Influence of meteorologyparameters on pulmonary Tuberculosis morbidity in two Eco-climatic zones in Nigeria

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SUMMARY

Weinvestigated the influence of weather parameters on the morbidity pattern of pulmonary tuberculosis (PTB) in the rain-forest (Ile-Ife)and guinea savanna (Ilorin) zonesof Nigeria. Retrospective clinic data on PTB (1996-2006) were collected from major hospitals in the zones while weather data (1996-2006) were collected from the Nigerian Meteorological agency. The highest reported cases of PTB were found in age-group 20-29 at Ile-Ife (19%) and Ilorin (27%). Gender distribution showed more casesamong malesinthetwo zones. More PTB cases were reported during wet season I and II at Ile-Ife while at Ilorin, wet season I and short dry season had higher concentration of cases. Periods of high PTB reporting at Ile-Ife associated with low ambient temperature, high relative humidity and wind speed. At Ilorin, periods of high PTB cases were characterised by low temperature and wind speed. Early onset of rains in the forest zone was linked with high PTB reporting during intense rainy period, characterised by high wind speed while high cases reporting was in the later phase of rains with low wind speed in the savanna zone. Intervention strategies for PTB control should therefore be sensitive to seasonal characteristics of locations for optimum outcomes.

Keywords: Tuberculosis, eco-health, respiratory diseases, weather parameters, associative analysis

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Introduction

Continuous research into the influence of meteorological parameters on infectious diseases is a veritable strategy for proffering sustainable solution to their morbidity. This is because climate affects infectious diseases more than other disease categories especially in Africa, where the burden of infectious diseases is highest [1]. Of the 56 million deaths per annum estimated by WHO as the global burden of diseases, infectious diseases accounted for more than 26percent. Tuberculosis and other respiratory infections are two of the four major contributors of these diseases [2].

Going by a recent WHO report [3], approximately 4,700 people die of TB infection daily and a total of 1.7 million deaths in 2009 were due to human infection by the disease. Furthermore, TB is the second leading cause of death among adults worldwide. It is equally reported that 13 million people suffer from active TB infection worldwide. These data portray a worrisome globally situation of TB but much more in developing countries where standard of living is low and health services are grossly inadequate. Besides the fact that the tropical countries suffer from high tuberculosis prevalence, they also show an increasing trend of the disease [4].

TB infection is caused by the bacillus, Mycobacterium tuberculosis[3]. It spreads through the inhalation of droplets from an infected person'ssneeze or cough by others people. Although the body immune system is capable of restraining the disease, if the immune status is low and the disease becomes active, the respiratory system and other body organs are subsequently attacked.Global attention targets early detection of the disease, development of effective drugs and combating the emergence of multi-drug resistant strains. In spite of this huge commitment, TB control poses challenges till today owing to its opportunistic association with HIV infection and the emergence of drug resistant strains among other things [3,5,6]. Hence the need to give substantial attention to components that could feed into strategies for prevention.

It is already known that weather variables influence the occurrence of diseases; the influence may be on the reproduction and survival of pathogen or the carriers of pathogens[1]. Moreover, weather condition may encourage the exposure of human to high concentration of pathogen characteristic of places where population (patients and healthy individuals) congestion is found [7]. According to Nakajiet al. [8] and Bragaet al. [9], mortality cases arising from tuberculosis, other

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respiratory diseases, diabetes and heart diseases among others peaked during the cold time of year. In the mid-90s, the Greater London recorded 150% increase in respiratory infections-related mortality at winter than summer [10].

Clinical cases of pulmonary and extra-pulmonary tuberculosis showed peak occurrence during the spring and summer seasons [11]. According to Nakajiet al. [8] and Ford [12], morbidity and mortality of respiratory diseases (including tuberculosis) were higher at winter period than summer. The plausible explanation of this apparent contradiction can be linked to the lag period of months between the infection of *M. tuberculosis* (possibly at winter) and clinical manifestation (during summer) [11]. Influence of weather parameters is also considered to be possibly indirect and contextual [13]; affecting human activities, nutrition status, body immune system and exposure to beneficial sun rays.

Generally, most investigations into tuberculosis epidemiology and intervention focus chemotherapy administration, the emerging resistant strains, and the contribution of socio-economic factors [5,14,15]. There is a dearth of studies on the influence of meteorological variables on PTB [16] especially in the sub-Saharan Africa countries [11]. Some of the available few studies submerged PTB under broad respiratory diseases [17]while the findings of some other studies are inconclusive or contradictory as study area varied [11] on the basis of climate or season types. From

available studies the specific influence of weather parameters on PTB occurrence are not well understood. Understanding the role of weather variables on the morbidity of PTB has potential for identifying weatherrelated markers that can assist effective allocation and efficient utilisation of health resources in the sub-Sahara African region. Moreover, identifying the role of weather parameters in PTB morbidity will contribute significantly to planning intervention strategies in response to climate change in this part of the world. In the current study, we investigated the relationship between monthly and seasonal pattern of PTB and weather parameters in two eco-climatic zones in Nigeria. Moreover, the correlation and influence of weather parameters on PTB morbidity in the study area was analysed.

Study Locations

Ile – Ife (7° 30¹N, 4° 31¹E) is situated in the humid forest zone of Nigeria (Figure 1). It hasan annual rainfall which exceeds 1400mm, which covers February to November but concentrated between March and October. Average relative humidity is about 55% duringthe dry season and 90% during the rainy season. The mean daily maximum temperaturesrange from 28 to 33°C, while the mean daily minimum temperatures range from 15to23°C. The mean daily wind speed ranges from about 2.5to 5m/s [18,19]. In 1991 the population of Ile-Ife was put at 261,900 while 2006, the figure was estimated at 644,373 people.

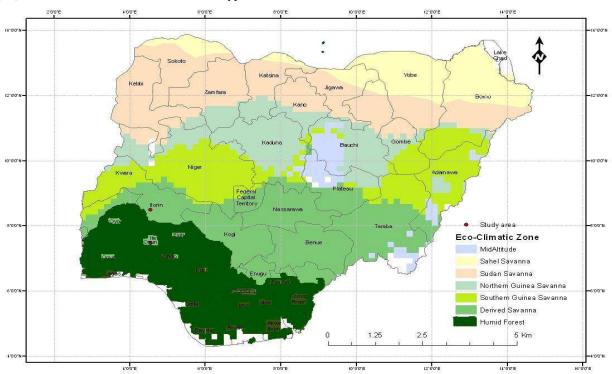


Figure 1: Map of Nigeria showing the study areas in the Eco-climatic zones of Nigeria

The second location, Ilorin (8° 30¹N, 4° 35¹E) is situated in the guinea savanna zone of Nigeria (Figure 1). It has an annual rainfall of about 1000mm to 1200mm, which covers the month of March to October. The relative humidity ranges from 75 to 85% during the rainy season while that of dry season is between 38 and 50%. The mean daily maximum temperature ranges from 27 to 37°C, while the mean daily minimum temperature ranges from 18 to 24°C [18,19]. Estimated population of Ilorin, as at 2007was 893,960.

Materials and Methods Data collection and Processing

Data on rainfall (mm), relative humidity (%), maximum and minimum temperature (°C) and wind speed (m/s) between 1996 and 2006 were collected from Nigeria Meteorological Agency. This is the agency that is accredited for meteorological data collection, documentation and dissemination. Secondly, retrospective clinic data on PTB (1996–2006) were extracted from the Diagnostic Index Card (DIC) of patients at the ObafemiAwolowo University Teaching Hospital, Ile–Ife, Osun State and University of Ilorin Teaching Hospital, Ilorin, Kwara State.

Access to clinic data was granted after the ethical committee of each of the two hospitals examined the study proposal and cleared it of any ethical implications. According to the coding system of the International classification of diseases, PTB carries J44.9 while the DIC code is 011.9. The specific information retrieved from the records of the patients includes age, sex, months and year of reporting of the disease. The ages of the patients were categories into 0–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79 and 80 years and above for analysis purpose.

Simple descriptive and quantitative analyses were employed to compute the monthly, seasonal and annual trends of PTB. Apart from the monthly and annual trends, six season groups adapted from Omonijo *et al.*[20]namely: dry season (January and February), transition to wet season (March and April), wet season I (May to July), short dry season (August), wet season II (September and October) and transition to dry season (November and December)also formed the basis of the temporal analysis.

Graphical representation was used to depict the possible modulation effects of weather parameters on monthly and seasonal group trends. In order to identify the specific weather parameter that showed significant association with PTB and those that explain the temporal pattern, correlation statistic and stepwise multiple regression analysis were conducted. The data entry was done on Excel spread sheet and imported into the Statistical package for the Social Sciences (SPSS version 18) for analysis.

Results

Between 1996 and 2006, 2056 and 2647 cases of respiratory diseases were reported at Ile-Ife and Ilorin with PTB occupying the third position (14.2 and 21.2%). Out of 292 and 562 cases of PTB reported in Ile-Ife and Ilorin, age-group 20-29 recorded the highest percentage(19.2% and 24.7%), followed by 30-39 (15.4% and 20.8%) as shown in Table 1.

Table 1:Demographic characteristics of PTB patients (1996-2006)

Demographic		
characteristic	Ile – Ife (%)	Ilorin(%)
Age Group		
Below 10 years	37 (12.7%)	67(11.9%)
10 – 19 years	3 (11.3%)	64(11.4%)
20 – 29 years	56 (19.2%)	139(24.7%)
30 - 39 years	45 (15.4%)	117(20.8%)
40 – 49 years	42 (14.4%)	49(8.7%)
50 – 59 years	29 (9.9%)	51(9.1%)
60 – 69 years	32 (10.9%)	49(8.7%)
70 – 79 years	13 (4.5%)	16(2.8%)
80 years and above	5 (1.7%)	10(1.8%)
Total	292(100%)	562(100%)
T-Test (t-value, α)	11.0, 0.001	12.6, 0.001
Gender		
Female	127 (43.5%)	228 (40.6%)
Male	165 (56.5%)	334 (59.4%)
Total	292 (100%)	562 (100%)

Other age-groups recorded fewer cases while 80 years and above had the least. Morbidity cases showed significant variation among the age groups at Ile-Ife and Ilorin (P<0.01). Moreover, the distribution of tuberculosis according to gender of patients in Ile–Ife and Ilorin showed higher percentage of cases among males (56.5% and 59.4%).

At Ilorin, the highest cases of PTB were reported in 1999, followed by a year preceding and after it. The highest cases at Ile-Ife were reported in 2002 followed by year 2000. While the annual trend of reported cases at Ile-Ife showed a decline, the trend at Ilorin appeared static during the study period (Figure 2).

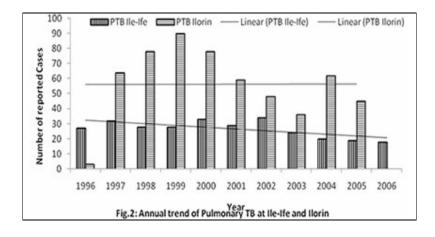
In September and October, PTB cases were higher than the monthly mean values of 47 cases at Ilorin area, followed by December and January. At Ile-Ife area, high cases of PTB (above monthly mean values of 25 cases) were reported between July and September. There was significant difference (P< 0.01) in the monthly pattern of PTB cases in the two areas within the study period. In order to present the concise seasonal pattern of PTB morbidity, six season categories were employed as shown in Table 2.

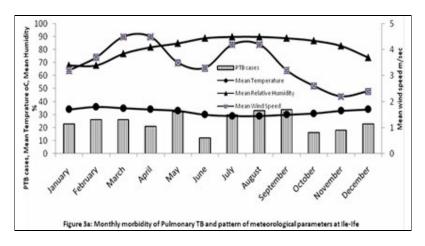
Table 2: Seasonal distribution of PTB cases (1996-2006)

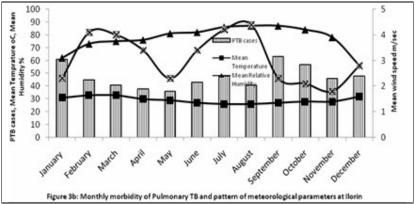
Season Group	Ile–Ife		Ilorin	
	Cases	Seasonal mean	Cases	Seasonal mean
Dry season	49	25	106	53
Transition to				
wet season	47	24	79	40
Wet season I	74	37	127	64
Short dry season	33	33	41	41
Wet season II	50	25	120	60
Transition to				
dry season	41	21	94	47
T-test (t-value, α)	6.2, 0.001		4.4, 0.001	

At Ilorin, the highest cases of PTB were reported during wet season I (July - September) with a seasonal mean value of 64 cases per month. Another season with almost equal mean monthly cases was wet season II (60 cases). Generally, the seasonal pattern was of the order: wet season I>wet season II>drv season>transition to dry season> short season>transition to wet season. The seasonal pattern at Ile-Ife was of the order: wet season I> short dry season> wet season II> dry season> transition to wet season> transition to dry season. In the two zones, wet season I and wet season II had the concentration of reported cases of PTB.

Figure 3a and 3b show the monthly pattern of PTB with the modulating effect of temperature, relative humidity and wind speed at Ile–Ife and Ilorin. From Figure 3a, high occurrence of PTBcoincided with temperature of 29.0°C to 31.0°C, relative humidity of 85.0 to 89.0% and wind speed of 3.5ms⁻¹ to 4.3ms⁻¹ in the months of May to September at Ile-Ife. At Ilorin (Figure3b), PTB cases peaked at 26.4°C to 27.5°C in the months of July to October. While the peak periods occurred during the wet season in the zones, it started and ended earlier at Ile-Ife.







Correlation analysis between PTB morbidity and mean maximum temperature (R=-0.16) was negative while mean wind speed (r=0.46) and mean relative humidity (r=0.17) had positive values. Only mean wind speed correlation coefficient (P=0.08) was near the significant level (p \leq 0.05), P values of other parameters were greater than 0.1. At Ilorin, the selected weather-related variables showed negative association with PTB morbidity. Only mean wind speed (R=-0.47) was significant at 0.06, P values of other parameters were higher than 0.1.

Moreover, stepwise regression analysis showed that mean wind speed, mean maximum temperature and mean relative humidity explained 18%, 2.4% and 1.2% of the monthly pattern of PTB morbidity in Ile-Ife area.In Ilorin area, a similar influence of weather related parameters was observed between each of mean wind speed (21.9%),mean maximum temperature (1.3%) and mean relative humidity (1.0%), and the monthly pattern of PTBmorbidity. At Ilorin (savanna zone), the negative correlation between mean wind speed and the morbidity pattern of PTB points to the prevalence PTB cases during the late wet season and early dry season.

The regression models involving all the weatherrelated parameters and PTB morbidity for the two locations involved in this study are given in equation 1 and 2.

Where: PTB denotes pulmonary tuberculosis, RH is the relative humidity, WS is the wind speed and T is the temperature.

Discussion

PTB stood as one of the three major respiratory diseases in the two eco-climatic areas in Nigeria. This finding is confirmed by other authors [21,22]. Although the absolute number of respiratory diseases varied between the forest and guinea savanna areas, the profiles are identical. The demographic analysis of tuberculosis patients in and outside Africa[23,24]agree with the high cases of PTB among ages 20-29 as indicated in this study. The concentration of PTB cases within this age cohorts may be connected with lifestyle of health care neglect, high mobility and the associated poor nutrition habit among people in this age-group who are largely new entrants into the labour-force.

Higher morbidity of PTB among males concurs with similar gender bias observed by Ane-Anyangwe, et al.[23] and Mabaera et al. [25]in parts of Africa and beyond. The global tuberculosis data presented by Fares [11] equally showed higher occurrence among males in different geographical locations. According to

the reports of Koren[26] and USEPA [27], environmental and occupational factors contribute to higher percentage of respiratory diseases among males. Higher exposure of males to pollens, dusts, indoor and ambient air pollutants among others in the course of their occupation is culpable. Gender differentiation of occupation and social roles in most African societies reserves tasks that involve exposure to pollutants and tress for males [17,28,29]; hence their health may be impaired with frequent exposure to pathogens.

Therelatively high cases of PTB reported in 1999 at Ilorin and 2002 at Ile-Ife may not be unconnected with better public awareness about TB detection and care, especially with the introduction of DOTS programme in the 1990sin Nigeria. Low public awareness of diseases generally contributes to low reporting apart from the negative attitude to medical facilities utilization [30,31] in less developed societies.

The temporal pattern of PTB showed a significant connection with the wet (rainy) season at both the forest and savannah zones. Ane-Anyangwe, et al. [23] equally pinpointed wet season as tuberculosis peak period in south-western Cameroon while some studies conducted outside the tropics pointed to winter period [8,32-34]. Since wet and dry seasons are the major season types in Nigeria, the wet season is characterised bycool temperature and ambient raining condition that constrainpeople to stay indoor for several hours. This leads to crowded indoor environment coupled with poor ventilation in low income areas, which has been identified as a significant factor in the spread of tuberculosis infection among human populations [11,35,36].

Mean wind speed has the highest positive correlation with and contribution to the temporal morbidity pattern of PTB at Ile-Ife. Ideally, intense wet season in the study area is characterised by rainstorms produced by strong convectional wind system, high relative humidity and low temperature. When rain falls, strong wind coupled with thunder prevails in the ambient environment and the associated cool temperature constricts most people indoor for several hours. In order to prevent the incursion of the strong wind into living apartments, doors and windows are shut, thereby leading to low airflow and poor ventilation indoor. According to Fares [11], low airflow in indoor environment is a risk factor in the transmission of tuberculosis. Escombe et al. [37] and Wood et al. [38] established through experimental studies that opening windows and doors drastically reduces the risk of PTB transmission. Besides, high wind speed from PTB prevalent areas (hot spots) is capable of dispersing droplets bearing M. tuberculosis to other residential areas thereby initiating tuberculosis infection among exposed communities "down-wind" [38].

The negative correlation between mean wind speed and PTB morbidity pattern at Ilorin agrees with high cases

reported during the late wet season and early dry season. This is attributed to existence of lag period of months as indicated by Fares[11]; hence PTB infections during intense wet season manifested about two months later in September and October. These months coincided with late wet season when the prevailing winds have low speed.

Conclusion

The temporal pattern of PTB showed a significant connection with the wet (rainy) season at both the forest and savannah zones of Nigeria although there was an earlier onset in the former area. PTB preparedness programme therefore can adopt wetness and the accompanying conditions as weather-related markers in the humid tropical region. In view of this, the study recommends an integrated public health education and mobilization of medical resources for PTB prevention response and adaptation from the onset of wet season, which is identified as critical season or PTB "cluster period" in the zones.

Finally, in view of climate change, the influence of weather parameters on the morbidity pattern of PTB has critical implications for the respiratory health of populations in the humid tropical region of Africa.

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References

- 1 Wilkinson P. Climate Change and Infectious Disease in Africa and the UK. In:Infectious Diseases: preparing for the future. Public and Environmental Health Research Unit, London School of Hygiene and Tropical Medicine, 2006. http://www.foresight.gov.uk. 30p
- 2 WHO (2004a) Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Ezzati, M., Lopez, A.D., Rodgers, A. & Murray, C.J.L. (eds.) Geneva.
- 3 WHO Global TB Report (2010). http://www.tballiance.org/why/tb-threat.php (cited in June 2011).
- 4 Prabhakar R. Tuberculosis--the continuing scourge of India. *Indian J Med Res.* 1996; **103**: 19-25.
- 5 Dye C and Espinal MA. Will tuberculosis become resistant to all antibiotics? *Proc. R. Soc. Lond. B. Biol. Sci.* 2001; **268**:45–52.

- 6 World Health Organization. Anti-tuberculosis drug resistance in the world, report #3. WHO; Geneva: 2004.
- 7 Checkley W, Epstein LD, Gilman RH, Figueroa D, Cama RI, Patz JA, BlackRE.Effect of El Niño and ambient temperature on hospital admissions for diarrhoeal diseases in Peruvian children. *Lancet* 2000; **355** (9202): 442-450.
- 8 Nakaji S, Parodi S, Fontana V, Umeda T, Suzuki K, Sakamoto J, Fukuda S, Wada S and Sugawara K. Seasonal changes in mortality rates from main causes of death in Japan (1970-1999). *European Journal of Epidemiology* 2004; **19**:905-913.
- 9 Braga ALF, Zanobetti A and Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities. *Environmental Health Perspectives* 2002; **110**: 859-863.
- 10 Kovats RS, Hajat S and Wilkinson P. Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. *Occupational and Environmental Medicine* 2004; **61**:893-898.
- 11 Fares A (2011). Seasonality of tuberculosis. *J. Global Infect Dis* 2011; **3**:46-55.
- 12 Ford MJ. The changing Climate: Responses of the Natural Fauna and Flora. George Allen and Urwin, London, United Kingdom. 1981.
- 13 Maes M, Stevens W, Scharpe S, Bosmans E, De Meyer F, Dhondt P, *et al.* Seasonal variation in peripheral blood leukocyte subsets and in serum interleukin-6, and soluble interleukin-2 and -6 receptor concentrations in normal volunteers. *Experientia* 1994;**50**:821-9.
- 14 Oguntoke O, Muili TH and Bankole MO. Morbidity pattern of pulmonary tuberculosis and housing quality in Lagos metropolis, Nigeria. *International Journal of Risk Assessment and Management* 2009; **13** (2): 115-126.
- 15 Sel'tsovskiĭ PP, Litvinov VI and Slogotskaia LV. Influence of social factors on tuberculosis mortality, effectiveness of socio-medical preventive measures in Moscow in the 20th century. *ProblTuberkBoleznLegk*. 2004; 2:11-16.
- Douglas AS, Strachan DP and Maxwell JD. Seasonality of tuberculosis: the reverse of other respiratory diseases in the UK. *Thorax* 1996; **51**: 944—6.
- 17 Ayres JG. Meteorology and respiratory disease. *Update* 1990; **40**: 596 605.
- 18 Ayoade JO. Introduction to climatology for the Tropics, John Wiley and Son,
- Chickheste, U.K. 1983; 167pp.

- 19 Philips G. Modern Atlas for Africa. John Wiley and Son, UK. 1996.
- 20 Omonijo AG, Oguntoke O, Matzarakis A and Adeofun CO. A study of weather related respiratory diseases in Eco-climatic zones. African Physical Review 2011; **5**(3): 41-56.
- 21 Nwonwu EU, Oyibo PG, Imo AOC, Ndukwe CD, Obionu CN and Uneke CJ. Radiological features of pulmonary tuberculosis in HIV-positive and HIV-negative adult patients in south-eastern Nigeria. Mera: *African Journal of Respiratory Medicine* 2008;20-23.
- 22 Akanbi MO, Ukoli CO, Erhabor GE, Akanbi FO and Gordon SB. The burden of respiratory disease in Nigeria.Mera: *African Journal of Respiratory Medicine* March 2009.
- 23 Ane-Anyangwe IN, Akenji TN, Mbacham WF, Penlap VN and Titanji VP. Seasonal variation and prevalence of tuberculosis among health seekers in the South Western Cameroon. *East Africa Medical Journal* 2006; **83**: 588-95.
- 24 Richter C, Ndosi B, Mwammy AS and Mbwambo RK. Extrapulmonary tuberculosis-a simple diagnosis?a retrospective study at Dar es Salaam, Tanzania. *Tropical and Geographical Medicine* 1991; **43**:375-78.
- 25 Mabaera B, Naranbat N, Katamba A, Laticevschi D, Lauritsen JM and Rieder HL. Seasonal variation among tuberculosis suspects in four countries. *International Health* 2009;1:53-60
- 26 Koren HS. Environmental risk factors in atopic asthma. *International Archives of Allergy and Immunology* 1997; **113**: 65 68.
- 27 United States Environmental Protection Agency (1998): National Air Quality and Emissions Report. CPA Pub. No. EPA 454/R-98-016. Research Triangle Park, NC: EPA, 1998.
- 28 Adefolalu DO. On Bio-climatological Aspects of Harmattan Dust Haze in Nigeria. *Archives of Meteorological*, *Geophysical and Bio-climatological Sciences*, 1984; B 33.
- 29 Rieder HL. Socialization patterns are key to transmission dynamics of tuberculosis (Editorial). *International Journal Tuberculosis and Lung Disease* 1999; **3**:177-8.
- Chukuezi AB. Profound and total deafness in Owerri, Nigeria. *East African Medical Journal* 1991; 68: 905–912.
- 31 Bandele EO and Olude IO. An analysis of deaths due to Tuberculosis at the University of Lagos Teaching Hospital, J. National Med. Association 1985; 77: 8
- 32 Atun RA, Samyshkin YA, Drobniewski F, Kuznetzov SI, Fedorin IM and Coker RJ. Seasonal

- variation and hospital utilization for tuberculosis in Russia: hospital as social care institutions. *European Journal of Public Health* 2005;**15**:350-4.
- 33 Nagayama N and Ohmori M. Seasonality in various forms of tuberculosis. *Int. J Tuber Lung Dis* 2006; 10:1117-22
- 34 Luquero FJ, Sancez-Padilla E, Simon-Soria F, Eiros JM and Golub JE. Trend and seasonality of tuberculosis in Spain, 1996—2004. *International Journal Tuberculosis and Lung Disease* 2008; 12:221-4.
- 35 Guzel R, Kozanoglu E, Guler-Uysal F, Soyupak S and Sarpel T. Vitamin D status and bone mineral density of veiled and unveiled Turkish women. *J. Women's Health Gender Based Med* 2001; **10**:765-70.
- 36 Kim JH and Moon SJ. Time spent outdoors and seasonal variation in serum concentrations of 25-hydroxyvitamin D in Korean Women. *Int. J Food SciNutr* 2000; 51:439-5.
- 37 Escombe AR, Oeser CC, Gilman RH, Navincopa M,Ticona E, Pan W, Martínez C, et al. Natural Ventilation for the Prevention of Airborne Contagion. *PLoS Med.* 2007; **4**(2)
- 38 Wood R, Johnstone-Robertson S, Uys P, Hargrove J, Middelkoop K, Lawn SD and Bekker L. Tuberculosis transmission to young children in a South African community: modelling household and community infection risks. *Clinical Infectious Diseases* 2010; **51** (4):401–8.