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# **Diabetic Eye Diseases: A Review**

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## **Review Article**

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Diabetes is a metabolic disorder in which the body functions gets affected which may even lead to death. The systems which are affected due to Diabetes are renal system, gastro intestinal system, urinary system, circulatory system and even eye complications. Eyes are one of the important organs of the human body. Diabetes may affect eyes leading to certain diseases like Cataract, Glaucoma, Retinopathy, Myeloma and Blurred Vision. This, if left untreated may even lead to permanent blindness. Proper diagnosis and treatment is important in order to treat eye disease. A review of the eye related diseases is discussed in this article.

ABSTRACT

## **INTRODUCTION**

Vision is most important for a man to survive and live in this world. Diabetes is a complex metabolic disorder, affecting the body metabolic functions leading to death in young age. One of the most common disorders associated with diabetes is eye complications. People with Diabetes develop a variety of eye disorders like retinopathy, glaucoma and cataract even sometimes leading to blindness. Although a number of treatments are available nowadays, people suffering with diabetes should go to regular eye checkups in order to avoid serious eye complications which may even lead to loss of vision. A glimpse of eye disorders associated with diabetes is discussed in this article for understanding the related mechanism and treatment.

## DIABETES

Diabetes is a condition in which body cannot produce insulin (hormone that regulates and controls the blood glucose levels) or cannot use sufficient insulin that is produced in the body which leads to the damage of organs, blood vessels and nerves <sup>[1-2]</sup>.

Diabetes also known as MadhuMeha (India) or Honey Urine is one of the diseases which was first described in Europe as "Too great emptying of the urine". Later Greek physicians described Diabetes as "the melting down of flesh and limbs into Urine". The term Diabetes was coined by Apollonius of Memphis (Greek) which means "to pass through". Later Diabetes was differentiated as Type-1, Diabetes Insupidus and Type-2, Diabetes Mellitus by Indian physicians Sushruta and Charaka. Thomas Wilis added the term Mellitus to diabetes to differentiate from Insupidus [3-4].

## **Types of Diabetes**

There are three main types of diabetes.

- Type-I Diabetes
- Type-II Diabetes
- Gestational Diabetes

#### Type-I Diabetes:

It is also referred as Juvenile or insulin dependent diabetes which usually develops in childhood or adolescence. In this condition, the human body removes insulin production due to the destruction of cells producing insulin by the immune system of the body due to which glucose levels get accumulated in the blood instead of using it in the form of energy <sup>[5-7]</sup>.

#### Type-II Diabetes:

It is also referred as adult onset or non-insulin dependent diabetes. In this type of diabetes, human body cells cannot use the produced insulin in a right way (insulin resistance) which may lead to decreased production of insulin (insulin deficiency) <sup>[8]</sup>. Type-II diabetes may be caused due to obesity <sup>[9-12]</sup>. Symptoms of Type-I and Type-II Diabetes:

Hunger, Fatigue, increased thirst and increased urination, slow healing sores and infections, Blurred Vision and sudden weight loss are the most common symptoms of Diabetes <sup>[13]</sup>.

# TREATMENT OF DIABETES

There is no treatment for the complete cure of diabetes. The goal of treatment is to lower the blood glucose levels so that we can prevent the complications caused by diabetes <sup>[14-16]</sup>.

#### **Gestational Diabetes**

It occurs during pregnancy in females and often resolves after childbirth but increases the risk of diabetes in mother and child as well <sup>[17-20]</sup>.

#### **Complications Associated with Diabetes**

Type-I Diabetes may affect central nervous system (Polydipsia, polyphagia, lethargy, stupor), eyes (Diabetic retinopathy, diabetic macular edema (DME), cataract, and glaucoma), Respiratory system (Hyper ventilation), Urinary system (polyuria, glysocuria), Gastrointestinal system (Nausea, Vomiting, Abdominal Pain), systemic circulation (Body weight) <sup>[21,22]</sup>.

## EYE COMPLICATIONS ASSOCIATED WITH DIABETES

Eye complications are common in people having high blood sugar. In order to understand what actually happens to our eye during diabetes, we should know how eye really works. Symptoms related to Diabetic Retinopathy and other Diabetes-Related Eye Problems include Fluctuating vision, Eye floaters and spots, Development of a scotoma or shadow in your field of view, Blurry and/or distorted vision, Corneal abnormalities such as slow healing of wounds due to corneal abrasions, Double vision, Eye pain, Near vision problems unrelated to presbyopia, Cataracts <sup>[23-25]</sup>.

#### Eye Mechanism

When light passes through the outer surface of the eye, cornea and retina focusses the light on to the retina which converts the light signals in to electric signals. These electric signals are sent to the brain through the optic nerves and then the brain interprets the signals to see the objects <sup>[26,27]</sup>.

#### **Complications Associated with Eye Disease**

Total 25% of the people with diabetes are having eye complications. The most common complications in people with Diabetes include <sup>[28-33]</sup>

- Blurred Vision
- Diabetic Retinopathy
- Cataract
- Glaucoma

#### **Blurred Vision**

Blurred vision is the most common complication associated with diabetes. When blood sugar levels gets increased, the lens of eye gets swollen which results in the blurred vision. It gets normal within 2-3 months after your blood sugar level gets normal.

#### **Diabetic Retinopathy**

Diabetic retinopathy can be seen in 21% of patients been diagnosed with Type-II Diabetes. It is the common cause of blindness among the working population. Retinopathy generally refers to the common disorders of retina caused due to Diabetes. As previously discussed retina of the eye converts the light signals in to electrical signals. When blood sugar levels are high, the tiny blood vessel which nourishes the retina gets blocked, cutting down the blood supply to the retina. If it is not treated on time, one may lose eye sight permanently <sup>[34-39]</sup>. Early Diabetic Retinopathy or non-proliferative diabetic retinopathy is a condition in which the tiny bulges known as microaneurysms, occur on the walls of blood vessels which may leak fluid and blood in to the retina <sup>[40-44]</sup>. Sometimes the central part of retina (Macula) begins to swell which is nothing but macular edema, which requires immediate attention. This may affect the central vision making difficult to see objects, recognizing people around. Around 2- 10% of people affected with diabetes has macular edema <sup>[45-50]</sup>.

Advanced Diabetic Retinopathy or Proliferative Diabetic Retinopathy: If Diabetic Retinopathy progresses, it causes the blood vessels blocked, which results in decreased oxygen supply to retina (Ischaemia). As a nature way of repairing this condition, the eye starts growing new blood vessels in the inner surface of retina, into the vitreous gel (fluid that fills the eye), that are fragile and starts to eventually break and bleed. Due to this the vision gets unclear as the light cannot pass due to the blockage due to blood. If the hemorrhages become extensive, scar tissue grows and thickens which leads to the detachment of retina from the back of the eye, which causes permanent eye loss. Treatment includes Laser treatment, Eye injections and Eye surgery (in case of advanced retinopathy) <sup>[51-53]</sup>.

#### Cataract

Aqueous humor is the fluid that surrounds the eye, which supplies nutrients, oxygen and glucose to eye's lens. In the case of Diabetes, when blood glucose levels are high, sugar levels increases in the aqueous humor and in the lens causing the lens to swell and unclear vision. Aldose reductase is an enzyme present in the lens, which converts glucose in to sorbitol. If blood sugar level gets increased sorbitol gets collected in the lens, which leads to opaque vision. This condition results in cataract which makes your vision blurred, yellowish, and opaque <sup>[54-59]</sup>. Treatment: Cataract operations are common in order to treat cataract replacing the clouded lens with artificial lens <sup>[58]</sup>.

#### Glaucoma

The main cause of glaucoma is Diabetes Mellitus among people suffering with Diabetes <sup>[60-64]</sup>. There are two types of glaucoma, open angle glaucoma and neo-vascular glaucoma.

If the fluid present in the eye doesn't drain out properly from the eye, it results in increased pressure inside the eye which damages the nerves and the blood vessels causing changes in vision. Glaucoma doesn't have any symptoms until one notices peripheral loss in the vision. The risk of glaucoma is high with increasing age and diabetes. Neo Vascular Glaucoma is commonly seen in people with diabetes, in which the abnormal blood vessels grow in the inner part of the eye, blocking the fluid flow out of the eye, thus raising eye pressure <sup>[65-71]</sup>. Treatment for glaucoma includes surgery, laser treatment <sup>[73-85]</sup>, eye drops and medications <sup>[86-100]</sup>.

## CONCLUSION

Diabetes is the most common metabolic disorders when body's ability to metabolize carbohydrates to energy fails, which lead to increase in the blood sugar levels due to which various disorders which may be nervous, eye related, cardiovascular etc. may develop. If not noticed in early stages it may even lead to death. Although it is not curable, several treatments came in to existence in order to maintain the blood sugar levels. This diabetes may even affect the eye, which may sometimes lead to blindness, if not noticed in the early stages. So, early diagnosis of the eye disorders is important in order to avoid serious complication of eye. People suffering with diabetes should go for regular eye checkups. Almost 40% of people with diabetes may have eye problems between 18 to 80 years of age.

#### REFERENCES

- 1. Tagliente I, et al. Management and treatment of type 1 and 2 diabetes: State of art. Gen Med. 2016;4:259.
- 2. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2010;33:S62-S69.
- 3. Baynes HW. Classification, pathophysiology, diagnosis and management of diabetes mellitus. J Diabetes Metab. 2015;6:541.
- 4. Ritu L. The history of diabetes mellitus. Sultan Qaboos Univ Med J. 2013;13:368-370.

- 5. Alemu F. Prevalence of diabetes mellitus disease and its association with level of education among adult patients attending at dilla referral hospital, Ethiopia. J Diabetes Metab. 2015;6:521.
- 6. Alberti KGMM and Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO Consultation. Diabetic Medicine. 2004;15:539-553.
- 7. Eiselein L, Schwartz HJ, Rutledge JC. The challenge of type 1 diabetes mellitus. ILAR. 2004;45:231-236.
- 8. Tosone G, et al. Diabetes mellitus type 1, latent autoimmune diabetes of adults and hepatitis c virus: what we know and what we need to know. J Diabetes Metab. 2013;4:301.
- 9. Kahn SE. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444:840-846.
- 10. Diabetes prevention program research group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346:393-403.
- 11. DeFronzo RA. pharmacologic therapy for type 2 diabetes mellitus. Ann Intern Med. 1999 131: 281-303
- 12. Norris SL, et al. effectiveness of self-management training in type 2 diabetes. Diabetes Care 2001;24:561-587.
- 13. Boulé NG, et al. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus. JAMA. 2001;286:1218-1227.
- 14. Zhao Y, et al. Type 2 Diabetes mellitus- disease, diagnosis and treatment. J Diabetes Metab 2015;6:533.
- 15. Pratley RE. The Early Treatment of Type 2 Diabetes. Am J Med 2013;126:S2-S9.
- 16. American diabetes association. The prevention or delay of type 2 diabetes. Diabetes Care 2002; 25:742-749.
- 17. Lu DY and Che JY. Rethink of diabetes treatment and drug development. Cell Dev Biol 2014;3: 125.
- 18. Hayashi A and Suganuma N. Physical activity for gestational diabetes mellitus. Clinics Mother Child Health 2016;13:238.
- 19. Bolognesi M. Overdiagnosis of gestational diabetes mellitus in pregnant woman: A case report. J Women's Health Care 2015;4:234.
- 20. Cheung KW and WongSF (2012) Gestational diabetes mellitus update and review of literature. Reproductive Sys Sexual Disord S2:002.
- 21. Shoar Z, et al. Maternal obesity, maternal gestational diabetes mellitus, and maternal and neonatal outcomes. J Obes Weight Loss Ther 2016;6:292.
- 22. Jain M, et al. Maternal vitamin d deficiency: a risk factor for gestational diabetes mellitus in north india. Gynecol Obstet 2015;5:264.
- 23. Mpondo BCT, et al. Gestational diabetes mellitus: challenges in diagnosis and management. J Diabetes Metab Disord. 2015;14:42.
- 24. Soumya D and Srilatha B. Late stage complications of diabetes and insulin resistance. J Diabetes Metab. 2011;2:167.
- 25. Bayramova AN. Gastroenterological diseases as a complications of type 2 diabetes mellitus. J Gastrointest Dig Syst. 2016;6:442.
- 26. Sharma NR and Rao GHR. Diabetes management: expectations and limitations. J Diabetes Metab. 2016;7:662.
- 27. Stolar M. Glycemic control and complications in type 2 diabetes mellitus. Am J Med. 2010;123: S3-S11.
- 28. Fowler MJ. Microvascular and macrovascular complications of diabetes. Clinical Diabetes. 2008;26:77-82.
- 29. Carle MV, et al. Patients with advanced diabetic retinopathy's understanding of diabetesmellitus and their diabetic eye disease: a survey of 100 patients currently undergoing treatment for diabetic retinopathy in a large retinal practice. J Clin Exp Ophthalmol. 2015;6:401.
- 30. UK prospective diabetes study group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ. 1998;317:703-713.
- 31. Aiello LP, et al. Eye complications of diabetes. Atlas of Diabetes. 2011;249-275.
- 32. Sabat D, et al. Understanding the structural and developmental aspect of simple eye of drosophila: The ocelli. J Cell Signal. 2016;1:109.
- 33. Sathyanarayanan V, et al. Homeomorphic model of the effect of impact trauma on the human eye. J Comput Sci Syst Biol. 2013;6:317-326.
- 34. Dhillon N, et al. Is Routine testing for proteinuria indicated in diabetic eye clinics? J Clin Exp Ophthalmol. 2014;5:333.
- 35. Norton AT. The mechanism of accommodation of the eye. Br Med J. 1873;2:749.
- 36. Magri CJ and Fava S. The diabetic eye: a window to the heart & vascular system. J Diabetes Metab. 2012;S3:008.
- 37. Charman WN. The eye in focus: accommodation and presbyopia. Clin Exp Optom. 2008;91:207-225.
- 38. Lundquist MB, et al. Patient perceptions of eye disease and treatment in Bihar, India. J Clinic Experiment Ophthalmol. 2012;3:213.

- 39. Fong DS, et al. Retinopathy in diabetes. Diabetes Care. 2004;27:s84-s87.
- 40. Lutty GA. Effects of diabetes on the eye. IOVS. 2013;54:ORSF81-ORSF87.
- 41. Kaštelan S, et al. Obesity and retinopathy in diabetes. J Mol Genet Med. 2014;S1:020.
- 42. Nwanyanwu KH, et al. Beyond HbA 1c environmental risk factors for diabetic retinopathy. J Clin Exp Ophthalmol. 2015;6:405.
- 43. Xie J, et al. Relative importance and contribiton of risk factors for diabetic retinopathy and macular edema. J Diabetes Metab. 2014;5:337.
- 44. Kumar TN, et al. Diabetic eye screening in multi ethnic population of Malaysia: epidemiological risk factors for development of diabetic retinopathy. Int J Res Med Sci. 2014;2:1045-1049.
- 45. Gupta S and Karandikar AM. Diagnosis of diabetic retinopathy using machine learning. J Res Development. 2015;3:127.
- 46. Bandello F, et al. Non-proliferative diabetic retinopathy. Clinical Strategies in the Management of Diabetic Retinopathy. 2014;19-63.
- 47. Pareja-Ríos A, et al. Management of diabetic macular edema in current clinical practice: A review. J Diabetes Metab. 2012;S3:004.
- 48. Lang GE. Diabetic macular edema. Ophthalmologica. 2012;227:21-29.
- 49. Semeraro F, et al. Erythropoietin and diabetic retinopathy. J Diabetes Metab. 2013;4:283.
- 50. Manjunathan R, et al. Evaluation of antiangiogenic potential of mmp 2 antisense oligonucleotide for the management of proliferative diabetic retinopathy using chicken chorioallantoic membrane. Mol Biol. 2016;5:148.
- 51. Shah, et al. Proliferative diabetic retinopathy. 2004;44:69-84.
- 52. Faghihi H, et al. Intravitreal triamcinolone injection as an adjuvant to standard laser therapy in management of proliferative diabetic retinopathy. J Clinic Experiment Ophthalmol. 2011;2:149.
- 53. Reyns GE, et al. Selection strategy of in vivo models for ophthalmic drug development in diabetic retinopathy. J Mol Genet Med. 2016;10:202.
- 54. Mohamed R and El-Remessy A. Imbalance of the nerve growth factor and its precursor: implication in diabetic retinopathy. J Clin Exp Ophthalmol. 2015;6:483.
- 55. Carle MV, et al. Patients with advanced diabetic retinopathy's understanding of diabetes mellitus and their diabetic eye disease: a survey of 100 patients currently undergoing treatment for diabetic retinopathy in a large retinal practice. J Clin Exp Ophthalmol. 2015;6:40.
- 56. Xu Q, et al. Recent progress in genetic polymorphisms and diabetic retinopathy (DR) in type 1 diabetes mellitus (t1dm). Endocrinol Metab Synd. 2014;3:131.
- 57. Alwadani F. The role and prevalence of polyol pathway and oxidative stress markers as risk factors for diabetic cataract in adult type-i diabetic and diabetic cataract saudi patients. J Clin Exp Ophthalmol. 2016;7:558.
- 58. Varma SD, et al. Diabetic cataracts and flavonoids. Science. 1977;195:205-206.
- 59. Rathi SS, et al. Prevention of experimental diabetic cataract by Indian Ayurvedic plant extracts. Phytother Res. 2002;16:774-777.
- 60. Bikbova G, et al. Diabetes mellitus and retinal vein occlusion as risk factors for open angle glaucoma and neuroprotective therapies for retinal ganglion cell neuropathy. J Clinic Experiment Ophthalmol. 2012;S3:002.
- 61. Ellisa JD, et al. Glaucoma incidence in an unselected cohort of diabetic patients: is diabetes mellitus a risk factor for glaucoma? Br J Ophthalmol. 2000;84:1218-1224.
- 62. Paula JS, et al. Long-term intraocular pressure control in a case of neovascular glaucoma treated with repeated intravitreal bevacizumab injections. J Clinic Experiment Ophthalmol. 2011;2:170.
- 63. Bonovas S, et al. Diabetes mellitus as a risk factor for primary open-angle glaucoma: a meta-analysis. Diabetic Medicine. 2004;21:609-614.
- 64. Balabathula P, et al. Combination therapy in glaucoma treatment. Clin Exp Pharmacol. 2013;3: 129.
- 65. Al Saikhan FI. Current options for treatment of glaucoma in pediatrics. Gen Med. 2015;3:1000189.
- 66. Cornish KS, et al. Intravitreal bevacizumab and augmented trabeculectomy for neovascular glaucoma in young diabetic patients. Eye. 2009;23:979-981.
- 67. SHAN LIN. Diabetes and primary open angle glaucoma. Br J Ophthalmol. 2000;84:1216.
- 68. Negi A, et al. An overview of the eye in diabetes. J R Soc Med. 2003;96:266-272.
- 69. Gavin S. Tan, et al. Diabetes, metabolic abnormalities and glaucoma. Arch Ophthalmol. 2009;127:1354-1361.
- 70. Katz J and Sommer A. Risk factors for primary open angle glaucoma. Am J Prev Med. 1988;4:110-114.
- 71. Nakamura M, et al. Diabetes mellitus as a risk factor for glaucomatous optic neuropathy. Ophthalmologica. 2005;219:1-10

- 72. Falavarjani KG, et al. Therapeutic effect of bevacizumab injected into the silicone oil in eyes with neovascular glaucoma after vitrectomy for advanced diabetic retinopathy. Eye. 2010;24:717-719.
- 73. T Oshitari, et al. Mitochondria and caspase dependent cell death pathway involved in neuronal degeneration in diabetic retinopathy. Br J Ophthalmol. 2008;92:552-556.
- 74. Klein R, et al. The NEI-VFQ-25 in people with long-term type 1 diabetes mellitus. Arch Ophthalmol. 2001;119:733-740.
- 75. Zhou M, et al. Diabetes mellitus as a risk factor for open-angle glaucoma: a systematic review and metaanalysis. Plos One. 2014;9:e102972.
- 76. Greenstein VC, et al. Chromatic and luminance sensitivity in diabetes and glaucoma. J Opt Soc Am A Opt Image Sci Vis. 1993;10:1785-1791.
- 77. Jeong HS, et al. Pars plana ahmed implantation combined with 23-gauge vitrectomy for refractory neovascular glaucoma in diabetic retinopathy. Korean J Ophthalmol. 2012;26:92-96.
- 78. Marilyn James, et al. Cost effectiveness analysis of screening for sight threatening diabetic eye disease. BMJ. 2000;320:1627.
- 79. Joanne WY, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35:556-564.
- 80. Leibowitz HM, et al. The framingham eye study monograph: an ophthalmological and epidemiological study of cataract, glaucoma, diabetic retinopathy, macular degeneration, and visual acuity in a general population of 2631 adults, 1973-1975. Surv Ophthalmol 1980;24:335-610.
- 81. Spranger J, et al. TNF-alpha level in the vitreous body. Increase in neovascular eye diseases and proliferative diabetic retinopathy. Medizinische Klinik 1983;90:134-137.
- 82. Wong TY, et al. The epidemiology of age related eye diseases in Asia. Br J Ophthalmol 2006;90:506-511.
- 83. Jose E. Pulido, et al. A role for excitatory amino acids in diabetic eye disease. Exp Diabetes Res 2007;
- 84. Gariano RF, et al. Retinal angiogenesis in development and disease. Nature. 2004;438:960-966.
- 85. Engerman R, et al. Relationship of microvascular disease in diabetes to metabolic control. Diabetes. 1977;26: 760-769.
- 86. Gohdes DM, et al. Age-related eye diseases: an emerging challenge for public health professionals. Prev Chronic Dis. 2005;2:1-6.
- 87. Pe'er J, et al. Hypoxia-induced expression of vascular endothelial growth factor by retinal cells is a common factor in neovascularizing ocular diseases. Laboratory Investigation; a Journal of Technical Methods and Pathology 1995;72:638-645.
- 88. Penas S, et al. Chronicity and recurrence as prognostic factors in central serous chorioretinopathy after half-dose photodynamic therapy. J Clin Exp Ophthalmol. 2016;7:594.
- 89. Tikmani SS, et al. Frequency of retinopathy of prematurity in a tertiary care hospital. J Preg Child Health. 2015;3:285.
- 90. Venkatesh P, et al. Results of investigations for tuberculosis in patients with serpiginous like choroiditis in comparison to patients with central serous retinopathy and non-serpiginous uveitis. J Med Diagn Meth 2016;5:194.
- 91. Man X, et al. Effects of cataract extraction on the outcomes of automated perimetry and retinal nerve fiber layer thickness measurements by optical coherence tomography in primary angle closure glaucoma. J Clin Exp Ophthalmol. 2016; 7:623.
- 92. Kwun ECCTS, et al. Virtual glaucoma clinic: do consultants agree on management outcomes? J Clin Exp Ophthalmol. 2016;7:585.
- 93. Shi H, et al. Correlations of primary angle closure glaucoma susceptibility gene and ocular biometry. J Clin Exp Ophthalmol. 2016;7:559.
- 94. Hasnain SS. Pathogenesis of orderly loss of nerve fibers in glaucoma. Optom open access 2016;1:110.
- 95. Jeganathan VSE, et al. Challenges in the management of glaucoma in a patient with severe ocular surface disease: A case report. Optom open access. 2016;1:111.
- 96. Carlotta F, et al. Changes in BDNF and MAPK signaling pathways in experimental glaucoma. J Clin Exp Ophthalmol. 2016;7:530.
- 97. Toyos MM, et al. Clinical outcomes of micropulsed transcleral cyclophotocoagulation in moderate to severe glaucoma. J Clin Exp Ophthalmol. 2016;7:620.

- 98. Grana ER, et al. Methotrexate as a Corticosteroid-Sparing Agent for Thyroid Eye Disease. J Clin Exp Ophthalmol. 2015;6:42.
- 99. Srilatha B. A Review on Age Related Eye Diseases and their Preventive Measures. J Clinic Experiment Ophthalmol. 2011;2:196.

100.Manzoor S, et al. Blue Eye Disease in Dog with Hyperthermia at Pindi Bhattian District Hafizabad, Pakistan. J Antivir Antiretrovir. 2014;6:84-85.