ORIGINAL ARTICLE

CLINICAL IMPROVEMENT AND DRUG-ADVERSE EFFECTS AMONG PATIENTS TAKING ANTI-TUBERCULOSIS DRUGS

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ABSTRACT

Introduction: *Although an optimal treatment is available for tuberculosis in most settings, the disease remains to be a major cause of morbidity and mortality worldwide. An assessment of treatment outcomes and anti-tuberculosis drug adverse effects will help in the fight against tuberculosis. There is a serious lack of information as to the picture of the Ethiopian TB patients' response to treatment and the adverse effects of treatment.*

Objective: *The main aim of this study is to assess tuberculosis clinical improvement and anti-TB drug adverse effects.*

Methods: *This is a cross-sectional descriptive study with some analytic components done on TB patients who came to the DOTS clinics in Gondar, Ethiopia. A well-structured and pre-tested questionnaire with socio-demographic and relevant clinical variables was used for data collection.*

Results and Conclusion: *The commonest TB symptoms seen in this study were fever, weight loss, cough, night sweating, and anorexia. Most of the symptoms improved within the conventional improvement time of 3 to 6 weeks. However, weight loss and fatigue improved late. Forty-six percent of the subjects experienced at least one drug-adverse effect at some time while on treatment. Major adverse effects were seen in 24.3% of the subjects. The commonly encountered adverse effects were GI upset (22.8%), neuropathic symptoms (13.5%), sleepiness (11.2%), and skin rash (9.0%). Fever improvement was delayed among patients co-infected with HIV. There was no significant delay in improvement of the other TB symptoms among HIV co-infected patients. HIV infection was not found to affect the occurrence of any of the drug-adverse effects in this study. However, cotrimoxazole use was found to increase the risk of skin rash by 4 fold.*

INTRODUCTION

Tuberculosis (TB) is one of the leading causes of death in all age groups despite a vigorous global struggle towards the achievement of a TB free world. It has been a historical enemy of the human generation since olden times. Currently one third of the world's population is said to be infected with the TB bacilli (*Mycobacterium tuberculosis).*[1] Ethiopia is one of the world's 22 countries seriously affected by TB. It ranks 7th in the world and 3rd in Africa in TB prevalence. According to the World Health Organization (WHO) Global TB Report 2006, the country had more than 267,000 TB cases in 2004. The occurrence of TB infection seems to have grown to around 420,420 among the Ethiopian population of 77,000,000 according to the WHO 2007 estimates.[2,3]

Directly Observed Treatment Short Course (DOTS) is the mainstay of TB treatment program which has started recently. Although it has resulted in optimal success, a lot of problems have been identified. Amongst many, one is failure of treatment. Failure of response to anti-TB treatment could be the result of a number of factors, like poor adherence to treatment, infection by drug resistant strains, inadequate treatment, personal variations, etc. In addition, wrong diagnosis, the co-existence of other diseases, like acute bacterial pneumonia and *Pneumocystis carinii* pneumonia (PCP) could also play a sensible role.[4]

Another problem in TB treatment programs is adverse events associated with anti-tuberculosis drugs. Most TB patients complete their treatment without any significant drug side-effects. However, a few patients do develop side effects. Different forms of adverse events from ant-TB treatment are seen in many patients including gastrointestinal disturbance, skin rashes, hepatotoxicity, neuropathies, etc. These

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adverse events are more common in HIV associated tuberculosis to the extent of throwing some of the anti-TB drug out of use.[4, 5] Among the commonly encountered, clinically identifiable side effects of the anti-tuberculosis drugs, which are considered to be the major drug side-effects (and hence indications to stop the culprit drug), are severe skin rash, hearing impairment, or balance disturbance (often due to streptomycin), poor vision and color perception (due to ethambutol), and jaundice (a sign for hepatotoxicity). The commonly encountered minor effects are burning sensations, lethargy, orange/red urine, gastrointestinal complaints (anorexia, nausea, vomiting, and abdominal pain) and the likes. HIV/AIDS is by far the most important factor for the development of all of these drug side-effects, the commonest in HIV infected individuals being skin rash.[5,6] This factor needs critical scrutiny for it accounts for more than 50% of tuberculosis patients in Ethiopia as some local researches show.[7]

On the other side of the tragedy, drug resistance, including multi-drug resistance and extensive drug resistance, is essentially a man made problem caused by the inappropriate use of drugs and, to a lesser extent, by non-adherence to prescribed treatment regimens by patients.[8] This problem can partly be brought about as a result of anti-TB drug-adverse effects. As in many other resource-constrained settings, TB treatment outcomes in Ethiopia have not been satisfactory. Numerous researches have been done on the assessment of treatment outcome in the country and abroad. Most of the researches were done by assessing sputum results at different times of treatment, mortalities, defaulters and the likes.[5, 9] Studies are few, particularly when it comes to symptomatic assessment of improvement among patients in Ethiopia. The same is true for clinical assessment of drug related adverse effects.[10] Symptomatology, though, a decisive component of the complex mesh existing over adherence, defaulting, clinical improvement, socioeconomic characteristics of patients, patient and health service delay, and TB treatment at large are serious problems in the Ethiopian context.[11, 12, 13]

This study is primarily designed for the elaboration of TB patients' response with a particular emphasis on clinical manifestations and also on anti-TB drug related adverse effects. In the investigators' opinion most Ethiopian studies tend to concentrate on laboratory profiles, like sputum examination, X-ray investigations, HIV seropositivity and success at the end of treatment. Results from this study, therefore, give highlight on the way TB patients respond clinically, consequently helping gear clinical expectations in treating TB patients. Moreover, the nature of side-effects from anti-TB drugs is another issue not well-addressed in the Ethiopian context. Hence, this study has the following specific objectives: the determination of improvement time for TB symptoms, finding out the commonest drug-related adverse effects, and investigating factors affecting symptomatic improvement and drug adverse effects of TB treatment.

METHODS

This is a health-institution-based cross-sectional study of TB patients at the DOTS clinics at Gondar University Hospital, Gondar Poly Clinic, and Azezo Health Center, Northwest Ethiopia. TB patients visiting these clinics in December 2008 and January 2009 constituted the study population for the research.

Patients were interviewed by trained nurses. All forms of TB patients on DOTS were recruited into the study. A total of 268 TB patients were encountered: 83 of them were from Gondar University Hospital; 160 were from Gondar Poly Clinic; and 25 were from Azezo Health Center. The composition was assumed to be homogeneous in that all patients were from Gondar town or its surroundings in all the three cases. The three health institutions are the only government health institutions which give comprehensive care to patients with TB. The researchers believe that TB patients coming for care at any time of the year are similar to each other in terms of the research title, justifying the representativeness of the sample.

All types of TB patients on treatment beyond the second week were included in the study. This is because clinical improvement among TB patients is expected to occur 2 weeks after the initiation of anti-TB drugs. Critically ill TB patients who could not give reliable information were excluded from the study and sent for evaluation. Their number was too low to cause a sort of non-response bias.

The study subjects were asked about presence of adverse drug effects, onset and types of clinical improvement. Other variables include age, sex, presence of co-infection, concomitant drug use, etc.
Data were collected mainly by using interview based questionnaire which was filled with the help of well oriented clinical nurses working at the study sites so that they may encounter all patients coming to the institutions at any time. Some data regarding diagnosis, concomitant drug use, and duration of treatment

were retrieved by using patient records. Well-structured, pre-tested questionnaire was used in the data collection process. A supervisor (one of the investigators) followed the completeness, accuracy, and procedure of data collection in order to help keep optimal quality of data.

Data were entered into a computer for cleaning and analysis. A statistical package SPSS version 15.0 was used for statistical analysis. Measures of central tendency and dispersion with graphical presentation of data were used for summarising the descriptive findings. Statistical associations were checked using chi-square and Fischer's Exact tests. Other statistical analyses like logistic regressions and t-tests were also used as necessary. A level of significance of 5% was used for the above statistical analyses used in this paper. This is considering the level of significance used in many researches.

The study participants were asked for their voluntary participation, and consent was taken by the data collectors verbally.

RESULTS

A total of 268 patients on TB treatment under the DOTS program were seen in this study with a sex composition of 53% male patients. The mean age was found to be 31.8 with a standard deviation of 13.1. The types of TB identified in the study are summarised as in Table 1.

Table 1: Table Showing the Frequency of Different Forms of Tuberculosis among the Study Subjects, Gondar, Dec 2008 to Jan 2009

Type of Tuberculosis	Frequency	Percent(%)
Smear positive PTB	110	41.2
Smear negative PTB	100	37.5
Isolated EPTB	53	19.9
Disseminated TB	4	1.5
Total	**267**	**100.00**

Out of all the patients, 94.8% were taking anti-TB drugs as newly diagnosed cases while 4.9% were relapse cases with only one treatment failure case. Thirty-three percent of the study subjects reported that they were using drugs while they were on TB treatment. Eighty-four percent of those using other drugs concomitantly, were taking anti-retroviral therapy (ART). Cotri-moxazole was the other most commonly used drug among the patients (taken by 29.1% of the patients). The five most common clinical symptoms at the time of initial presentation were fever (81.7%), weight loss (81.3%), cough (79.4%), night sweating (78.7%) and loss of appetite (76.5%). Table 2 shows the relative duration of recovery for each symptom with some important measures to depict the difference clearly.

Table 2: Table showing the average duration of recovery for each TB symptom, Gondar, Dec. 2008 to Jan 2009

TB Symptom	No of patients with the symptom recovered	Mean duration of recovery in days	Standard deviation of recovery duration
Cough	178	33.3	27.4
Sputum Production	131	33.3	27.7
Hemoptysis	43	26.2	23.8
Chest Pain	150	30.5	24.1
Fever	191	28.8	22.7
Loss of Appetite	175	31.6	23.7
Night Sweating	187	28.6	22.7
Weight Loss	182	37.8	26.3
Discharging Wound	25	46.7	25.4
Swelling	40	47.3	31.1
Fatigue	144	41.2	30.8

Drug adverse effects in the order of their occurrence were reddish urine (94.4%), gastrointestinal upset (22.8%), neuropathic symptoms (13.5%) (symptoms like paresthesia, numbness and tingling sensation), sleepiness (11.2%), skin rash (9.0%), balance disturbance (8.6%), vision problem (8.2%) and yellow sclera (7.1%). All in all, excluding reddish urine as an adverse effect, 45.7% of the patients have experienced one or more of the above adverse effects at some time in their treatment period. Twenty-four percent were found to have experienced one or more of the major anti-TB related adverse effects.

The five commonest TB symptoms identified in this study were evaluated in relation to the presence of HIV infection. Patients who had already improved from their symptoms were seen with respect to their HIV status and duration lapsed until improvement. The duration of improvement of fever was found to be significantly delayed among HIV positive TB patients when compared to HIV negative TB patients using independent samples t-test (mean difference = 9.4, $p = 0.01$, 95% CI: 2.2 – 16.7). Independent samples t-test showed no significant difference in the mean duration of improvement of cough ($d = 4.98$, $p = 0.26$, 95% CI: -3.7 – 13.6) and weight loss ($d = 4.2$, $p = 0.28$, 95% CI: -3.4 – 11.7) between HIV positive

and HIV negative TB patients. Marginal significance was seen for mean duration of improvement of chest pain (d = 7.6, p = 0.06, 95% CI: -0.4 – 15.5) and night sweating (d = 6.9, p = 0.06, 95% CI: -0.4 – 14.1) between HIV positive and HIV negative TB patients.

The multivariate analysis showed that HIV negatives were significantly different from HIV positives in terms of weight gain while on treatment for TB. However overall significant associations were not seen with the variables considered in the model. A similar analysis pointed out that elderly patients were significantly different from children less than 20 in terms of improvement of fatigue within 6 weeks of treatment. Overall significance was not seen here either. These findings are summarised in Tables 3 and 4.

Table 3. Logistic regression output showing the effect of different variables on persistence of weight loss, Gondar, Dec 2008 to Jan 2009

Predictor Variables	Weight Gain within 6 weeks		Crude OR (95% C.I)	Adjusted OR (95% C.I.)
	Yes	No		
Age (in years)				
0 – 19	12	3	1.0	1.0
20 – 59	60	61	0.246 (0.066, 0.915)*	0.313 (0.076, 1.294)
≥ 60	4	4	0.250 (0.038, 1.633)	0.237 (0.034, 1.653)
Sex				
Male	45	36	1.0	1.0
Female	32	34	0.75 (0.392, 1.445)	0.803 (0.391, 1.648)
Residence				
Urban	67	64	1.0	1.0
Rural	8	7	1.09 (0.374, 3.185)	0.835 (0.267, 2.604)
HIV Status				
Positive	24	38	1.0	1.0
Negative	47	29	2.57 (1.288, 5.113)*	2.130 (1.002, 4.528)*
Not tested	6	4	2.38 (0.607, 9.295)	1.504 (0.335, 6.747)

* Significant Association

Table 4. Logistic regression output showing the effect of different variables on the persistence of fatigue, Gondar, Dec 2008 to Jan 2009

Predictor Variables	Fatigue Improvement within 6 weeks		Crude OR (95% C.I)	Adjusted OR (95% C.I.)
	Yes	No		
Age (in years)				
0 – 19	6	2	1.0	1.0
20 – 59	47	59	0.266 (0.051, 1.376)	0.322 (0.058, 1.772)
≥ 60	2	7	0.095 (0.010, 0.897)*	0.880 (0.009, 0.879)*
Sex				
Male	30	38	1.0	1.0
Female	27	10631	1.103 (0.546, 2.230)	0.902 (0.422, 1.928)
Residence				
Urban	51	62	1.0	1.0
Rural	6	6	1.216 (0.370, 3.999)	1.435 (0.404, 5.094)
HIV Status				
Positive	24	32	1.0	1.0
Negative	27	34	1.059 (0.509, 2.201)	1.049 (0.466, 2.361)
Not tested	6	4	2.000 (0.508, 7.882)	2.195 (0.484, 9.954)

* *Significant Associations*

Logistic regression was also done to see the effect of treatment duration until the interview, age, sex, HIV status and concomitant use of other drugs on the experience of any potentially drug related adverse effect. And it was found out that none of the above independent variables were found to be associated with the occurrence of drug adverse effects. Details of the logistic regression are summarised as in Table 5.

Table 5. Logistic regression output showing the effect of different variables on the occurrence of drug related adverse effect among patients, Gondar, Dec 2008 to Jan 2009

Predictor Variables	Presence of Drug Related Adverse Effect		Crude OR (95% C.I)	Adjusted OR (95% C.I.)
	Yes	No		
Age (in years)				
0 – 19	10	18	1.0	1.0
20 – 59	100	118	1.525 (0.673, 3.455)	1.074 (0.440, 2.620)
≥ 60	10	6	3.000 (0.840, 10.721)	3.108(0.811, 11.915)
Sex				
Male	65	75	1.0	1.0
Female	55	70	0.907 (0.558, 1.472)	0.930 (0.553, 1.565)
HIV Status				
Positive	52	53	1.0	1.0
Negative	61	77	0.807 (0.485, 1.343)	1.034 (0.405, 2.646)
Not tested	9	15	0.612 (0.246, 1.520)	0.679 (0.207, 2.232)
Use of Other Drug				
Yes	44	44	1.0	1.0
No	78	100	0.780 (0.467, 1.302)	0.745 (0.286, 1.940)

In all the above three logistic regression tests, the effect of multicollinearity among the predictor variables was checked as most of the associations were not significant. Multicollinearity was ruled out with small Variance Inflation Factors for each predictor variable (all values much lower than 2.5).

Chi-square tests were done for associations between three of the most common drug related adverse effects in this study and concomitant use of antiretroviral therapy or cotrimoxazole: gastrointestinal upset, neuropathic symptoms, and skin rash. A chi-square association test done between ART and GI upset showed no significant association (OR = 1.3, P = 0.40, 95% CI = 0.7 to 2.4). The same was true between ART and neuropathic symptoms (OR = 0.7, P 0.49= 95%, CI = 0.3 to 1.7) and between ART and skin rash (OR = 1.1, P = 0.8, 95% CI = 0.4 to 2.8). Findings were also the same for cotrimoxazole except that Fischer's Exact test showed a significant association between cotrimoxazole use and experience of skin rash (OR = 3.9, P = 0.015, 95% CI = 1.4 to 11.1).

DISCUSSION

Comparable figures of male and female patients (53% and 47%, respectively) were seen in this study. The age distribution of the study population included virtually all age groups but a relatively larger frequency (93.9%) was seen among productive people within the age range of 15 to 59. This is a reflection of how tuberculosis affects the economy of a country by harming the productive force. The predominantly non child population depicted here has additional public health importance in the transmission of tuberculosis in a community in that adults are more likely to be responsible for maintaining the transmission of TB in the public than children.[14]

The type of TB diagnosis which is an important factor for the clinical symptoms one will have, also has an influence on the symptomatic improvement in patients under TB treatment. What is compatible with other studies done in Ethiopia[9,10], is that most of the patients (79%) had a diagnosis of pulmonary TB. Out of these, more than half (52.4%) had smear positive pulmonary TB. This is a big share and has a significant public health importance in that coughing smear positive pulmonary TB patients are the primarily responsible sector for the transmission of TB among the public. Even though the above figure is high, an even higher proportion of smear positivity (73.3%) was of course seen in a study done 4 years back in Addis.[10] Additionally a higher number of smear positive pulmonary TB patients were found to be HIV negative. But this was not statistically significant (OR = 0.72, P = 0.26, 95% CI = 0.39 to 1.33). Contrary to this finding there is a higher tendency of smear negativity among HIV infected TB patients.[5]

With regard to the presence of diagnoses other than tuberculosis, nearly half of the study subjects (46.3%) had additional diseases potentially boosting

problems associated with clinical improvement as well as experience of a variety of drug adverse events. In about 85% of these cases, HIV/AIDS was found to be an additional diagnosis. Overall, 43% of the TB patients tested for HIV were found to have been co-infected with HIV. This is in agreement with the prevalence of HIV infection among tuberculosis patients in Ethiopian studies[15,16], although some studies in the country showed a prevalence as low as 18%.[17] A relatively higher figure (52.1%) was found out by a research done in the same setting by Kassu A et al.[7]

The clinical picture of the study subjects was consistent with the usual presentation of TB patients seen in other studies, the commonly encountered symptoms being fever, weight loss, cough, night sweating, and anorexia.[18] Most experts agree that signs and symptoms of tuberculosis can be used to gauge response to treatment. And in most of the cases, TB symptoms improve 2-6 weeks after initiation of anti-TB therapy.[19] In line with this, improvement of the clinical symptoms was assessed. On average chest pain, fever, night sweating and anorexia took roughly a month to improve. Even though the difference is not that pronounced, a relatively longer time was taken by the TB symptoms, cough and sputum production (33 days). This slight distinction in the duration of stay of symptoms may have resulted from the tendency of patients to remember time duration in units like weeks and months. A higher degree of precision would have been possible had the study been designed in a follow up way. Despite this problem, the improvement of weight loss, TB related swellings, discharging wounds, and fatigue took extended time (on average, 38, 47, 47 and 41 days, respectively).

According to some beliefs, weight loss and fatigue are thought to reflect the body's reaction to substances elaborated during ongoing tissue damage, lysis of mycobacterium tubercles, and inflammatory effecter cells. Therefore they should improve earlier than cough, hemoptysis, and chest pain which could persist despite microbiologic clearance because of longstanding anatomical and physiological changes.[19] The findings observed in this study could be due to the concomitant occurrence of other diseases in almost half of the study subjects. These findings could also suggest the possibility of delayed treatment response as a peculiar character of TB patients of the area as a result of factors associated with nutrition, immunity, and socioeconomic issues.

Logistic regression tests done on factors for persistence of TB symptoms, weight loss and fatigue beyond the 6th week of anti-TB treatment, suggested that HIV status could influence whether a patient has a persisting weight loss or not, while patient age could have a similar effect on fatigue. In these tests, HIV negatives were expectedly less likely to have a persisting weight loss than HIV positives. And it was found out that the tendency of having fatigue persisting beyond the 6th week was higher among the elderly than the younger patients. This means, younger patients are likely to recover from fatigue. But this was seen with a very wide confidence interval showing the inadequacy of the sample with regard to this conclusion.

Concerning drug related adverse effects in this study, the commonly encountered ones were reddish urine, gastrointestinal upset, neuropathic symptoms (like numbness, tingling, paresthesia, etc) and sleepiness. According to WHO, these symptoms are considered to be minor drug adverse effects of anti-TB drugs. Concerns are big regarding the major anti-TB drug adverse effects like jaundice and vision problem. A good number of the jaundiced patients were encountered in this study (7.1%) though this figure is a bit lower than those of other studies.[20] Vision problem prevalence of 8.2% is another more detrimental adverse effect, particularly in relation to a recommendation of routine vision check up for patients on a long term ethambutol treatment.[21] In these study settings and in many others throughout the country, routine visual examination for TB patients is not a common practice. And this makes the situation worse.

HIV infection is an important factor which can presumably contribute to delay in the clinical improvement of patients under TB treatment for a number of reasons. One of these is the presence of undetected opportunistic infections. The other is the very nature of HIV disease itself (symptoms like fatigue, weight loss, fever, etc). Surprisingly, it was only fever which had significantly protracted improvement period among HIV infected TB patients compared to non HIV infected TB patients with a mean difference in the average improvement period of 9 days (mean difference = 9.4, p = 0.01, 95% CI: 2.2 – 16.7). The other symptoms were not found to differ between HIV positive and HIV negative TB patients.

The overall occurrence of drug adverse effects in 45.7% of the subjects in this study is compatible to some researches done elsewhere although this is a bit higher. For example, according to a research done in Rio De Janeiro, Brazil, adverse effects of anti-TB chemotherapy were seen in 45.9% of the elderly and

34.3% of non-elderly TB patients.[22] On the other hand, the figure is much lower than that shown by a Nepalese study (80%)[20] and also reasonably very low when compared with that among those being treated with second-line drugs for multi-drug resistant TB during which as many as 86% of the patients may develop medication side-effects.[23] 24.3% of the study population developing severe forms of drug-adverse reactions which could prompt immediate discontinuation of one or more anti-TB drugs is a serious concern identified in this study although this proportion is a bit lower than the result of a research done among urban Nepalese(34.3%).[20] On the other side of the coin, side effects like hepatitis, dyspepsia, exanthema and arthralgia could be responsible for termination of therapy in up to 23% of patients during the intensive phase.[23]

The effect of different factors on the occurrence (at any time during treatment) of any drug adverse effects was also assessed in this study. The binary logistic regression showed that treatment duration, age, sex, HIV status and concomitant drug use did not affect the patients' chance of developing drug related adverse effects. This, in fact, was done by excluding reddish urine as an adverse effect mainly because it has little impact on adherence and treatment discontinuation and also because it is an expected effect of taking rifampin.

Detailed scrutiny of each of the variables is an important task here. Age and sex predilection was not seen in the development of drug adverse effects contrary to some research findings abroad.[22] In line with this, a research done in Malaysia showed that age and sex did not show a significant effect on the occurrence of drug related hepatotoxicity.[24] Unlike major beliefs, HIV status and the concomitant use of other drugs were not found to increase the likelihood of developing drug related adverse effects. A conflicting finding was reported by Marzuki A O et al in Malaysia, and also in Addis Ababa, Ethiopia, related to drug induced hepatotoxicity.[10,24] Treatment duration also, paradoxically, did not have any effect. Logistic regression done separately for each adverse effect also did not show any effect of age, sex, treatment duration and HIV status on the occurrence of each of the drug adverse effects. This is against some established findings and could have resulted from the very nature of the study design, patients' failure to recall remote experiences of drug adverse effects.

Separate tests for association were also done between antiretroviral therapy and cotrimoxazole and GI upset, skin lesion, and neuropathic symptoms. Results showed a significant association between cotrimoxazole use and skin rash with those on cotrimoxazole 4 times at risk for skin lesion than those not taking cotrimoxazole (OR = 3.9 P = 0.015, 95% CI = 1.4 to 11.1). This research failed to show any statistically significant relation between ART and the above three adverse effects, and also between cotrimoxazole treatment and GI upset. Also, age, sex, HIV status, and use of other drugs were not found to have an effect in the experience of any side effect. The major reason for this finding to deviate from the common expectation could be the role of recall bias as patients were being asked about events which might have taken place a long time ago as TB treatment is a long process.

CONCLUSIONS

Most of the TB symptoms improved within the universally acceptable period of 3 to 6 weeks after initiation of anti-TB therapy. However, unexpectedly longer time for improvement was taken by weight loss and fatigue. The most commonly encountered anti-TB drug related adverse effects were reddish urine, GI upset, neuropathic symptoms, and sleepiness. Another concern in this study was the relatively good number of cases with jaundice, vision, and balance problems. Factors like HIV infection, ART, cotrimoxazole use were seen to have no influence on the occurrence of any of the adverse effects except that patients taking cotrimoxazole were found to be at a higher risk for skin rash than those who are not taking it.

RECOMMENDATIONS

Health professionals working in DOTS clinics have to be trained to work in such a way that they will follow strictly the clinical profile of patients and act accordingly when improvement is delayed. Drug adverse effects are fairly common among TB patients under DOTS. Some of the adverse effects are fatal while some could contribute to a high rate of defaulting. Therefore, health workers have to strictly follow adverse effects with routine clinical and laboratory tests and treat them accordingly. TB patients taking additional drugs like cotrimoxazole have to be given special attention for the possibility of higher rate of drug adverse effects.

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