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Effects of Ethambutol on Visual Acuity, Contrast & Colour Vision; A Descriptive Analysis

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ABSTRACT

Objective: To determine the effects of Ethambutol on visual acuity, contrast sensitivity and colour vision in tuberculosis patients taking Ethambutol drug.

Place and Duration: This study was conducted in Rawalpindi Leprosy Hospital and time duration was 2 months.

Methodology: It was hospital based, descriptive, cross-sectional study. Written consent was taken from every patient to take part in this study.

Results: A total 50 participants were included in this study, in which 26 (52%) were male and 24 (48%) were female Participants having age groups of 10-25 years old were 15 (30%) and 26-40 years were 14 (28%) while having 41-55 years were 11 (22%) 56-70 were 7 (14%) and 71-85 were 3 (6%). In total 7 (14%) patients develop visual functions defects after 2 months of taking 25mg/kg dose of Ethambutol out of which in right eye 3 (6%) patients developed visual acuity defects, 1(2%) showed decline in contrast sensitivity and 5 (10%) acquired color vision defects while in left eye 3 (6%) patients developed visual acuity defects, 2(4%) developed contrast sensitivity defects and 5 (10%) developed color vision defects.

Conclusion: Long term use of Ethambutol causes serious visual functions disorders which may lead to permanent vision loss. Vision is the basic human right so medical professional and patients both should take serious precautions and care when administrating and using Ethambutol.

Keywords: Ethambutol, Visual Acuity, Contrast, Colour Vision

Introduction

Tuberculosis is highly contagious disease caused by infection with Mycobacterium tuberculosis. It usually affects lungs but it can affect other organs of the body. Ethambutol is the first line treatment for tuberculosis. It is being used to treat TB since 1960s. It is usually given with the combination of other antibiotics such as isoniazid, pyrazinamide and rifampicin. TB treatment takes much longer than other type of bacterial infection. A person diagnosed with TB must take antibiotic for at least six to nine months. The exact drug, dose and length of treatment depend upon age, general health, dug resistance and form of TB[i].

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No safe dose of Ethambutol has been reported and major pathway of excretion of Ethambutol is via the kidneys. To help patients stick to their treatment, a program is recommended. The program is called direct observed therapy (DOT). In this program a health care person or a worker administers your medication so that you do not have to remember it at your own[i].

The most common toxic effect of ETH is optic neuropathy, generally reversible although irreversible blindness has been reported. Hepatotoxicity has been reported; baseline and periodic assessment of hepatic function should be performed during treatment. Other side effects that have been observed are pruritus, joint pain, gastrointestinal upset, abdominal pain, malaise, headache, dizziness, mental confusion, disorientation, and possible hallucinations.[i]

It is most frequent to have impaired vision, decreased visual acuity, central scotomas, and loss of the ability to discern green and occasionally red. As a result, visual acuity and colour vision may not be compromised, but peripheral visual field constrictions are. Both kinds of retrobulbar neuritis have a normal-looking fundus on opthalmological testing. When EMB is stopped in most cases, the visual defects disappear. When EMB is stopped, some patients' vision continues to decline for a month or two before improving in further months.[ii].

Tuberculosis may be categorized into followings.

Active TB Infection

In this type of TB the bacteria are rapidly multiplying and invade different organs of the body. Active pulmonary TB is highly infectious and may spread through coughing[iii].

Latent TB Infection

Many people that are infected with TB do not develop disease. They do not show any symptom and their chest X-ray may be normal. They are at risk of developing active TB. The risk of developing active

TB is often increased when immune system is compromised e: g AIDS or immunosuppressive drugs[iii].

Four subjects with tuberculosis developed ocular toxicity 2 1/2, 7 1/2, 8 and 12 months after starting Ethambutol. Normal visual acuity returned in three cases; one patient has severe, permanent visual impairment. Language difficulties were present in three subjects[iv].

Ethambutol, and to a lesser extent isoniazid, are both implicated in the development of visually related side effects. There is documentation of ocular toxicity with Ethambutol when administered at dosages generally pronounced as being safe. Controversy as to what constitutes a safe and effective dose of these medications still exists[v].

Of 1317 patients 67 (5.1%) had 70 reactions to anti-tuberculosis drugs requiring modification of treatment. The frequency of drug reactions increased from 2.3% at age 0–19 to 4.6% at age 20–39, 7.1% for age 40–59 and to 8.4% for those aged 60 and over. Females had significantly higher reactions rates than males. White patients had higher reaction rates than Pakistani and Indian patients, mainly due to the average age being greater[vi].

The interval between cessation of ethambutol treatment and the initial visit ranged from 1 week to 3 months. All patients had visual deficits characteristic of ethambutol-induced optic neuropathy at their initial visit, and the follow-up examination was performed within 12 months. Compared with the initial RNFLT, there was a statistically significant decrease in the mean RNFLT of the temporal,

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superior and nasal quadrants (p=0.009, 0.019 and 0.025, respectively), with the greatest decrease in the temporal quadrant (mean decrease 26.5 μm)[vii].

At the beginning of the study, no visual impairment was found. On follow-up, colour vision, visual field parameters and anterior and posterior segment findings were not affected in any patients. Mean visual acuity before starting therapywas0.00 –0.08 Log-MAR and after therapy was 0.08–0.18 Log-MAR. Visual acuity improved by a significant amount (p=0.004). Both monocularly and binocularly, the difference in contrast sensitivity before and after therapy was statistically significant (p0.005 in both cases). P1 amplitudes (in terms ofnV/deg2and mV) of ERG waves were significantly reduced and their P1 latencies were significantly increased in all the rings after ethambutol therapy ($p<0.05$). There was no significant change in N1 amplitudes and N1 latencies after therapy in any of the rings[viii].

EMB ocular toxicity was found in 6% of 139 patients on daily medication, compared to 0 of 90 patients on intermittent therapy ($p = 0.05$). None of the patients who exhibited signs of EMB eye toxicity were diagnosed with routine vision screenings, such as an eye exam or colour vision test. After stopping EMB, all individuals with EMB-related ocular illness restored to their pre-EMB status. In this patient cohort, intermittent rather than daily EBM dosing was linked with lower ocular toxicity.[ix].

Methods

A study was conducted in Rawalpindi Leprosy Hospital which is located in the crowded part of Rawalpindi city. The hospital was setup in 1904 by the British Leprosy Mission. Leprosy patients from all over British India used to come here for treatment. Since 1968 (ALP) Aid to leprosy patients is running this hospital. This hospital also runs TB (Tuberculosis) control program, Community based inclusive development program (CBID), POB (Prevention of blindness control program), General skin clinic, General physiotherapy department, a orthopedic shoe shop, many permanent handicapped patients are also catered here, operations are performed in surgical unit, group of Doctors, nurses and medical students visits hospital for lectures and last but not the least training programs are conducted in hospital for medical officers, ophthalmic technicians, leprosy technicians and laboratory technicians.

Data was collected using specialized medical equipments, after assessing each patient and then forms were filled. The variables that were used on the forms include; (1) demographic data: like name, age, gender, contact, file number; (2) clinical data: visual acuity, contrast and colour vision. There were two types of patients (i): those who were admit in wards and (ii): coming in weekly OPD.

First complete eye assessment for visual acuity, contrast sensitivity and colour vision was done on patients diagnosed with TB before start of ethambutol therapy then after two month of using ethambutol eyes of patients were again examined for change in visual functions, patients admitted in wards was an easy approach for reexamination but those who were either discharged or was visiting outpatient department were contacted repeatedly for follow up as some of them belong to far-flung areas.

Two patients belonging to kahuta were visited ourselves as they were not able to come for follow up while one of the patients died hence her reassessment was not done.

Results

A total 50 participants were included in this study, in which 26 (52%) were male and 24

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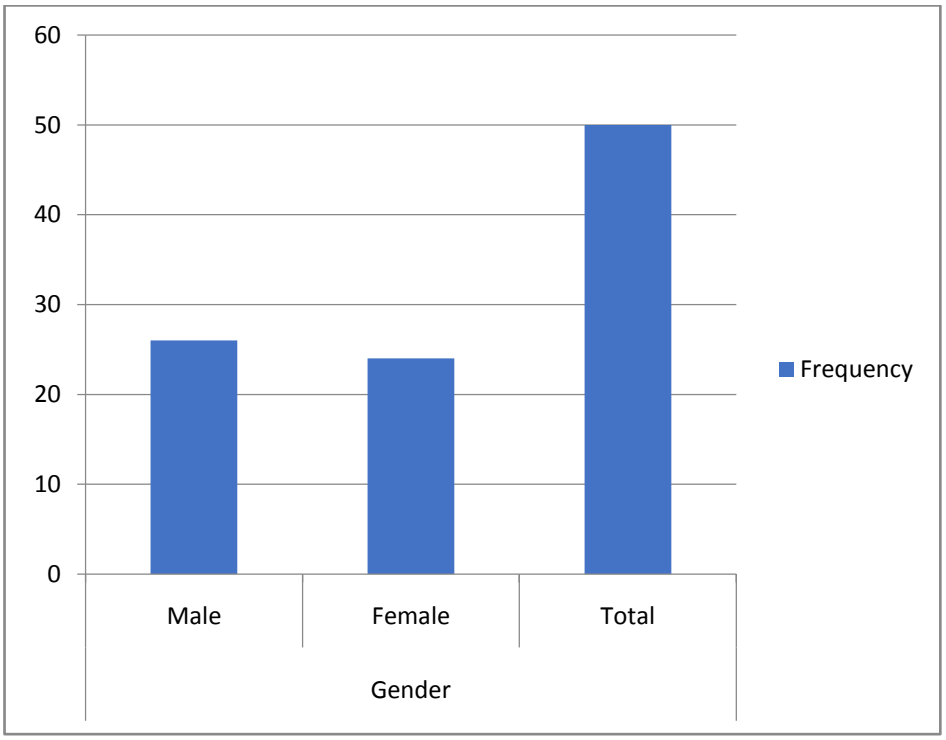
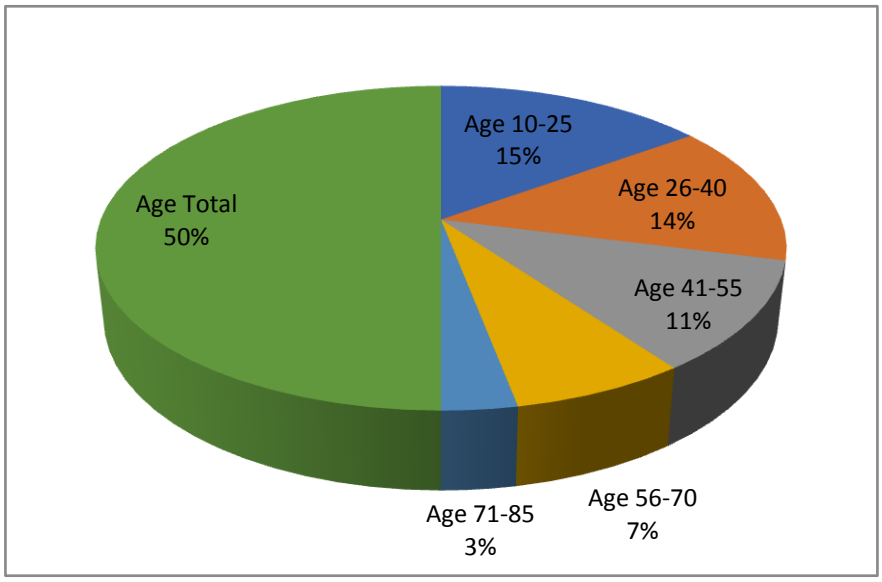
(48%) were female (Fig: 1).Participants having age groups of 10-25 years old were 15 (30%) and 26-40 years were 14 (28%) while having 41-55 years were 11 (22%) 56-70 were 7 (14%) and 71-85 were 3 (6%) (Fig: 2). At first follow up their visual acuity of right eye in group 6/6-6/12 were 34 (68%), 6/18-6/36 were 8 (16%), and 6/60 and lower were 8 (16%) (Fig: 3) while in second follow up 6/6-6/12 were 33 (66%), 6/18-6/36 were 7 (14%) and 6/60 and lower were 10 (20%) (Fig: 4). The visual acuity of left eye at first follow up in group 6/6-6/12 were 38 (76%), 6/18-6/36 were 6 (12%), and 6/60 and lower were 6 (12%)(Fig: 5) while during second follow up visual acuity of left eye in group 6/6-6/12 were 35 (70%), 6/18-6/36 were 9 (18%), and 6/60 and lower were 6 (12%)(Fig: 6).

(Fig:1)Gender Wise Distribution





(Fig:2) Age Wise Distribution

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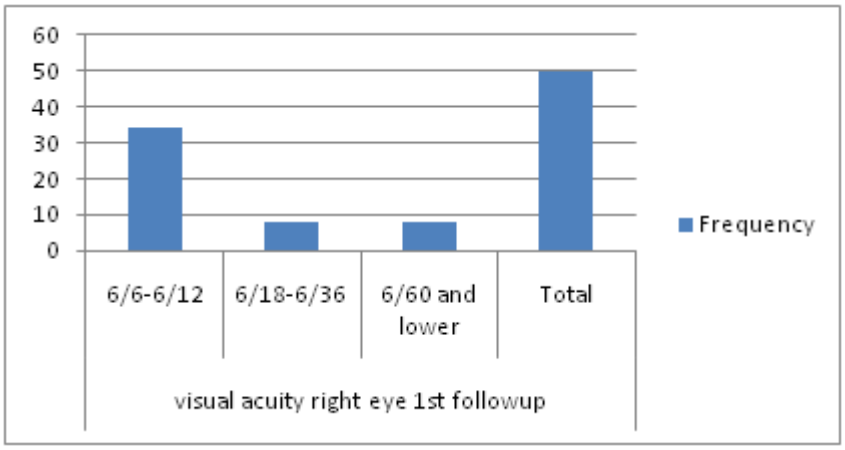
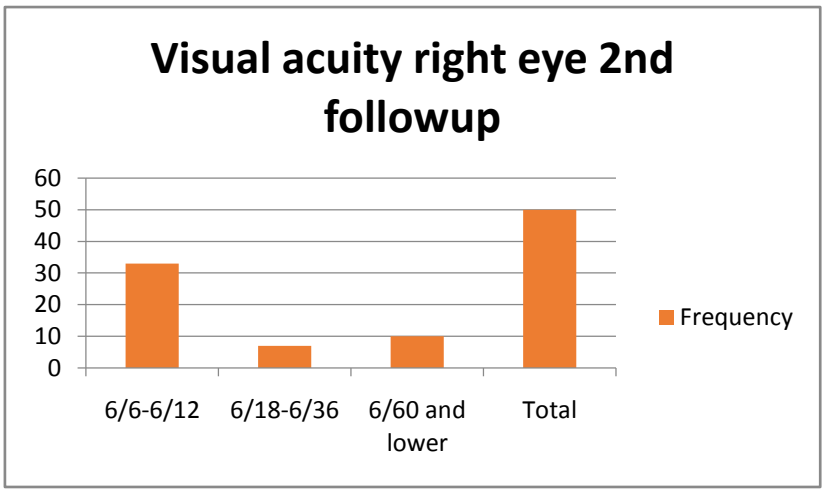
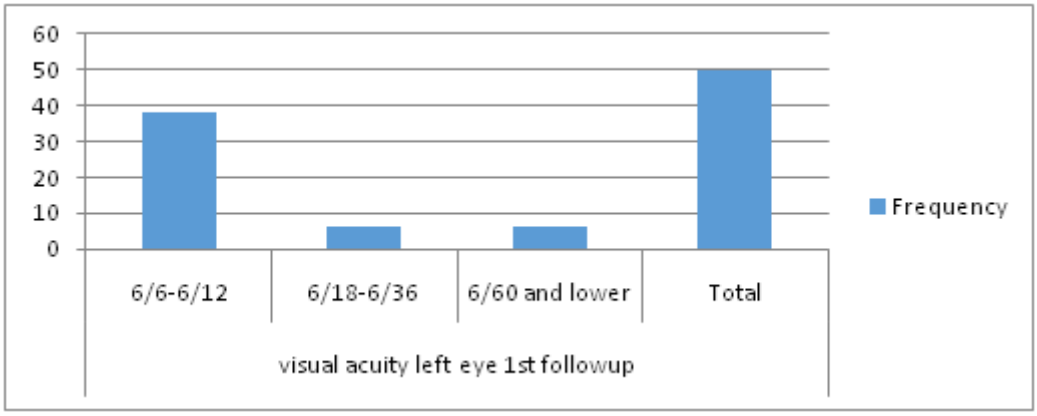


(Fig:3) VA (OD) 1st follow up



(Fig:4)
VA (OD) 2nd Follow Up



(Fig:5) VA (OS) 1st Follow Up

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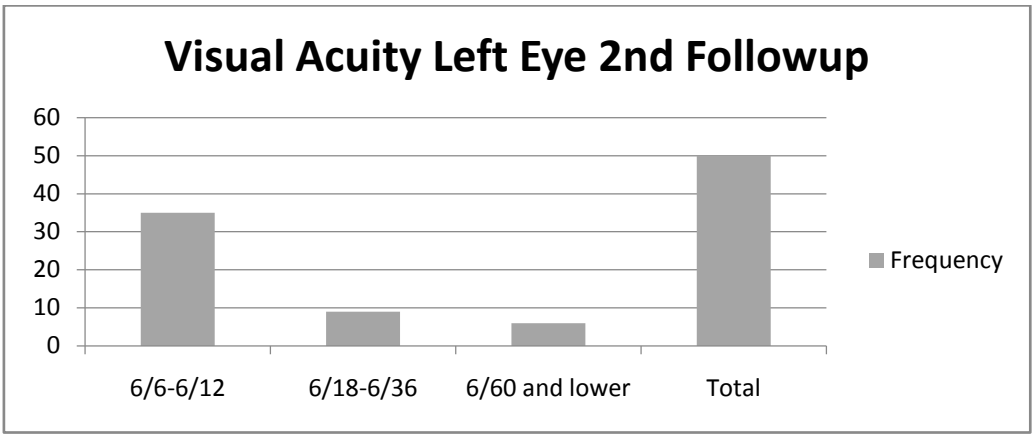
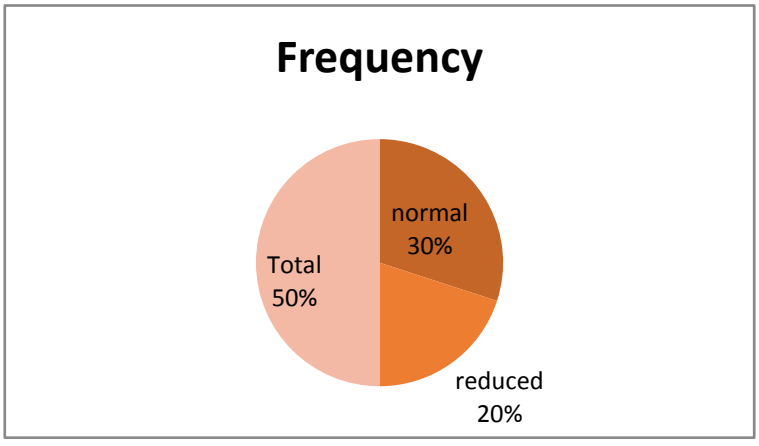


(Fig:6) VA (OS) 2nd Follow Up

During contrast sensitivity of right eye patients found normal were 31 (62%) and reduced were 19 (38%)(Table:7) while in second follow up normal were 30 (60%) and reduced were 20 (40%)(Fig: 8). Similarly in assessing left eye in first follow up patients with normal contrast sensitivity were 32 (64%) and reduced were 18 (36%)(Fig: 9) while in second follow up normal were 30 (60%) and reduced were 20 (40%)(Fig: 10).

(Table:7) Contrast Sensitivity (OD) 1st Follow Up

	Frequency	Percent
Normal	31	62.0
Reduced	19	38.0
Total	50	100.0



(Fig:8) Contrast Sensitivity (OD) 2nd Follow Up

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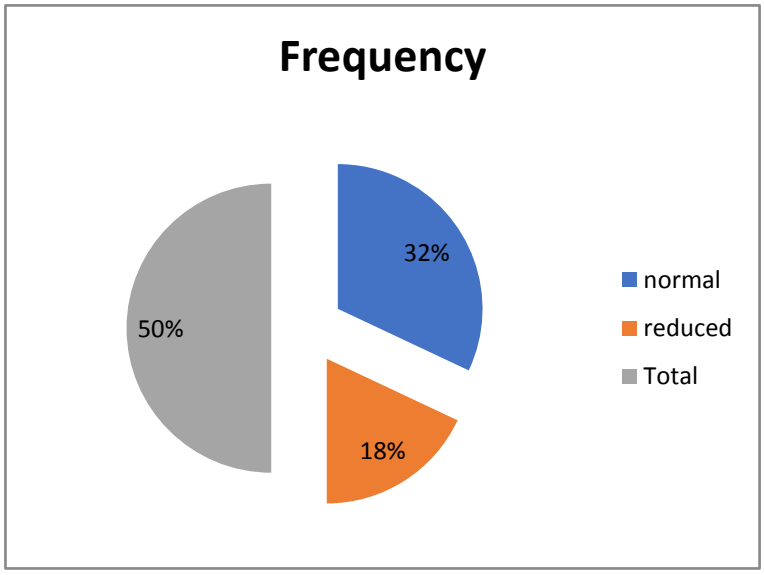
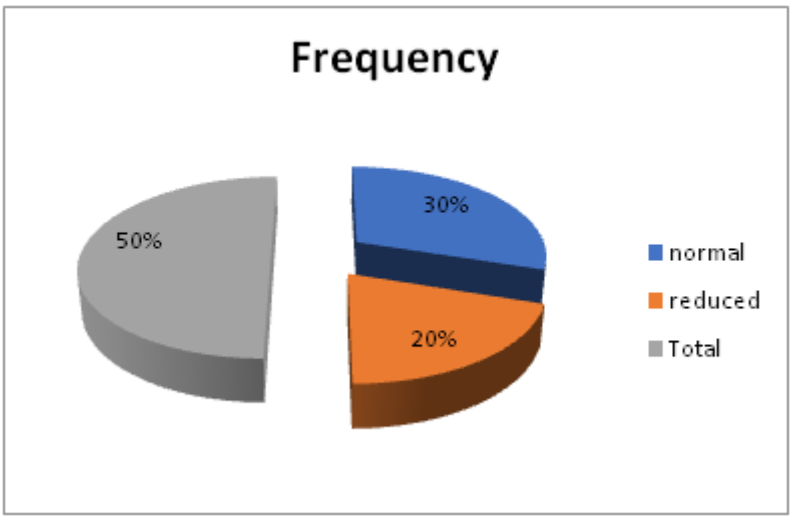


(Fig:9) Contrast Sensitivity (OS) 1st Follow up



(Fig:10) Contrast Sensitivity Left Eye 2nd Follow-up

At first follow up while assessing color vision of right eye no patients was found with protan and tritan defect but deutan defects were found and it was 2 (4%) and a total of trichromate were 48 (96%)(Fig.11) and in second follow up patient with protan defect were 4 (8%), deutan defect were 3 (6%) and trichromate were 43 (86%) but no tritan defect was found(Fig.12) while for first follow up of left eye a total of 49 (98%) were found trichromate and 1 (2%) was found with deutan defect but no protan and tritan defect was found (Fig.13) and in second follow up patients with protan defect were 4 (8%), deutan defect were 2 (4%),tritan defect was not found and a total trichromate were 44 (88%)(Fig.14).In total 7 (14%) patients develop visual functions defects after 2 months of taking 25mg/kg dose of Ethambutol.

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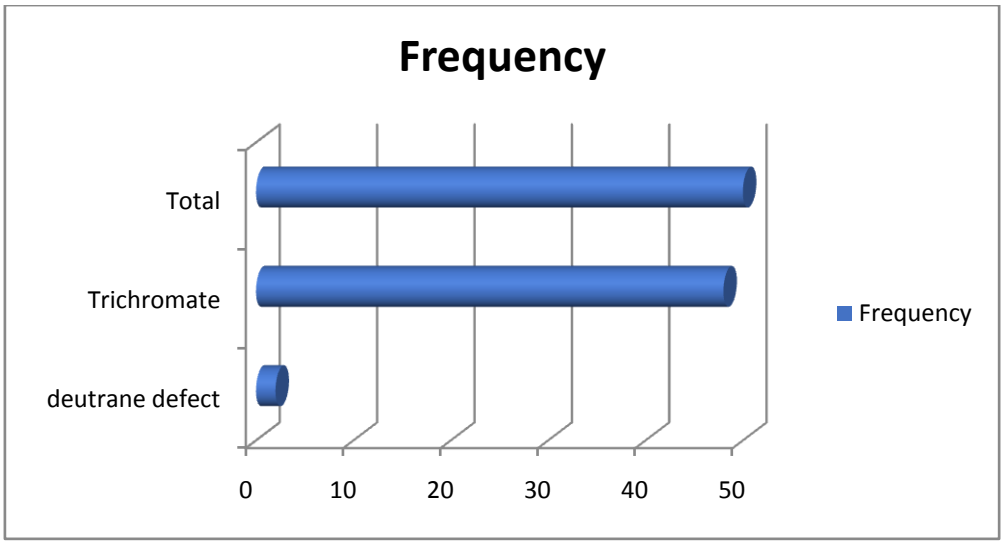
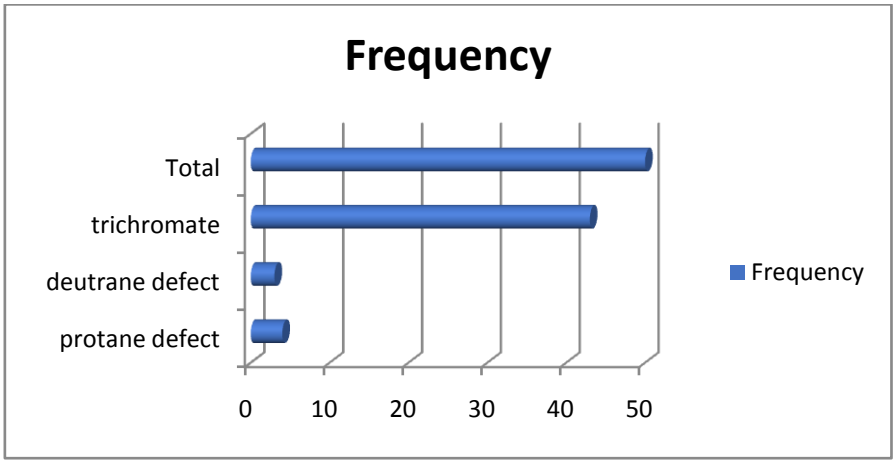
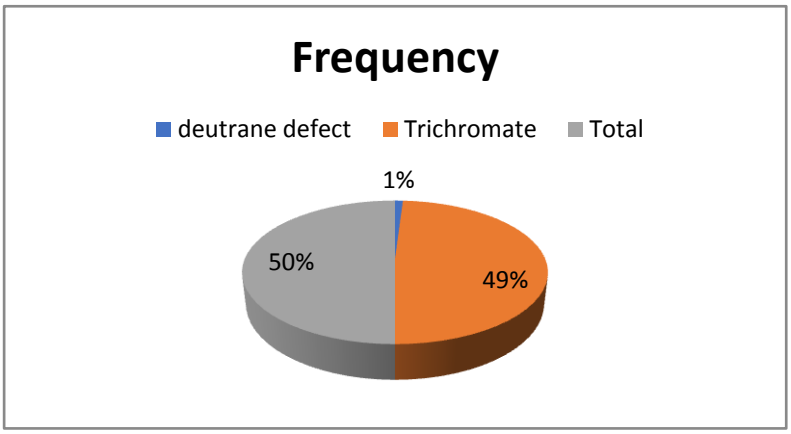
(Fig:11) Color Vision Right Eye First Follow-up



(Fig:12) Color Vision Right Eye 2nd Follow-up





(Fig:13) Color Vision (OS) 1st Follow Up

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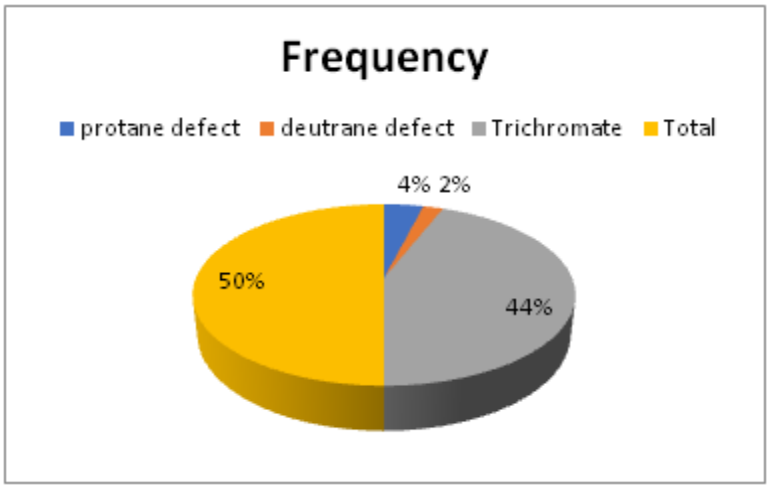

(Fig:14) Color Vision (OS) 2nd Follow Up

Discussion

Visual functions defects found in subjects admitted in Rawalpindi Leprosy Hospital were 14% another study done in United States Visual functions defects were 5.1% which is quite different from ours study it could be because the basic living standards of both countries are quite different, Pakistan is one of third world developing country and there is a lot of poverty and tuberculosis affects people whose immune system is compromised while America is super power and developed country.

In that study the patients who developed visual loss after 9-months of Ethambutol therapy was presented while in this study the patients who had just started Ethambutol within one week or two were examined. Examination of visual acuity, contrast sensitivity and colour vision was done and after two months of Ethambutol therapy they were reexamined for any change in their visual functions.

Well in current study we have found significant colour vision defects but a study in Nepal no colour vision defects were found after 2 months of taking Ethambutol under DOT program However according to Polak et al[x] changes in colour vision is the baseline indicator for optic neuropathy due to Ethambutol.

Conclusion

The use of Ethambutol cannot be stopped and a disease like Tuberculosis can't be eradicated specially form third world countries like Pakistan but we can work together in an attempt to save our humans from the toxicity of ethambutol.

Patients' visual functions must be examined before start of ethambutol therapy by ophthalmologists and optometrists and examination should be follow at 1 month interval for that a separate eye unit must be made in TB hospitals.

Prescribing doctor show know the potential ocular toxicity of ethambutol and should discontinue drug as soon as ocular toxicity is reported.

Ethical Approval: Pakistan Institute of Rehabilitation Sciences (PIRS) Ethical committee and MD (Medical Director) of Rawalpindi Leprosy Hospital approved this study.

Patients' Consent: Written consent was taken from every patient before taking any data.
Conflict of Interest: No conflict of interest by any Author.

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