INTRODUCTION

- Cataract is a consequence of the ageing of the lens and is the major priority in the global initiative to eliminate avoidable blindness by the year 2020. At present, the only means of treating cataract is by surgery, which initially restores high-quality vision and this is currently the most performed operation in developed countries.***(*Mc Carty CA *et al., 2001).***

- Unfortunately, Posterior Capsular Opacification PCO is the most common complication of cataract surgery occuring in a significant proportion of patients to such an extent that secondary visual loss happens. It also can cause impaired contrast sensitivity, glare disability, and monocular diplopia.**.(Wormstone et al.,*2009)* .**

- Posterior capsular opacification (PCO) is the most frequent complication of cataract surgery. Advances in surgical techniques,intraocular lens materials and designs have reduced the PCO rate, but it is still a significant problem ***(Buehl et al., 2005).***

- PCO is caused mainly by remnant lens epithelial cell proliferation and migration, epithelialmesenchymal transition, collagen deposition and lens fiber generation.All of these processes are influenced by

cytokines, growth factor and extracellular matrix proteins ***(Meacock et al., 2000).***

- The only effective treatment of PCO is Nd:YAG laser Capsulotomy, which involves clearing the visual axis by creating a central opening in the opacified posterior capsule. Although this procedure is easy and quick, it carries vision-related complications and risks, including retinal detachment, damage to the IOL, cystoid macular edema, increase in intraocular pressure, iris hemorrhage, corneal oedema, IOL subluxation and exacerbation of localized endophthalmitis ***(Aslam et al., 2003).***

- Moreover, PCO can have a significant impact on the ability to examine the posterior segment and as many diagnostic devices used in ophthalmology rely on a clear visual axis **(Claesson MKL *et al., 1994).***

- Nd:YAG capsulotomy is still the golden standard for treating PCO with success rate of more than 95%. Fortunately, the overall incidence of PCO and the incidence of (Nd:YAG) laser posterior capsulotomy has decreased from 50% in the 1980s and early 1990s to less than 10% today **(Pandey SK *et al.,2004*) .**

- Macular oedema is caused by movement and damage in the vitreous cavity and release of inflammatory mediators due to the damage of blood-aqueous barrier, elevated IOP is associated with an increased amount of aqueous particle following Nd:YAG laser capsulotomy. Ari et al, underlined that the severity and duration of increased IOP and macular thickness are less when a total energy level less than 80 mj is used ***(Ari et al., 2012) .***

- Optical coherence tomography (OCT) has emerged as an important imaging modality in the evaluation and management of retinal diseases. Before OCT, the standard method for assessing macular thickness in the clinic or within clinical research studies was stereoscopic bio microscopy or stereoscopic color fundus photographs. Optical coherence tomography (OCT) has provided an objective and potentially more sensitive means of assessing macular edema and provides data that can be collected and interpreted in a standardized fashion which can facilitate outcome assessments. **(*(Aslam et al.,2003*) .**

AIM OF THE WORK

The aim of this study is to evaluate the influence of Nd: YAG laser capsulotomy on visual outcomes and macular thickness in patients with opacified posterior capsule.

ANATOMY OF THE LENS

The adult human lens is an asymmetric oblate spheroid that does not possess nerves, blood vessels, or connective tissue (***Kuszak and Brown, 1994).*** The lens is located behind the iris and pupil in the anterior compartment of the eye. The anterior surface is in contact with the aqueous; the posterior surface is in contact with the vitreous. The anterior pole of the lens and the front of the cornea are separated by approximately 3.5 mm (***Saude, 1993).***

The lens is held in place by the zonular fibers (suspensory ligaments), which run between the lens and the ciliary body. These fibers, which originate in the region of the ciliary epithelium, are fibrillin rich and converge in a circular zone on the lens. Both an anterior and a posterior sheet meet the capsule 1–2 mm from the equator and are embedded into the outer part of the capsule (1–2 μm deep). It is also thought that a series of fibers meets the capsule at the equator ***(Forrester J et al., 1996).***

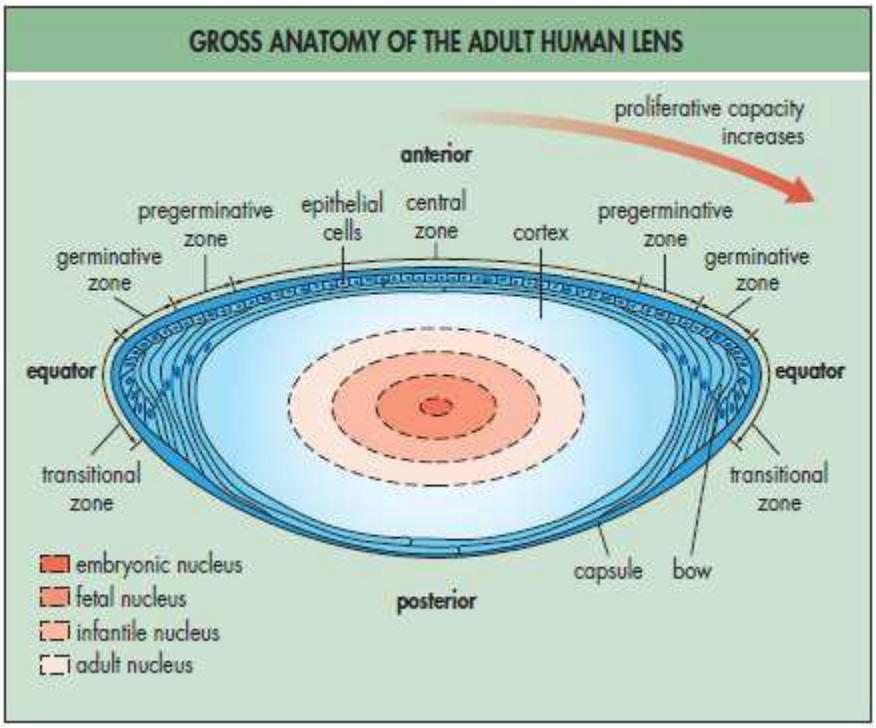

Figure (1): Gross anatomy of the adult human lens ***(Snell and Lemp, 1980)***

Histologically the lens consists of three major components –capsule, epithelium, and lens substance (Fig. 1).

LENS CAPSULE

The lens capsule is the ensheathing elastic basement membrane that helps to maintain epithelial cells and lens fibers as one unit. It acts as a semi-permeable membrane that allows the passage of small molecules into and out of the lens. The lens capsule is the thickest basement membrane in the body as it is continuously produced throughout life.

The capsule is produced anteriorly by the basal membrane of the epithelial cells while posteriorly it is produced by the basal membrane of elongating fiber cells. The thickness of the capsule depends on the region of the capsule being measured. The thickest region of the capsule is located just anterior and posterior to the equator (up to 23 microns). The thinnest area is that of the posterior pole (4 microns). Capsular thickness is also age dependent as the capsule is continuously produced throughout life ***(Forrestre et al., 1996).***

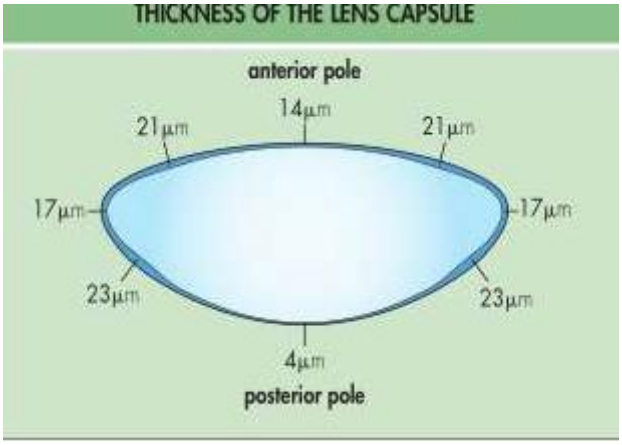

Figure (2): Changes in thickness of the adult lens capsule with location ***(Snell and Lemp, 1980)***

By light microscope the capsule is homogenous, transparent membrane that under polarized light appears birefringent indicating a lamellar structure. The lamellae are narrowest near the outside of the capsule and widest near the cell mass. The layer of inserting zonular fibers and the related capsular layer were termed the zonular lamella by Berger (also termed pericapsular membrane) ***(Seland, 1974).***

Under electron microscope, the capsule appears to have a relatively amorphous appearance in which the lamellar structure is suggested by coarse scattered filamentous elements. There are up to 40 lamellae, each of which is about 40 nm in thickness. The lamellae are formed of fine fibrils as seen under higher resolution ***(Fisher and Hayes, 1979)***.

The capsule is basically formed of type IV collagen but also contains type I and III collagens in addition to other extracellular matrix components as laminine, fibronectin, heparin sulphate proteoglycan, entactin and vitronectin ***(Dische and Zelmenis, 1965; Lisa, 1999).***

Epithelial Cells:

The lens epithelium arises as a single layer of cells beneath the anterior capsule and extending to the equator of the lens. There is no corresponding posterior layer since the posterior embryonic epithelium is involved in the formation of the primary lens fibers. The cells are polygonal (in surface view) cuboidal (in sagittal section), being approximately 10 microns high and 15 microns wide. The central cells are located near the anterior pole. They are polygonal with rounded nuclei that show no mitotic figures except when stimulated mechanically.

Peripheral to the central cells, the cells become smaller and more cylindrical. Mitosis is occasionally seen. The pre-equatorial and equatorial cells are the major site of cell division although mitotic figures are still rare. From these cells new cells migrate posteriorly to form lens fibers, the basal surface of the epithelial cells adheres to the capsule. The rest of the cell membrane is relatively complex. The lateral margin shows undulations whereas the apical membrane shows interdigitations with the underlying lens fibers. The cells are attached to each other's by desmosomes and to the underlying capsule by hemidesmosomes. Gap junctions lie between the cells allowing free movement of small molecules. Gap junctions are infrequent between apical membranes and adjacent lens fibers; however the apical membranes are abundant of receptors mediating endocytotic transferring processes of metabolites ***(Bron et al., 1997).***

With age the height of the epithelial cells decreases and the width increases. It has been reported that a decrease in the number of epithelial cells occurs with cataract formation; other reports have been unable to find decreased number of cells. No anatomical features of the epithelium exist that influence surgical technique, but all ophthalmic surgeons recognize that the epithelium is exquisitely sensitive to trauma as during cataract extraction ***(Chylack, 1995).***

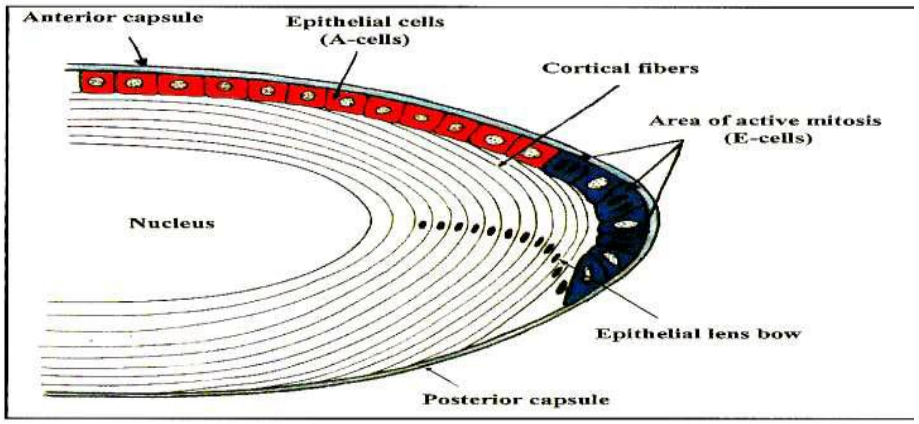

Figure (3): Histology of the anterior and posterior capsule. A cells: anterior subcapsular cells. E cells: equatorial cells ***(Pandey et al., 2004)***.

Lens Substance

The lens substance, the bulk of the lens, is composed of densely packed lens cells with very little extracellular space. The adult lens substance consists of the nucleus and the cortex which are often histologically indistinct. Although the size of these two regions is age dependent, a study of lenses with an average age of 61 years indicated that the nucleus accounted for approximately 84% of the diameter and thickness of the lens and the cortex for the remaining 16*% **(Taylor et al., 1996).***

The nucleus is subdivided into embryonic, fetal, infantile, and adult nuclei (Fig. 1). The embryonic nucleus contains the original primary lens fiber cells that are formed in the lens vesicle. The rest of the nuclei are composed of secondary fibers, which are added concentrically at the different stages of growth by encircling the previously

formed nucleus. The cortex, which is located peripherally, is composed of all the secondary fibers formed after sexual maturation. Fibers are formed constantly throughout life by the elongation of lens epithelial cells at the equator. Initially, transitional columnar cells are formed, but, once long enough, the anterior end moves forward beneath the anterior epithelial cell layer and the posterior end is pushed backward along the posterior capsule. The ends of this U-shaped fiber run toward the poles of both capsular surfaces. Once fully matured, the fiber detaches from the anterior epithelium and the posterior capsule. Each new layer of secondary fibers formed at the periphery of the lens constitutes a new growth shell. Lens fibers are bound by the interlocking of the lateral plasma membranes of adjacent fibers. Both desmosomes and tight junctions are absent from mature lens fibers, although desmosomes are found between elongating fibers ***(Kuszak, 1995).***

Posterior Capsular Opacification:

Visually significant posterior capsular opacification is the most common late complication of uncomplicated cataract surgery. It occurs in 50% of cases within 2-3 years after surgery***(Emery, 199),***and now,the incidence of PCO **is** 11.9% in 5 years after operation **(Karin et al.,2014).**

The overall estimates of posterior capsular opacification were 11.8% at one year, 20.7% at 3 years and 28.4% at 5 years after cataract extraction ***(Schaumberg et al., 1998).***

Another report is that it is about 50% at 5 years after surgery, and almost 100% in pediatric age groups ***(Saxby et al., 1998).***

Pathogenesis

Capsular opacification is a misnomer as it is not really an opacification of the lens capsule but an opaque material that lines the capsule rendering it non transparent ***(Pandey et al., 2004).***

This opaque material could be:

- Capsular remnants.
- Capsulolenticular remnants.
- Inflammatory or haemorrhagic elements**.**

The pathogenesis of capsular opacification is multifactorial.

It has been found that anterior epithelial cells undergo fibrous metaplasia whereas equatorial cells proliferate and migrate ***(Apple et al., 1992).***

Normally no cells line the posterior capsule. Pathological cells lining the capsule in posterior capsular opacification are either epithelial cells or fibrocytes ***(Nagamato et al., 1992).***

The anterior lens epithelium proliferates onto the posterior capsule at the site of apposition of the anterior capsule flaps to the posterior capsule ***(Mc Donnell et al., 1983).*** The contraction caused by the myoblastic features, acquired through fibrous metaplasia, of the lens epithelial cells produces wrinkling of the posterior capsule. Collagen deposition results in white fibrotic opacities ***(Chan et al., 1982).***

In a study to determine whether LECs are transcriptionally activated after a foreign body is attached to the anterior lens surface, the anterior capsule was rubbed with blunt 27 gauge needle 10 times. After cataract extraction in Wister rats, the protein c-Fos was transiently expressed in equatorial LECs after rubbing of the anterior capsule, indicating that the equatorial LECs are transcriptionally activated by minor mechanical stimuli to the anterior lens surface ***(Shirai et al., 2003).***

Postoperative lens epithelial cell proliferation is also involved in the pathogenesis of other entities. These include anterior capsular opacification (ACO) and inter lenticular opacification (ILO), a more recently described complication

related to piggyback IOLs. Thus there are three distinct anatomic locations within the capsular bag where clinically significant opacification may occur postoperatively ***(Werner et al., 2002).***

Less common factor in the pathogenesis of capsular opacification is the break down of blood ocular barrier with release of inflammatory mediators and cells into the aqueous humour, These cells may precipitate on the anterior and posterior capsule resulting into anterior and posterior capsular opacification ***(Saxby, 1999).***

Pigmentations arising from the posterior surface of the iris and ciliary body may also play a role in posterior capsular opacification. Iris melanocytes are sometimes found on the posterior capsule ***(Saxby, 1998).***

Delayed localized endophthalmitis is another condition that may lead to capsular opacification. A white plaque formed of inflammatory cells and the organism is formed on the posterior capsule ***(Clayman and Jaffe, 1988).***

Apoptosis (programmed cell death), was found in residual epithelial cells after cataract extraction. Apoptosis can be induced by many cell surface-specific factors as withdrawal of cytokines, growth factors and ultraviolet radiation ***(Nishi et al., 1996).***

Certain chemical substances play a role in the pathogenesis of capsule opacification namely:

- **Cytokines:** Cytokines are peptides secreted from cells after cell injury and act either in a paracrine or autocrine manner on their target cells ***(Duncan et al., 1997).***
- **Transforming growth factor –beta [TGF-b]: TGF-b** promotes cellular adhesions and therefore stimulates epithelial cells to undergo hyperplasia to bridge the gap that hinders cellular adhesions ***(Hynes, 1987).***
- **Hepatocyte growth factor [HGF]:** HGF is secreted by mesenchymal cells and acts upon epithelial cells influencing their migration and survival as well as promoting junctional breakdown ***(Grierson et al., 2000).***
- **Osteopontin**: Extracellular matrix in human postoperative capsular opacification and anterior subcapsular cataract contains osteopontin ***(Saika et al., 2003).***
- **Fibroblast growth factor [FGF]:** FGF was found to increase epithelial mitosis and collagen production ***(Nishi et al., 1996).***

Pathology

Pathological types of posterior capsular opacification include:

- Elschnig's pearls.
- Fibrous type.
- Soemmerring‟s Ring.