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Short Communication

Glaucoma in diabetic patients and the need for further research

Omyma Abbas Banaga Salih, Zaid Al Hamadani, Bayan Alemrayat, AlAnoud AlFehaidi, Ehab Hamed*

Primary Health Care Corporation, Qatar

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***Correspondence:**
Dr. Ehab Hamed,
E-mail: ehabaziz@gmail.com

ABSTRACT

Glaucoma is considered the leading cause of irreversible blindness worldwide. Patients with diabetes are at risk of different eye complications, mainly retinopathy. Patients with diabetes are also at risk of developing cataract, uveitis and glaucoma. Three systematic reviews examined the associations between diabetes and glaucoma. Pooled analysis from those studies reported different OR 1.37, (95% CI=0.72-2.02), OR=1.36, (95% CI=1.25-1.50) and OR=1.48, (95% CI=1.29-1.71). Although the results seem close and suggest an increased risk in the diabetic population, the systematic reviews report significant heterogenicity and come short in explaining causality. Indeed, in one systematic review where 3 out of 7 studies suggested a non-significant association, the results were skewed to the positive side with a one-record based study that had a population size exceeding 2 million patients, while the rest of the studies had collectively 100 thousand patients. In our view, a case control study design that combines the patient surveys and electronic medical records ensure accurate data and more valid study results to validate or refute the association. This short communication article discusses the condition associations, theories for increased risk in the diabetic population and implications for future research.

Keywords: Glaucoma, Diabetes, Blindness

INTRODUCTION

Glaucoma is considered the leading cause of irreversible blindness worldwide. The term describes a group of progressive disease where the optic nerve damage leads to vision loss. Open angle glaucoma and closed-angle glaucoma are the most common forms. The condition affects the patient's quality of life, physical ability and emotional well-being.[1,2]

Patients with diabetes are at risk of different eye complications; mainly retinopathy.[3] Diabetic retinopathy is one of the most devastating complications and results in vision loss. The disease is the leading cause of blindness in working-age adults.[4] Patients with diabetes are also at risk of developing cataract, uveitis, and glaucoma.[5-9]

Pathophysiologic changes of diabetic retinopathy and glaucoma and theories for the association

Glaucoma was believed to occur from solely elevated Intraocular pressure (IOP) mechanical stress. Though raised IOP is associated with the condition, other pathophysiological factors include genetics and impaired microcirculation.[10,11] Impaired microcirculation was implied as a contributory factor that causes glaucomatous optic neuropathy in the diabetic eye. Microvascular abnormalities are central to the development of diabetic retinopathy and related to the number of years since diagnosis and blood sugar control. The microvascular changes ultimately result in macular oedema and retinal neovascularization, the hallmark of proliferative diabetic retinopathy.[12]

Different theories were suggested to explain the associations between diabetes and glaucoma. First, Long-standing hyperglycaemia might increase the risk of neuronal stress damage.[13] A second theory that might explain the condition in diabetic eyes is dysregulation of blood flow due to retinal vascular endothelial cell dysfunction.[13] A third one is a remodelling of the connective tissue of the optic nerve head with the increasing of intraocular pressure (IOP).[13] Raised IOP causes mechanical stress that ultimately results in the loss of the neuroretina rim of the optic disc and enlargement of the optic cup.[14] Such theories are suggesting that such damage is caused either directly by hyperglycaemia or through the microvascular changes secondary to hyperglycaemia or secondary to the diabetic eye structural changes secondary to the microvascular changes due to the persistent hyperglycaemia.

Different genetic variants are associated with cases of glaucoma in young and early adult age and glaucoma cases that happen in normal IOP.[6] Several studies suggest that genetic abnormality is also implicated in glaucoma cases even in the diabetic population, but in such studies, the population is not compared to non-diabetic population.[15]

Three systematic reviews examined the associations between diabetes and glaucoma.[7-9] Pooled analysis from those studies reported different OR 1.37, (95% CI=0.72-2.02), OR=1.36, (95% CI=1.25-1.50) and OR=1.48, (95% CI=1.29-1.71). Alhough the results seem close and suggest an increased risk in the diabetic population, the systematic reviews report significant heterogenicity and come short in explaining causality. The methodology of the results varied between cross-sectional, case-control, and cohort studies. Results varied across no association, positive associations and in rare cases, negative associations (protective effect). Indeed, in one systematic review where 3 out of 7 studies suggested a non-significant association, the results were skewed to the positive side with a one record-based study that had a population size exceeding 2 million patients, while the rest of the studies had collectively 100 thousand patients.[7,10] Different theories tried to explain the association between diabetes and glaucoma, but in our view, further studies are needed to confirm or refute the association.

Implications for future research design

Future research should focus on possible causes rather than only associations. Research studies reporting on glaucoma in patients with diabetes should include variables such as time since disease development and should consider associations with diabetic control. Also, a record of family history of glaucoma might help to confirm or refute the association between genetic predisposition and glaucoma development. There is no research to compare the difference in genetic predisposition to glaucoma between diabetic and non-diabetic population. One could assume that genetic predisposition is unlikely to differ from the non-diabetic population.

Such studies would be of interest but would be challenging to conduct due to the rarity of the condition. A suitable design might be a case-control design, which will allow for proper sampling and patient validated history may warrant more accuracy. The downside of such a design might provide a smaller sample size and some researchers suggested that patient surveys are largely inaccurate. A retrospective record-based design might form another possibility with the advantage of a larger sample size but the concerns regarding data accuracy remains valid. Though medical diagnosis on electronic medical records seems to be accepted as the gold standard, there is always the chance of incomplete data set or inaccurate diagnosis. A prospective cohort study would be ideal, but the numbers of patients to recruit and the time to follow up would make that unfeasible. In our views a case control study design that combines the patient surveys and electronic medical records ensures accurate data and more valid study results.

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