ASSESSMENT OF FACTORS AFFECTING CHILDREN ADHERENCE TO ANTI-TB DRUG IN ADAMA REFERRAL HOSPITAL, OROMIA, ETHIOPIA

Kelifa Osman Yusuf[1]*, Muluneh Fromsa Seifu[1], Belayneh Kefale Gelaw[1], Tirumurgan Gunasekaran[1], Esayas Tadesse Gebremariam[1],Mustefa Ahmed Mohammed[1]

[1]Ambo University, College Of Medicine and Health Sciences, Department Of Pharmacy
P.O.Box: 19, Ambo, Ethiopia

Abstract

Objective: *The objective of this study was to assess of factors affecting adherence of pediatric TB patients to anti TB drugs in Adama referral hospital.*

Methodology: Retrospective cross sectional study has been conducted from March 19th to May 20th, 2014 to assess factors affecting adherence of pediatrics TB patients to anti TB drugs in Adama referral hospital. Data collection format was used to collect data from available data sources such as patients' medical cards and DOT registration book. Simple random sampling technique has been used in this research and data was presented in table and categorized and analyzed by using SPSS computer software package.

Result: Among 91 patients 42(46.1%) were males and 49(53.8%) were females. And 16 (17.6%) of patients were below 5 years of age, 30(32.96%) and 45(49.5%) of patients were between age of 6-10years and between11-15 years of age, respectively. Among all pediatrics patients 59(64.83%) of them adhered to treatment program while 27(29.67%) patient defaulted (not adhered to) the treatment program. But for 5(5.5%) patients at end of program it was not known whether they defaulted or completed the treatment. At the end of treatment program 14(15.38%) of patients were cured while 6(6.6%) of the patients were not cured due to either MDRTB development or relapse, and 6(6.6%) of the patient were died. The most common factor identified to affect pediatrics adherence to anti TB medication were parents' knowledge of TB, parents relationship with provider, presence or absence of other reason like feeling better, forgetfulness and residence area.

Conclusion: As this study shows 29.67% of patients did not adhere to their treatment program. Also, this study shows that adherence of pediatric patients to their medication is not only affected by patient taking medication as prescribed but also by parent knowledge of TB, parent relationship with provider, presence or absence of other reason like feeling better, forgetfulness and residence area.

Key word: pediatric patients, Adama, Adherence, TB patients

Correspondence author:
Kelifa Osman Yusuf

QR code

Please cite this article in press as Kelifa Osman Yusuf et al, Assessment of Factors Affecting Children Adherence to Anti-Tb Drug in Adama Referral Hospital, Oromia, Ethiopia, Indo American J of Pharm Sci, 2015;2(5):903-911.

INTRODUCTION

Background Information

Tuberculosis is an infectious disease caused by mycobacterium tuberculosis which is transmitted through the air, by ingesting infected milk or meat and it is both preventable and curable disease. People who have pulmonary tuberculosis can infect other through droplet infection when they cough, sneeze, and talk. If TB is detected early and fully treated, people with disease quickly become non infectious and eventually cured (1).

The WHO in its global plan to stop TB report that poor treatment has resulted in evolution of mycobacterium TB strain that do not respond to treatment with standard first line combination of anti TB drug. Emergency of multi drug resistant TB, extensive drug resistant TB, HIV associated TB and weak health system are the major challenge to TB control program globally (2).

One of the greatest challenges facing most TB program is that of patient who do not complete their TB treatment for one or more reasons such as patient are not only at risk of relapsing ,but also they may develop resistances to one or more potent first line TB drug ,such as isoniazid (INH),rifampcin(RMP) Pyrazinamide (PZA), ethambutol (ETH)and streptomycin(2).

Out of approximately one million estimated case of TB in children world wide,75% occur in the 22 high burden countries and majority of children with smear positive TB who are <15 years of age were in Africa and south east Asia. In low income countries childhood TB is associated with malnutrition, poverty, over-crowding, higher death rate and lower treatment success rate (3).

Although the true burden of childhood TB is not well known, it is one of the 10 major causes of childhood mortality with estimated annual death of 74,000_130,000 .Ethiopia is one of 22 high burden countries in which TB is the second leading cause of death ,it is estimated that children contribute to 16% of national TB burden. Childhood TB is marker of recent transmission in population; moreover, children are the primary victims of poor TB control programs and TB is significant childhood morbidity and mortality in the country (4).

Adherence to long term therapy is a multi-dimensional phenomenon determined by the interplay of five set factors namely social and economical factor, health care team, conditional related factor, therapy and patient related factor (6).

Poor adherence to treatment of chronic disease including TB is a worldwide problem of striking magnitude, however patient with TB are expected to have adherence level greater than 90% in order to facilitate cure .The failure for cure increase the risk of

development of drug resistance TB and further spread in community which in turn increase morbidity and mortality (5)

In sub sub-Saharan Africa there is high rate of loss to follow up of TB patient that range from 11.1% -29%. Ethiopia is one of the seventh countries that reported lower rate of treatment success and patient who take TB treatment irregularly and unreliable way are at greatly increased risk of treatment failure(5).

Statement of the Problem

Compliance to TB treatment continues to be one of the major obstacles that TB control program worldwide have to deal with, especially in developing countries (7). Poor compliance and defaulting anti TB treatment contribute to the increase of multi drug resistant mycobacterium tuberculosis (8). In addition, comprehensive studies on resistance to anti TB drug in children are lacking, because they are not included in global survey. Surveillance of anti TB drug resistance during 1995-2007 among children from south Africa showed a significant increase in resistance to INH and RMP from 2.3%-6.7%. Drug-resistance among children has been documented in clinical trial of both pulmonary and extra pulmonary tuberculosis (4). Therefore, children under treatment for TB who default from treatment are at risk for clinical deterioration and complication and can continue to be infectious to other and at risk of premature death (11).

Furthermore, mortality from tuberculosis is highest in early childhood due to children non adherence to TB treatment (4). Approximately one million children develop active TB annually comprising 30%-40% of the total TB case load in high burden countries, out of this 75% occur in high burden countries of whom 450,000 die each year, even though there is highly effective medication (12). According to 2012 WHO report estimate, half of million children ill with tuberculosis in 2011 of which nearly 64000 children die of TB, even though there is effective medication(9).

In Ethiopia, even though TB drug are given free of fee TB continues to be major cause of TB related child hood death (10). In developing countries including our country large number of family have no balanced diet for their child normal growth? In these types of children when they are infected with mycobacterium tuberculosis with underlying malnutrition, they develop drug side effect such as drug intolerance and vomiting in intensive phase of the treatment which result in child non adherence to their treatment. In this type of countries poor adherence is major concern of child hood TB treatment and usually less than one third of

participant to the treatment program complete full course of poorly supervised treatment (13).

Treatment is challenging since no pediatric drug formulations are currently commercially available and with a long and burdensome disease, especially in the case of MDR-TB when treatment can take up to two years, adherence to treatment is difficult for patients and their families. Children lack the emotional resources to cope with the disease on their own and rely heavily on practical and emotional support from their care giver. (14)

Significance of the Study
The result of this study would identify the major problems that account for children non adherence to their medication and TB relapse. It also notifies the development of MDR TB in children who are being treated and who will be treated at Adama hospital. The finding of this study also gives an insight to health professional about major factors affecting the children adherence to their anti TB drug treatment schedule. If it is implemented, also it will improve children cure rate and minimize death from MDR TB in children. Once the factors are identified, then targeted strategies to address them can be formulated. The finding may also be used to formulate strategies to improve quality of care for TB pediatric patient.

OBJECTIVE
General objective
To assess factors affecting children adherence to anti TB drug in Adama referral hospital, East Shewa Ethiopia
Specific objective
To determine the magnitude of non adherence in children attending anti-TB drug in Adama referral hospital

To determine reasons for MDR TB in children

To determine factors affecting children adherence to anti TB drugs in Adama referral hospital

To assess factors contributing to children defaulting TB treatment program

Methodology
Study Area
Adama is one of the towns of Oromia regional state, East Shewa zone and located 99Km far from Addis Ababa. There are different governmental and non-governmental institutions in the town such as 8 health Centers, one referral hospital, one general hospital, 50 private clinics, and 105 pharmacies. The study was conducted in Adama hospital medical college on pediatrics patients who had attended TB treatment program from September 2002 EC-September 2006 EC. Adama hospital was established & started its full function in 1965. The hospital is now providing several health services including TB treatment program for the community.

Study Design
In this research a cross sectional study based on retrospective data was conducted by reviewing patient`s DOT registration book and patient medical charts. The study period had been from April 1 to May 20, 2014.

Source Population
All pediatric patients' s DOT registration book and medical charts of who had attended TB treatment program in the previous five year from 2002 E.C-2006 E.C

Study Population
All sampled pediatric patients s DOT registration book and medical charts of who had attended TB treatment program at TB clinic for the past five year from 2002 E.C-2006 E.C were included.

Inclusion and Exclusion Criteria
All medical charts of pediatrics patients below sixteen years old were included and all adult TB patients above fifteen years old were excluded from the study.

Sample Size Determination
The proportion to be studied was (p) =10% of the population, allowed deviation was ''w' 'which was 5 % and confidence interval was 95% therefore minimum sample size required was obtained by the formula:

$$n=z^2p\ (1-P)/W^2$$
$$n= (1.96)^2 0.1x0.9/(0.05)^2$$

n=138 sampled for the study
but because N was relatively small adjustment was made for the above ''n'' required by the following formula

$$n/(1+n/N)$$
$$=138/(1+138/1500)$$

=126 Patient were included

Sampling Technique
In this study simple random sampling was used.

Study Variables
Independent Variables
- Age
- Sex
- address
- quality of service
- parent educational status

- parent socioeconomic status

Dependent Variables

- Adherence/non adherence to the treatment
- Defaulting the treatment
- MDRTB development

Data Processing and Analysis

After data was collected, it was categorized and analyzed using SPSS computer soft ware package. And the result was summarized and presented in table and written form.

Data Quality Control

To ensure data quality, data collection technique and format was pretested at study area in 5% of sample population of the same source population.

Ethical Consideration

Permission letter or ethical clearance was obtained from college of medical and health science department of pharmacy and was given to Adama hospital administrative office and permission was obtained from administrator. In addition the patients' information was kept confidentially.

Operational Definition

Adherence = extent to which the patient take their medication as prescribed by physician

Non adherence = not taking medication as prescribed

Defaulting = discontinuing taking medication

Tuberculosis = disease caused by mycobacterium tuberculosis

RESULTS:

In this study 126 pediatric TB patients' medical charts were sampled from 1500 medical charts of pediatrics TB patient population using simple random sampling. Among whom 35 patients were transferred to other health institution for close follow up of DOT therapy. Thus, 91 pediatrics medical charts were analyzed.

Socio-demographic characters

Table 5.1 demonstrate demographic characteristics and patient sources of sample population

Variable		frequency	Percent
Sex	Male	42	46.1%
	Female	49	53.8%
Age	0-5	16	17.6%
	6-10	30	32.96%
	11-15	45	49.5%
New to program	YES	86	94.5%
	NO	5	5.5%

Among 91 patients 42(46.1%) were males and 49(53.8%) were females, the association between sex and patients completion of the treatment was identified by calculating "p" value for both variables and the association was found to be insignificant 0.66 (>0.05). 16(17.6%) of patients were below 5 years of age, 30(32.96%) and 45(49.5%) of patients were between age of 6-10 years and between age of 11-15 years, respectively. The association between age of patients and treatment completion behavior of the patients was obtained to be statistically insignificant (p = 0.87 at 0.05 level of significance).

In this study 86(94.5%) of the patients were new for treatment program while 5(5.5%) of patients had attended the treatment program before they were readmitted to the treatment program.

Out of all pediatrics TB patients analyzed 52(57.1%) of patients were treated for extra pulmonary TB while the rest 39(42.82%) of patients were treated for pulmonary TB. The association between type of TB and treatment completion behavior was obtained to be insignificant (p=0.769).

Table 5.2 Demonstrates initiation missed dose, phase in which dose was missed ,duration for which dose was missed, side effect, type of side effect ,other reason and defaulting behaviors of patient

Variable		Frequency	Percent
Initiation missed dose per week	none	68	74.5%
	One dose	1	1.1%
	Two dose	10	10.99%
	Three dose	9	9.9%
	Four dose	3	3.3%
Side effect	yes	26	28.6%
	Unknown	65	71.42%
Type of side effect	none	64	70.33%
	Vomiting and headache	13	14.28%
	Nausea	1	1.1%
	Hepatotoxicity	8	8.78%
	Vomiting and nausea	5	5.49%
Other reason	Feeling better	15	16.48%
	Forget	4	4.39%
	Missed	2	2.19%
Phase in which dose was missed	Initiation	17	18.7%
	Continuous	19	20.87%
Duration	None	64	70.33%

for which dose was missed	Two week-one month	14	15.4%
	Two month-four month	13	14.3%
Default	yes	22	24.17%
	No	66	72.52%
	unknown	3	3.3%

In initiation phase 17(18.7%) of the patients were recorded to missed their dose up to two weeks of initiation phase because of side effect or other reason while 19(20.87)of the patients default the treatment in continuous phase due to other reason like feeling better, forgetfulness, being far away and due to missing. But statistical p value (0.857) indicates that there was no association between presence of side effect and treatment completion behavior of patients. But other reasons like feeling better, forget fullness and death together with treatment completion behavior had association (p=0.00).

The side effect of anti TB medication was identified in 26(28.6%) of patients and not identified in 65(71.42%) of the rest patients. The most common identified drug related side effect were vomiting and nausea in 18(19.78%) of patients, followed by hepatotoxicity in 8(8.7%). The other reasons for which most of the patients missed their dose were feeling better in15 (16.48%) of the patients, forget in 4(4.39%) of the patients and being far away in 2(2.19%) of the patient.   Most of these reasons were very common in continuous phase of treatment program. The patient who defaulted treatment program for two weeks –one month were 14(15.4%) while 13(14.3%) of the patient discontinued their medication for two months-four months. There was statistically significant association between defaulting and treatment completion with (p=0.00).

Table 5.3 demonstrate type of TB the patient was treated for, patient co morbid condition, type of ART the patient had been taking and MDRTB status of the patient.

Variable		Frequency	Percent
Co morbid condition	HIV	20	21.97%
	DM	5	5.49%
	No other condition	66	72.52%
Type of TB	Pulmonary	39(42.85)	42.85%
	Extra pulmonary	52(57.1)	57.1%
ART medication	None	71	78%
	D4T+3TC+EFV	11	12.1%
	TNF+3TC+EFV	9	9.9%
MDRTB	Yes	7	7.69%
	No	14	15.38%
	Unknown	70	76.92%

The most common co morbid condition reported in these patients were HIV in 20(21.97%) of pediatric TB patients who analyzed for the study and DM in 5(5.49%) of the patients. Among the patients who had HIV as underlying disease to tuberculosis 11(55%) of patients were treated with D4T+3TC+EFV and 9(45%) of the patients were treated with TDF+3TC+EFV regimen. Statistical p-value that indicates association between co morbid condition and treatment completion was 0.868 indicating insignificant association.

MDRTB was identified in 7(7.69%) of the patients, while 14(15.38%) of the patients were cured and 70(76.92%) of the patients were not reported whether they had MDRTB or not. The statistical association between adherence and MDRTB was found to be insignificant (p=0.121).

Table 5.4 demonstrates parent TB knowledge, parent relation with provider, economic status and patient health status at the end of treatment program and completion status.

Variable		Frequency	Percent
Parent economy	No any information	91	100%
Parent TB knowledge	Good	58	63.73%
	Poor	20	21.97%
	Unknown	13	14.28%
Parent relation with provider	Good	56	61.54%
	Poor	22	24.17%
	Unknown	13	14.28%
Patient health at end of the treatment	Cured	14	15.38%
	Not cured	6	6.6%
	Missed	6	6.6%
	Unknown	65	71.43%
Did the patient complete the treatment course	Yes	59	64.83%
	No	27	29.67%
	Unknown	5	5.5%

The knowledge of parents of TB patients for 58(63.73%) were good while poor for 20(21.97%), and those whose parent's TB knowledge status was unknown were 13(14.28%) of the patient. The statistical association between adherence and parents' TB knowledge was (p=0.000). Parents of 56(61.54%) patients had good relationship with health care providers of the program while parents of 22(24.17) patients had poor relation with health care provider and parents relation with provider for 13(14.28%) of pediatrics patients was unknown. The statistical association between patient adherence and parent relation with service provider was significant (p=0.00). At the end of treatment program 14(15.38%) of patients were cured while 6(6.6%) of the patients were not cured and 6(6.6%) of the patients died. However, patients health at the end of the program were not known for 65(71.43%) of patients. The statistical association between adherence and patient's health status at the end of treatment program was found to be significant (p=0.00). Among all pediatrics TB patients 59(64.83%) were successfully complete (adhere to) treatment program while 27(29.67%) patient default ed treatment program (non adhere) and for 5(5.5%)

patient at end of program whether they complete or not were not known.

Table5.5 Relationship of patient address to treatment completion

Address	Completeness				P value
	yes	no	unknown	total	
Urban	43	17	5	65	
Rural	16	10	0	26	

Out of patients who attended treatment from urban area 66% completed their treatments while 26% of patients from urban area did not. But 61% of patients from rural area completed the treatment while 38.4% of patient did not complete the treatment. The statistical association between adherence and address was obtained to be insignificant (p= 0.220).

DISCUSSION:
In this study 46.1% of patients were found to be males while 53.8% of the patients were females, this result is similar with study conducted in Kenya in which 44.9% of the patients were males and 55.1% of the patient was females (15). In this study there was no significant association between sex, age and patient's adherence to their medication. This result is also consistent with finding of the study conducted in Kenya (15). In addition, it is similar with result reported by study conducted in Nigeria (18). Both studies concluded that there was no significant association between age, sex and patient adherence to medication. This could be due to the fact that in pediatric patients adherence is highly dependent on care giver of the patients (15). The result of this study showed that extra pulmonary TB was found to be more common in patients when compared with pulmonary TB, 57.1% and 42.82%, respectively. This result was not reported in study conducted in different countries. This indicates that diagnosis of TB in children is made at advanced stage of TB in pediatrics patient in Adama referral hospital. Furthermore, there was no statistically significant association (p = 0.76) between type of TB and patient adherence to their medication. This means that there is no difference in adherence to medication between the types of TB.

The patients who completed the treatment course at the end of the program were 64.83% while 29.67% of the patients defaulted the treatment, because caregiver may thought that their children were cured or due miss. This result is in line with a study

conducted in Uganda which reported similar non adherence (25% of the study population) (17). Among these patients those whose sputum result recorded for three consecutive months showed that they were cured, were 15.38% while 6.6% of patients failed to be cured. 6.6% of patients died while they were on treatment. And those for which their health status was not known at end of treatment program were 64.83%. This result is not consistent with study conducted in Nigeria where higher cure rate and lower failure rate were reported (17). But it is consistent with result reported in retrospective study conducted in Ethiopian rural hospital in 2010 in which almost similar defaulter rate (16.8%) was reported, but the patients who died were lower than that obtained in this study (12).

Adherence in this study (64.83%) is slightly lower than that reported in study conducted on children registered for TB treatment at 23 health centers (85%) in Addis Ababa, but lower death rate (3.3%) of patients was reported (4). But it is in contrast with study conducted in Egypt in which lower adherence (16%) and higher non adherence (51%) of studied patients were reported (16).

As this study indicates vomiting and headache in 19.68% of the patients and hepatotoxicity in 8.78% of patients were found to be the most common drug related side effects which appear on patients in initiation phase. This result is in contrast with the result reported in study conducted in Nigeria in which hepatotoxicity (72.1%) and nausea and vomiting (25%) of the side effects reported in the patients (18). But according to the finding of this study, there was no significant association between treatment completion and presence of side effect. This means presence or absence does not bring difference in the extent treatment completion (18).

The finding of this study shows 24.17% of the patients defaulted the treatment program in continuous phase due to feeling better in (16.48%), forget in(4.39%) and missed(died) in 2.19% of patients. Similar result was reported by the study conducted in Uganda (17). As the above finding shows other reasons like feeling better, forgetfulness and miss had significant association with adherence of the patients, this is also in contrast with what has been obtained in study conducted in Kenya which showed that there was no significant relationship between side effect and adherence to anti TB medication (15).

The finding of this study also showed that the most common co morbid conditions were HIV in 21.97% and DM in 5.49% of studied patients. There was no significant association between co morbid condition and adherence. However, the patient who had been taking ART had good adherence to medication than non HIV co morbid patients, because their family might think that their children would die if they discontinue taking anti TB drug as they were told by service providers. This result was similarly reported in study conducted in Uganda (17).

MDRTB was found in 7.69% of patients. According to the finding of this study there was no association between MDRTB development and adherence to medication as it was shown by p value (p=0.121 CI=95%). It might be due to poor adherence of patients to their medication or patients were caught by MDRTB from other patients. As the finding of this study shows there was no significant association between parent monthly income and patient adherence to anti TB medication. This result is in line with finding reported in study conducted in Kenya which states that family average monthly income had no statistically significant association with patient adherence to their medication (15). This was because TB treatment was given free and readily available to all patients.

As one can observe from the finding of this study the patients whose caregiver had TB knowledge (like nature of the disease, the effect of discontinue the treatment and the effect of irregular medication taking behavior) had good adherence to their medication when compared to patient whose care giver had poor TB knowledge, and there was statistically significant association between parent TB knowledge and adherence to medication .This result is in contrast with finding reported in Kenya which state that caregiver knowledge of TB had no significant association with adherence to medication (15). But it is consistent with study conducted in Uganda (17).

It was found that pediatric patients whose care giver had good relation with service provider had good adherence when compared with patient whose parent had poor relation with service provider. In addition, the quality of services has been shown to have significant association with adherence to the medication. This might be due to the parents were getting advice properly from health service providers. This finding is, however, in contrast with what reported in study conducted in Kenya which states that there was no statistically significant association between pattern of health care and patient adherence to medication (15).

In this study, even though higher defaulter were obtained in patients attended treatment from rural

area when compared with those attended treatment from urban area, there was no significant association between address and adherence of patients to their medication (p=0.220, CI, 95%). This finding is in line with study conducted in Uganda (17). It is also consistent with finding reported in Kenya (15)

Conclusion and Recommendation
CONCLUSION:
This study shows that adherence of pediatric patients to their medication is not only affected by patient taking medication as prescribed but also parents' knowledge of TB, parents' relationship with health providers, presence or absence of other reasons like feeling better, forgetfulness and residence area . As the finding of this study shows presence of underlying disease like HIV have no effect on adherence of patient to anti TB drug. The parent monthly income also have no effect on adherence of the patient to anti TB medication .The result of this study indicate that MDRTB and TB relapse were most common in patients with poor adherence to their medication.

RECOMMENDATION:
Health professionals should give special consideration for parents of children who come from rural area and parents should be informed and made aware about TB because pediatrics adherence to their medication is highly dependent on parent's TB knowledge.
Unlike adult patients children do not know the effect of discontinuing their medication; therefore treatment adherence of pediatrics patient should be monitored only by health professionals even during continuous phase of the treatment.
Health status of pediatrics patient should be checked at least every two months.
Side effect and other reasons which account for missing the dose should be monitored early so that children will adhere more to their medication.
Adama hospital TB clinic should be staffed by qualified health personnel so that pediatrics patients will get high quality of service.
Health professionals should focus on how to create awareness about factor affecting adherence in the community.
Parents should be educated about the causes and the effects of TB, and possible adverse reactions of the medication, and the importance of children completing their medication according to the treatment plan.

Abbreviation and Acronyms :
DOT = directly observed therapy
EDR TB = extended drug resistant tuberculosis
ETH = Ethambutol
HIV = human immune deficiency virus
INH = Isoniazid
MDR TB = multi drug resistant tuberculosis
PZA = pyrazinamide
RMP = rifampcin
SRP = streptomycin
TB = Tuberculosis
WHO = world health organization
D4T = stavudine
3TC = lamivudine
EFV = efaverenz
TDF = tenofovir

REFERENCES:
1. Kudakwashe Ch. Factor affecting compliance to tuberculosis treatment in Andra Kanvango region in Namibia, Journal of compliance to TB treatment, 2010, and 5-6.
2. Rieder, L. H. Interventions for tuberculosis control and elimination; journal of International Union against Tuberculosis and Lung Diseases, 2002, 5.
3. Soumya Swaminatha and Banu rekha. Burden of child hood tuberculosis and DOT in childhood in India, journal of medical science ,2010,6-7
4. Dereje hailu ,et al. Child hood tuberculosis and its treatment out come in Addis Ababa, Journal of BMC,Pediatrics2014,14:61 doi.10.1186/1471-2431-14-61
5. Akilew ,Kefyalew and mulugeta Belay. Non adherence to anti TB treatment November 11, 2013,DOI: 10.1371/journal. pone. 0078791;1
6. Bernand N Muture,Mergaret N Keraka,Peter K Kimu. Factor associated with defaulting from treatment among tuberculosis patient in Nairobi provinces, Journal of BMC Public Health 2011, 11:696 doi:10.1186/1471-2458-11-696

7. Tessema, B, Muche, A, Bekele, A, Reissig, D, Emmrich, F and Sack, U. Treatment outcome o f tuberculosis patients at Gondar University Teaching Hospital, Northwest Ethiopia,2009. A five   year retrospective study.Biomedical Central journal 9:371;1-2

8. B Castlen Vovo.A review of compliance to anti tuberculosis treatment and risk factors for defaulting treatment in Sub Saharan Africa, journal of   African Health Science ; Dec 2010;v.10(4),1-3

9. Alyysa Finlay. et al.Patient and provider level risk factor associated   with defaulting from tuberculoisis treatment South Africa 2002,1-2

10. Ibrahim Ali , Yimtubeznash Woldeamnuel , Amha Mekasha , Markos Abebe , Demissew Beyene, Shiferaw Bekele Abraham Aseffa . Drug Resistant Pattern of M. tuberculosis Among TB Suspected Children at Tikur Anbesa Specialized Hospital, Ethiopia,2011:1-4

11. WHO   report. Burden of TB on children 2012:14-15

12. Ramos, et al. Childhood and adult tuberculosis in rural hospital south east Ethiopia, Journal of BMC, public health ,2010,10:215

13. B.J Maris ,et al. The burden of child hood tuberculosis in south Africa,Journal of public health 2005,4:35

14. Tajakistan   ministry of health. Improving pediatric TB care inTajakistan,report of 2013:3-5

15. Dr Mario Nyamokami Ongayo ,etal. Determinant of adherence to anti TB drug among pediatrics TB patient in urban Kenya, journal of pharmacology 2011,1-2

16. Aida Mohey Mohammed .Adherence of children to INH preventive therapy in Alexandria ,Egypt journal of community medicine 2010:5-7

17. Monica G Amuha,1 Paul Kutyabami,1 Freddy E Kitutu,1 Richard Odoi-Adome,1 and Joan N Kalyango. Non-adherence to anti-TB drugs among TB/HIV co-infected patients in Mbarara Hospital Uganda: Prevalence and associated factors, Afr Health Sci. Aug 1, 2009; 9(Suppl 1): S8–S15. PMCID: PMC2890989

18. Bello S.I and Itiola O.A. drug adherence among tuberculosis patient in university of Ilorin teaching hospital, Nigeria, African journal of pharmacy and pharmacology.vol. (4)pp(109-114) march 2010.