% were Non-Bahrainis, 67% were males and 64% had pulmonary disease. TB incidence in Bahrain is declining with no any reported cases of miliary diseases among pediatrics, but with few sporadic cases of meningeal TB among pediatric Bahraini population appear over the period (2009 - 2011), albeit with no further cases of meningeal disease since 2012.

Conclusion: Implementation of selective BCG vaccination policy in Bahrain didn't result in any apparent harmful effect in terms of increase in TB incidence or sustained resurgence of meningeal or miliary TB among pediatric population.

Keywords: *Tuberculosis; Vaccine; BCG; Miliary; Meningeal*

Introduction

Bacillus Calmette-Guérin (BCG) is an attenuated strain of *Mycobacterium bovis* and the only available vaccine against TB since its introduction in 1921, it is most effective in preventing pediatric TB, in particular, miliary TB and tuberculous meningitis. However, it has a limited effect in preventing pulmonary TB, which occurs more frequently in adults [1,2].

WHO published the last BCG position paper [3] in 2004 and recommends that, in settings where TB is highly endemic or where there is high risk of exposure to TB, a single dose of BCG vaccine should be given to all infants at birth, while low TB countries may limit BCG vaccination to selective risk groups.

The International Union Against Tuberculosis and Lung Diseases(IUATLD) [4] had set criteria to help countries in defining low endemicity and to consider discontinuation of BCG vaccination or changing its policy from universal to targeted approach.

As the incidence of TB continues to decline in most developed countries [5], selective BCG vaccination strategies in high-risk populations are increasingly being considered as an alternative to universal vaccination [6-9], particularly among countries that fulfill the IUATLD criteria for discontinuation [4].

In real practice, BCG immunization policies vary widely in countries with low TB burden, many countries have continued universal BCG vaccination practice despite their low incidence, others; BCG vaccination has been replaced by intensified case detection and supervised early treatment with contact tracing, while some countries have chosen to continue BCG vaccination, but adopt a selective approach to be targeted for high-risk group only [10].

In the kingdom of Bahrain, since 2003, the national BCG vaccination strategy was shifted from universal to selective approach targeting high risk group infants (high risk group was defined as newborn to a parent originally from high TB burden country), since the implementation of selective BCG vaccination program, there was no any increment of TB incidence in Bahrain, but there was resurgence of few sporadic cases of TB meningitis among Bahraini pediatric population during 2009 - 2011 as reported in MOH statistics [11] which might be perceived as warning indicator and should justify revising our national TB program, in particular BCG vaccination policy.

Our study aims to explore any adverse trend in TB epidemiology in Bahrain since 2005 (2 years after changing the policy of BCG vaccination from universal to selective approach) with particular emphasis on miliary and meningeal disease among children and to link this data with the recommended national BCG vaccination policy and disclose the challenges in adherence and implementation of selective BCG vaccination policy, along with the dispute of going back to universal approach, bearing in mind the influx of large number of foreign workers from TB endemic countries; given the fact that; according to 2015 statistics in Bahrain 52% of Bahraini population are non-nationals [12] which might adversely affect the TB control in the kingdom.

Materials and Methods

In the kingdom of Bahrain; notification and reporting of all new cases of TB to the disease control section of the public health directorate in ministry of health is obligatory at the time of initiating anti-tuberculous treatment. To ensure such reporting; supply of anti-tuberculosis medication is restricted to the pharmacy of the main governmental hospital where a special registration number is needed to initiate therapy. Collected data were organized in the public health directorate, tabulated and published in the annual report of ministry of health.

In this study, TB surveillance data were retrieved form ministry of health annual report, then further organized and analyzed. Relevant information about TB epidemiology were also extracted and tabulated in reference to IUATLD criteria for defining low TB endemicity.

Further structured review with retrospective analysis of all reported cases of miliary and meningeal TB among pediatric (< 15 years old) were conducted by the authors by reviewing their medical records to select relevant information, and extract necessary data and important risk factors for better defining of target group with high risk of TB exposure among Bahraini infants.

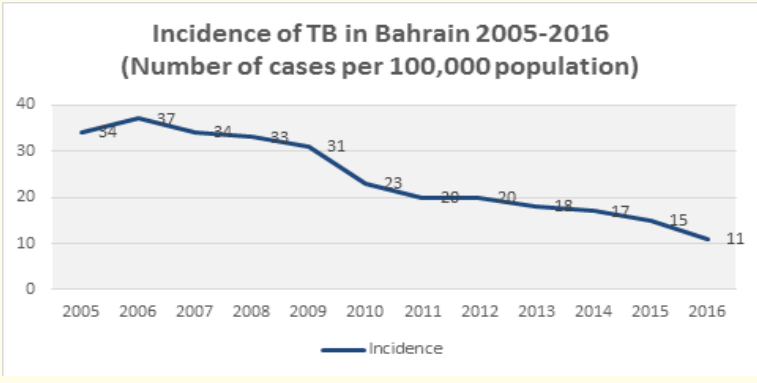
Accompanying that; authors took the initiative to review the current policy of BCG vaccine in Bahrain, its targeted population, process of implementation, reported percentage of vaccine coverage and the method of calculating the coverage rate.

Results

Incidence of TB

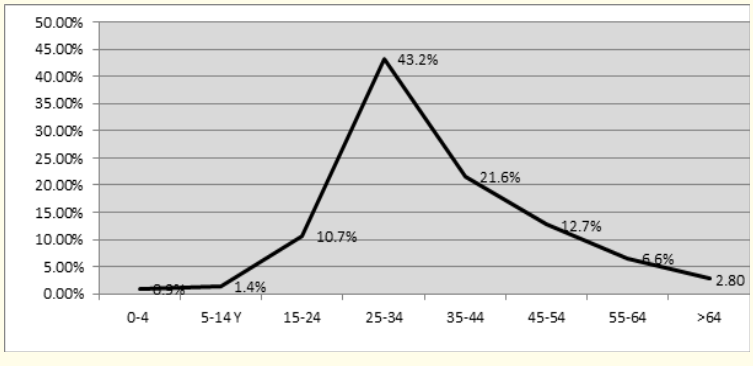
There was a total of 2,997 TB cases reported to the Ministry of Health during 2005 - 2016; out of those total cases 81% were Non-Bahrainis; 64% had pulmonary disease with male predominance of 67%.

The annual incidence of TB started with 34/100,000 in 2005, then it showed a declining trend over the 12 years of the study period till it reached 11/100,000 population in 2016 (Graph 1).

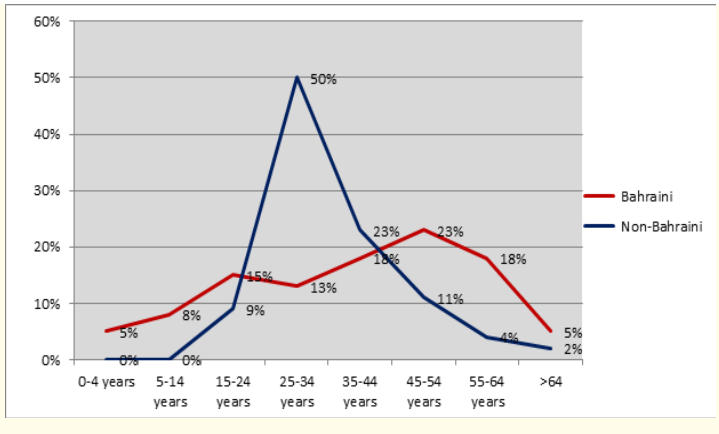


Graph 1: *Annual incidence of TB in Bahrain (2005 - 2016).*

The total number of TB cases were broken down by age groups (Graph 2). 43% of all TB cases were from young adults (aged 25 - 34 years) further stratifying the distribution of cases among different age groups by nationality (Graph 3) revealed that the predominance of young age group (25 - 34 years) among TB cases was basically among the Non-Bahraini population, where there was a peak of distribution of 50% of all TB cases in this young age group, while among Bahraini population the age distribution curve was much smoother with higher proportion of cases around the middle age group (45 - 54 years).



Graph 2: *Distribution of TB cases (2005 - 2016) by age groups.*

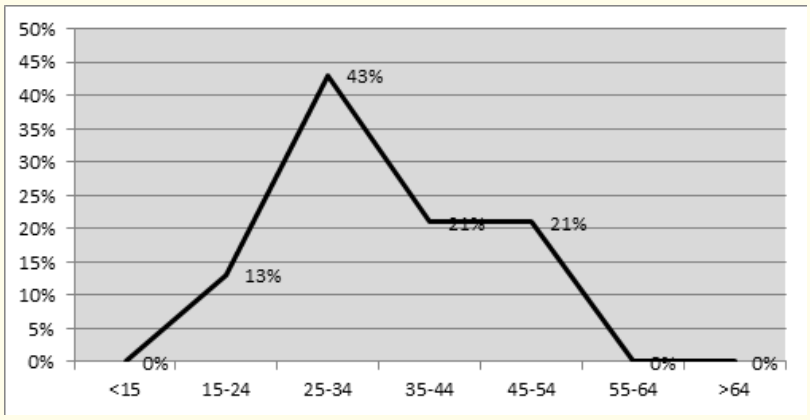


Graph 3: *Distribution of TB cases by age groups stratified by nationality.*

Miliary TB

During the study period, there were 23 reported cases of miliary TB, giving an average annual incidence of 0.16 per 100, 000 population, the trend of incidence was stable over this 12 years with no single reported case over the last 2 years of the study.

As shown in graph 4; the majority of cases were among young adults (aged 25 - 34 years) with no single reported case during the whole study period from pediatric age group (< 15 years).



Graph 4: *Distribution of miliary TB cases by age group.*

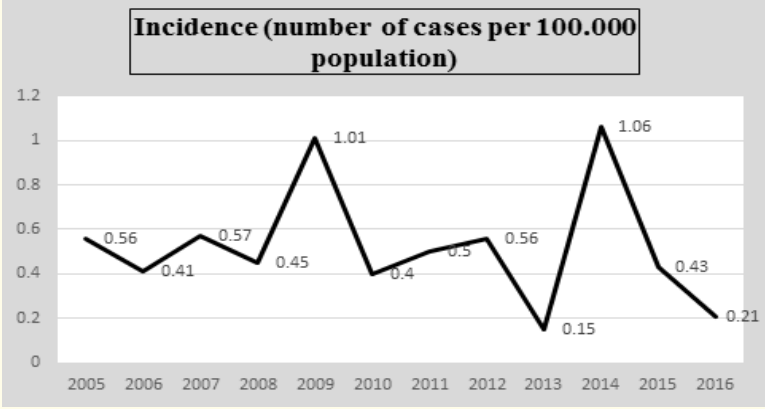
Meningeal TB

There were 75 reported cases of meningeal TB during the study period, giving an average annual incidence of 0.52/100,000 population, the trend of incidence showed some fluctuation, with peaks during 2009 and 2014; where the incidence became > 1/100,000 population.

In 2009, there was a peak of 12 cases of meningeal TB, out of which there was one Bahraini child of 10 years old with remaining 11 cases in the age group (15 - 34 years).

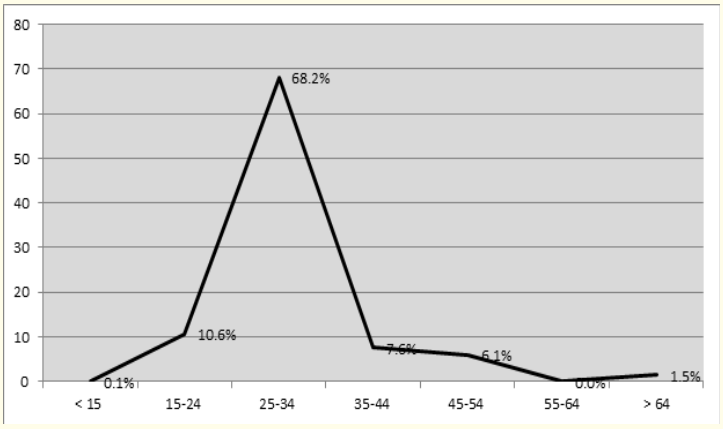
In 2014, a second peak of 14 cases of meningeal TB, all in the age group (15 - 34 years).

During the whole period of study, most cases of meningeal TB were among males and Non-Bahrainis (72.7% and 78.8% respectively) and most are in the age group between 25 and 34 years (Graph 5).



Graph 5: *Annual incidence of meningeal TB in Bahrain (2005 - 2016).*

Further review of all reported meningeal TB among pediatric during the study period revealed the following, total of 4 Pediatric patients (< 15 years) were reported as meningeal TB, they were all Bahrainis in nationality and of Bahraini parents in origin; the first case is 10 years old boy reported in 2009, the second is 14 years old girl reported in 2010 and then 2 cases in 2011 (1 and 4 years old); obtaining risk factors of the four cases: only one of the cases (1 year old that reported in 2011) had a documented history of contact with Non-Bahraini housemaid diagnosed with active pulmonary TB, while there was no other known documented risk factors or exposure among the remaining three cases. All the affected four children didn't receive BCG vaccine in infancy; as all were originally Bahrainis, and not from the target group of BCG vaccine (Graph 6).



Graph 6: *Distribution of meningeal TB cases by age groups.*

Following 2012, there was no any further reported cases of meningeal TB in pediatric age group (< 15 years).

BCG vaccination policy in Bahrain

Before 2003, BCG was administered to all newborns at birth, while since 2003 BCG vaccine is administered only for targeted infants (defined as babies of Non Bahraini nationality or newborns of parents originally from high TB burden countries), vaccine is usually administered routinely for the target group of newborns at maternity hospitals just before discharge.

Defaulters who were targeted for BCG vaccination but didn't receive the vaccine at birth hospitals in Bahrain for any reason are channeled to assigned heath center to receive the BCG vaccine the earliest possible once been recognized by the health care system, identification of such babies usually will take place at the time of registering them in their assigned primary health centers for maternity and child health service which is provided freely for all residents in Bahrain (nationals and non-nationals) or some babies who missed such registration will be identified by their pediatrician or family physician during any visit to the health care system.

BCG coverage rate in Bahrain incremented from 73% in 2011 to about 99% during 2015, but we have to be careful in interpreting this figure of coverage rate which might be wrongly biased or inflated because it considers non-Bahraini children registered in the health care system as the denominator, which might not accurately count all target group of newborns at high risk of TB exposure as it includes only babies who are officially registered as Nan-Bahraini and this will miss a big proportion of babies who might be Bahraini by nationality but originally newborn of parents from high TB burden countries, another pitfall is that babies will be included in the calculation of denominator once they have registered in the health care system, this again will miss children that are born at their country of origin and then brought to Bahrain with their families and not been registered in the health care system.

Discussion

Incidence of TB in Bahrain is decreasing over the last 12 years. Its rate is in 2016 is comparable to other Arabian Gulf countries like Qatar, Kuwait, Kingdom of Saudi Arabia, Oman and United Arab Emirates where the reported incidence per 100,000 population was 34, 22, 12, 8.4 and 1.6 respectively [13]. Male sex predominance among reported TB cases observed in our study (67%), in agreement with other studies as being reported in Saudi Arabia where male contributed for about 62% of TB cases [14], as in other international studies as well [15-19].

Our study revealed that 81% of TB cases were from Non-Bahraini populations, which confirms and extends the results of other previous studies in Bahrain with regard the high proportion of TB among non-national populations [20-22].

Similar demographic data of TB predominance among Non-Nationals was observed in a recent study conducted in Qatar who shared same demographic characteristics of population; who reported 93% of TB patients as been among non-Qataris [23]. However, Other Arabian Gulf countries reported different distribution; with equal proportion between Nationals and Non-nationals was reported from Saudi Arabia in a study conducted by Al-Orainey., *et al*. [24]; over a 20 years' period (1991 - 2010) which showed 52% of the reported tuberculous patients were Saudis. On the other hand, other Arabian Gulf countries such as United Arab Emirates and Oman showed marked predominance of tuberculous cases (76.7% and 79% respectively) among nationals [25,26]. This difference could be explained by more strict pre-employment screening criteria for foreign worker from high TB burden countries been applied in Arabian gulf countries other than Bahrain and Qatar.

Our study showed predominance of TB in general and its severe form of meningeal and miliary among the age group (25 to 34 years), similar results were obtained from Qatar which share the high rate of immigration and high proportion of non-nationals among reported TB cases [23]. This epidemiological data are explained by the vast influx of foreign workers from TB endemic countries in the age group of 25-to- 34 years which account for the majority of TB cases in both countries in addition to the effect of limited screening process for most worker to chest X-ray only without PPD skin testing.

Other studies from neighboring countries like Saudi Arabia where there was equal proportion of TB between nationals and non-nationals, TB incidence increased with age and was highest for those older than 45 years [24], with predominance of miliary form among elderly above 65 years.

Reviewing the meningeal TB statistics in Bahrain with reporting of 4 cases over the period (2009 - 2011) arouses some uncertainties about the best preventive track of implementing BCG vaccination in term of selective Vs. universal approach.

Further review of literature with regard the pros and cons of selective BCG vaccination and its cost effectiveness revealed that the evidence of the benefits of universal BCG vaccination in low endemic settings is uncertain [7-9,27] and as been published in WHO last BCG position paper [3] once the country been defined as low endemic for TB and fulfill IUATLD criteria [4], it would be appropriate to shift its BCG vaccination policy from universal to selective approach provided efficient TB notification system is in place and all other elements of TB control program are been implemented.

In reference to IUATLD criteria [4], BCG vaccination can be discontinued if:

- The average annual notification rate of smear-positive pulmonary TB is < 5 per 100,000 or
- The average annual notification rate of TB meningitis in children aged < 5 years has been < 1 per 10 million population over the previous 5 years or
- The average annual risk of infection is < 0.1%.

Bahrain was defined as low endemic for TB and met the first 2 criteria since 2003 and based on that BCG vaccination policy was changed by MOH authority to the current policy.

In view of reappearing few sporadic cases of TB meningitis during 2009 - 2011, we reevaluate TB statistical data in Bahrain, if it still satisfy IUATLD criteria: the first two criteria are met, as the average annual notification rate of smear-positive pulmonary TB cases is 1.4/100000, and the average annual notification rate of TB meningitis in children aged < 5 years during the last five years of the study (2012 - 2016) is below 1/10 million population. The last criterion was not met as the average annual risk of tuberculous infection in children during the study period (PPD converter among pediatric < 7 years) is about 0.25% [11].

So, in our opinion, changing BCG vaccination policy from universal to selective didn't adversely affect TB control program in Bahrain as evidenced by sustained declining TB incidence with absence of any miliary TB among pediatrics population, on the other hand; resurgence of few sporadic cases of TB meningitis during 2009 - 2011 among Bahraini children might be partly explained by lax of implementing other elements of TB control program in addition to vast influx of foreign workers from TB endemic countries keeping in mind the incremental prevalence of expatriate housemaids and baby sitters in our community, with majority being from high TB burden countries which might adversely affect TB control.

Our opinion is supported by no further reporting of TB meningitis among pediatric population after 2012 (over the last 5 years of the study) with implementation of strict pre-employment criteria for foreign worker (by deporting any foreign worker with abnormal chest X-ray highly suggestive of previous TB infection or exposure accompanied by intensified surveillance for case detection accompanied by early treatment and contact tracing with fully supervised INH post exposure prophylaxis particularly among children, those measure alone were enough to bring the condition under control without any amendment of BCG vaccination policy.

Conclusion

Changing in BCG vaccination policy since 2003 had no apparent harmful effect, as there was no increase in TB incidence in general and no sustained increment in cases of tuberculous meningitis or miliary disease in children.

Accordingly BCG vaccination of special high risk group is favored over the universal approach, however, there is a need for concerted effort to identify eligible infants at high risk of TB exposure and subsequent early vaccine delivery to them by filling the bridge gap to reach this target groups of infants who might not participate fully in the usual health care system as Non-Bahrainis to be identified as defaulters.

Additionally, Optimum surveillance with vigilance for any new case of meningeal or miliary TB among pediatric age group is crucial, as if further cases continue to resurge despite efficient implementation of all other elements of TB control program, there will be a need to revise and possibly to amend the current BCG policy.

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Volume 12 Issue 1 September 2017