Clinical Spectrum and outcome of Childhood Tuberculosis in Mohammed Al-Amin Hamid Hospital for Children 2017-2018, Sudan

Walyeldin Elnour Mohamed Elfakey[1], Sara Altayeb AbdAlgader[2], Karimeldin Mohamed Ali Salih[1, 3], Omaima Abdel Majeed Mohamed Salih[4],

[1] *Faculty of Medicine, University of Bahri, Khartoum North, Sudan*

[2] *Federal Ministry of Health, Khartoum, Sudan.*

[3] *Faculty of Medicine University of Bisha, Saudi Arabia*

[4] *Faculty of Medicine Omdurman Islamic University, Sudan*

***Correspondence to Walyeldin Elnour Mohamed Elfakey,** Faculty of Medicine, University of Bahri, Sudan. walyeldin@aol.co.uk*

Abstract:

Background:

The WHO report in 2018 estimated 234.000 deaths due to tuberculosis in children less than 15 years, 40.000 of them occurring in HIV infected children, these deaths represent 15% of all tuberculosis deaths.

Objectives: This study aimed to determine the clinical spectrum and outcome of child hood tuberculosis in Mohamed Al-Amin Hamid Pediatric Hospital TB management unit (TBMU).

Methods: This retrospective observational hospital based study was co nducted in Mohammed Al-Amin Hamid hospital during a period of 24 months from (January2017 to December2018) .The study was conducted among children aged (0-18) years and diagnosed with Tuberculosis .Data was collected and analyzed using statistical package for social science (SPSS-24).

Result: A total of 174 patients were enrolled in this study. The majority of patients' ages ranged from 5-17 years 111(63.8%). Most of the patients were male 92(52.9%) and There were 142(81.6%) resided in Khartoum. Lung opacity and hailer parenchymal shadows were the most presenting features 83 (47.7%) in chest x-ray. Sputum for Acid Fast Bacilli (AFB) was positive only in 20 (11.5%) patients. HIV was negative in 41 (23.6%) patients and was not done in 133 (76.4%).

A hundred and seven (61.5%) children were diagnosed as having pulmonary Tuberculosis, extra pulmonary Tuberculosis was 67 (38.5%). Tuberculous lymphadenitis was the commonest type of extra pulmonary tuberculosis where it was diagnosed in 38(56.7%) patients.

There were 94(87.9%) complete their treatment and 13(12.1%) with smear positive were cured. Defaulter were20 (11.5%), and 6 patients (3.4%) were retreated after default, and 11(6.3%) were transferred out, and 14(8%) still on treatment, there were 13 patients (7.5%) dead, and 3 patients their outcome not documented.

Conclusion: The most affected children were male patients aged above 5years.with extrapulmonary Tuberculosis being the most common presenting type especially tuberculous adenitis with favorable outcome among the study group as patients who completed their treatment successfully were approaching 90%

Keywords: Tuberculosis (TB), Tuberculosis Management Unit (TBMU), pulmonary /Extra-pulmonary, Treatment outcome

Introduction

Tuberculosis is one of the major hazards to communities in the developing countries [1], The WHO estimated that 9 million persons infected yearly in developing countries with an estimated mortality of 2 million [1,2,3] and 19-43.5%of the pollution in the world are affected by M tuberculosis. [4]. Tuberculosis usually has non-specific symptoms and signs and hence diagnosis is challenging [5], however technology successfully addresses this issue [5, 6]. The usual complaint are low or high grade fever ,cough or running nose and majority of cases have pulmonary tuberculosis ,however 3rd of the patient developed extra pulmonary tuberculosis [7].Great variation in clinical presentation across different age group :whereas in pre-school age and adolescent symptoms and signs are usually exciting, no symptoms and signs among school age children [7,8]. On the other hands great number of children with positive radiological findings, have symptoms or signs, diagnosed only during tracing process [7]. In fact radiology in children shows clear lymphadenopathy but less parenchymal infiltration [9]. Since the positivity of culture of gastric aspirate is insignificant, culture is not needed to make a diagnosis and suggestive symptoms, signs, positive skin test, positive radiological changes with known contact enough to start treatment in children [7, 10]. We conducted this study to determine the clinical

presentations and risk factors of child hood tuberculosis identify the radiological finding and laboratories investigations, the association of age with type of tuberculosis and the treatment outcome.

Materials and methods:

This is a Retrospective cross sectional hospital based study, which was conducted in Mohamed Al-Amin Hamid Pediatric Hospital (TBMU) TB management unit from January 2017-December 2018. Mohamed Al-Amin Hamid Pediatric Hospital is a general pediatrics hospital in the capital Khartoum. It is of 320 beds with neonatal intensive care unit, pediatric intensive care unit, infectious diseases word, and renal dialysis unit and referred clinics for Tuberculosis, asthma, sickle cell disease, HIV-AIDS clinic and nephrology clinic. The hospital serves population from Omdurman city and from all other states and different parts of Sudan. We included any child from birth -18 years with tuberculosis those who agreed and their care giver agreed to be part of the study after full explanation of the study purpose ,data about the main study variable (classification of Pulmonary versus extra-pulmonary and treatment outcome) was extracted from the patients 'record , Using specially designed data collection sheet as patient were classified and their treatment outcome was recorded as per WHO guidelines, patients with incomplete records were excluded. Secondary data was extracted from the patient's records and then re-entered into a predesigned data collection form, cleaned and analyzed using SPSS version 24.

Statistical analysis

All collected data were cleaned, entered and analyzed using SPSS version 24 Descriptive statistics in term of frequency tables with percentages and graphs. Means and standard deviations were presented with relevant graphical representation for quantitative data Bi-variable analysis to determine the associations between the main outcome variable (disease outcome) and the other relevant factors with Chi square test (for categorical variables) and t-test (quantitative variables) statistical tests. P value of 0.05 or less is considered statistically significant.

Ethical clearance and approval

Ethical clearance and approval for conducting this research were obtained from ethical committee from the SMSB and the Khartoum state Ministry of the health research department.

Results

A total of 174 patients were enrolled in this study. The majority of the studied population age ranged from 5-17 years 111(63.8%). Most of the patients were male 92(52.90), and 142(81.6%) of them were resided in Khartoum as shown in table 1.

Regarding the clinical presentation of the studied population, prolonged fever was the most common presenting feature 170 (97.7%), followed by weight loss 139 (79.9%), cough 125 (71.8%), lymphadenopathy 103 (59.2%) and the come the rest of the clinical features which shown in table 2.

The specific investigations done to the studied group was sputum for acid alcohol fast bacilli GeneXpert test. The GeneXpert test done for 149 (85.6%) of the patients, from this number only 20 were positive.

The Mantoux skin test done for the entire studied group, 25 (14.4%) were negative, 93 (53.4%) were borderline and 56 (32.2%) were positive.

The erythrocyte sedimentation rate (ESR) done for all patients, in 168 (96.6%) it was more than 40 mm/hour, 5 (2.9%) their ESR was between 20 – 40 mm/hour and only one (0.6%) was less than 20 mm/hour.

Fine needle aspiration (FNA) cytology of lymph nodes done for 90 of the patients, out of those 90, 41 (45.6%) were suggestive of tuberculosis and 49 (54.4%) were not suggestive.

Only 41 (23.6%) of the studied group were screened for human immunodeficiency virus (HIV), all of them were negative.

The opacity and hailer parenchymal shadows were the most presenting radiological features in almost half of them 83 (47.7%). Other findings include hilar parenchymal shadow 18 (10.3%), opacity 18 (10.3%), lung collapse three (1.7%), pleural effusion three (1.7%), features of miliary tuberculosis two (1.1%), cavity one (0.6%) and in one (0.6%) of those selected for chest x-rays the scan was normal. In 45 (25.8%) chest x-rays not done. The X-ray findings shown in figure 1

Regarding the pattern of tuberculosis in the studied group, we found that the majority 107 (61.5 %) were pulmonary tuberculosis. Tuberculous adenitis was 38 (21.8%), gastrointestinal tuberculosis was 11 (6.3%), tuberculous meningitis was 7 (4%), Pott's disease of spine was 6 (3.4%), miliary tuberculosis was 2 (1.1%) and other types of tuberculosis were 3 (1.7%). These illustrated in figure 2.

In correlation between the age, treatment and the outcome, as shown in table 3, we found that generally the prognosis is better in the age group between 5 to 18 years than those who were less than 5 years with significant statistical differences in retreatment after default and in those who completed treatment with cure.

Table 1: General characters of the studied group

Variable	Frequency	Percent %
Age		
5 and less	63	36.2
>5 – 17	111	63.8
Gender		
Male	92	52.9
Female	82	47.1
Residence		
Khartoum	142	81.6
Outside Khartoum	32	18.4
Risk factors		
History of contact	105	60
Not vaccinated	33	19

Table 2: **Clinical Presentations**

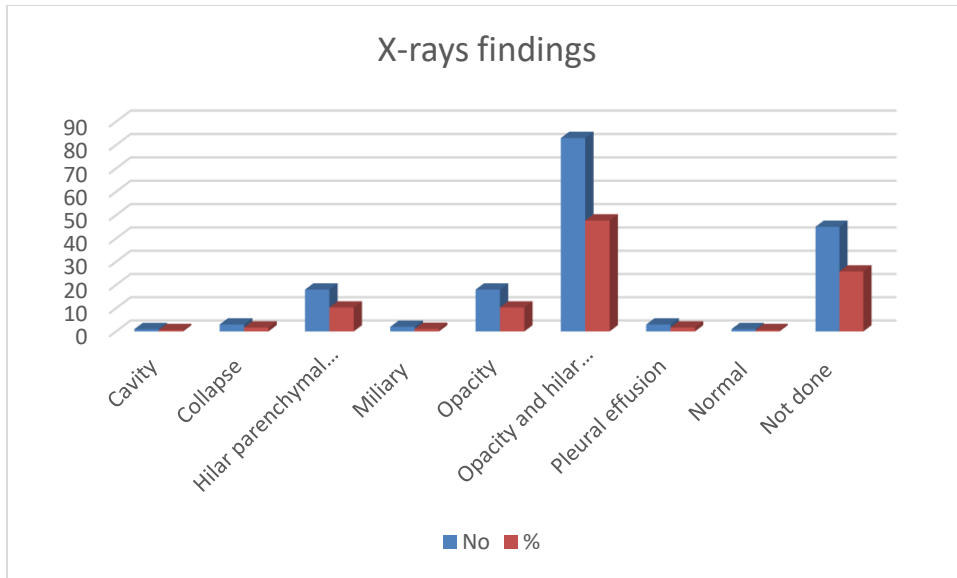| Clinical Presentation		
Variable	Frequency	Percent %
Fever	170	97.7
Weight loss	139	79.9
Cough	125	71.8
Sweating	78	44.8
Fatigue	80	46.0
Convulsion	3	1.7
liver enlargement	9	5.2
Splenomegaly	6	3.4
ascites	8	4.6
Lymphadenopathy	103	59.2
Hemiplegia	1	0.6

Figure (1) Distribution of chest X- ray Finding among the studied participants, n= 174
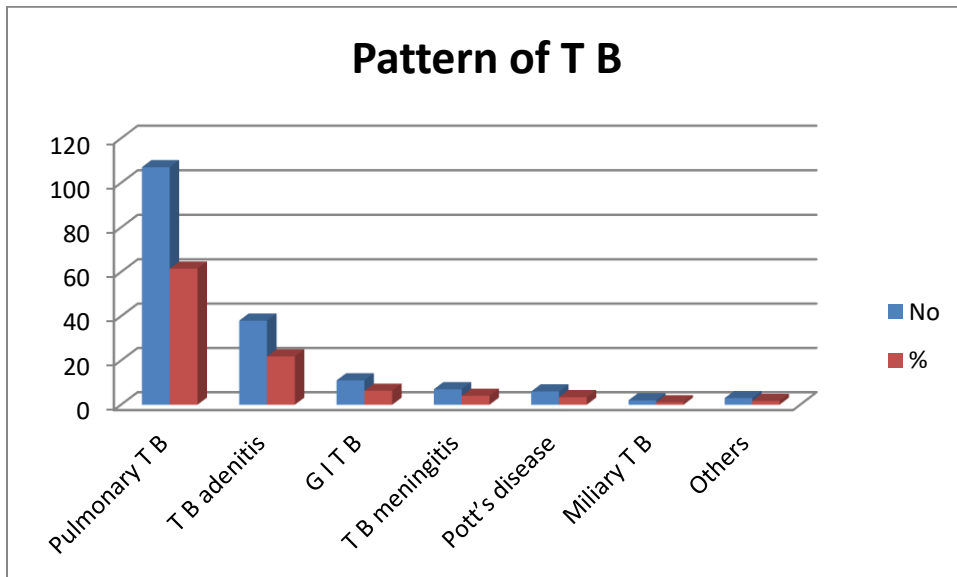

Figure (2) Distribution of pulmonary and Extra pulmonary and among the studied participants, n = 174

Table 3: Correlation between the age, treatment and the outcome:

Outcome	Age		P value
	Less than 5 years	**5-18 years**	
Death	8	5	0.405
Default	8	12	0.371
Not documented	1	2	0.564
On treatment	5	9	0.285
Retreatment after default	1	5	0.000
Transferred out	2	9	0.000
Treated (complete/cured)	38	69	0.003

Discussion:

In our study, the majority (Almost two thirds) of patient's age range from 5-17 years 111(63.8%) This may reflects the uncertainty of symptoms in younger patients and difficulties of confirmatory investigations. The other factors contributing to this result is that most probably because the older age are more mobile in community more than the younger so they had a big chance to contact with diseased adult patients and their peers. These findings are in agreement with other local, regional and international studies, (Sudan, Nigeria, and Nepal) studies. [11, 12, 22]

Most of the patients were males 92(52.9%) which is comparable to other studies done in Sudan [11], South Africa [13] and Pakistan [14]. However our study differs from that done in Iran where female patients were the majority. [15]. It is very difficult at this age to explain this gens differences.

The general signs of fever, weight loss and lymph-adenopathy were similar to the study done in Sudan by Wadie 2016 [11], and other international studies in Nepal, Turkey and Iran [12, 17,15]. Signs of extra pulmonary tuberculosis such as paralysis, convulsions, ascites, hepatomegaly and splenomegaly were similar to the study done in Izmir, Turkey 2014 [17].

The chest x-ray findings is in agreement with the study done by Verma SK etal in India 2006 [19] and the study done in developed countries by Tomà P etal 2017 [20] .

In our study, the sputum for AAFP was positive only in 20 (11.5%) which is comparable to the local study by Wadie etal 2016 [11] and other studies by Osman etal 2014 [21]

In our study the Manteux test showed induration in our cases less than reported in   Philippine 2018 [26], Izmir, Turkey 2014 [17]. Nepal 2018 [12]. Whether these differences related to coexisting infection in our context needs further work up.

In our study the ESR was significant (more than 40) in 168(96 .5%). This was similar to studies done in Nepal 2018[12] and Turkey 2014 [17]. In our study FNA was suggestive of tuberculosis in 41(45.6%) of patients. In the study done in Nepal 2018 [12], there were 5 children with lymph node TB and FNAC was diagnostic in all of them which was less than in our study but is considered as a helping tools in diagnosis.

In almost two thirds (61.5%) of our cases diagnoses was pulmonary tuberculosis which was similar to Wadie 2016 [11] and Osman Osman 2014 [21] studies in Sudan. Regionally in Nigeria 2016 [24] Pulmonary TB (PTB) was seen in 58 (76.3%) which is similar to our study .In sub-Saharan Africa Congo 2016 [24] it showed 159 (56.1%) patients had extra-pulmonary tuberculosis (EPTB) which was higher than in our study.

Again the study done in Turkey 2014 [17] showed that Ninety-two (78.6%) of the cases had PTB and 25 (21.4%) of the cases had EPTB), which is similar to our findings. In Delhi, Dhaked etal (2019) [24], a study found that extra pulmonary TB (70.2%) was almost three times more prevalent than pulmonary. The Nepal study found the Extra-pulmonary TB (59.38%) was more common than pulmonary TB (40.62%), and these results were not similar to our result [12]. These differences in occurrences of pulmonary and extra pulmonary tuberculosis may be due to age distributions' in studies, presences of other co morbidities and efficacy and availability of diagnostic methods. Tuberculosis cases are primarily pulmonary and are easier to diagnose than extra pulmonary, which requires high index of suspicion. Majority of studies show that pulmonary tuberculosis was more common than extra pulmonary, and the non-specific symptoms of extra pulmonary tuberculosis make its diagnosis more difficult and missed in younger patients.

The commonest type of extra pulmonary tuberculosis was tuberculous lymphadenitis 38(21.8%). In sub-Saharan Africa in Kinshasa 2016 [24] the EPTB cases included 118 (74.2%) of cases of peripheral lymphadenitis, 11 (6.9%) cases of pleural effusion , 8 (5.0%) cases of meningitis , 6 (3.8%) cases of vertebral TB, 5 (3.1%) cases of abdominal TB, 4 (2.5%) cases of military TB and pericardial TB, and 3 (1.9%) cases of osteoarticular TB. Also in a study done in Delhi (2019) [24], the commonest site involved in approximately two thirds of EPTB cases were lymph nodes (72.7%), which is similar to our study. Other types of tubersculosis we found were as follows: gastrointestinal tuberculosis 11(6.3%), tuberculous meningitis 7 (4.0%), Pott's disease 6 (3.4%) and military which was the least one2 (1.1%) and in others 3 (1.7%). All these results were similar to the above studies. In Nepal study [12], pleural effusion (39.47%) and abdominal TB (26.31%) were the most common types which were different from our study findings. Lotfian 2016 in Iran showed pleural tuberculosis to be more common, which is different from our study [15].

87.9%completed their treatment. 12.1% with smear positive were cured. This is considered as a favorable outcome and similar to study done in Sudan by Wadie 2016 [11] where the cure rate was (76.5%). In study done in Nigeria 2018 [22] Majority 51(67.1%) completed treatment but is less than in our study. 12 (15.8%) were cured which were more than in our study.

Defaulters were 20 (11.5%) which was similar to study done in Sudan by Osman etal 2014 [21] where they were (17.3%). Regionally in Nigeria 2018 [22], the defaulters were only1 (1.3), which is less than in our study. In Iran 2016 [15], the defaulters were more in adults where fifty-four (39%) adolescents were identified. This is more than in our study. Thirteen Patients (7.5%) died which was similar to a study done in Sudan 2016 [11] and higher than the study done in Nigeria [22], where the deaths were 3(3.9%)

The extra pulmonary TB occurred in 52% of females which is similar to studies done elsewhere [20, 21, and 26],

Limitations:

In this is retrospectives study there were many-missed information's and follow up data. The study not covers the social and psychological aspects, which are, considered an effective factor in the outcome and clinical presentations. The determinations of contact and their distribution were difficult to assess in our methodology.

Conclusion:

The most affected children were male patients aged above 5years. With extrapulmonary Tuberculosis being the most common presenting type specially Tuberculos adenitis with favorable outcome among the study group as patients who completed their treatment successfully were approaching 90%

Recommendations:

Improving the notification system and increasing researches in alternatives investigative tools .The adolescents need more focusing in their adherence to follow up and treatment **and transitional clinic with medicine department is needed**. As adults are the main source of infection, so they need specialized center for psychological support to deal with stigma of the disease. Improving the knowledge about tuberculosis transmissions and importance of screening.

References

1. Gupta R, Garg A, Venkateshwar V, Kanitkar M. Spectrum of childhood tuberculosis in BCG vaccinated and unvaccinated children. Medical Journal Armed Forces India. 2009 Oct 1;65(4):305-7.

2. Global Tuberculosis Control Report and WHO guidelines for National Tuberculosis programme on the management of Tuberculosis in Childhood, 2006. Available at http://www.who.int/tb/publications/global_report/2008/pdf/fullreport.pdf.

3. Amdekar YK. Consensus statement of IAP working group: Status report on diagnosis of Childhood Tuberculosis. Indian Pediatr. 2004;41:146–155. [PubMed] [Google Scholar

4. WHO. Laboratory XDR-TB definitions. Geneva: Meeting of the global XDR TB task force 2006. World Health Organization. Available at http://www.who.int/mediacentre/factsheets/fs104/en/index.html. Accessed: October 1, 2008

5. Zar HJ, Workman LJ, Little F, Nicol MP. Diagnosis of pulmonary tuberculosis in children: assessment of the 2012 National Institutes of Health expert consensus criteria. Clinical Infectious Diseases. 2015 Oct 15;61(suppl_3):S173-8.

6. Bates M, O'Grady J, Maeurer M et al. Assessment of the Xpert MTB/RIF assay for diagnosis of tuberculosis with gastric lavage aspirates in children in sub-Saharan Africa: a prospective descriptive study. Lancet Infect Dis 2013; 13:36–40. [PubMed] [Google Scholar]

7. Jahromi MK, Sharifi-Mood B. Pulmonary tuberculosis in children. Int J Infect. 2014 Sep 1;3:e21116.

8. Perez-Velez CM, Marais BJ. Tuberculosis in Children. *New England Journal of Medicine.* 2012; **367**(4) : 348 -61 [PubMed

9. Newton SM, Brent AJ, Anderson S, Whittaker E, Kampmann B. Paediatric tuberculosis. *The Lancet Infectious Diseases.* 2008; **8**(8) : 498 -510

10. Phongsamart W, Kitai I, Gardam M, Wang J, Khan K. A Population-Based Study of Tuberculosis in Children and Adolescents in Ontario. The Pediatric Infectious Disease Journal. 2009; 28(5) : 416 -419 10.1097/INF.0b013e3181920d4d

11. Elmadhooun WM, Salah ET, Noor SK, Bushara SO, Ahmed EO, Mustafa H, et al. Prevalence of tuberculosis among children in North Sudan: Are we only seeing the tip of the iceberg? Journal of natural science, biology, and medicine. 2017;8(1):114

12. Shah B, Mishra S. Clinico-laboratory Profile of Childhood Tuberculosis Admitted at a Tertiary Hospital in Nepal. Journal of Advances in Medicine and Medical Research. 2018:1-6.

13. Marais B, Obihara C, Warren R, Schaaf H, Gie R, Donald P. The burden of childhood tuberculosis: a public health perspective. The International Journal of Tuberculosis and Lung Disease. 2005;9(12):1305-13.

14. Laghari M, Sulaiman SAS, Khan AH, Memon N. Epidemiology of tuberculosis and treatment outcomes among children in Pakistan: a 5 year retrospective study. PeerJ. 2018;6:e5253.

15. Lotfian F, Bolursaz MR, Khalilzadeh S, Baghaie N, Hassanzad M, Velayati A. Features of adolescents tuberculosis at a referral TB's Hospital in Tehran, Iran. Mediterranean journal of hematology and infectious diseases. 2016;8(1).

16. Hunter RL. Tuberculosis as a three-act play: a new paradigm for the pathogenesis of pulmonary tuberculosis. Tuberculosis. 2016;97:8-17.
17.   Devrim I, Aktürk H, Bayram N, Apa H, Tulumoğlu Ş, Devrim F, et al. Differences between pediatric extra-pulmonary and pulmonary tuberculosis: a warning sign for the future. Mediterranean journal of hematology and infectious diseases. 2014;6(1).
18. Panigatti P, Ratageri VH, Shivanand I, Madhu P, Shepur T. Profile and outcome of childhood tuberculosis treated with DOTS—an observational study. The Indian Journal of Pediatrics. 2014;81(1):9-14.
19. Verma SK. Assessment of Radiologic Manifestation of Pulmonary Tuberculosis in paediatric patients: Retrospective study. Journal of Advanced Medical and Dental Sciences Research. 2016;4(2).
20. Tomà P, Lancella L, Menchini L, Lombardi R, Secinaro A, Villani A. Radiological patterns of childhood thoracic tuberculosis in a developed country: a single institution's experience on 217/255 cases. La radiologia medica. 2017;122(1):22-34.
21. Osman T, El Sony A. Case management of childhood tuberculosis in children's hospitals in Khartoum. 2014.
22.   Ogbudebe CL, Adepoju V, Ekerete-Udofia C, Abu E, Egesemba G, Chukwueme N, et al. Childhood Tuberculosis in Nigeria: Disease Presentation and Treatment Outcomes. Health services insights. 2018;11:1178632918757490.
23.   Aketi L, Kashongwe Z, Kinsiona C, Fueza SB, Kokolomami J, Bolie G, et al. Childhood tuberculosis in a sub-Saharan tertiary facility: epidemiology and factors associated with treatment outcome. PloS one. 2016;11(4):e0153914.
24.   Dhaked S, Sharma N, Chopra K, Khanna A, Kumar R. Socio-demographic profile and treatment outcomes in pediatric TB patients attending DOTS centers in urban areas of Delhi. Indian Journal of Tuberculosis. 2019; 66(1):123-8.
25.   Joshi S. Association of type of tuberculosis with treatment outcome among pediatrics tuberculosis patients in Bhopal city. International Journal of Community Medicine and Public Health. 2017; 4(11):4205-8.
26. Aldaba JG, Ama MCG, Salonga AM, Sylim PG, Sarol Jr JN, Lopez AL. Diagnosis and Management of Childhood tuberculosis in Public health Clinics in a rural Area in the Philippines: results from Community surveillance. Acta Medica Philippina. 2018; 52(4):312.