The nutritional status of patients with tuberculosis in comparison with tuberculosis-free contacts in Delft, Western Cape

Lombardo CC, MPH, RD(SA), Lecturer
Swart R, PhD, RD(SA), Head of Department
Visser ME, PhD, RD(SA)
Division of Nutrition and Dietetics, University of the Western Cape
Correspondence to: Candice Lombardo, e-mail: clombardo@uwc.ac.za
Keywords: malnutrition, tuberculosis

Abstract

Objective: To report on the nutritional status of newly diagnosed patients with pulmonary tuberculosis in comparison to contacts who are tuberculosis free.

Design: This was a community-based case-control study.

Setting and subjects: The study was conducted in Delft, a periurban community in the Western Cape. Forty-three newly diagnosed patients with tuberculosis were recruited as cases and matched according to age, gender and race to 43 tuberculosis-free contacts.

Outcome measures: Each participant was interviewed and completed a structured questionnaire to provide demographic information. Weight was measured to the nearest 0.1 kg and height to the nearest 1 mm. Mid-upper-arm circumference (MUAC) was measured to the nearest 1 mm and skinfold thickness measurements to the nearest 0.2 mm. The 24-hour dietary recall method was used to obtain dietary information and analysed in the nutrition database of the Medical Research Council in order to translate foods into nutrients. Biochemical analyses were carried out to measure concentrations of transferrin, albumin, C-reactive protein (CRP), ferritin, zinc, copper and vitamins A and E. Means (± standard deviation) and confidence intervals were used to describe serum micronutrient and biochemical levels. Medians (minimum and maximum) were used to describe the nutrient intake and anthropometric status of patients.

Results: The median body mass index for tuberculosis cases was 18.80 kg/m² [interquartile range (IQR) 14.35, 32.11] and for tuberculosis-free contacts 21.17 kg/m² (IQR 16.75, 34.98), with a significant difference between the groups with a p-value = 0.001. There was a statistically significant difference in weight (p-value = 0.002) and MUAC (p-value = 0.000) between groups; and in ferritin (p-value = 0.000) and CRP (p-value = 0.000) in patients with tuberculosis; while albumin (p-value = 0.000), serum zinc (p-value = 0.000) and serum vitamin A (p-value = 0.000) were significantly lower in cases.

Conclusion: Newly diagnosed patients with tuberculosis have a poorer nutritional status than their tuberculosis-free counterparts. This may be a result of the acute phase response, increased metabolism and anorexia.

Ⓟ Peer reviewed. (Submitted: 2011-11-21. Accepted: 2012-07-30.) © SAJCN **S Afr J Clin Nutr 2012;25(4):180-185**

Introduction

Pulmonary tuberculosis is caused by *Mycobacterium tuberculosis,* which usually affects the apices of the lungs. According to the World Health Organization report on global tuberculosis control,[1] 8.8 million new cases of tuberculosis were reported in 2010. Although there has been a decrease of 3.4% per year in incident rates, tuberculosis remains a major public health problem in most developing countries. In 2009, South Africa had an incidence rate of 971 and a prevalence rate of 808 per 100 000.[2] In 2008, 50 000 new tuberculosis cases were diagnosed in the Western Cape. This is an incidence rate of 892 per 100 000.[3] Therefore, tuberculosis remains a major public health concern, especially in developing countries.

Infection with the bacillus does not necessarily lead to active disease, as the immune response of most individuals can successfully contain, but not eliminate, the infection. A decline in the immune response caused by the human immunodeficiency virus (HIV), ageing, alcohol or drug abuse and poor nutritional status may lead to active infection.[4] Cytokines, including tumour necrosis factor, interleukin-4 and interleukin-1β, are responsible for the high fever, weight loss and acute phase response (APR) that is seen in patients with active tuberculosis. Malnutrition and nutrient deficiencies may result. Alternatively, malnutrition, including micronutrient deficiencies, may affect immunity, leading to increased susceptibly to active infection.

For this reason, malnutrition and tuberculosis have a long history of association.[5] Numerous studies have detailed the poor nutritional status of patients with tuberculosis in terms of body mass index (BMI), mid-upper-arm circumference (MUAC) and skinfold thickness. A study that was conducted by Kennedy et al[6] in Tanzania used BMI to assess the nutritional status of 148 patients who presented with active tuberculosis. They found that malnutrition was evident before and after treatment for tuberculosis. Karyadi et al[7] conducted a case-control study in Indonesia and found that patients had significantly lower BMI, MUAC and skinfold measurements than the controls. It was also noted that patients had varying degrees of malnutrition. Micronutrient deficiency positively related to the level of malnutrition. Therefore, supplementation in this group may prove to be beneficial.

In the Western Cape, the Nutritional Therapeutic Programme (NTP) is currently in place to provide nutritional supplementation to individuals who are malnourished or at risk of malnutrition. Patients with tuberculosis with a BMI of < 18.5 kg/m², or those who have lost 10% of their body weight in six months or 5% in one month, qualify for supplementation.[8] However, these guidelines may need to be adjusted in order to appropriately address malnutrition in patients with tuberculosis.

The purpose of this study was to compare the nutritional status of newly diagnosed patients with tuberculosis, prior to receiving any nutritional supplementation, with tuberculosis-free contacts in Delft, Western Cape.

Method

Study design

A community-based case-control study design was used.

Study population

The study population included adults aged 18-65 years, residing in Delft, a low-level socio-economic, periurban settlement in the Western Cape.

Selection of subjects

Cases

Newly diagnosed patients with tuberculosis aged 18-65 years receiving treatment from the Delft Community Health Centre (CHC) were recruited. Cases were included when two sputum specimens tested positive for acid-fast bacilli by smear microscopy or more than one positive sputum specimen, and a chest X-ray that indicated active tuberculosis was present. Cases that were HIV positive or who had elevated alanine aminotransferase (ALT) levels were excluded from the study.

Controls

All tuberculosis patients who were recruited were used as a point of contact to recruit controls from other households (family and neighbours) who were interested in participating in the study. A sampling frame from the interested households was constructed. It included adults aged 18-65 years who were willing to participate in the study. This sampling frame was used to select controls that matched cases for age, gender and population group. A sputum sample was collected from the controls to confirm the absence of active tuberculosis. Subjects who had positive sputum samples were referred to the Delft CHC for counselling and treatment. Controls who were HIV-positive or who had elevated ALT levels were excluded from the study.

Sample size

Eighty-six subjects were included in the study (43 cases and 43 controls).

Data collection

All cases and controls were interviewed using a structured questionnaire. The following information was obtained:

- *Socio-demographic data:* Socio-demographic characteristics were documented for each subject, including type of housing, housing density, household income and smoking habits.
- *Dietary and anthropometric data:* The dietary intake of participants was assessed by means of one 24-hour recall using a standardised form. According to Rankin et al,[9] the 24-hour recall method may be simple to use and applicable across populations, but respondents may have difficulty recalling intakes and portion sizes which may affect the accuracy of the results. However, it would not have been useful to repeat the 24-hour recall method in cases in this study as symptoms generally improve two weeks after treatment and this may affect the appetite. Portion sizes were determined with the use of food models and examples of common household measures. All data were coded, captured and analysed in the nutrition database of the Medical Research Council in order to translate foods into nutrients.
- *Anthropometrical measurements* included body weight to the nearest 0.1 kg (A & D Personal Precision Scale, Tokyo, Japan) and height on a portable stadiometer to the nearest 1 mm. MUAC was measured to the nearest 1 mm on the left arm using a standardised measuring tape. Skinfold thickness measurements were carried out on the left arm to the nearest 0.2 mm using a skinfold caliper (Scales 2000, Durban, South Africa) and included triceps, biceps, subscapular and suprailiac skinfold measurements. All measurements were taken by a registered dietitian and performed three times. Then the average value was recorded. The percentage of body fat was calculated with the use of Durnin and Womersley equations.
- *Blood sampling:* Venous blood was drawn aseptically from each case and control by the registered study nurse. One 7-ml blood sample, serum-separating tube serum, was collected to determine the ALT level. The samples were analysed and stored at 37ºC. One 7-ml blood sample was collected in a trace-element-free tube, protected from light and stored at -70ºC after centrifugation. The following biochemical investigations were performed using high-pressure liquid chromatography: serum albumin, retinol, zinc, copper, ferritin, transferrin receptor and C-reactive protein (CRP).

- *Sputum samples*: All cases and controls were required to provide the study nurse with a sputum sample, which was collected and transported to the Groote Schuur Hospital laboratory for analysis. Sputum smears were examined by means of fluorescent microscopy (auramine stain). Sputum samples were cultured on liquid (using an automated nonradiometric MGIT™ 960 tuberculosis system) and solid media (Löewenstein-Jensen) slopes to confirm the presence of tuberculosis in cases and the absence of disease in controls.

Statistical analysis

All data were cleaned, coded and entered into SPSS® version 17.0 (SPSS, Chicago, Illinois, USA) by the study leader for analysis. A one-sample Kolmogorov-Smirnov test was used to determine whether variables were normally distributed, and appropriate parametric and nonparametric statistics applied. Means (± standard deviation) and confidence intervals were used to describe serum micronutrient and biochemical levels. Medians (minimum and maximum) were employed to describe the nutrient intake and anthropometric status of patients. Independent t-tests were included to investigate differences between biochemical and micronutrient indicators. The Mann-Whitney test was used to investigate differences between the characteristics of the participants, such as nutrient intake and anthropometric status. Chi-square was employed to determine differences in categorical data.

Ethics and institutional approval

Ethics approval for this study was obtained from the University of the Western Cape Research Ethics Committee. Written informed consent was obtained from all participants. An information sheet that outlined all aspects of the study made it clear that the subject could terminate participation in the study at any time without having his or her health care affected in any way.

Results

The study sample comprised 86 participants (43 cases and 43 controls). The mean age of the sample was 28.21 (± 10.36). The sample included 40 males and 46 females. Socio-demographic data, as presented in Table I, revealed no statistical differences between cases and controls, except for the number of people per household and money spent on food per month. However, the number of controls who were unaware of how much money was spent on food might have affected the latter.

Dietary intake

The dietary intake of energy, macronutrients, zinc and vitamin A, as presented in Table II, was similar between groups. No significant differences between the dietary intake of energy, protein, carbohydrate, fat, zinc and vitamin A between the case group and the control group were found at the time of diagnosis. The vitamin A intake in both cases and controls was found to be inadequate [recommended daily allowance (RDA) 700 µg, which is equivalent to 700 retinol equivalents]. The median intake of zinc in cases was inadequate when compared to RDA. However, the median intake in controls fell in the normal range.

Table I: Socio-demographic information

Categories	Cases (n = 43)	Controls (n = 43)	p-value (chi-square)
Smoking			
Daily	27 (63%)	31 (72%)	0.250
Occasionally	1 (2%)	3 (7%)	
None	15 (35%)	9 (21%)	
Alcohol misuse			
Yes	8 (19%)	4 (9%)	0.213
No	35 (81%)	39 (91%)	
Type of dwelling			
Brick	37 (86%)	41 (96%)	0.361
Tin	1 (2%)	1 (2%)	
Plank	3 (7%)	1 (2%)	
Other	2 (5%)	0	
Number of people living in the house			
1-4	17 (40%)	22 (51%)	0.043
5-8	23 (53%)	20 (47%)	
> 8	3 (7%)	1 (2%)	
Drinking water			
Own tap	38 (89%)	41 (95%)	0.411
Communal tap	4 (9%)	2 (5%)	
Borehole	1 (2%)	0	
Type of toilet			
Flushing	40 (93%)	43 (100%)	0.211
Pit	2 (5%)	0	
Bucket	1 (2%)	0	
Fuel for cooking			
Electric	41 (96%)	40 (93%)	0.366
Gas	1 (2%)	3 (7%)	
Paraffin	1 (2%)	0	
Refrigerator or freezer			
Yes	37 (86%)	39 (91%)	0.501
No	6 (14%)	4 (9%)	
Employment status			
Unemployed	25 (58%)	34 (79%)	0.104
Self-employed	4 (9%)	1 (2%)	
Wage earner	14 (33%)	8 (19%)	
Total money spent on food per month			
R0-100	10 (23%)	6 (14%)	0.002
R101-200	7 (16%)	4 (9%)	
R201-300	11 (26%)	9 (21%)	
> R300	8 (19%)	7(16%)	
Unknown	7 (16%)	17 (40%)	

Anthropometric status

There was a statistically significant difference in the anthropometric measurements between cases and controls, measured at the time of diagnosis, as presented in Table III. Weight, BMI and MUAC were

Table II: Median energy, carbohydrate, protein, fat, zinc and vitamin A

Measurement	Cases (n = 43)			Controls (n = 43)			p-value
	Median	Minimum	Maximum	Median	Minimum	Maximum	
Energy (kJ)	6 434.55	3 047.90	16 475	6 773.38	2 492.50	21 016	0.675
Protein (g)	53.30	53.30	11.90	53.15	17.97	170.49	0.799
Carbohydrate (g)	206.40	63.26	483.31	182.36	54.80	858	0.739
Fat (g)	59.39	11.47	212.56	57.38	14.70	188.52	0.746
Zinc (mg)	7.58	2.13	23.04	9.60	3.01	34.60	0.096
Vitamin A (RE)	425.74	28.02	7701.70	433.26	18.36	1 975.05	0.746

Table III: Median weight, body mass index, mid-upper-arm circumference and percentage body fat

Measurement	Cases			Controls			p-value
	Median	Minimum	Maximum	Median	Minimum	Maximum	
Weight (kg)	49.63	37.38	76.25	58.20	40.25	84.05	0.002*
BMI (kg/m²)	18.80	14.35	32.11	21.17	16.75	34.98	0.001*
MUAC (cm)	23.45	18.40	31.60	26.00	20.90	34.60	0.000*
Body fat (%)	14.90	3.70	35.90	14.10	4.80	37.50	0.645

* p-value < 0.05 (indicates statistical significance)
BMI: body mass index, MUAC: mid-upper-arm circumference

Table IV: Mean serum micronutrient concentrations: zinc, copper, vitamin A and vitamin E

Measurement	Cases		Controls		p-value
	Mean (SD)	CI	Mean (SD)	CI	
Zinc (µg/dl)	59.49 (± 10.96)	56.03-62.90	77.03 (± 14.88)	72.39-81.66	0.000*
Copper (µg/dl)	173.35 (± 36.50)	161.83-184.87	166.61 (± 28.30)	157.79-175.43	0.351
Vitamin A (µg/dl)	23.55 (± 10.08)	20.37-26.73	38.88 (± 10.93)	35.47-42.28	0.000*
Vitamin E (mg/l)	9.92 (± 3.32)	8.87-10.97	9.69 (± 4.92)	8.16-11.23	0.860
Transferrin (ng/ml)	6.73 (± 2.13)	6.08-7.39	5.85 (± 2.21)	5.17-6.53	0.062
Albumin (g/l)	37.65 (± 4.55)	36.24-39.05	43.70 (± 2.51)	42.93-44.48	0.000*
CRP (mg/l)	49.13 (± 33.14)	38.93-59.33	2.82 (± 2.23)	2.13-3.51	0.000*
Ferritin (ng/l)	214.18 (± 155.72)	166.26-262.11	57.28 (± 38.72)	45.36-69.20	0.000*

* p-value < 0.05 (indicates statistical significance)
CI: confidence interval, CRP: C-reactive protein, SD: standard deviation

all significantly lower in the case group. The median BMI and MUAC in cases were at the lower end of normal, indicating suboptimal nutritional status.

Serum micronutrient concentrations

The mean zinc status of cases fell just below the lower end of the normal range (60-110 µg/dl), as presented in Table IV. Serum concentrations of vitamin A in cases were considerably lower than the reference range (30-85 µg/dl), while the levels of vitamin E and copper were in the normal range (5-18 mg/l and 70-170 µg/dl respectively). The mean serum concentrations of micronutrients in the control group were all in the normal range.

Biochemical values

The mean albumin level in cases was at the lower end of the normal range (35-50 g/dl). CRP and ferritin levels were markedly increased in this group, indicating the presence of inflammation. Transferrin receptor levels remained within reference ranges, with similar values between groups.

Discussion

The results demonstrate a significant degree of malnutrition in tuberculosis cases, as evident from their lower median weight, BMI and MUAC values. Micronutrient malnutrition was also evident in the case group, which had significantly lower serum vitamin A and zinc.

Malnutrition in patients with tuberculosis has been documented in many studies[6,7,10] and is once again reflected in the above results. Karyadi et al[7] conducted a case-control study to determine the nutritional status of patients in Indonesia. They demonstrated a significant decrease in BMI, skinfold and body fat percentage in tuberculosis cases. They reported that patients had significantly lower BMI (18.5 kg/m² for males and 17.8 kg/m² for females), MUAC (24 cm for males and 22.3 cm for females) and skinfold measurements compared to controls (BMI 21.9 kg/m² for both females and males, and MUAC of 28.4 cm for males and 26.6 cm for females). Serum vitamin A and zinc were also considerably lower in tuberculosis cases compared to controls.

Malnutrition, as evidenced by a decreased BMI, weight and body fat percentage, may be attributed to an increase in energy expenditure as a result of the APR and reduced nutrient intake, as well as fatigue and shortness of breath in the case of severe infections. The latter may make it difficult to prepare and ingest food.[11] In the initial phase of the disease, the APR is responsible for the increase in energy expenditure in patients, but once they are on treatment, the APR declines and nutritional status may improve. The APR is also responsible for the often lower levels of albumin and increases in ferritin that are seen in patients with active disease. Albumin is a negative acute phase protein whose production is reduced in periods of acute stress, trauma or infection, because of the APR. Therefore, the statistically significantly lower levels of albumin that were seen in cases can be attributed to the APR. Generally, the APR also results in increases in CRP,[12] as well as elevated levels of ferritin.[13] In this study, the BMI was significantly different between the groups, yet body fat percentage showed no association. This may be due to the limitation of the BMI in differentiating between fat and lean body mass. There were also no significant differences between genders in this regard.[14]

Serum vitamin A and zinc concentrations were statistically significantly lower in cases than in controls. These results are similar to those of other studies and reviews that were conducted to assess the micronutrient status of patients with tuberculosis. Ramachandran et al[15] conducted a case control study to assess the vitamin A status of patients with tuberculosis and found that it was significantly lower than household contacts and healthy "normals". They also found that vitamin A levels returned to normal after anti-tuberculosis therapy (ATT) and that supplementation of vitamin A was not necessary.

Karyadi et al[16] found that supplementation with vitamin A improved sputum smear conversion after two months of ATT. These results may be attributed to the co-supplementation of zinc. However, a randomised control trial that was conducted in the Western Cape by Visser et al[17] showed no effect on treatment outcomes after eight weeks of supplementation with vitamin A and zinc. Serum vitamin A may also be affected by the APR as albumin is decreased, with a consequent decrease in retinol-binding protein which is responsible for transport of retinol to various tissues.[7,16] Urinary losses of vitamin A associated with fever and infection may also be responsible for the low vitamin A levels that were seen in patients with active disease.[7,16]

Serum zinc concentrations were significantly lower in cases than in controls, which may also affect the level of vitamin A. Zinc plays an important role in many enzymatic processes, including vitamin A metabolism.[7] A zinc deficiency may cause a secondary vitamin A deficiency by impairing the production of retinol-binding protein, leading to a decrease in vitamin A. Therefore, zinc supplementation may improve vitamin A metabolism, especially in patients with tuberculosis,[5] and may be responsible for the improved sputum conversion seen in patients after two months of ATT.[15]

Therefore, zinc and vitamin A supplementation, when administered together, may be beneficial in improving the treatment outcomes in already malnourished patients after two months of therapy. Since levels appear to return to normal after treatment, supplementation in "normal" nourished individuals may not be necessary.

Even though the results of this research revealed similar outcomes to those of other studies, no new solutions have been reached to address malnutrition in tuberculosis patients. Many studies have discussed medical treatment outcomes, different strains of the tuberculosis pathogen and emerging treatment, yet there is little documentation on the follow-up of patients who present to the tuberculosis clinic who qualify for the NTP. According to Sudarsanam et al,[18] nutritional supplementation provides a low-cost intervention that may improve treatment outcomes. Abba et al[19] suggest that dietary assessment and advice may improve weight gain. Hence research should be conducted at facility level to ascertain whether at-risk patients are appropriately identified and then referred for nutrition counselling and to the NTP. However, this may sometimes be difficult as facilities are overcrowded and short-staffed, and it likely that these important processes are sometimes missed.

There were no significant differences between serum vitamin E, copper and transferrin between cases and controls. This was not expected, as copper tends to increase in APR due to the increased synthesis and release of the copper-binding protein, ceruloplasmin.[5,10] However, serum copper was not significantly increased in cases in this study. According to Kasvosve et al,[20] transferrin receptor levels tend to increase during periods of inflammation, independent of iron status. In this study, transferrin receptor levels in cases did not significantly increase compared to controls.

Conclusion

Newly diagnosed patients with tuberculosis tend to have a poorer nutritional status than tuberculosis-free contacts. Patients with active tuberculosis present with malnutrition, as evidenced by the lower anthropometric indices, as well as decreased serum levels of vitamin A and zinc. This may be attributed to the APR and increased metabolism and anorexia seen in these patients. Even though evidence from this study suggests the presence of malnutrition in active tuberculosis cases, it is still unclear whether the disease precipitates malnutrition or malnutrition leads to the disease.

Limitations

The sample of the current study may be too small and therefore lack the power to enable any significant recommendations to be made regarding nutritional guidelines for tuberculosis cases. Consideration should be given to constructing a multi-centre study design so that adequate numbers may be recruited for future research in this field.

Recommendations

According to Cegielski and McMurray,[21] case-control studies are not effective in determining the cause and effect of disease, as tuberculosis causes wasting and depresses the immune system. This resembles malnutrition. Therefore, the role of malnutrition in the development of the disease cannot be determined. A longitudinal study design should be applied in future studies to assess the role of malnutrition in the development of disease. Since newly diagnosed patients with tuberculosis tend to have increased catabolism and energy expenditure due to APR, nutritional supplementation for the first two months of treatment may improve outcomes, irrespective of body weight.

Declaration

This study was supported by the National Research Foundation (NRF) South Africa (2067444); the Norwegian Programme for Development, Research and Education (NUFU) (NUFUPRO-2007/10183); the Royal College of Nursing (RCN) (183694/S50) and NRF (South Africa)/RCN 180353/S50; Helse Vest (2007-2009-Grewal) and the South African Society of Anaesthesiologists (SASA) (2000).

References

1. World Health Organization. Global tuberculosis report. WHO [homepage on the Internet]. 2011. Available from: http://www.who.int/tb/publications/globalreport/gtbr11_executive_summary.pdf
2. World Health Organization. Tuberculosis country profile: South Africa. WHO [homepage on the Internet]. 2010. Available from: http://www.who.int/tb/data
3. Western Cape Department of Health (DOH).World TB day: Kick TB out of Cape Town. Western Cape DOH [homepage on the Internet]. 2010. Available from: http://www.capetown.gov.za/en/Pages/worldTBdaykickTBoutofcapetown.aspx
4. Flynn JL, Chan J. Immunology and tuberculosis. Annu Rev Immunol. 2001;19:19-129.
5. Gupta KP, Gupta R, Atreja A, et al. Tuberculosis and nutrition. Lung India. 2009;26(1):9-16.
6. Kennedy N, Ramsay A, Uiso L, et al. Nutritional status and weight gain in patients with pulmonary tuberculosis in Tanzania. Trans R Soc Trop Med Hyg. 1996;90(2):162-166.
7. Karyadi E, Schultink W, Nelwan RHH, et al. Poor micronutrient status of active pulmonary tuberculosis patients in Indonesia. J Nutr. 2000;130(12):2953-2958.
8. Western Cape Department of Health. Circular NOH/10: policy and implementation guidelines for the Nutrition Therapeutic Programme of the health facility based nutrition programme. Western Cape DOH; 2010.
9. Rankin D, Hanekom SM, Wright HH, MacIntyre UE. Dietary assessment methodology for adolescents: a review of reproducibility and validation studies. S Afr J Clin Nutr. 2010;23(2):65-74.
10. Van Lettow M, Fawzi WW, Semba RD. Triple trouble: the role of malnutrition in tuberculosis and human immunodeficiency virus co-infection. Nutr Rev. 2003;61(3):81-90.
11. Winkler MF, Malone AM. Medical nutrition therapy for metabolic stress: sepsis, trauma, burns and surgery. In: Mahan LK, Escott-Stump S, editors. Krause's food, nutrition and diet therapy. 11th ed. Philadelphia: Saunders, 2008; p. 1022-1037.
12. Koyanagi A, Kuffo D, Gresely L, et al. Relationships between serum concentrations of C-reactive protein and micronutrients, in patients with tuberculosis. Ann Trop Med Parasitol. 2004;98(4):391-399.
13. Beard JL, Murray-Kolb LE, Rosales FJ, et al. Interpretation of serum ferritin concentrations as indicators of total-body iron stores in survey populations: the role of biomarkers for the acute phase response. Am J Clin Nutr. 2006;84(6):1498-1505.
14. Romero-Corral A, Somers VK, Sierra-Johnson J, et al. Accuracy of body mass index to diagnose obesity in the US adult population. Int J Obes (Lond). 2008;32(6):959-966.
15. Ramachandran G, Santha T, Garg R, et al. Vitamin A levels in sputum-positive pulmonary tuberculosis patients in comparison with household contacts and healthy "normals". Int J Tuberc Lung Dis. 2004;8(9):1130-1133.
16. Karyadi E, West CE, Schultink W, et al. A double-blind, placebo-controlled study of vitamin A and zinc supplementation in persons with tuberculosis in Indonesia: effects on clinical response and nutritional status. Am J Clin Nutr. 2002;75(4):720-727.
17. Visser ME, Grewal HMS, Swart EC, et al. The effect of vitamin A and zinc supplementation on treatment outcomes in pulmonary tuberculosis: a randomized control trial. Am J Clin Nutr. 2011;93(1):93-100.
18. Sudarsanam TD, John J, Mahendri V, et al. Pilot randomized trial of nutritional supplements in patients with tuberculosis and HIV-tuberculosis coinfection receiving directly observed short-course chemotherapy for tuberculosis. Trop Med Int Health. 2011;16(6): 699-706.
19. Abba K, Sudarsanam TD, Grobler L, Volmink J. Nutritional supplements for people being treated for active tuberculosis [Cochrane review]. In: The Cochrane Library, Issue 1, 2010. Oxford: Update Software.
20. Kasvosve IK, Gomo ZAR, Nathoo KJ, et al. Association of serum transferrin receptor concentration with markers of inflammation in Zimbabwean children. Clin Chem Acta. 2006;371(1-2):130-136.
21. Cegielski JP, McMurray DN. The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. Int J Tuberc Lung Dis. 2004;8(3):286-298.