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Indicators Used to Measure the Impact of TB Control by World Health Organization

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Abstract

The indicators of tuberculosis (TB) burden not only estimate the epidemic of TB but also assess the effectiveness of national TB control program. This article introduces the estimation and definition of three indicators-incidence, prevalence, mortality-to measure the impact of TB control program by World Health Organization (WHO).

Estimation of TB burden was based on case notification data in approximately 80% countries in the world. WHO suggested four formulas to estimate TB incidence: (1) adopting case notification and case detection to estimate the incidence; however, if the poor quality of case notification or case detection varies in different periods, incidence would be difficult to estimate; (2) using mortality and case fatality rate to estimate, the incidence would be influenced by the vital statistics system and death coding;(3) estimating incidence with annual infection rate multiplied by Styblo coefficient; and (4) estimating incidence by prevalence divided by duration of disease; however, accurate prevalence and infection rate are difficult to obtain and estimation may vary by different duration of disease. Therefore, the WHO recommended that the completeness and reliability of surveillance data should be improved as much as possible to evaluate the TB burden, especially in morbidity and mortality. The research suggested by adopting the WHO

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formulas, Taiwan could estimate its TB burden, and monitor these indicators regularly among HIV positive cases and multidrug resistant TB patients.

Keyword：tuberculosis, burden, indicators, World Health Organization

Introduction

Millennium Development Goals of United Nations target to “combat HIV/AIDS, malaria, and tuberculosis…and by 2015, to decrease incidence, prevalence, and mortality of tuberculosis” [1, 2]. The Stop TB Partnership advocated by 2015, halve TB prevalence and mortality (compared with the baseline of 1990) [3, 4], and in its Global Plan to Stop TB 2006-2015, aims to halve TB prevalence and mortality in 2015 [4, 5].

Since 2004, Taiwan Executive Yuan had launched national initiative of “improving TB control strategy III” (five-year plan), and in 2006 “full-scale promotion plan to reduce tuberculosis by half in a decade” was implemented. The objectives are to decrease the TB cases to 7500 in 2015, and incidence to 34/100000 [6].

Indicators such as incidence, prevalence and mortality were quantitative items for WHO to estimate global TB burden. These indicators not only estimate the global epidemiological situation but also provide health authorities evaluation indicators of effectiveness for TB control program e.g. whether the medication shorten the duration of disease and decrease TB death risks [1]. Therefore, WHO in 2009 set incidence, prevalence and mortality as indicators as the assessment of national tuberculosis control program [7].

These indicators will be published annually on “Global Tuberculosis Control” around October (since 1997, WHO published global report on March 24 every year; but from 2010 onwards, WHO will publish the annual report around October every year [8].), and which are also reference sources of major health indicators of WHO World Health Statistics Report and Global Competitiveness Report organized by World Economic Forum.

The WHO estimated TB burden indicators could serve for health policy evaluation and health plans assessment; besides, those results were estimated by WHO formulas, and could differ from each country’s national TB indicators. Therefore, this article introduces the WHO TB disease burden indicators and organizes relevant researches for reference of public health and health care workers.

Estimated burden of TB: Incidence

Incidence hereby referred to cumulative

incidence in epidemiology. The cumulative incidence is defined that the number of new cases during a time period divided by the number of individuals at risk in the population at the beginning of the study. According to this definition, TB new cases include pulmonary cases (pulmonary combined with extra-pulmonary categorized as pulmonary), extra-pulmonary cases, and TB cases co-infecting with HIV [1, 9, 10]. WHO estimates TB incidence via following four formulas [1, 10]:

(1) Incidence = case notifications / proportion of cases detected
(2) Incidence = annual risk of TB infection × Styblo coefficient
(3) Incidence = prevalence / duration of disease
(4) Incidence = death rate (mortality) / proportion of incident cases that die (case fatality rate)

Formula (1) was estimated from case notification. The case notification was defined that the number of all cases diagnosed as TB patients and reported to national surveillance system and WHO divided by the number of study population. All cases with TB included pulmonary TB patients, extra-pulmonary TB patients, and those patients co-infecting with HIV [1, 9, 10]. The proportion of cases detected referred to the percentage of cases that were notified among the estimated TB cases in that year [1, 9-11]. The estimated TB cases included pulmonary TB cases with smear-positive, pulmonary TB cases with smear-negative, and extra-pulmonary TB cases. If those pulmonary TB cases with smear-positive were the target population of TB control program, the proportion of cases detected for pulmonary TB patients with smear-positive could be calculated and equaled the rate of case detection [10].

Formula (2): estimates by annual risk of infection multiplied by Styblo coefficient. The definition of annual risk of infection indicates percentage of Mycobacterium tuberculosis infection in a group [1, 9, 10]. The Styblo coefficient is an empirical constant value, varied between 40 and 60. WHO estimated that under HIV/TB co-infection rate less than 5 %, if the annual infection rate increased 1 %, the sputum smear positive incidence increases 50 (range 35-65) / 100000 [10]. If the country had good TB control, the Styblo coefficient would be higher (above 50), even over 70. On the contrary, if the epidemic was poorly controlled, the coefficient would be significantly lower, even lower than 40 [9].

On the other hand, if precise or low error prevalence research results were available, formula (3) could be used to estimate the incidence of tuberculosis. Or use death registration system with formula (4) to estimate the incidence of tuberculosis as well.

Although annual risk of infection or prevalence investigation could estimate incidence more precisely, but researches with good study design, high validity and reliability were very few. Even with good study design, TB incidence could be hardly estimated due to fail to precisely calculate duration of TB disease [10]. In addition, when using the annual infection rate and prevalence rate to estimate the incidence, it may difficult to explain the relationship between occurrence of TB and HIV infection [10, 12]. Therefore, WHO in 2008 noted that the annual infection rate of survey

findings are not suitable for widely use in estimating TB incidence [11, 13]. From December 2009, WHO no longer estimated TB incidence from the prevalence of infection at the suggestion of the WHO Global Task Force on TB Impact Measurement [8].

Estimated burden of TB: Prevalence

In epidemiology, the prevalence of a disease in one population is defined as the total number of cases of the disease in the population at a given time. Here, the TB prevalence means at a given time, the total number of TB cases among the total population in a group [1, 9, 10]. TB cases include pulmonary cases, extra-pulmonary cases, and cases with TB/HIV co-infection [1, 9, 10]. The TB prevalence could be estimated by following approaches [1]:

(1) Population-based prevalence survey:

This is a direct estimate of TB prevalence. However, the survey at least recruited 200,000 samples (above 400,000 favored), and needed resources of two million US dollars. The potential error which varied from 25 % (China, Rep. of Korea) to 60% (Eritrea in Africa), was higher than estimating via notification data (potential error, 10%) [7, 11]. Thus, the WHO suggested that those countries of low TB burdens should estimate TB prevalence indirectly by using notification data and formulas. For some high disease burden or high incidence countries, TB prevalence survey should be needed [7].

(2) Case notifications:

This is an indirect way to estimate the prevalence of tuberculosis and is the current WHO approach to estimate TB prevalence in the world [1]. First, estimating TB incidence by case notifications, and then use formula: TB incidence multiplied by duration of disease is TB prevalence, to obtain the prevalence [1, 10]. While the duration of disease means the time of a disease from beginning to the end, that is, the difference of the time between the onset of disease and the end of completed treatment. Since TB has no obvious and specific symptoms, the determination of onset time is difficult due to either the appearance of clinical signs, delay from patient, or delay of diagnosis from physicians. Therefore, the duration of disease for TB is difficult to estimate [10].

Nevertheless, WHO still use mathematical models to estimate the average duration for TB, two years, without medication or therapy. For those who did not receive medication, with HIV/TB co-infection, due to low immunity, the average duration of disease is 0.5 years. In addition, for the DOTS high effectiveness countries (i.e. US and some Western European countries), the average duration of disease was 0.8 years; for the DOTS poor effectiveness countries (i.e. some African countries), the average duration of disease was 1.5 years [10]. Furthermore, for countries with no significant DOTS effectiveness, the duration of TB varied from 1 to 3.5 years, such as 1 year for Singapore and Hong Kong, 1.3 years for Japan, 2.5 years for Philippines, and 3.5 years for Indonesia [10].

TB prevalence was influenced by both incidence and the duration of disease. Therefore, the interpretation on changes of TB prevalence needs more conservative. For example, if higher TB prevalence was observed, it could be due to TB incidence increasing or prolonging the duration of disease. On the contrary, if lower TB

prevalence was observed, it could be due to TB incidence decreasing or shortening the duration of disease by effective medication [11].

Estimated burden of TB: Mortality

Mortality is defined as the total number of TB deaths among the total population at a given time. Here, the number of TB deaths includes the number of pulmonary cases and extra-pulmonary cases [1, 9, 10]. There are three ways to obtain TB mortality: (1) vital statistics (direct estimates), (2) investigating cause of death by autopsy and (3) product of TB incidence and case fatality rate (indirect estimates) [11]. TB case fatality rate is defined as the proportion of deaths due to TB among the same cohort TB cases [1, 9, 10]. TB case fatality rate could be influenced by DOTS program, anti-TB medication, and prevalence of HIV co-infection [1].

For TB patients with positive sputum smears, if not receiving medication, the case fatality rate could be 70%; for those patients with negative sputum smears, if not receiving medication, the case fatality rate could be 20% [10]. For patients with HIV/TB co-infection, if not receiving medication, the case fatality rate could be 90% [10]. Therefore, if cases could be detected early, with higher case detection rate, and appropriate treatment, case fatality rate could decrease and TB mortality could be lower as well [12].

WHO suggested vital statistics would be the ideal approach to direct estimate TB mortality. The main reason is that the vital statistics provide continuous and long-term trends of TB mortality [11]. WHO analyzed the quality of death notification based on completeness and coverage and the results indicated that some countries have high quality of death statistics (i.e. United States, Canada, United Kingdom, Japan, and Singapore); some countries have medium-high quality of death statistics (i.e. Republic of Korea and Philippines); some countries have medium-low quality of death statistics (i.e. Brazil and Russia) [14, 15]. Of the twenty-two TB high burden countries, Philippines, Brazil, and Russia have well quality and reliable death statistics; while China and India have registration statistics only in partial areas, and lack of national statistics [14, 15].

When the vital statistics system becomes more complete and more accurate in coding on cause of death, the estimate of TB mortality will be less biased [1]. When estimating TB mortality, cross validate and cross-referencing TB cohort and vital statistics could help improving data quality [11]. Or the mortality under DOTS program could be adopted since the bias was the least and could close to the true value of TB mortality in a population [7, 9].

Discussion

WHO recommended that each country should collect notification data on a regular basis to estimate TB disease burden (especially mortality and incidence) [7, 11]. WHO suggested each country should increase the reliability of case notifications, and then enhance the convenience and completeness of national surveillance system [10, 11, 16]. TB surveillance system plays a great part in DOTS implementation and serves as key element in Global Stop TB Strategy. The surveillance system could not only help the implementation

of DOTS, but also provide accurate estimation on the TB situation [1, 10]. WHO published policy package in 2009 for measuring rates of TB incidence, prevalence, and mortality: (1) improve surveillance systems to include all (or almost all) incident cases in TB case notification data and to account for all (or almost all) TB deaths in vital registration system; (2) strengthen national capacity to monitor and evaluate the TB epidemic; (3) review and update periodically the data, assumptions and analytical methods used to produce WHO estimates of TB incidence, prevalence, and mortality [7].

Most countries needed to use the case notifications to estimate TB disease burden (Table); therefore, WHO suggested the method of evaluating the quality of notification data (Figure 1) and included three steps: (1) assessment of the completeness and reliability of notification data, including checking whether there are duplicate or misclassified records and whether data meet the criteria for internal and external consistency; (2) analysis of trends in notification data; (3) evaluation the coverage of notification data, with the objectives of realizing notification including all incident TB cases [7, 11]. The internal consistency means that no matter when or where, same results of notification data would be obtained; while, external consistency means the results of analysis from notification data should correspond with existing evidence in epidemiology, including male cases are more than female cases and the number of cases with positive smears are lower than the number of all new cases by 50% [7, 11]. After the evaluation of notification data, countries should improve the completeness and reliability of national surveillance system.

Table. Estimated burdens of tuberculosis, 2007 [7, 17]

Regions	Subgroups	Notified cases[a]			Case detection rate[b]		Incidence[a]		Prevalence[a]	Mortality[a]
		New & relapse	New	New pulmonary, sputum smear +	All new	New sputum smear +	All forms	Sputum smear +	All forms	All forms
America	Canada	5	4	1	84	62	5	2	4	<1
	USA	4	4	2	105	87	4	2	3	<1
Europe	U.K.	13	13	3	84	39	15	7	12	2
	Denmark	7	7	2	81	69	8	4	6	<1
	Netherlands	6	6	1	74	34	8	3	6	<1
Southeast	India	111	103	51	61	68	168	75	283	28
Asia	Thailand	86	83	45	58	72	142	62	192	21
Western	Australia	5	5	1	83	49	6	3	6	<1
Pacific	New Zealand	7	7	2	90	60	7	3	7	<1
	China	74	70	35	71	80	98	44	194	15
	Japan	19	19	7	88	78	21	9	28	3
	Hong Kong	74	69	21	111	75	62	28	63	5
	Singapore	31	28	11	106	96	27	12	27	3
	Rep. of Korea	78	72	23	80	56	90	40	126	10
	Vietnam	111	104	62	61	82	171	76	220	24
	Philippines	160	156	98	54	75	290	130	500	41
	Cambodia	246	242	134	49	61	495	219	664	89
	Malaysia	61	59	36	57	80	103	45	121	18
	Taiwan	66	63	25	74	77	85	32	111	3

[a]Unit: Per 100,000 persons.

[b]Unit: %.

The second step concerns time series of TB notifications, distinguishing between changes that are due to incidence and changes that are due to other factors [7, 11]. The purpose of this step would assess whether notification data can be a good proxy for estimates of TB burden [7, 11].

The final step concerns whether notification data could include all incident TB cases [7, 11]. Capture recapture studies could be used, and evidence-based data also could be collected, such as the knowledge and practices of health-care workers, the requirement and regulations about notifications of cases, and the accessibility to health services [7]. Furthermore, "onion" model could be applied to identify where cases would be lost or missed. Cross-validate between estimate of TB incidence and TB deaths recorded in vital registration system also could improve the coverage of notification data.

On the other hand, because the prevalence of HIV and multidrug-resistant tuberculosis (MDR-TB) would influence the national TB disease burden, the WHO estimated routinely the number of cases with HIV-positive or MDR-TB cases [7]. If the number of estimated MDR-TB cases was over 4,000 cases every year

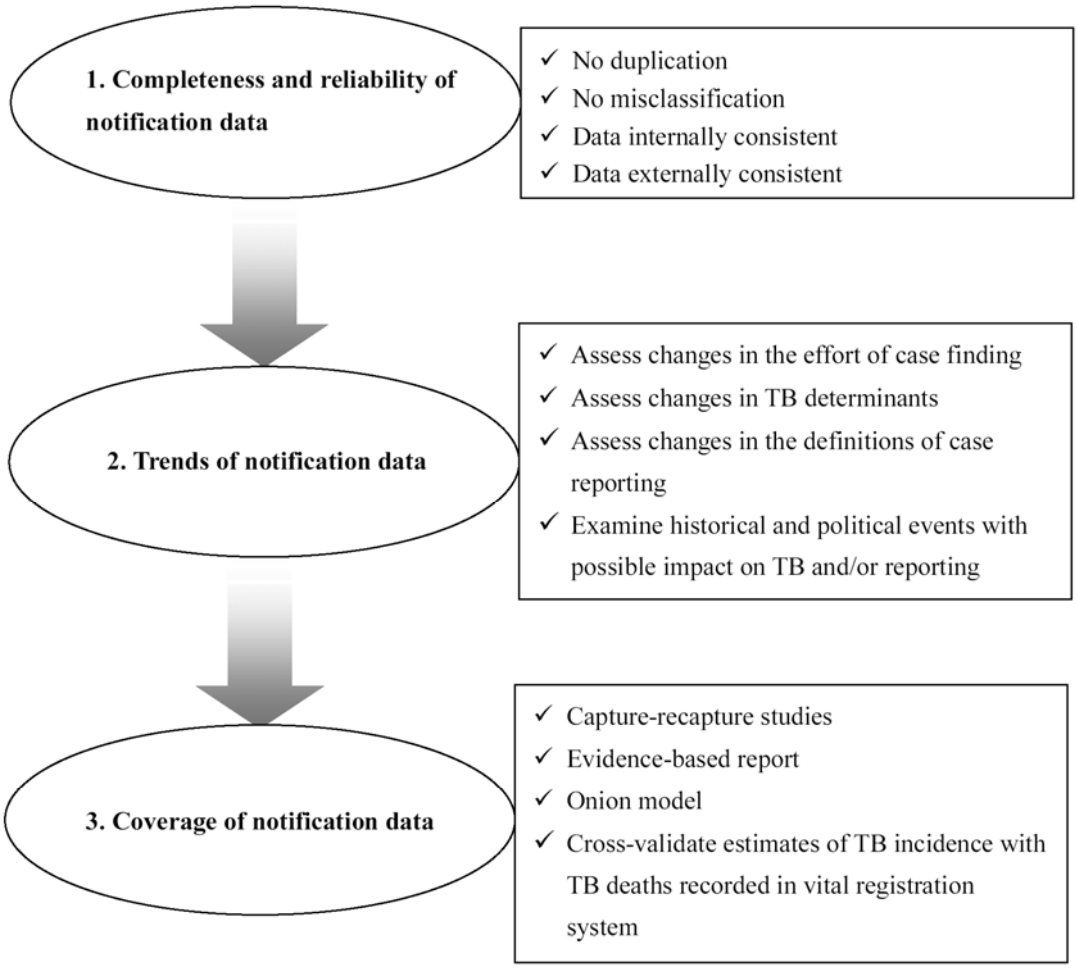

Figure 1. Method of evaluating the quality of notification data [7, 18]

and/or the proportion of estimated MDR-TB cases was over 10% of all TB cases, WHO would regard those countries which satisfy above criteria as countries of high MDR-TB burden [7]. There were 27 countries of high MDR-TB burden in 2007, and 13 countries of these high MDR-TB burden countries were also countries of high TB burden (Figure 2).

Conclusion and suggestion

The estimates of TB burden could be used as the tools of assessing the effectiveness of national TB control program, and monitor long-term changes and trends of TB epidemiology as comparing with other countries. These estimates could understand the epidemiology of TB in Taiwan and relative severity of TB epidemics in the worldwide to amend preventive strategies in a timely manner. At present, the staffs in most countries would report TB notifications to the WHO on a regular basis. The experts in the WHO would verify the reported data and publish the final outcomes on the global annual report. However, the estimates of TB burden in Taiwan could not regularly be validated by internal experts and compared with other countries because of lack of the official channels of international communication.

Thus, the article suggests: (1) to establish the official channels of communicating with WHO, and report actively TB notifications to WHO to improve the precision of estimates of global TB burden; (2) to estimate the burdens of TB in Taiwan by using WHO formulas, and validate the data by inviting WHO or international recognized experts; (3) to refer to the practice of WHO, estimate the disease burden of TB among HIV positive patients as well as MDR-TB cases on a regular basis.

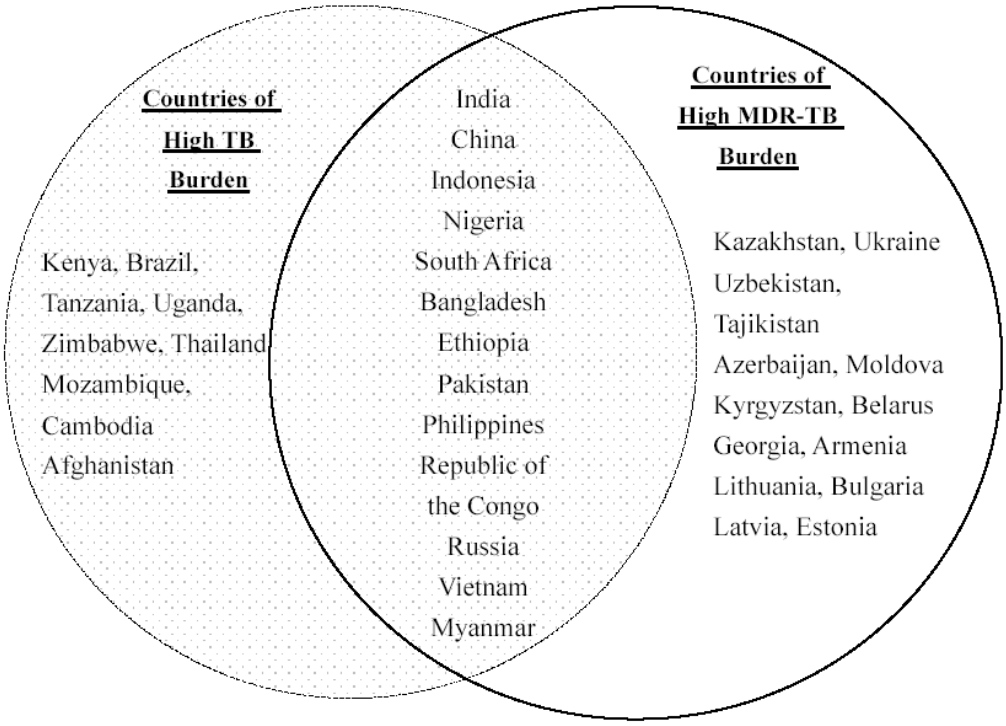

Figure 2. Countries of high TB and/or MDR-TB burden

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Tuberculosis Cluster among Health Care Workers in a Hospital, Taiwan, 2005

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Abstract

About four-fifth of tuberculosis patients decide to receive medical treatment in general hospitals due to changing of medical environment and communicable diseases prevention system in Taiwan. Thus, the risk of exposure to the pathogen for health care workers is increasing. Taiwan CDC received a report of suspected tuberculosis cluster in a hospital from a public health bureau on August 12, 2005. During this investigation, except the index case, 1,194 contacts were screened and 19 health care workers were confirmed as tuberculosis cases. Among the 20 confirmed cases in the cluster (3 males and 17 females), 65% of these cases were nurses in the pulmonary ward. Clinical symptoms were reported in 12 cases and most of which was cough (11 cases). One case showed abnormal with cavitary, 5 pleural effusions and 14 abnormal without cavitary by chest x-ray radiographic examination. However, only 7 cases (35%) were confirmed by laboratory testing. The genotype analysis of the M. tuberculosis isolated from 3 nurses who work in the pulmonary ward showed the same pattern as that of the isolate from the source patient, 11 had epidemiological related linkage but sputum cultures were negative. These 14 cases were considered as a tuberculosis clustering based on the investigative findings. No pathogen was isolated with no epidemiological linkage or different genotypes were found in other 6 cases and, thus, were not listed in the cluster. The infection source was a patient with terminal stage of laryngeal carcinoma. The clinical symptoms of tuberculosis may be concealed by the tumor diseases to delay diagnosis. The exposure risk to tuberculosis in the health care workers is higher than other people and it is important to strengthen the infection control measurements. Any respiratory symptoms should be concerned and the risk of tuberculosis should be evaluated.

Keywords: health care workers (HCWs), tuberculosis, cluster, infection control

Introduction

Based on the data of Taiwan CDC, there were 14,480 new tuberculosis cases confirmed in 2007. The incidence was 63.18 per 100,000 population [1]. Unfortunately, most of the tuberculosis patients may become the infectious source and spread pathogens in the hospital causing hospital-acquired infection before accurate diagnosis. In the event of individual infection or the cluster, the infection source may be the patients, health care workers (HCWs), visitors, or contractors. The transmission route

may occur between patients, patients and workers, and staffs themselves, while transmission between patients and HCWs was most commonly reported [2-4].

On June 18, 2005, a nurse in the pulmonary ward (ward 16S) of a hospital (hospital A) was reported as suspected tuberculosis with negative sputum smear for M. tuberculosis but revealed abnormal chest films. This hospital performed contact investigation through the chest X-ray examination (CXR) based on the “Guidelines for Prevention and Control the Hospital-acquired Tuberculosis”. Few HCWs revealed abnormal chest films, or with clinical symptoms of cough, fatigue or weight loss, which were suspected as a cluster outbreak. The Taiwan CDC established an investigation group to investigate the event, and a medical evaluation group for identification and classification of the cases.

This is the first report for tuberculosis cluster among HCWs in a medical center in Taiwan. This report described the epidemiological investigation, chest radiography and molecular biological methods and discussed the risks of exposure to the M. tuberculosis during health care. This report could be a reference for improving infection control procedure in the hospital.

Background

Hospital A is a medical center in the city, which has 40 negative pressure isolation rooms, 1,485 beds and 3,074 employees (short-term rotators not included). In ward 16S, there are 38 beds, 37 HCWs including 21 nurses and 16 medical doctors. The hospital requests all HCWs wear surgical mask while on duty. Every year, 1-2 times of CXR examination is also arranged. For those who contact to or accidentally exposed to tuberculosis patient unprotected, further CXR examination will be proceeded, but not tuberculin skin test (TST). The infected HCWs will be suspended for at least two weeks and receive medical treatment.

Methods and materials for the investigation

Investigation method: Retrospective research

Investigation period: From August 12, 2005, to January 12, 2007 (the research was concluded when no case was reported within one year after the last epidemiological- linked case diagnosed).

Investigation subjects: The person who had contacted to the index case and qualified to the definition for tuberculosis, while the last regular CXR examination before clinical symptoms occurred still normal.

Data collection: Using the “Questionnaire for listed tuberculosis-related HCWs group” of Taiwan CDC to collect clinical, demographic and epidemiologic data. We also compared the patient lists (August 2004 - August 2005) in the divisions of Internal Medicine and Infectious Disease in this hospital to the CDC tuberculosis database, retrieved the anamneses and conducted field investigation.

Medical evaluation group: Diagnosis and classification of the cases are based on the CXR and sputum examinations, smear, and culture for M. tuberculosis (PCR test included). Group members included 1 radiologist, 2 chest specialists and 3 infectious disease specialists.

Case definitions

Laboratory diagnosis: In each case, acid-fast stain (AFS) smears or cultures were positive for M. tuberculosis in the samples collected from

respiratory tract ; or representative pathology report of tissue biopsy [5].

Clinical diagnosis: Patients (chronic cough, fever, weight loss etc., or abnormal CXR result of tuberculosis) had good improvement in clinical symptoms or CXR examination after anti-tuberculosis medical treatment [5]. Clinical diagnosis should be made by group of specialists.

Definition for cluster and case classification

Cluster: Conformed to person, time and place relationship and identical genotypic examinations performed by the Research and Diagnostic Center, Taiwan CDC, for at least 2 M. tuberculosis isolates collected from the cases.

Case classification:

Cases with Identical genotype

Cases with epidemiological relationship and without genotypic examination

Others (not qualified to 1 and 2)

Results

Twenty tuberculosis-confirmed cases [6 doctors and 14 nurses, index case included) were reported in this cluster. The ratio of male and female was 3:17. The average age was 27 years, ranged from 22-38 years. The average working seniority was 3.3 years, ranged from 0.7-12.6 years (Table 1). In these confirmed cases, 14 (70%) presented abnormal CXR result without cavity, 1 (5%) presented abnormal CXR result with cavity, and 5 (25%) presented pleural effusion. The sputum smear for M. tuberculosis of each confirmed patient was between 1-3 times. Four cases (20%) revealed negative sputum smear for M. tuberculosis, but culture were positive. Three cases (15%) had positive result in both sputum smear and culture. Seven cases (35%) were confirmed as tuberculosis by laboratory diagnosis, while 13 (65%) were based on clinical symptoms (Figure 1). Twelve confirmed cases presented clinical symptoms and coughing was most identical (11 cases); 8 cases revealed 2 or more symptoms (coughing and fever in 4 cases). During the investigation, 1,194 contacts were examined by CXR and 1,175 were confirmed normal, while 19 were reported abnormal based on the examination result. The average number of contact per case was 59.7 (range: 1-135).

From August 2004 to August 2005, there were 13,758 patients in outpatient department and 1,055 hospitalized patients in hospital A. Compared with the tuberculosis database in Taiwan CDC, fifteen patients hospitalized in ward 16S were laboratory confirmed of tuberculosis during hospitalization. The M. tuberculosis isolates collected from 6 patients were stored in the Research and Diagnostic Center, Taiwan CDC. The genotypes of these M. tuberculosis isolates were compared with those collected from 7 cases in the cluster. The M. tuberculosis genotypes were identical between 3 nurses (case 2, 4, 11) and one patient (patient A, the original source case), while the genotype of the other 4 cases (case 16, 17, 18, 20) are different.

Three cases were identical in M. tuberculosis genotype and 11 cases (index case and case 3, 5-10, 12-14) had epidemiological links but without strain isolated; these 14 cases were classified as “a cluster”. We were unable to include other 6 cases in this cluster due to different M. tuberculosis genotypes (case 16, 17, 18, and 20) or no data of genotypic analysis and no epidemiological relationship (case 15, 19).

Table 1. The characteristics of the 20 tuberculosis-confirmed cases in a hospital cluster－Taiwan, 2005

Case no.	Gender	Age	Seniority	Workplace	Position	Symptom#	Date of diagnosis	CXR result	Smear AFS	Culture MTB	Genotype
1 index case	F	22	0.7	16S	Nurse	N/A	2005/6/9	Abnormal without cavitary	－	－	
2	F	23	1	16S	Nurse	Y	2005/8/4	Pleural effusion	－	＋	Identical
3	F	27	5.8	16S	Nurse	N/A	2005/8/9	Abnormal without cavitary	－	－	
4	F	23	1.8	16S	Nurse	N/A	2005/8/11	Abnormal without cavitary	＋	＋	Identical
5	F	32	7	16S	Nurse	Y	2005/8/11	Abnormal without cavitary	－	－	
6	F	25	1	16S	Nurse	N/A	2005/8/11	Abnormal without cavitary	－	－	
7	F	23	2.3	16S	Nurse	Y	2005/8/11	Abnormal without cavitary	－	－	
8	F	27	2.9	16S	Nurse	Y	2005/8/22	Abnormal without cavitary	－	－	
9＊	F	26	1.1	16S	Doctor	N/A	2005/7/18	Abnormal without cavitary	－	－	
10＊	F	25	2.1	16S	Doctor	Y	2005/6/20	Pleural effusion	－	－	
11	F	22	2	16S	Nurse	Y	2005/9/30	Abnormal without cavitary	－	＋	Identical
12＊	F	38	12.6	16S+17N	Nurse	Y	2005/11/16	Abnormal without cavitary	－	－	
13＊	F	25	1.9	16S+17N	Nurse	Y	2005/12/12	Abnormal with	－	－	
14	M	28	1	16S	Doctor	N/A	2006/1/12	Pleural effusion	－	－	
15	F	32	0.9	14S	Nurse	Y	2005/8/8	Pleural effusion	－	－	
16	M	32	1.1	14S	Doctor	N/A	2005/8/18	Abnormal without cavitary	＋	＋	Un-identical
17	F	30	3.6	14S	Doctor	Y	2005/8/26	Abnormal without cavitary	＋	＋	Un-identical
18	F	22	6.9	20N	Nurse	N/A	2005/9/5	Abnormal without cavitary	－	＋	Un-identical
19	M	26	0.8	20S	Doctor	N/A	2006/1/25	Abnormal without cavitary	－	－	
20	F	32	9.5	PICU	Nurse	Y	2005/10/28	Pleural effusion	－	＋	Un-identical

#：Fever, chronic cough, respiratory difficulty, weight loss, weakness, decreased appetite, night sweat… etc.

＊：Worked in ward 16S for at least 6 months before this event.

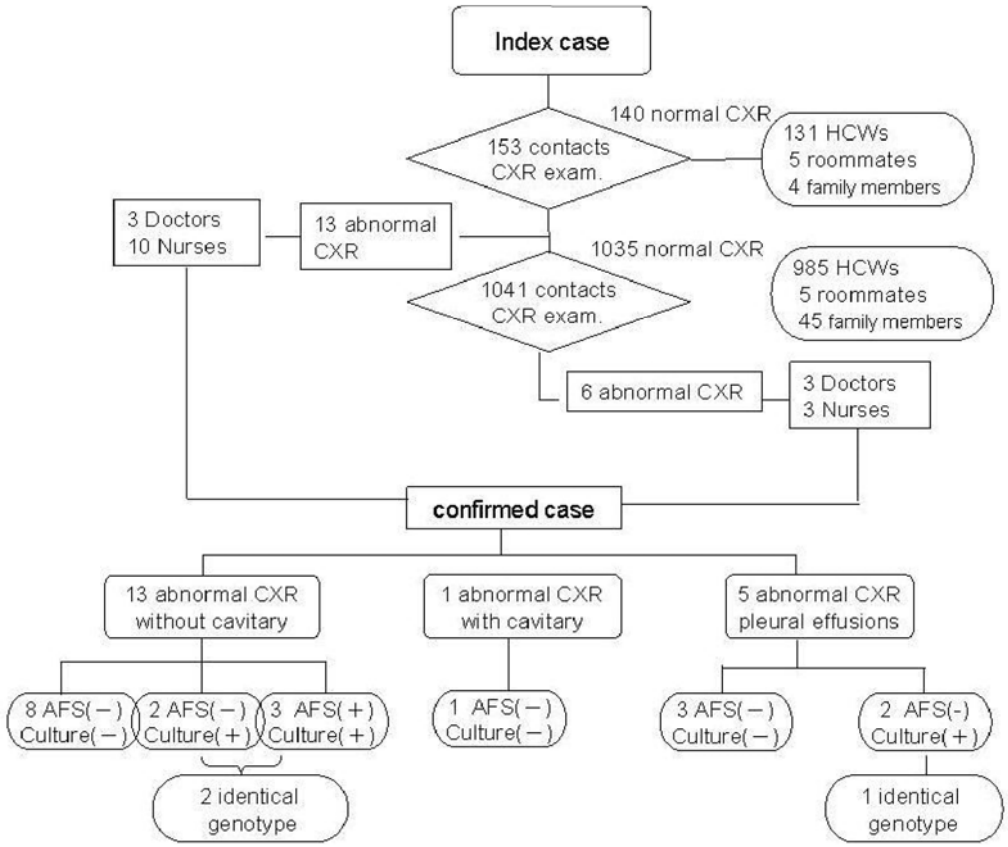

Figure 1. Overview of the contact investigation by CXR examination, smear, and culture results for 20 cases of tuberculosis in a hospital cluster－Taiwan, 2005

Tracing the case history and nursing shift schedule, case 2, 4, and 11 were not the main care-taking nurses for patient A, but they might have contacted to the patient during night shift while checking and assisting medical procedures. Patient A was born in 1949 and was diagnosed for laryngeal carcinoma stage Ⅳ in May, 2004. Three consecutive sputum smears and culture for M. tuberculosis were collected in November 4-6 and all were negative. He was hospitalized on February 3, 2005, due to productive cough, fever and pneumonia in the right middle lobe. Only one sample of sputum smear and culture for M. tuberculosis was collected and was negative. He was moved to the treatment room in order to monitor closely on February 6; his condition deteriorated and chest films showed suspicion of pulmonary abscess on February 14. Pleural fluid was collected on February 17, 2005, through Echo-guided lung aspiration for acid-fast stain (negative in result) and culture. This patient received several cough-inducing and aerosol-generating procedures, including sputum suction, nebulization, laryngoscopic examination, and tracheotomy, during hospitalization. The family members approved for hospice care, and therefore, the patient stayed in the treatment room till passed away on March 1. On May 13, the pleural fluid culture revealed positive for M. tuberculosis and all sensitive to first generation anti-tuberculosis drugs.

During environmental investigation, the treatment room was behind the nurse station and the space of which was smaller than a single

ward (61.41 m^3 vs. 37.13m^3). The left exit of the treatment room was usually closed, but the right exit was not (Figure 2). There were 4 air inlets for the nurse station and 2 exhaust fans situated at both ends of the hallway. Furthermore, there were 2 diffuse-type air inlets in both treatment room and preparation room, but no exhaust port existed. The air flow was directional toward the room and down to the floor based on visualization and smoke tube testing, which was in accordance with standard procedure.

Discussion

CXR is an important and convenient tool for diagnosis of tuberculosis. Most of contacts in this event received only CXR, similar to those in other health care settings, and may be unable to detect subtle changes. Over diagnosis and medical misuse may occur while there is only CXR examination without sufficient bacteriology and pathology evidence [6-9]. Several studies indicated that the risk of exposure to tuberculosis was higher in HCWs than in other people and the prevalence of latent tuberculosis infection (LTBI) in HCWs was 33-79% in low-middle income countries [3, 7, 8]. Other supplemental diagnostic tools, such as tuberculin skin test or QuantiFERON-TB® [3, 7, 9-12], should be offered in order to diagnose the early-stage active tuberculosis or the possibility of LTBI.

The clinical symptoms of tuberculosis were not specific and may be different in cases. Initially these would be easily neglected due to misdiagnosis of upper respiratory infection, only if typical CXR images, clinical symptoms of coughing for at least 3 weeks and weight loss, or epidemiologic evidence for contacting TB patient are presented. In this event, 12 cases had respiratory symptoms of fever, cough and chest discomfort, associated with weight loss,

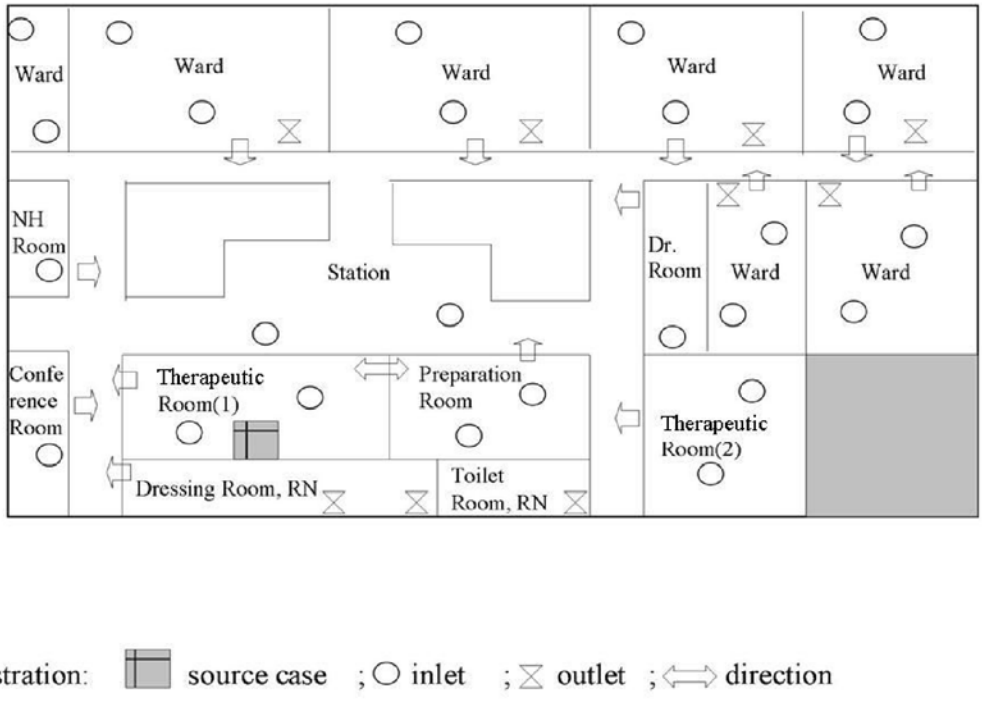

Figure 2. Ward 16S floor plan of hospital A

afternoon fever or night sweat, which were typical tuberculosis symptoms. These cases did not notice the possibility of tuberculosis initially until the investigation. Thus, the risk of tuberculosis should be evaluated while any respiratory symptoms occurred, especially for those who work in the high-risk areas, to fulfill self-protect measures.

The incidence of tuberculosis in HCWs was different in countries and investigations, ranged from 2-50 times higher than community residents. The incidence of those who work in pulmonary, infectious disease ward and emergency departments was 2.9-10.5 times higher than those who work in other sections in the hospital [3, 4, 8, 12]. Studies also indicated that the risk of infection was also related to the age, seniority and work position. Alonso-Echanove et al. found that junior varsity was an independent factor for increasing risk of tuberculosis infection [13]. The result of this investigation was similar to the research described above. The seniority of 5 nurses was less than 2 years in the 14 nurses in this investigation, especially those 3 nurses who had identical genotype for M. tuberculosis (0.9 vs. 3.7; p=0.026). Even though seniority may be related to the risk of exposure, personal characteristics and self-protection measures may also affect. HCWs with higher seniority may not follow standard operation procedures during daily work. Furthermore, HCWs may be exposed to the risk of infection unconsciously because of work overloading. Thus, the relationship between seniority and risk of exposure still needs further study.

Some clinical symptoms of tuberculosis and cancers are similar or overlap and are not easy to differentiate, which may misleads the clinicians or delay the diagnosis. The nosocomial tuberculosis infection may increase when delayed diagnosis occurs or delayed medical treatment [14]. As for the source patient in this investigation, the possibility of tuberculosis infection could not be ruled out, although the sputum smear and culture were all negative in November, 2004. The patient frequently had clinical signs of fever, tachypnea and coughing, while these signs were also usually seen in other diseases and difficult to be distinguished. Therefore, HCWs should evaluate the possibility of tuberculosis when patients of cancer, diabetes mellitus, AIDS, etc. had fever with unknown cause or respiratory symptoms. Although the anti-tuberculosis medicines may have limited help for the patient with critical illness, they were still necessary for decreasing the possibility of disease spread [2, 15, 16].

Three nurses (case 2, 4, 11] had identical genotype with the source patient, which indicates that these nurses may have some levels of interaction with this patient. These 3 nurses fell ill within 1 year (about 6-7 months) after the source patient moved into the treatment room. As previous studies, the risk of falling ill was increased with closer exposure, especially in 1 to 2 years. However, what was the situation when they were infected? Based on the life cycle and transmission mode, the spread of air droplet with infective tubercle bacillus was affected by clinical symptoms and activity of the patient, environmental space, and air circulation [8, 17]. Furthermore, based on the environmental investigation, the transmission may also be related to the personal protective equipment for HCWs and movement of the patient to the treatment room. Reviewing the

records, the patient was arranged in the positive-pressure treatment room about 2/3 period of hospitalization before suspicion of tuberculosis and received some cough-inducing and aerosol-generating procedures. As for environmental infection control, the direction of air flow should be from the nursing station (clean area) toward other wards and then exhausted. Infective tubercle bacillus produced by coughing or nebulization in the treatment room and preparation room behind nursing station could be transmitted toward other wards and clean areas while no air exhaust existed. Clean areas may be contaminated due to mixture of clean air and infectious aerosols, and could be one of the possible causes of this event. Under the situation, personal protective equipment was the last line of defense against tuberculosis infection. The hospital requested all HCWs to wear surgical masks while on duty, however, the practice level was questionable. It was speculated that these nurses were exposed to this disease during preparing medicines (in the preparation room), proceeding charting work or caring for the source patient without sufficient respiratory protection. The accumulation of risk was increased with passing in and out frequently and staying time. In order to protect HCWs and to prevent nosocomial infection, we strongly recommend that all patients with respiratory symptoms should not be arranged and receive any invasive procedures for respiratory tract in the room without air exhaust.

There were 14 personnel affected in the tuberculosis cluster in the ward 16S. These cases may be affected by transmission between each other instead of by the source patient simultaneously, but we could not determine the priority of infection. However, it was affirmative that the transmission route was between the source patient and HCWs or among HCWs themselves. The possible causes for this event include: 1. it was difficult to distinguish the clinical symptoms of respiratory tract cancer and tuberculosis and hence delayed the diagnosis; 2. the source patient received cough-inducing and aerosol-generating procedures in the treatment room resided in the clean area, and the environment was contaminated by the infective tubercle bacillus; 3. personal protective measures were not fully proceeded or lack of sufficient awareness.

This event occurred in May 2007, before revision of “The Definition for Suspected Tuberculosis Cluster”. The investigation and tracing time frame was according to the resolution of the meeting of epidemic investigation group. All the TB confirmed cases were successfully treated in this event. In order to complete tuberculosis control procedures, to prevent public panic, and to prevent disease spreading, this event relied on effective communication between hospitals, mass media, and public health authorities.

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