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MORPHOLOGY AND BIOCHEMISTRY OF HUMAN CATARACTS STUDIED IN PAKISTAN*

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Abstract. Human cataractous lenses were studied *in vivo* and *in vitro* in this Department. The site and extent of opacities were the basis of classifying immature cataracts *in vivo*. *In vitro* cataracts were classified on the basis of colour, consistency and transparency. There is an early age incidence of cataracts in Pakistan as compared to European countries. Diabetics get an early senile change, starting with posterior subcapsular opacities probably due to metabolic changes in vitreous.

In the light of biochemical studies and the views presented by van Heyningen and Kinoshita it was concluded that glutathione when present in high concentration inhibits oxidative mechanism in the lens which causes inhibition of soluble proteins leading to cataract formation. A parallel decrease of reduced ascorbic acid with respect to reduced glutathione suggested that in the energy metabolism of lens ascorbate reductase is the key enzyme.

There is a vast difference in the prevalence of senile cataract in Western countries and in Asia. The lens opacity which is due to aging process appears at a much earlier age group in Asian countries than in Europe. There is some difference in the incidence of cataract in the different regions of Pakistan where this study has been made. It is more common in the plains and the desert areas of Sind than in the valleys of the five rivers of the Punjab and other Northern areas near the mountains.

Ghosh *et al.*[2] Chaterjee, Rambo, and Raanken[3] have studied the prevalence of cataract in northern India, in the dry belt of southern Punjab and Haryana with a population of 3.5 million and they have concluded that roughly 31.4% of all persons above the age of 60 years have a cataract formation. Franken and Mehta[4] estimated that the prevalence of cataract in one district of northern India is astonishingly high. In a study of the incidence of cataract in western countries by van Heyningen[1] in Oxford area, she found that the incidence was much less and the average age of the patients with cataract was 72 years, whereas in Pakistan, the average age of the patients suffering with defective vision due to cataract was 56 years.

During a period of five years in an ophthalmic survey in rural areas, carried out through Mobile Eye Units of the Mobile Eye Service of Pakistan, cataract was found to be the most common cause of blindness followed by corneal opacities due to trachoma, small-pox and glaucoma. The relative frequency of cataract extraction has increased each year, and has considerably gone up in the province of Sind. The compaign of preventing blindness through mobile eye teams in rural areas has been most successful.

The etiology of cataract formation has never been fully explained; an attempt has, therefore, been made in the present investigation to study the morphology of senile cataract in Pakistan. The paper further throws light on the etiological basis and the biochemical aspects of formation of these opacities which is to this date remained obscure. There is undoubtedly an early age incidence in cataract formation in Asia and there is also some genetic basis of formation of certain types of opacities.

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Material and Methods

Two thousand patients who had defective vision of various degrees, between the age of 30 and above, were selected on random basis from the regular Ophthalmic Outpatients of the Jinnah Postgraduate Medical Centre. These patients were refracted and when their corrected vision did not improve beyond 6/12 (20/40), then these patients were included in the study. The patients were then examined thoroughly on the slit lamp after dilatation of their pupils with mydiatric and the lens opacities were noted according to their site and type of opacity, 1040 eyes were thus examined and they were classified in the 'immature cataract group' and further subclassified *in vivo* on morphological basis. Similarly 1420 patients from the Diabetic Eye Clinic were selected on random basis in the same age group (30 and above) and were examined by slit lamp microscopy which included 2780 eyes, here also the same criteria of the inclusion in the study, i.e. if their vision is not improved beyond 6/12 with glasses, they were included in the study. Morphology of the lens *in vitro*, includes patients who suffered from gross visual loss due to advanced opacities in the lens and with vision between 3/60. 585 patients were thus selected on random basis. These lenses were extracted in routine manner and nearly all of them were removed by cryo-probe (Amoils) and immediately on extraction were placed on the filter paper and were examined by a magnifying glass on the basis of their colour, texture of the cortex, site, extent and degree of their opacities, and they were classified. After studying the morphology of these lenses, they were weighed in preweighed plastic containers and actual wet weight of every lens recorded. The biochemical variation which causes these morphological changes were studied by Kirmani *et al.*[5] and also discussed in this paper.

Results

In five years duration, 169360 patients were examined with defective vision at various Eye Relief Camps and 10% were found to be suffering from cataract formation.

The non-diabetic patients had an immature cataract or early senile cataract formation Of 600 patients with 1040 eyes 35% of them were nuclear opacities, 20% equitorial and peripheral, 12% anterior cortical, 4% cortical and 30% posterior cortical and posterior subcapsular opacities.

Similarly out of 1420 diabetic patients with 2780 eyes, 18% of them were cortical, 12% anterior cortical. Equitorial and peripheral opacities were not observed in this group. Whereas posterior cortical and subcapsular were much higher (41.7%), while nuclear opacities were 28.3%.

It was observed that the cataracts were almost equally distributed in both sexes. Mature cataract was most common, other cataracts like hypermature variety were 18.29%, immature 9.74%, rest were mixed variety that is about 10%. It was found that the cataracts in diabetics were more common in females than in males (Table 2).

In Oxford the sequence of the distribution of no. and percentage in each age group is just the reverse as compared to Pakistan. Senile cataract in diabetics also appeared much earlier than in the nondiabetics (Table 3).

In vitro, cases were classified into six main groups. The description of each group is as follows :

(1) *Immature Cataract*. Lenses were pale uniform colour, the state of cortex was still clear, or partly translucent. In some cases, the cortical opacities were small and the cortex was mostly translucent; and in some, extensive cortical opacities existed. The immature cataracts found were anterior cortical 10%, cortical 2%, peripheral 20%, nuclear 30% and posterior cortical 38%.

(2) *Mature Cataract*. The lenses showed visible discontinuity between cortex and nucleus, with complete opacification of the capsule.

(3) *Hypermature Cataract*. The cataracts were swollen capsules, the liquified cortex sometimes of brown in colour. The hypermature cataract found were anterior cortical 15%, cortical 15% nuclear 60% and nuclear and cortical 10%.

(4) *Morgagnian Cataract*. It is the swollen capsules in which a brown nucleus was suspended in the turbid fluid. All (100%) were nuclear opacities with liquification of cortex and opacification of capsule.

(5) *Senile Cataract in Diabetes*. The cataracts were brown, nucleus invisible in turbidity.

(6) *Complicated Cataract*. It includes groups of cataractous lenses which appeared in various intraocular diseases such as glaucoma, uveitis and corneal diseases and were mostly of posterior cortical variety. The average wet weight of lenses were determined and found to be 206.91, 197.59, 159.94, 158.07, 129.94 and 210.11 mg for immature, mature, hypermature, morgagnian senile cataracts in diabetes and complicated cataracts respectively. The values are expressed with standard deviation, standard error and number of determination in each case.[6] The wet weight of immature cataract and complicated

TABLE 1. PREVALENCE OF CATARACT IN PATIENTS WITH OCULAR SYMPTOMS OBSERVED IN 5 YEARS.

Duration of survey	No. of cataract found	Miscellaneous	Total
January 1969–June 1973	17,136	152,224	169,360
Percentage	10·1	89·9	100

TABLE 2. MORPHOLOGY OF CATARACTS STUDIED AFTER EXTRACTION.

Cataracts	No.	Percentage
Immature	57	9.74
Mature	346	59.15
Hypermature	107	18.29
Morgagnian	39	6.67
Senile cataract in diabetics	18	3.07
Complicated	18	3.08
Total	585	100.00

TABLE 3. AVERAGE AGE OF CATARACT EXTRACTION OF EACH TYPE IN PAKISTAN AND OXFORD.

Cataracts	Average age of cataract extraction in Pakistan	Average age of cataract extraction in Oxford	Group
Immature	55·00	70·7	I
Mature	57·70	72·8	II
Hypermature	60·30	76·8	III
Morgagnian	56·76	75·5	IV
Senile cataract in diabetics	53·76	—	—
Complicated	56·90	—	—

were found to be a few mg higher as compared to the mature, hypermature, morgagnian and senile cataract in diabetes.

Discussion

This paper gives some observation on the morphology of cataracts in Pakistan. These changes in human lenses can be observed in early stages, i.e. when it is immature, because once the opacification of cortex and nucleus is complete, the picture merges from one type into another and no distinction can be made as to where the opacity began and how it progressed.[7]

Cataract was surveyed in Pakistan and was found to be unevenly distributed in different regions, being more common in the plains and desert areas than in the mountains. Mann[8] reports an uneven distribution throughout the world, but in Pakistan it is astonishingly high as compared to Oxford[1] and relatively higher than findings of Franken and Mehta.[4]

Immature senile cataract in nondiabetes shows that 35% of lens opacities results as a senile change, are nuclear and to aging process, whereas 30% are posterior cortical opacities which are equally important giving an indication of some metabolic change in the vitreous pointing to the etiology towards biochemical basis.

Kirby[9] studied the morphology of cataract, particularly in the diabetics, and noted 64% suffering from cataract formation and in his study, nuclear opacities were 29%, equitorial and peripheral 52% and nuclear and cortical 3%, posterior cortical 7% and mixed variety 9%.

Previously, with rare exceptions, only the post-mortem lenses were used for the study of morphology and they usually had undergone physical and biochemical changes after death.[10] In our study we have included patients who suffered from gross visual loss due to advanced opacities in the lens and with vision lower than 3/60.

This goes to show that there is possibly a biochemical basis of senile cataract formation which is accentuated in diabetics and the first sign that appears is a small dot of an opacity in the back of the cortex of lens expanding later in star shape and eventually invading the rest of the cortex. This process may be very rapid in a number of cases or it may be delayed for several decades in others. It is similar in complicated cases of cataract as in glaucoma, uveitis, high myopia and other degenerative disorders of the vitreous.

In most of the age groups, the cataractous lens from female patient was on average, a few mg lighter than that from the male. This is just in accordance with the finding of van Heyningen.[1]

The lens weight increases with age as the total protein content increases. The loss in weight of the lenses with opacities may be due to the loss of soluble protein from the lens.

For a long time it was thought that crystalline lens is a dead tissue but subsequent studies showed that it is a living tissue and substances or factors which interfere with energy metabolism, also causes cataract. Hence dinitrophenol, iodoacetate, cyanide all opacify the lens tissue, when lenses are incubated *in vitro*. Scientists to this date have failed to pinpoint any lacunae in the normal energy metabolism of the lenses undergoing opacification.

The metabolic breakdown of glucose by the lens appears qualitatively the same as in other tissues, but graded to condition of relative anoxia (Fig. 1).[11]

Recently van Heyningen[12] has described another method of glucose metabolism which is almost unique to the lens and which, although scarcely operative under normal condition, becomes active under conditions of high blood sugar. Figure 2. summarises our present knowledge of the metabolism of glucose by the lens and show possible interaction between different pathways. Nicotinamide adenine dinucleotide phosphate ($NADPH_2$) is formed in the metabolism of glucose by pentose phosphate path and is used in the reduction of glucose to sorbitol. Kinoshita[11] has found that increase of glucose concentration which stimulates formation of sorbitol will also stimulate the breakdown of glucose by the pentose phosphate path. This type of energy metabolism for the lens has been proposed by Kinoshita (Fig. 3).[13]

We have tried to find out the impediments of this energy pathway in the lenses studied by us. An attempt was made to modify and elaborate the microestimation methods for the determination of reduced glutathione and reduced ascorbic acid in the blood, aqueous humour and homogenates of different cataractous lenses.[7]

The bar diagram (Fig. 4) shows that the concentration of reduced glutathione increases as the opacity of lens increases. It is maximum in case of morgagnian and in cataract of diabetic patient. The rise in concentration level is reduced if glutathion was accompanied by the rise in blood and aqueous humour.

Milligram per cent concentration of ascorbic acid in blood, aqueous humour and lens homogenate were plotted, the type of cataract studied as shown in Fig. 5. This showed a gradual fall in the concentration with the appearance maturation of cataractogenesis. In the blood there was a little decrease in ascorbic acid concentration of lens, while there was an appreciable increase in the ascorbic acid concentration of lenses specially in case of morgagnian cataract and cataracts in diabetics.

Now referring back to the energy metabolism (Fig. 3). It was concluded from the observation that as the reduced form of glutathione has shown to be increased with advancement of opacities parallel by a decrease in concentration of reduced ascorbic acid we propose that if at all the mechanism suggested by Kinoshita[13] be the major source of energy in the lens, then the bottle neck seems to lie at stage of ascorbate reductase and hence it was suggested that in the energy metabolism of lens ascorbate reductase is the key enzyme. We are extending our work towards investigating the action of this enzyme under normal and cataract conditions.

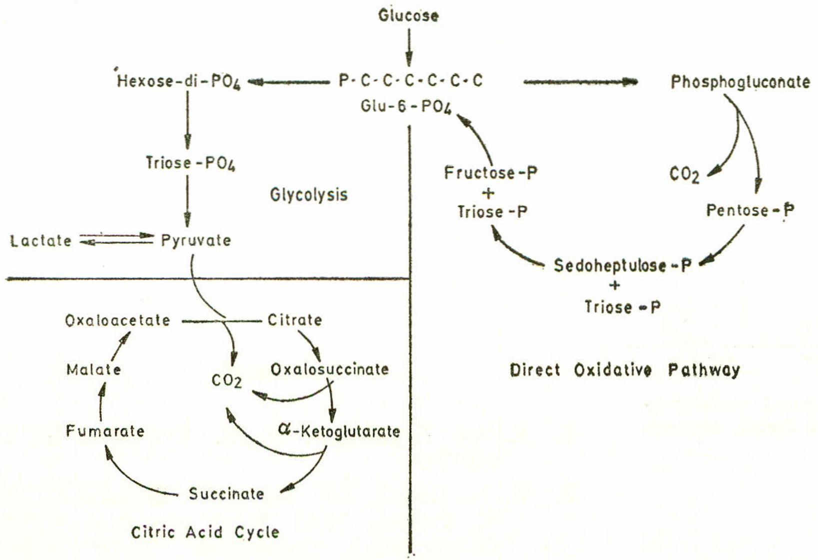

Fig. 1. Pathways of glucose metabolism.

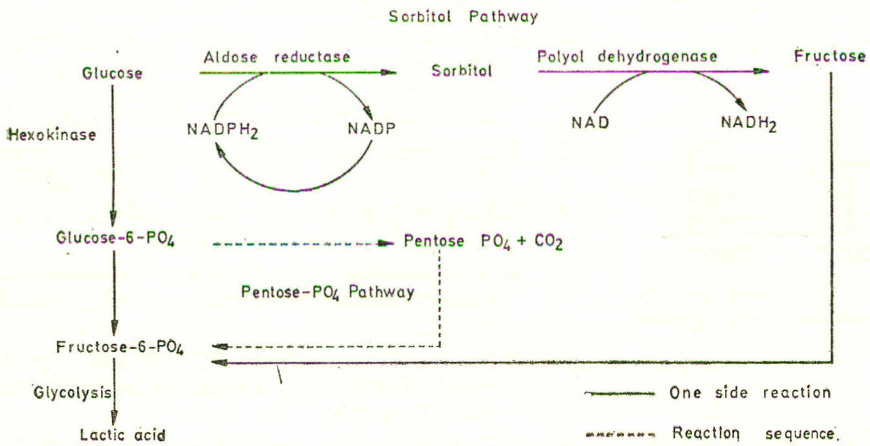

Fig. 2. Main paths of metabolism of glucose by the lens showing interaction between sorbital and pentose phosphate pathways through the coenzymes.

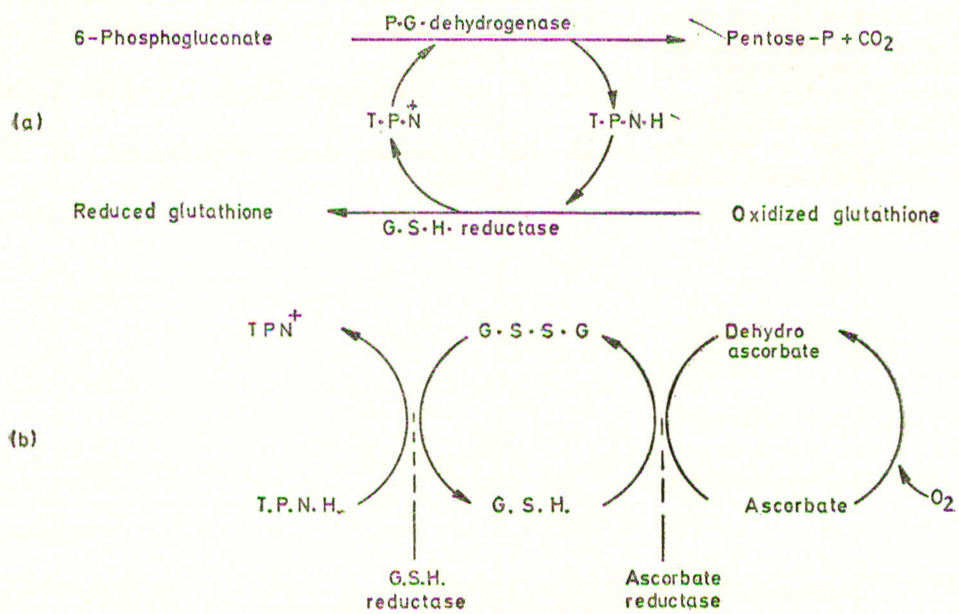

Fig. 3. (a) Coupled oxidation reduction reaction, (b) G.S.H. ascorbic acid oxidation mechanism.

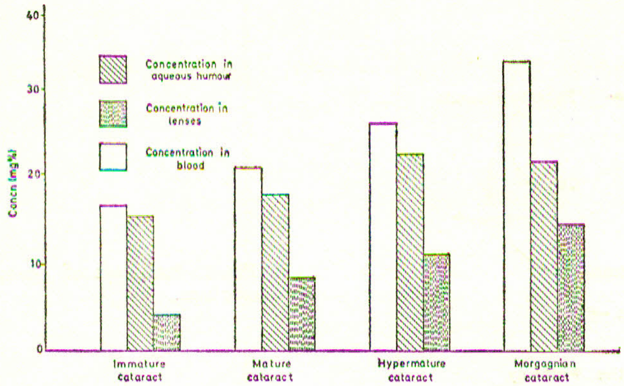

Fig. 4. Variation in concentration of reduced glutathione due to the different types of cataract in blood, aqueous humour and lenses.

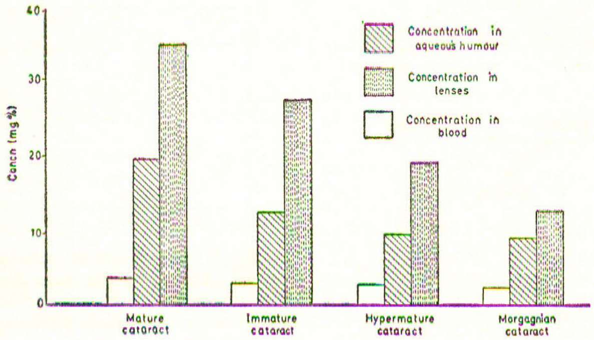

Fig. 5. Variation in concentration of reduced ascorbic acid due to the different types of cataract in blood, aqueous humour and lenses.

Conclusion

Lens opacities are mostly due to nuclear sclerosis or senile changes. Posterior cortical opacities form one-third of these producing effective loss of vision at an early age. Typical senile changes, i.e. cart wheel appearance is relatively rare, nuclear and posterior cortical opacification is predominant.

Diabetics get an early senile change and in this group 41% of lens opacities appear in posterior cortical region, of course associated with nuclear and cortical chances as well. This points to the metabolic changes of the vitreous as the etiological basis of these changes.

In the light of biochemical studies and the view presented by van Heyningen and Kinoshita it is easy to conclude that glutathione when present in high concentration inhibits oxidative mechanism in the lens which causes inhibition of soluble proteins leading to cataract formation. A parallel decrease of reduced ascorbic acid with respect to reduce glutathione suggest that in the energy metabolism of lens ascorbate reductase is the key enzyme.

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