International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 8; Issue 02(E); February 2018; Page No.17430-17433
DOI: http://dx.doi.org/10.24327/ijcar.2019.17433.3306

Recerch Report

PREVALENCE AND PRESENTATION OF TUBERCULOSIS IN ESRD IN PORT SUDAN

Murwan Mohamed Saeed Elnour., Yasir Mohammed Mahmmoud and Shimoos Obied Margani

Department of Medicine

A R T I C L E I N F O

Article History:

Received 15th November, 2019
Received in revised form 7th December, 2018
Accepted 13th January, 2019
Published online 28th February, 2019

Key words:

prevalence, presentation, tuberculosis, ESRD, haemodialysis, port sudan

A B S T R A C T

Tuberculosis is the commonest infectious communicable disease in Red sea state- Sudan, in the last years the percentage of extrapulmonary tuberculosis exceeding that of pulmonary tuberculosis, multiple factors may contribute in this and these factors must be investigated. At same time incidence of renal failure also increased in the last years in Red sea state.

Several factors contributed in transmission of tuberculosis, and renal failure is one of these factors, as it affect the immunity, reducing body mass and responsible for reduction of vitamin D. In addition over crowd in dialysis centre and contamination of dialysis sets represent other factors making those on dialysis at higher risk to develop tuberculosis. At same time tuberculosis may be a cause of CKD secondary to genitourinary tuberculosis or through haematological spread from latent or active pulmonary tuberculous lesion. Both tuberculosis and renal failure worsening morbidity of each other.

Diagnosis of tuberculosis in those of ESRD is more difficult than in normal population as symptoms of ureamia mimicking general symptoms of tuberculosis. Pulmonary tuberculosis in those patient has atypical radiological presentation, Mantoux test usually negative, Z- N stain usually negative, and TB usually presented as EPTB, so This is a prospective, descriptive, and interventional study done in Port Sudan dialysis centre in 246 patients of ESRD on haemodialysis to know the prevalence and pattern of tuberculosis among patient of ESRD in Red sea state and to find out criteria for early detection of tuberculosis in ESRD. In this study M: F is 2:1 mean age is 47 years, Bija tribe 75%, non Bija 25%.. The commonest cause of ESRD was hypertension followed by diabetes. Prevalence of TB among ESRD in Port Sudan is 11.4% presented as post primary 21.4%, latent TB 18%, tuberculous pleural effusion 21.4%, tuberculous peritonitis 21.4%, tuberculous pericarditis 10.7% and tuberculous lymphadenitis 7.1%. Risk factors for tuberculosis among those patient were over crowd in dialysis centre, poor ventliation of the centre, lag of infection control measurement, poor neutritional state and diabetes.

INTRODUCTION

Tuberculosis is an infectious caseating granulomatous disease that caused by mycobacterium bacilli, mainly mycobacterium tuberculosis, it transmitted mainly by inhalation of bacilli contained in a droplet nucleus, but other mode of transmission play less common role. In 90% of immunocompetant individuals the infection remain in a latent state while 10% progress to TB disease (1), multiple risk factors contributing in developing active disease rather than latent infection such as: contact to smear positive pulmonary tuberculosis, poverty, malnutrition, overcrowd, alcohol, HIV infection, diabetes and end stage renal disease, the later is stage 5 chronic kidney disease in which GFR is less than 15 ml/ min/ 1.73m^2 (2). Symptoms of tuberculosis are varies according to case definition, host immune, bacterial load , comorbidity or contributing risk factor. Most symptoms of pulmonary tuberculosis such as cough, chest pain, breathlessness and weight loss can presented in renal failure due to metabolic state of ESRD or due to uraemic complications and that of most type of extrapulmonary tuberculosis also may mimic symptoms of ureamia or that result from dialysis.

Diagnosis of pulmonary tuberculosis depend on symptomatological presentation, sputum Z-N stain, CXR, TST, IGRA and geneXpert, while that of extrapulmonary tuberculosis need further and even advance investigation that varies according to site, these include FNA, ultrasonology, PCR and histopathology. In immunosupressed patient like those with ESRD the diagnosis is more difficult because of energy and atypical presentation therefore, BTS guidelines prefer interferon gamma release assay rather than tuberculin skin test (3).

Incidence of both tuberculosis and ESRD increased in the last years in Port Sudan – eastern Sudan. New cases of tuberculosis in 2017 was 1185 which represent detection rate of 97%, in

Corresponding author:* **Murwan Mohamed Saeed Elnour
Department of Medicine

this year EPTB represent 53% of all detected cases (4), this is high percentage when comparing to WHO suspicion that shows up to 25% of all detected cases may present as EPTB (5) While cases of ESRD increased from January 2017 to October 2017 by 15.5% (from 213 in January to 246 in October) (6), those patient on haemodialysis in Port Sudan haemodialysis centre, the only centre in Red sea state – eastern Sudan so those patient represent all state population. Both increase in EPTB and ESRD need advanced investigations and research to know and manage the cause.

Both tuberculosis and ESRD affecting the morbidity and mortality of each other, those with ESRD at increase risk to develop tuberculosis by 6 to 25 times than normal individuals (7) while tuberculosis can affect genitourinary tract and result in CKD and ESRD, decrease in renal function affecting the immunity and hence affecting the progress of tuberculosis. Ethambutol is secreted by the renal in up to 80% and in those with ESRD its clearance is affected and adverse effect increase (3), rifambucin as enzyme increasing the serum level of several drugs and so affecting the kidneys in those with ESRD.

There are view evidence regarding treatment of tuberculosis in patient with end stage renal disease, BTS guideline suggest positive pressure isolation for TB patient and to start standard regimen of four drugs rifampicin, isoniazid, pyrazinamide and esambutol with interval days and close monitoring for drugs serum level (3), here in Port Sudan a daily fixed dose of these four drugs is used and there is no facilities for detecting antituberculous serum level. There are three methods for chemoprophylaxis these are 6 month of isoniazid, 3 month of rifampicin plus isoniazid and 4 – 6 month of rifampicin (3), in Port Sudan there is no routine chemoprophylaxis, despite recent WHO recommendation to give prohylactic isoniazid for all ESRD (4). There is no strong evidence guideline shows when and how to screen patients with ESRD for tuberculosis and no guideline shows treat or not those with latent tuberculosis but BTS guideline suggest CXR for all CKD patient and those with radiological abnormality need further investigation, this guideline suggest IGRA rather than tuberculin skin test as negative TST doesn't exclude tuberculosis (3), so these area for further studies.

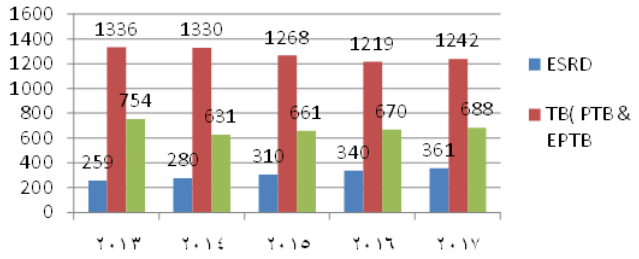

Figure (1) shows incidence of TB, EOTB & ESRD in Red sea state in period 2013 – 2017

Objectives

This study done to know the prevalence and pattern of tuberculosis among patients with ESRD in Port Sudan haemodialysis centre as those patient are at high risk to develop tuberculosis and there is no study in this field in this area. And to find out criteria for early detection of tuberculosis in patient with ESRD and to participate in explanation for rapid rising in both ESRD and EPTB.

METHODOLOGY

Study area

Port Sudan dialysis centre the only haemodialysis centre in Red sea state, in which there are 33 haemodialysis units and it work six days/week for three sessions/day under supervision of national Sudanese dialysis centre.

Study Population

All adult patient on haemodialysis in Port Sudan haemodialysis centre who accept to be enrolled in this study and fulfilling including criteria.

Study Period

This study done in period from January 2017 to October 2017

Data Collection

Data was collected through questionnaire, personal interview, and from patients files and statistic record.

Excluding Criteria

Those who refused to be enrolled in study, peadiatrics patients and those with HIV were excluded,(this centre didn't received HIV patients).

Study Design and Procedures

This is a prospective, descriptive interventional hospital based study. 245 patients were enrolled in this study, questionnaire was designed and submitted, followed by personal interview and physical examination for those who showed respiratory symptoms. CXR and sputum for AAFB using Z-N stain done for all patient. Abdominal ultrasound done for those who showed symptoms suggesting involvement of gastrointestinal tract and this was reported by radiologist, from those who showed radiological or sonological feature of pleural effusion or ascites 20 ml of pleural fluid or ascitic fluid was aspirated and sent for PCR.

Echocardiography done for those who showed radiological feature of pericardial effusion. FNA done for those who showed hilar enlargement in CXR and had peripheral enlarged lymph node in clinical examination and these samples examined for cytology. Mantoux test done for those who had negative smear but had radiological feature suggestive of tuberculosis.

Those with smear positive, PCR positive, radiological feature suggestive of TB with positive mantoux, FNA and echocardiography feature suggesting tuberculosis was diagnosed as TB patients. Those who diagnosed as TB patients received six month antituberculous under DOTS according to Sudan national TB control program (fixed dose of rifampicin, isoniazid, pyrazinamide, and ethambutol for two month followed by four month of rifampucin and isoniazid) and those patients followed during treatment course.

RESULT

245 patient with ESRD were enrolled in this study, M: F was 2:1, mean age was 47 years (22 – 70). The causes of ESRD in those patient was hypertension 41.6 %, diabetes mellitus 16.3%, glomerulnephritis 5.3 %, urinary tract infection 2.9 %, and 25.7 remain unknown. Respiratory and / or cardiac symptoms (cough , breathlessness, chest pain, haemoptysis) appear in 192 patient 78.4 %. GIT symptoms (abdominal pain,

abdominal distension dyspepsia) appear in 63 patient (25.7 5%). Sputum for AAFB was positive in 6 patients (2.4%), CXR showed pleural effusion in 36 patients (14.7%), lower lobe consolidation in 16 patients (6.5%), upper lobe consolidation in 8 patients (3.3%), pericardial effusion in 9 patients (3.7%), upper lobe fibrotic changes in 3 patients (1.2%), lobar collapse in 2 patients (0. 8%) and prominent hilar shadow in 12 patient (5%).

Mantoux test done for 70 patient and was positive in 6 (8.6%) of them which represent 2.4 % of all patients, while FNA was done for 3 patient of those who showed prominent hilar and it showed cytological features of TB in 2 (16.7%) of them that represent (0.8%) of all patients. Ascites appear in 42 patients (17%). Echocardiography was done for those 9 patients with radiological feature of pericardial effusion and just 3 (33 %) of them showed features of tuberculous pericarditis which represent 1.2% of all patient. Qualitative PCR was positive for mycobacterium bacilli in 6 patient of ascites (2.4%) and in 6 patient of pleural effusion (2.4%) of all study population. According to our diagnostic criteria 28 patient diagnosed as tuberculosis and so prevalence of TB among patients with ESRD is 11. 4 %, EPTB 6.9 % and PTB 4.5 %.

In those who diagnosed as tuberculosis male : female was 2:1, presenting symptoms were cough in 16 (57%) patients, breathlessness 16 (57%) patients, fever 15 (53.6%) patients, chest pain 12 (39.3%) patients, weight loss 10 (32%) patients, abdominal distension 3 (10.7%) patients, and abdominal pain in 2 (7%) patients. In those tuberculous patient 17 patients (60.7%) were EPTB and 11 patients (39.8 %) was PTB.

In patient of PTB 54.5 % (6 patients) were post primary TB, and 45.5 % (5 patients) were latent TB while in those of EPTB 21.4 % (6 patients) were tuberculous pleural effusion, 21.4 % (6 patients) tuberculous peritonitis, 10.7 % (3 patients) tuberculous pericarditis, and 7.1 % (2 patients) tuberculous lymphadenitis.

The risk factors for tuberculosis in ESRD in Port Sudan haemodialysis centre are over crowd, poor ventilation, lag of infection control procedures, low body mass, diabetes and poor nutrition. All tuberculous patient are declared as completed without major addverse reaction.

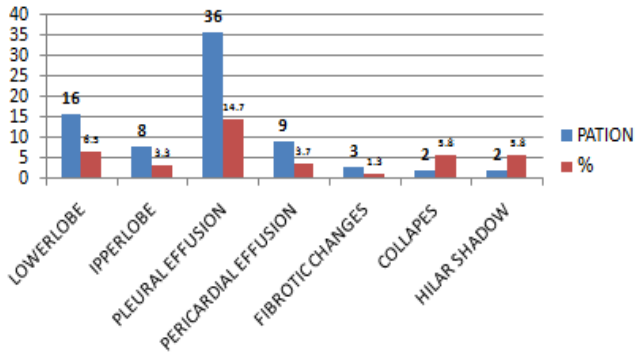

Figure (2) shows radiological presentation in all ESRD patients

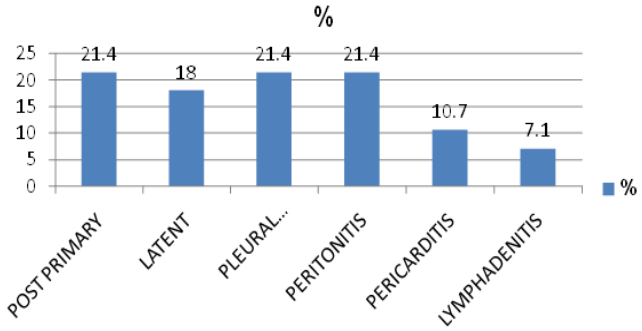

Figure (3) shows pattern of TB in ESRD

DISCUSSION

The prevalence of tuberculosis in patient with ESRD in Port Sudan is 11.4% in our study this percentage may be lower than real prevalence because of study limitation as we depend on sputum examination using Z-N stain which is has low diagnostic yield in those patient because of energy, and we used mantoux test which is usually give false negative result in those immunocompromised patient rather than IGRA which is more sensitive, but not available in this area, in addition we avoid invasive diagnostic procedures in diagnosing of tuberculous peritonitis and pericarditis and in those who suspected to have tuberculous lymphadenitis but have no peripheral enlarged lymph node, due to these limitation this percentage is low comparing to other study done in Morroco that showed 24 % as prevalence of TB in ESRD patients (7) while it was 1.4 in study done in Khartoum – Sudan (8), this wide variation due to various diagnostic policies as there is view diagnostic guidelines (3), and this study may be the first step toward local or national diagnostic guideline as the study done in Khartoum involved those already diagnosed as TB patients.

There is many avoidable risk factors for tuberculosis such as improving ventilation system, improving infection control procedure, control diabetes in those patient of ESRD, involving nutritionist in management team. Vitamin D prevent infection of mycobacterium through induction of several antimicrobial peptide (9), but in patient with ESRD there is reduction in vitamin D due to impaired hydroxycaciferol production secondary to renal insufficiency or due to defect in receptors (2) and this need regular measurement of serum calcium, parathyroid hormone and serum vitamin D and correct any defect early to decrease the risk of TB.

Ureamia may produce both cough and breathlessness through metabolic complication or uremic pulmonary oedema, this delay the suspicion of tuberculosis and so the diagnosis of TB. In those of pulmonary tuberculosis the radiological features were atypical as lower lobe consolidation presented twice than upper lobe consolidation which the feature in immunocompromised patient for unknown cause, but still this delays the suspicion of tuberculosis, again mantoux test usually negative in immunocompromised patients while it is an earlier indicator of TB infection this due to activation of suppressor lymphocyte (10).

Extrapulmonary tuberculosis more than pulmonary 1.5 : 1 and this is extra factor that make diagnosis of tuberculosis in those with ESRD more difficult than normal population, in addition to that the commonest pattern of extrapulmonary tuberculosis (tuberculous pleural effusion, tuberculous peritonitis and

tuberculous pericarditis) mimicking complication of ureamia and dialysis, pericarditis occurs in advanced ureamia more often in under dialysis which is the condition in our centre (2), so special consideration and high suspicion should be taken. Latent tuberculosis also appear in significant percentage and it need regular radiological follow up (10). All patient of ESRD are at increased risk of tuberculosis so they need chemoprophylaxis, secondary chemoprophylaxis which is given in this condition (third category according to American recommendation) should be accompanied by regular follow up because of high index of suspicion even after receiving chemoprophylaxis (10).

CONCLUSION

Diagnosis of tuberculosis in patient with ESRD is more difficult than in normal population because there are many factors affecting diagnosis and delays suspicion, such as atypical presentation and interference of symptoms of ureamia and complication of dialysis, so high suspicion and early intervention should be there.

The prevalence of tuberculosis in patient with ESRD in Port Sudan although it looks high comparing to that appear in study done in Khartoum but still it is low comparing to global rate. Most of the risk factors can be managed and this may decrease the incidence. Extrapulmonary tuberculosis presented as tuberculous pleural effusion, tuberculous peritonitis, tubercuolus pericarditis and tuberculous lymphadenitis and all need to be differentiated from other causes of pleural effusion, ascites and pericardial effusion. Latent tuberculosis occurs in considerable percentage and need regular monitoring as it may convert to active disease. Fortunately the treatment outcome with standard treatment is similar to that of normal population, but delayed diagnosis may associated with several morbidity and may affecting the outcome. All patient with ESRD should receive three month chemoprophylaxis with 300 mg isoniazid according to American recommendations for secondary prophylaxis. Those ESRD patient who diagnosed as tuberculosis would received haemodialysis in separate isolated unit, and would received their antituberculous dose after dialysis.

Abbreviation

AAFB: Alcohol acid fast bacilli
BTS: British thoracic sosciety
CKD: Chronic kidney disease
CXR: Chest X ray
DOTS: Direct observe therapy strategy
EPTB: Extrapulmonary tuberculosis
ESRD: End stage renal disease
FNA: Fine needle aspiration
GFR: Glomerular filtration rate
HIV: Human immunodeficiency virus
IGRA: Interferon- gamma release assay
PCR: Polymerase chain reaction
PTB: Pulmonary tuberculosis
TB: Tuberculosis
TST: Tuberculin skin test
WHO: world health organization
Z - N: Ziel - Neelsen

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How to cite this article:

Murwan Mohamed Saeed Elnour *et al* (2019) 'Prevalence and Presentation of Tuberculosis in Esrd in Port Sudan', *International Journal of Current Advanced Research,* 08(02), pp.17430-17433.
DOI: http://dx.doi.org/10.24327/ijcar.2019.17433.3306

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