INTRODUCTION

Glaucoma is a potentially blinding disease which is defined as an optic neuropathy with characteristic appearance of the optic disc and specific pattern of visual field defects that is associated frequently but not invariably with raised intraocular pressure. Glaucoma is the 2nd most common cause of blindness worldwide and the 4th most common cause in Pakistan. Optic nerve, which transmits visual information from retina to visual cortex, is made up of axons of ganglion cells. Throughout the course of life, a reduction of axons is observed annually even in healthy person. In glaucoma, loss of axons is at a higher rate than normal. The diagnosis of glaucoma is currently based on the appearance of optic disc and standard achromatic perimetry. It has been estimated that 30% to 50% of retinal ganglion cells may be lost before an abnormality appears on the standard achromatic perimetry.

Optical coherence tomography, first described in 1991 by Huang, is a high-resolution cross-sectional imaging technique. The third-generation machine, Stratus optical coherence tomography received food and drug administration approval in May 2002. Optical coherence tomography is a non-invasive imaging technique that uses low coherence interferometry to create high resolution (8µ) cross-sectional and topographic images of any optically accessible tissue. It provides a high resolution and reproducible image of retinal nerve fiber layer that discriminate glaucomatous from healthy subjects. This high resolution by optical coherence tomography makes it a potentially more objective technique to diagnose glaucoma and detects glaucomatous progression much earlier. The technology is completely objective and dependent on neither patient cooperation (visual fields) nor clinician’s interpretation (optic disc appearance). Besides this test would be immediately beneficial for many patients who are unable to perform visual field testing due to mental or physical disabilities.

The objective of this study was to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of measurements of the retinal nerve fiber layer using the Stratus optical coherence tomography for perimetric glaucoma.

METHODOLOGY

Fifty glaucoma patients and 50 normal subjects were taken from outdoor of Layton Rehmatulla Benevolent Trust Hospital (LRBT), Lahore.
Trust Hospital, Lahore. All the subjects were older than 17 years and both genders were included. Any specific diagnostic types of glaucoma patients with visual field defects in at least one eye regardless of intraocular pressure (IOP) were studied. Glaucmatous subjects having visual acuity less than 6/12, diabetes mellitus, cataract and history of ocular surgery were excluded from the study. Normal subjects having IOP more than 22 mmHg in either eye, diabetes mellitus, cataract, history of amblyopia, refractive error of > 5 diopters sphere and > 2.5 diopters cylinder were excluded.

The study was conducted after the approval of research/ethical committee of the hospital. Informed consent was taken. Sociodemographic profile like name, age, gender and history of current disease with respect to symptoms, severity and duration was taken. Examination included detailed anterior segment examination with slit lamp, best-corrected visual acuity with Snellen's chart, intraocular pressure measurement with Goldmann's applanation tonometer and dilated fundus examination with indirect ophthalmoscope. Patients were assessed using the peripapillary Fast RNFL program of the Stratus OCT, model 300-1222, and analyzed using software version 3.0. With this scan type, during a single scan the RNFL thickness was determined at 256 points around a set diameter (3.4 mm) around the centre of the optic disc three times. These values were averaged to yield four quadrant (superior, temporal, nasal, inferior) thicknesses and a single RNFL thickness measurement. These values were then compared against a normative database of age-matched control to derive percentile values. Minimal criteria for glaucomatous visual fields (VF) defect were, glaucoma hemifield test outside normal limits, pattern standard deviation with a p-value of < 5% or a cluster of ≥ 3 points in the pattern deviation plot in a single hemifield (superior or inferior) with p-value of < 5%, one of which must have a p-value of < 1% on two consecutive occasions. Visual field abnormalities were classified as mild, moderate, or severe glaucomatous defects using the Hodapp-Anderson-Parrish system. This criterion used the size of the VF defect, the depth of the defects, and proximity of the defects to fixation to separate visual field severity into mild, moderate and severe. All this information was collected through specially designed proforma.

All information was entered into Statistical Package for Social Sciences (SPSS) version 10. A 2 x 2 table was generated. The sensitivity, specificity positive predictive value, negative predictive value and diagnostic accuracy were assessed using achromatic perimetry as gold standard. The quantitative data (age, intraocular pressure, retinal nerve fiber layer thickness) were presented with simple descriptive statistics like mean and standard deviation. The qualitative data (gender, visual field severity) were presented as frequency and percentage.

RESULTS

In the group with normal subject there were 24 males (48%) and 26 females (52%). In the group with glaucoma patients there were 19 males (38%) and 31 females (62%).

In the normal group the mean age was 35.52 ± 10.69 years, while in glaucoma group the mean age was 60.78 ± 6.45 years.

Mean intraocular pressure in normal subjects was 15.8 ± 2.68 mmHg in left eyes while in right eyes was 15.4 ± 2.64 mmHg. Mean intraocular pressure in glaucoma patients was 15.52 ± 1.83 mmHg in left eyes while in right eyes was 15.52 ± 1.54 mmHg.

Mean cup-disc ratio in right eyes of normal subjects and glaucoma patients was 0.26 ± 0.04 and 0.60 ± 0.14 respectively. Mean cup-disc ratio in left eyes of normal subjects and glaucoma patients was 0.29 ± 0.03 and 0.63 ± 0.15 respectively.

There were 18 patients (36%) of primary open angle glaucoma, 16 patients (32%) of chronic angle closure glaucoma and 16 patients (32%) of pseudoxefoliation glaucoma.

There were 19 patients (38%) with mild visual field defect, 22 patients (44%) with moderate visual field defects and 9 patients (18%) with severe visual field defects. Mean retinal nerve fiber layer thickness of normal and glaucomatous eyes is given in Table I.

The sensitivity and specificity of retinal nerve fiber layer measurement for perimetric glaucoma using Stratus OCT were 82% and 96% respectively. The positive predictive value, negative predictive value and diagnostic accuracy were 95%, 84% and 89% respectively.

Table I: Mean retinal nerve fibre layer thickness (n=100).

<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Eye</th>
<th>Mean ± SD RNFL</th>
<th>Mean ± SD temporal RNFL</th>
<th>Mean ± SD superior RNFL</th>
<th>Mean ± SD nasal RNFL</th>
<th>Mean ± SD inferior RNFL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Right</td>
<td>102.38 ± 9.61µ</td>
<td>77.64 ± 13.02µ</td>
<td>131.06 ± 15.71µ</td>
<td>81.26 ± 11.58µ</td>
<td>132.68 ± 17.36µ</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>102.44 ± 10.42µ</td>
<td>76.44 ± 12.46µ</td>
<td>130.04 ± 15.48µ</td>
<td>81.42 ± 11.64µ</td>
<td>129.36 ± 17.37µ</td>
</tr>
<tr>
<td>Glaucomatous</td>
<td>Right</td>
<td>75.04 ± 14.71µ</td>
<td>51.76 ± 10.10µ</td>
<td>90.88 ± 15.36µ</td>
<td>61.65 ± 7.98µ</td>
<td>87.21 ± 19.04µ</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>75.35 ± 14.97µ</td>
<td>51.76 ± 10.10µ</td>
<td>93.91 ± 21.82µ</td>
<td>61.22 ± 7.52µ</td>
<td>86.97 ± 18.27µ</td>
</tr>
</tbody>
</table>

Key: n = number of cases; RNFL = retinal nerve fiber layer; SD = standard deviation; µ = micron.
The current study demonstrated that measurements of RNFL thickness using the Stratus OCT may be useful in distinguishing normal from glaucomatous eyes, at least those that have VF (visual fields) defects. The mean RNFL thickness alone has a sensitivity of 82% and specificity of 96%, one potential source of bias in the current study is the differences in age of the patients in the glaucoma and normal groups. This is true of most glaucoma studies of this nature, but is particularly important to consider when the outcome measured is RNFL thickness because the RNFL is known to become progressively thinner with age. Ideally, the study should include age-matched controls.

Currently, visualization of a change on optic disc photographs, which takes years to occur, or VF defects seen on achromatic automated perimeter, which may not show-up until many thousands of axons are already lost, are the only reliable criteria used to diagnose glaucoma.9

Kim et al. showed that in cases of early glaucoma OCT detected RNFL defects while standard automated perimetry results were within normal limits.10 Leung et al. proved that the RNFL defects detected by OCT expanded in size as the glaucoma progressed. The measurement of RNFL defect can provide an additional dimension for the measurement of glaucoma.11 The work of Blumenthal indicated that RNFL measurements by OCT were reproducible for both normal and glaucomatous eyes.12 Budenz showed that the sensitivity and specificity of RNFL measurements using the Stratus OCT for glaucoma with manifest VF defects are excellent. The sensitivity and specificity were 89% and 92% respectively.5

Parikh et al. showed that the Stratus OCT had 75% sensitivity and 89.6% specificity for the diagnosis of early glaucoma. The positive and negative predictive values were 75% and 98% respectively.13 Pieroth studied 19 glaucoma patients and 14 normal controls using OCT and found a sensitivity of only 65% and specificity of 81% for clinically detectable RNFL defects using clinical examination, red free photography, or automated VFs.14 Guides et al. measured RNFL thickness in glaucoma patients and normal subjects and found significant difference between the two groups.15

In the current study, an attempt was made to recruit glaucoma subjects with a wide range of glaucoma severity, as measured on the VF. This may account for the slightly higher sensitivity in the current study compared with others, because we did include subjects with mild, moderate, and severe VF defects. Alternatively, the higher resolution technology may indeed be more sensitive and specific than earlier versions.

Other imaging technologies such as confocal scanning laser ophthalmoscopy (Heidelberg Retinal Tomography [HRT], Heidelberg Engineering, Heidelberg, Germany) and scanning laser polarimetry (GDx Nerve Fiber Analyzer, Laser Diagnostic Technologies, San Diego, CA) have been developed for imaging the optic nerve and RNFL in glaucoma. Sensitivities and specificities of the HRT for glaucoma have ranged between 62% and 96% and between 84% and 94% respectively, depending on the patient population studied and criteria used for diagnosis of glaucoma by the HRT.16-18 The GDx without corneal compensation has shown sensitivities and specificities of 74% to 96% and 92% to 93%, respectively.19,20 The OCT seems to compare favorably to these alternate technologies, although direct comparison is not possible given the differences in patient populations and parameters studied.

The current study clearly demonstrates the value of detecting glaucoma accompanied by VF defects using the Stratus OCT. In addition to having relatively high sensitivity and specificity for glaucoma accompanied by VF defects, this technology is completely objective because it depends on neither patient cooperation (VFs) nor clinician interpretation (optic disc appearance). The test would be immediately beneficial for the many patients who are unable to perform VF testing due to mental or physical disabilities. It may also be helpful in reassuring clinicians that patients with large optic nerve cups do not have significant loss of nerve fibers. It may also be helpful in demonstrating the progression of glaucoma before VF could detect. Future studies are needed to determine the sensitivity and specificity of this new technology for glaucoma without visual field defects.

**DISCUSSION**

**REFERENCES**


