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Research Article

A Review on Association Between Diabetes Mellitus and Cataract Formation

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Abstract

Major cause of blindness among diabetic patients is cataract both in developed and developing countries. Diabetic ocular complications are most common in both type-1 and type-2 diabetes, considering the fifth most common cause of legal blindness. This review aims to systematically evaluate the studies on occurrence of cataract formation among diabetic patients, types of cataract and its mechanisms of pathogenesis. According to WHO, cataract is 33% of all type of visual impairment. Prevalence of cataract increased with increasing age in both younger and older onset diabetic persons. Females had higher rates than males. The pathogenesis of diabetic cataract development is still not fully understood. Population-based studies have greatly increased our knowledge concerning the association between diabetes and cataract formation and have defined risk factors for the development of cataract. Simply diabetic cataracts are characterized by cortical or posterior sub-capsular opacities. Aldose reductase and polyol are responsible for diabetes ocular complications. Mechanisms of diabetic cataractogenesis have been studied in less detail than those of other diabetic complications. Both animal and human studies support important contribution of increased aldose reductase activity. Several clinical studies investigated the role of phacoemulsification surgery and its post-surgery complications. Researchers are trying to develop aldose reductase inhibitors and antioxidants, may be effective treatment to prevent or cure diabetes cataract.

Keywords: Diabetes mellitus; Cataract; Aldose Reductase; Polyol Pathway; Sorbitol; transient hyperopia

Introduction

Diabetes mellitus is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period resulting both microvascular and macrovascular complications in body though there is other complications (Deshpande AD et al, 2008). Microvascular complications include neuropathy, nephropathy, and retinopathy, while macrovascular complications consist of cardiovascular disease, stroke, and peripheral artery disease (PAD). Worldwide more than 285 million people are affected by diabetes mellitus. This number is expected to increase to 439 million by 2030 according to the International Diabetes Federation. In 1990, cataract was in South Asia as well as worldwide the most common cause of blindness, followed by uncorrected refractive error, glaucoma, age-related macular degeneration, corneal disease, trachoma and diabetic retinopathy. This pattern was mostly maintained in 2015 and also in the projection up to 2020, with the only difference of diabetic retinopathy occupying the second-last position from trachoma in exchange for the last position (Nangia V et al, 2018). Signs of diabetic retinopathy occur, in 95% of type 1 diabetics and 60% of type 2 diabetics with disease duration longer than 20 years. According to Guillausseau PJ and UK Prospective Diabetes Study (1998) severe cases of proliferative diabetic retinopathy are found in patient suffering from type 1 diabetes. Cataract is considered a major cause of visual impairment in diabetic patients as the incidence and progression of cataract is elevated in patients with diabetes mellitus (Stratton IM et al, 2001; Harding JJ et al, 1993).For instance, the Wisconsin Epidemiologic Study of Diabetic Retinopathy19 reported a 10 year cumulative incidence of cataract surgery of 24.9% in those with type 2 diabetes. The association between diabetes and cataract formation has been shown in clinical epidemiological and basic research studies. Globally, Cataracts occur remain the leading cause of blindness, affecting approximately 18 million people. Cataracts occur at later age and 2-5 times more frequently in patients with diabetes, thus the visual loss has a significant impact on the working population (KAHN HAet al, 1977; Klein BEet al, 1995). Cataract surgery is the most common ophthalmic procedure used worldwide. Rate of cataract and cataract surgery is high as cataract is most common cause of visual impairment. But to delay or prevent the development of cataract in diabetes patients remains a challenge. Particularly in developing countries, both diabetes and cataract become health and economic burden, where diabetes treatment is insufficient and cataract surgery often inaccessible (Tabin G et al, 2008).

Pathogenesis and Types of Cataract

Diabetes manifests various complications including eye. Among several retinopathies cataract is the most common ocular complication which is characterized by nuclear, cortical and sub-capsular opacities (KINOSHITA JH et al, 1974).

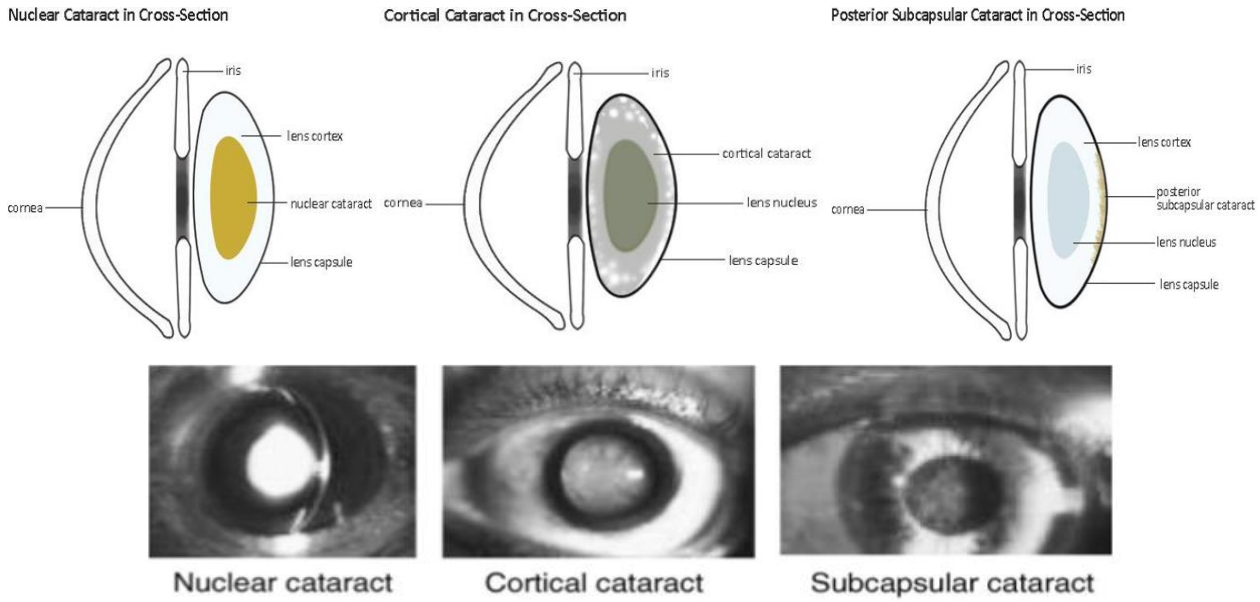

Figure 1: *Types of Cataract*

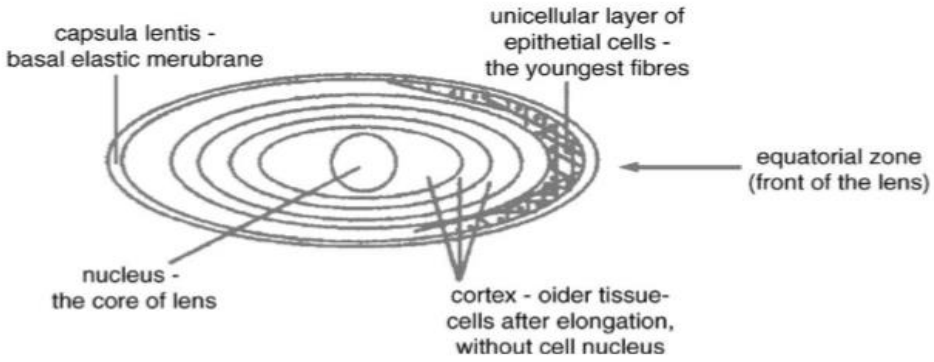

Figure 2: *illustrations of lens anatomy*

When large amounts of glucose are present in blood (as in diabetes mellitus), hexokinase becomes saturated and the excess glucose enters the polyol pathway when aldose reductase (AR), a cytosolic enzyme present in most of the mammalian cells, reduces it to sorbitol.

In the lens, sorbitol is produced faster than it is converted to fructose by the enzyme sorbitol dehydrogenase.

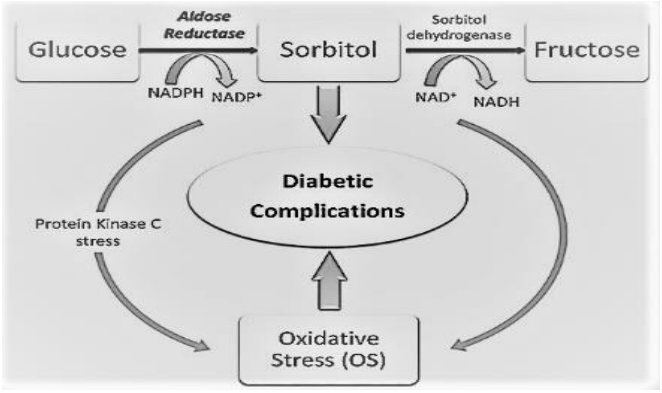

Figure 3: *pathogenesis of cataract formation.*

Intracellular accumulation of sorbitol causes osmotic changes that leads-

- The Lens to swell up which is associated with biochemical complex biochemical changes ultimately producing cataract (Moher D et al,2015;KINOSHITA JH et al, 1974 & 1979)
- Hydropic lens fibers to degenerate resulting cataract formation.(Moher D et al,2015;KINOSHITA JH et al, 1974 & 1979).

The objective of this review is to systematically perceive the published work on understanding the occurrence cataract formation, the pathophysiological significance of aldose reductase in mechanism of pathogenesis and types of cataract among diabetics.

Methods

A systematic review of published studies about on cataract formation in diabetic patients was assumed in accordance with PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis) statements (Moher D et al, 2015).

Search Method

An effective search for diabetic retinopathy related articles was performed in Google scholar, BioMedCenter. A manual google search of the reference lists of studies was performed to obtain the data. Data were also obtained from the search of Retinopathies related web sites.

Inclusion and exclusion criteria

The following inclusion principles were considered; a)human adults (>18 years old), b) Observational study design c) chronic diabetic patients. The following exclusion principles were considered; a) adults having others NCD,b) those with having genetically ocular disease and c) seminar proceedings, perspectives, comments and book chapters/book reviews.

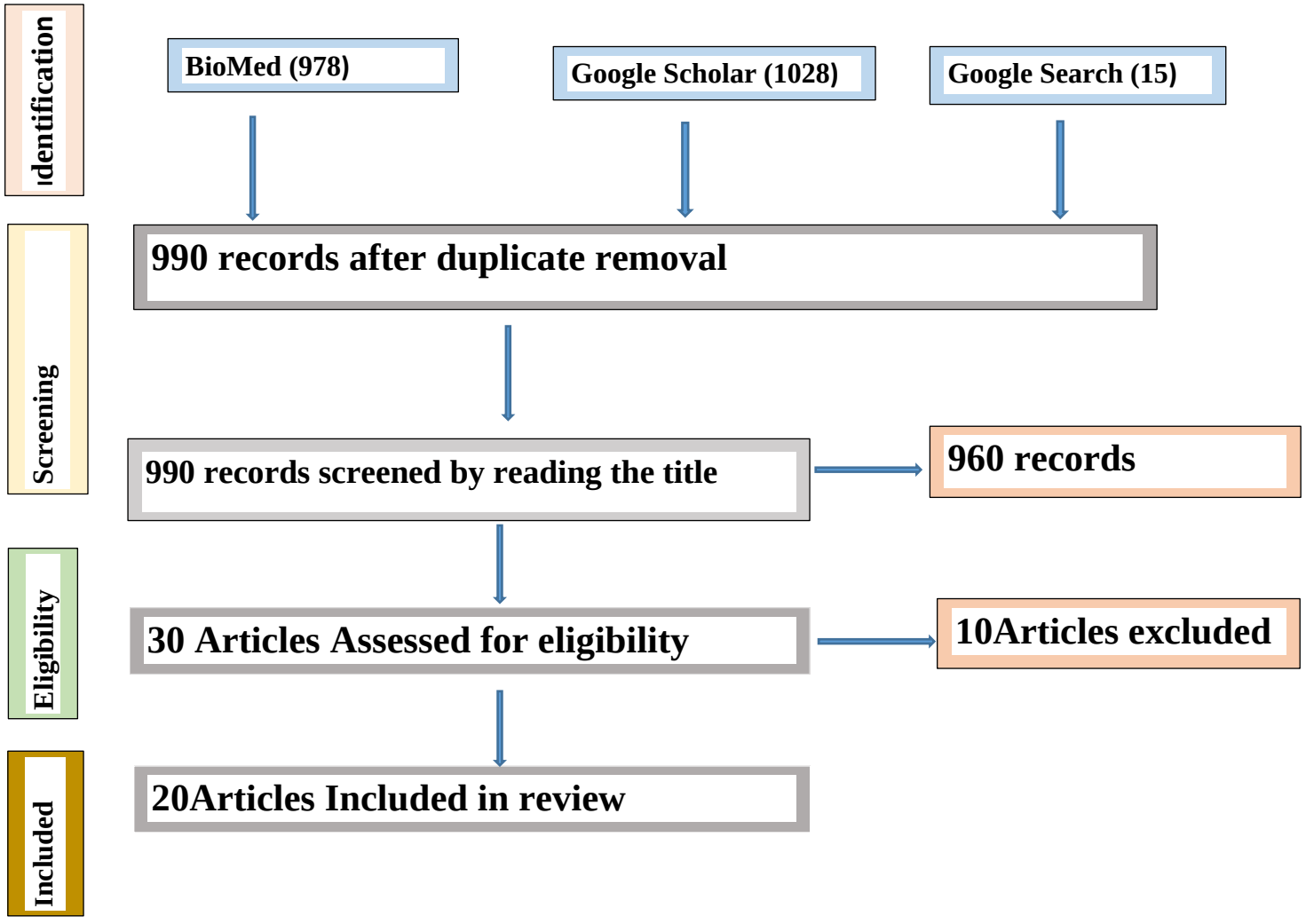

Figure 4: *Summarised Search Protocol*

Results:

Studies related to cataract formation in diabetic patients have shown that hyperglycaemia is associated with loss of lens transparency in a cumulative manner. Hyperglycaemia may induce temporary lens opacification and swelling as well as transient hyperopia. The occurrence of diabetic cataract was higher among those with a longer duration of diabetes, higher levels of glycated haemoglobin (HbA1c) and fasting glucose, papillary excavation ≥ 0.5, and among individuals in older age group (Lima CG et al, 2018). Using the log-binomial regression model,

diabetes duration >24 months and HbA1c≥6.5% were significantly associated with the occurrence of diabetic cataract (.Lima CG et al, 2018). The UK Prospective Diabetes Study (UKPDS) found that every 1% reduction in glycated haemoglobin (HbA_{1c}) was associated with a 37% decrease in microvascular disease including cataract formation (Litwak L et al, 2013). Usually prevalence of cataract was higher in female than male diabetic patients (Klein BE et al, 1985;Srinivasan S et al, 2017).

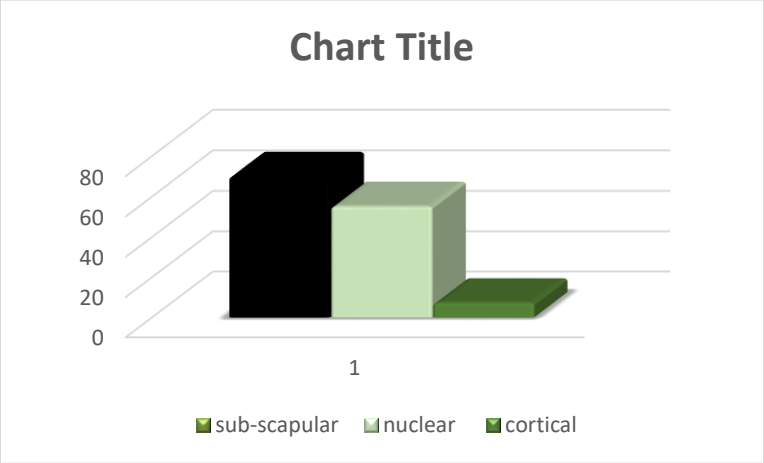

Figure 5: *Rates 0f different types of cataract formation.*

Prevalence of subscapular (70%) and nuclear cataract (55.2%) are higher among diabetic patients then cortical cataract (7.3%).

Types of cataract	OR	95% CI for OR		p-value
Nuclear cataract	1.15	1.03	1.28	<0.001
Sub-scapular cataract	1.12	1	1.125	<0.001
Posterior sub-scapular cataract	1.55	1.27	1.90	<0.001

Table: *probability of cataract formation in association with HbA1C.*

The incidence rates of cataract diagnosis seems to be slightly higher (overall 20.4 per 1000 person-years (py) vs. 11.7 and 17.8 per 1000 py, for non-insulin treated T2DM and insulin-treated T2DM respectively, in the study by Janghorbani et al.

There is an increased rate of nuclear and cortical cataract among diabetics with increasing levels of HbA1C (OR 1.15 [95% CI 1.03, 1.28] and OR 1.12 [95% CI 1.00, 1.25], respectivelywhereas posterior sclerotic cataract (OR = 1.55, 95% CI: 1.27,1.90). The rate of Posterior capsular opacification development has been reported to be higher after cataract extraction in patients with diabetes than in the general population (Peterson SR et al, 2018).But in another study, both visual acuity and the vision related quality of life of the patients with diabetic retinopathy improved significantly after cataract surgery though phacoemulsification surgery severely affects the blood aqueous barrier in diabetic patients with proliferative diabetic retinopathy than non-diabetic patients (Zhu B et al, 2017).

Discussion:

This paper provides an overview of the pathogenesis of diabetic cataract, clinical studies investigating the association between diabetes and cataract development, and current treatmentof cataract in diabetics. Besides we tried to show the types of cataract formation and its prevalence among diabetic patients with respect to gender. In case of high blood sugar the enzyme aldose reductase, present in mammalian cell, converts glucose to sorbitol. Increased accumulation of sorbitol causes swelling of lens with complex biochemical changes and creates a hyperosmotic effect that results in an infusion of fluid to countervail the osmotic gradient.This biochemical alterations leads to a collapse and liquefaction of lens fibre, which ultimately results in the formation of lens opacities.

Usually three types of cataract prevails in medical terminology. We observe thatamong them nuclear and cortical cataract are higher in diabetic retinopathy whereas posterior capsular opacification appears after cataract surgery. Several studies found that diabetic retinopathy e.g. cataract prevalence is higher in females with compared to male diabetic patients

We also observe that anti-cataract treatment has achieved popularity among diabetic patients. Usually aldose reductase inhibitors are used to delay cataract formation as preventive use. Again a number of different antioxidants such as alpha lipoic acid have been reported to delay cataract formation in diabetic animals.

However, knowledge, attitude and practices towards diabetic care will reduce the complications resulted from diabetes.

Conclusion

Diabetes mellitus is widely recognized as an emerging epidemic that has a cumulative impact on almost every country, age group, and economy across the world as it has both short and long term complications. Cataract is a major cause of vision impairment in the general population worldwideas well as in people with diabetes as long term complications. As diabetes mellitus is increasing along with its complications, preventive measures can minimizes the losses. More researches should be carried out to find alternate ways of leading vision related quality of life.

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