International Journal of Medical Science in Clinical Research and Review
Online ISSN: 2581-8945
Available Online at http://www.ijmscrr.in Volume 05|Issue 06 (November-December)|2022 Page: 1097-1110

Review Paper

IMPACT OF CARDIOVASCULAR AND METABOLIC DISORDER IN DEVELOPMENT OF CATARACT

Authors:

Ragni Kumari1, Pragti Garg2 Jamshed Ali3*, Vibha Kumari4, Paramita Deb5, Nitika Kumari6, Momin Khan7, Zeba Hayat8, Alina Malik9, Sunil Kumar Gupta10

1. *Ph. D. Scholar, Amity Institute of Public Health, Amity University, Noida India*
2. *Professor, AIIMS, Raebareli, Uttar Pradesh*
3. *Assistant Professor, Department of Optometry, Era University, Lucknow*
4. *Assistant Professor, Department of Paramedical Sciences, Jamia Hamdard New Delhi India*
5. *Assistant professor, Department of Allied health sciences, Brainwear University, Barasat, Kolkata*
6. *Clinical Instructor, School of Nursing Sciences and Allied Health, Jamia Hamdard, New Delhi*
7. *Clinical Instructor, School of Nursing Sciences and Allied Health, Jamia Hamdard, New Delhi*
8. *School of Nursing Sciences and Allied Health, Jamia Hamdard, New Delhi*
9. *School of Nursing Sciences and Allied Health, Jamia Hamdard, New Delhi*
10. *Assistant Professor, Department of Optometry, Era University, Lucknow.*

Corresponding Author:

Jamshed Ali, Assistant Professor, Department of Optometry,
Era University, Lucknow

Article Received: 15-10-2022 Revised: 04-11-2022 Accepted: 24-11-2022

ABSTRACT

Diabetes mellitus (DM) is an ailment of insufficient manipulate of blood tiers of glucose. It has many subclassifications, which include kind 1, kind 2, maturity-onset diabetes of the younger (MODY), gestational diabetes, neonatal diabetes, and steroid-induced diabetes. Type 1 and two DM are the major subtypes, every with exclusive pathophysiology, presentation, and management, however each have a achievable for hyperglycemia. Definition of hypertension given by way of Seventh Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure in 2003, systolic blood stress (SBP) increased than a hundred- and forty-mm Hg and/or diastolic blood stress (DBP) higher than ninety mm Hg. The 2014 JNC Report centered on hypertension therapy objectives with dichotomized advice to provoke pharmacological remedy relying on a cut-off age of 60 yrs. to decrease blood stress to <150/90 mm hg. A cataract is a main purpose of blindness in developed and growing countries. Various cardiovascular and metabolic stipulations have been proposed as feasible contributors to the etiopathology of the disease, such as diabetes mellitus (DM), arterial hypertension, and dyslipidemia, on the grounds that sufficient manipulate of these parameters have been proven to be helpful to forestall cataract improvement and minimize its development rate. The incidence and development price of cataract is observed to be improved in diabetic patients, who are additionally at a greater threat of intra- and postoperative problems related to cataract surgical procedure in contrast to non-diabetics.

Keywords: cataract; arterial hypertension; diabetes mellitus; dyslipidemia.

INTRODUCTION:

A cataract is a primary motive of blindness in developed and growing countries. Various cardiovascular and metabolic prerequisites have been proposed as viable contributors to the etiopathology of the disease, which include diabetes mellitus (DM), arterial hypertension, and dyslipidemia, due to the fact sufficient manage of these parameters have been proven to be beneficial to forestall cataract improvement and reduce its development rate1,2. The incidence and development charge of cataract is determined to be accelerated in diabetic patients. A current learn about proven that arterial hypertension will increase the chance of cataract, particularly the posterior subcapsular subtype three A learn about executed in aged Australians published no tremendous affiliation between baseline serum lipids or fibrinogen four Another learn about completed on Chinese topics additionally did now not locate any hyperlink of dyslipidemia to nuclear, cortical, or

subcapsular cataract 5. Dyslipidemia has been in a roundabout way related with cataract development, because statin use in regular papulation seems to be related with a decrease hazard of nuclear cataract formation6. A find out about of 2794 Malay adults determined that cataract occurrence extended with greater quartiles of blood glucose, systolic blood stress (BP), and metabolic syndrome aspects whilst excessive BP was once related with all three cataract types. Diabetes used to be related with cortical and posterior subcapsular (PSC), and low high-density lipoprotein (HDL), excessive physique mass index (BMI), and metabolic syndrome had been related with cortical cataract 7. The presence of each excessive BP and diabetes used to be related with a four-fold make bigger in having cataract8. Available guidelines and reports from various professional forms reflect different thresholds for hypertension classification and managements,[9-11] indicating uncertainty and a need for worldwide synchronization[12]. The Seventh Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure in 2003 defined hypertension as systolic blood pressure (SBP) greater than 140 mm Hg and/or diastolic blood pressure (DBP) greater than 90 mm Hg. The 2014 JNC Report focused on hypertension treatment targets with dichotomized recommendation to initiate pharmacological treatment depending on a cut-off age 60 years to lower blood pressure to <150/90 mm hg[10]. The updated 2016 National Institute for Health and Care Excellence (NICE) Guidelines characterized Stage 1, Stage 2, and severe hypertension (180/ 110 mm Hg)[11]. Recently, the Association of Anesthetists of Great Britain and Ireland (AAGBI) and British Hypertension Society (BHS) produced joint guidelines8 for simplified anesthesia management and categorized hypertension into 4 grades:

Grade 1 (SBP 140–159 mm Hg and/or DBP 90–99 mm Hg)

Grade 2 (SBP 160–179 mm Hg and/or DBP 100–109 mm Hg)

Grade 3 (SBP 180–209 mm Hg and/or DBP 110–119 mm Hg)

Grade 4 (SBP 210 mm Hg and/or DBP 120 mm Hg).

Recent NICE guidelines[7] iterates the important role of hypertension as a preventable cause of premature morbidity and mortality. A blood stress threshold of systolic one hundred eighty mm Hg and diastolic one hundred ten mm Hg is viewed unsafe and heralds an affiliation with goal organ damage. It is argued that the grades of hypertension may no longer be relevant to the perioperative setting. Perioperative hypertension can fluctuate in mechanism, therapy responsiveness, as nicely as penalties relying on affected person traits and invasiveness of surgical procedure. This leads to controversies with regards to perioperative goals for blood pressure[10].

DIABETES MELLITUS

Diabetes mellitus (DM) is a metabolic disease, involving inappropriately improved blood glucose levels. DM has a number of categories, which includes kind 1, kind 2, maturity-onset diabetes of the younger (MODY), gestational diabetes, neonatal diabetes, and secondary motives due to endocrinopathies, steroid use, etc. The fundamental subtypes of DM are Type 1 diabetes mellitus (T1DM) and Type two diabetes mellitus (T2DM), which classically end result from faulty insulin secretion (T1DM) and/or motion (T2DM). T1DM offers in teens or adolescents, whilst T2DM is concept to influence middle-aged and older adults who have extended hyperglycemia due to negative lifestyle and dietary choices. The pathogenesis for T1DM and T2DM is appreciably different, and consequently every kind has several etiologies, presentations, and treatments. Unfortunately, even today, diabetes is one of the most frequent persistent ailments in the United States and worldwide. In the US, it stays as the seventh main reason of death. In the islets of Langerhans in the pancreas, there are two most important subclasses of endocrine cells: insulin-producing beta cells and glucagon secreting alpha cells. Beta and alpha cells are always altering their ranges of hormone secretions primarily based on the glucose environment. Without the stability between insulin and glucagon, the glucose degrees come to be inappropriately skewed. In the case of DM, insulin is both absent and/or has impaired motion (insulin resistance), and for that reason leads to hyperglycemia. TIDM is characterized by means of the destruction of beta cells in the pancreas, usually secondary to an autoimmune process. The outcomes is the absolute destruction of beta cells, and consequentially, insulin is absent or extraordinarily low. T2DM includes a greater insidious onset the place an imbalance between insulin tiers and insulin sensitivity reasons a purposeful deficit of insulin. insulin resistance is multifactorial however commonly develops from weight problems and aging. Globally, 1 in eleven adults has DM (90% having T2DM). The onset of T1DM regularly will increase from start and peaks at a while four to 6 years and then once more from 10 to 14 years13. Approximately 45% of teens current earlier than age ten years[14]. The occurrence in human beings underneath age 20 is about 2.3 per a thousand While most autoimmune illnesses are greater frequent in females, there are no obvious gender variations in the incidence of childhood T1DM. In some populations, such as in older adult males of European starting place (over thirteen years), they might also be

greater possibly to enhance T1DM in contrast to ladies (3:2 male to woman ratio)[15]. The incidence of T1DM has been growing worldwide. In Europe, Australia, and the Middle East, costs are rising by using 2% to 5% annually[16-18]. In the United States, T1DM fees rose in most age and ethnic organizations by using about 2% yearly, and fees are greater in Hispanic youth[19]. The specific cause for this sample stays unknown. However, some metrics, such as the United States Military Health System information repository, discovered plateauing over 2007 to 2012 with a occurrence of 1.5 per a thousand and incidence of 20.7 to 21.3 per a thousand[20].

HYPERTENSION AND CATARACT:

Hypertension is regarded to motive elevation of inflammatory cytokines such as tumor necrosis factor-alpha (TNF-a), interleukin-6(IL-6)[21]. Besides, an elevation of C-reactive protein (CRP) degree has been detected when man or woman blood stress raises[22,23]. Considering that cataract is intently associated to severe systemic irritation [23,24], hypertension is consequently concerned in the pathological pathway of cataract improvement thru an inflammatory mechanism. Beyond that, Lee et al[25] suggested that hypertension ought to set off conformation shape alteration of proteins in lens capsules, thereby exacerbating the cataract formation. Although countless achievable mechanisms have been proposed based totally on laboratory results, the conclusions from epidemiologic research stay inconsistent. It is necessary to decide the results of hypertension on cataract risk, due to growing hypertension morbidity. Many pupils preserve the opinion that hypertension may be linked to cataract by using different primary aspects of Metabolic Syndrome (pathoglycemia, weight problems and dyslipidemia)[26,27].

As per Cumming et al.[28] full-size affiliation between cataract threat and potassium-sparing diuretics, which is biologically plausible, as this sort of anti-hypertension medicinal drugs can disturb the electrolyte stability throughout the lens fiber membrane[29]. Several different research indicated that publicity to beta-blockers can additionally promote cataract formation[30,31], which is supported via experimental research demonstrating that the use of beta-blockers ought to bring up ranges of intracellular cyclic adenosine monophosphate, thereby ensuing in the amendment of lens proteins [30, 32, 33]. It is well worth noting that protecting roles towards cataract improvement have been additionally found. Klein et al.[31, 34] additionally confirmed that human beings taking thiazide diuretics or angiotensin-converting enzyme inhibitors (ACEI) have a lowered nuclear cataract risk. It ought to be mentioned that the outcomes of anti-hypertension tablets and hypertension on cataracts may be conflated with the aid of every other. Several pathophysiological pathways might also be beneficial to recognize the mechanisms of cataract improvement promoted by way of hypertension. Bautista et al.[21,22] have determined that expanded plasma tiers of IL-6 and TNF-a seemed in persons with hypertension, which are intently associated to extreme systemic irritation with more desirable degrees of C-reactive protein and promote the improvement of cataract [23,24]. Hypertension was once stated to purpose conformational adjustments in lens tablet 25, thereby interfering with the transportation of potassium ion in lens epithelial cells. And this pathological procedure in the end leads to a sickness of lens short-circuit contemporary that performs a defensive function towards cataract formation [35, 36]. Ornek et al.[37] confirmed that hypertensive sufferers would have a extensively greater degree of nitrite in their cataractous lenses; the ensuing nitric oxide performs an necessary function in the pathogenesis of human cataract. One greater find out about completed by means of Johnson et al.[38] mentioned a novel gene mutation associated to each cataract and hypertension, which may also be useful in discovering the plausible fundamentals of genetics. outcomes of anti-hypertension tablets and cardiovascular disease on cataracts is also conflated with the help of each different. many pathophysiological pathways may additionally be helpful to acknowledge the mechanisms of cataract improvement promoted by manner of cardiovascular disease. Bautista et al.21,22 have determined that expanded plasma tiers of IL-6 and TNF-a appeared in persons with cardiovascular disease, that square measure intently associated to extreme general irritation with a lot of fascinating degrees of serum globulin and promote the advance of cataract twenty three,24. cardiovascular disease was once declared to purpose conformational changes in lens pill twenty five, thereby busybodied with the transportation of K particle in lens animal tissue cells. And this pathological procedure within the finish results in a illness of lens short-circuit modern that performs a defensive perform towards cataract formation thirty five, 36. Ornek et al. thirty seven confirmed that hypertensive sufferers would have a extensively bigger degree of chemical group within their cataractous lenses; the following gas performs associate degree necessary perform in the pathological process of human cataract. One bigger resolve concerning completed by suggests that of Johnson et al.38 mentioned a completely unique mutation associated to every cataract and cardiovascular disease, which can even be helpful in discovering the plausible fundamentals of biology. According to Sabanayagam et al. 39, individuals with severe cardiovascular disease have the next risk of cataract than those with delicate cardiovascular disease. many studies

indicated a linear correlation between pressure and cataract risk [40,41], that is in unison with our results. length of cardiovascular disease is additionally a crucial issue, indicating a relationship between longer length and enhanced cataract risk [42].

DIABETES MELLITUS AND CATARACT:

The protein simple sugar reductase (AR) catalyzes the reduction of aldohexose to sorbitol through the polyol pathway, a method connected to the event of diabetic cataract. in depth analysis has centered on the central role of the AR pathway because the initiating because the consider diabetic cataract formation. it's been shown that the living thing accumulation of sorbitol results in diffusion changes leading to hydropic lens fibers that degenerate and kind sugar cataracts [43,44]. within the lens, sorbitol is made quicker than it's reborn to laevulose by the protein sorbitol dehydrogenase. additionally, the polar character of sorbitol prevents its living thing removal through diffusion. The enhanced accumulation of sorbitol creates a hyperosmotic result that ends up in associate degree infusion of fluid to countervail the diffusion gradient. Animal studies have shown that the living thing accumulation of polyols results in a collapse and physical change of lens fibers, that ultimately ends up in the formation of lens opacities[42,43]. These findings have light-emitting diode to the "Osmotic Hypothesis" of sugar cataract formation, action that the living thing increase of fluid in response to AR-mediated accumulation of polyols ends up in lens swelling related to complicated organic chemistry changes ultimately resulting in cataract formation [43,44,45]. moreover, studies have shown that diffusion stress within the lens caused by sorbitol accumulation [46.] induces caspase-mediated cell death in lens animal tissue cells (LEC) resulting in the event of cataract [48]. Transgenic hyperglycemic mice overexpressing AR and phospholipase D (PLD) genes became vulnerable to develop diabetic cataract in distinction to diabetic mice overexpressing PLD alone, associate degree protein with key functions within the osmoregulation of the lens [49]. These findings show that impairments within the osmoregulation might render the lens vulnerable to even little will increase of AR mediate diffusion stress, probably resulting in progressive cataract formation. The role of diffusion stress is especially vital for the fast cataract formation in young patients with sort one polygenic disorder mellitus[50,51] thanks to the in depth swelling of plant tissue lens fibers[51]. A study performed by Oishi et al. investigated whether AR is connected to the event of adult diabetic cataracts[52]. Levels of AR in red blood cells of patients underneath sixty years ancient with a brief length of polygenic disorder were absolutely related to with the prevalence of posterior subcapsular cataracts. A correlational statistic has been shown in diabetic patients between the quantity of AR in erythrocytes and therefore the density of lens animal tissue cells, that square measure acknowledged to be slashed in diabetics compared to nondiabetics suggesting a possible role of AR during this pathomechanism[53]. The polyol pathway has been represented because the primary negotiator of diabetes-induced aerophilous stress within the lens[54]. diffusion stress caused by the buildup of sorbitol induces stress within the endoplasmic reticulum (ER), the principal web site of macromolecule synthesis, ultimately resulting in the generation of free radicals. ER stress may additionally result from fluctuations of aldohexose levels initiating associate degree flat macromolecule response (UPR) that generates reactive chemical element species (ROS) and causes aerophilous stress injury to lens fibers[55]. There is square measure various recent publications that describe aerophilous stress injury to lens fibers by radical scavengers in diabetics. However, there's no proof that these free radicals initiate the method of cataract formation however rather accelerate and worsen its development. peroxide (H2O2) is elevated within the body fluid of diabetics and induces the generation of radical radicals (OH–) once getting into the lens through processes represented as Fenton reactions [56]. The radical gas (NO•), another issue elevated within the diabetic lens fifty-seven and within the body fluid fifty eight, might cause associate degree enhanced peroxynitrite formation, that successively induces cell injury thanks to its oxidizing properties. moreover, enhanced aldohexose levels within the body fluid might induce glycation of lens proteins, a method leading to the generation of superoxide radicals (O2 −) and within the formation of advanced glycation end products (AGE) fifty-nine. By interaction ancient with cell surface receptors like receptor for advanced glycation end products within the epithelial tissue of the lens additional O2 − and H2O2 square measure generated sixty. additionally, to enhanced levels of free radicals, diabetic lenses show associate degree impaired inhibitor capability, increasing their condition to aerophilous stress. The loss of inhibitors is exacerbated by glycation and inactivation of lens antioxidant enzymes like enzyme [61]. Copper-zink enzyme one (SOD1) is that the most dominant enzyme isoenzyme within the lens [62], that is vital for the degradation of superoxide radicals (O2 −) into peroxide (H2O2) and chemical element [63]. Data from the Framingham and different eye research point out a three to fourfold expanded incidence of cataract in sufferers with diabetes underneath the age of 65, and up to a twofold extra occurrence in sufferers above 6567, 70. The threat is multiplied in sufferers with longer period of diabetes and in these with negative metabolic control. A

unique kind of cataract recognized as snowflake cataract is considered predominantly in younger kind 1 diabetic sufferers and tends to growth rapidly. Cataracts can also be reversible in younger diabetics with enhancement in metabolic control. The most often considered kind of cataract in diabetics is the age-related or senile variety, which tends to manifest in the past and progresses greater unexpectedly than in nondiabetics. The Wisconsin Epidemiologic Study of Diabetic Retinopathy investigated the incidence of cataract extraction in humans with diabetes. Furthermore, extra elements related with greater hazard of cataract surgical treatment have been determined. The 10-year cumulative incidence of cataract surgical procedure was once 8.3% in sufferers struggling from kind 1 diabetes and 24.9% in these from kind two diabetes. Predictors of cataract surgical procedure blanketed age, severity of diabetic retinopathy and proteinuria in kind 1 diabetics whereas age and use of insulin have been related with extended danger in type two diabetics seventy one A follow-up examination of the Beaver Dam Eye Study cohort, consisting of 3684 members forty three years of age and older, carried out 5 years after the baseline comparison confirmed an affiliation between diabetes mellitus and cataract formation[72]. In the study, the incidence and development of cortical and posterior subcapsular cataract used to be related with diabetes. In addition, increased ranges of glycated hemoglobin have been proven to be related with an extended chance of nuclear and cortical cataracts. In a similarly evaluation of the Beaver Dam Eye find out about the incidence of cataract improvement was once studied in a populace of 4926 adults seventy-three Diabetic sufferers had been extra possibly to strengthen cortical lens opacities and confirmed a greater price of preceding cataract surgical treatment than nondiabetics. The evaluation of the statistics proved that longer period of diabetes used to be related with an expanded frequency of cortical cataract as properly as an accelerated frequency of cataract surgery. The intention of the population-based cross-sectional Blue Mountains Eye Study used to be to study the relationship between nuclear, cortical, and posterior subcapsular cataract in 3654 individuals between the years 1992 to 199474. The find out about supported the preceding findings of the damaging outcomes of diabetes on the lens. Posterior subcapsular cataract used to be proven to be statistically extensively related with diabetes. However, in distinction to the Beaver Dam Eye Study, nuclear cataract confirmed a weak, no longer statistically significant, affiliation after adjusting for different regarded cataract danger factors. A population-based cohort learn about of 2335 humans older than forty-nine years of age performed in the Blue Mountains area of Australia investigated associations between diabetes and the 5-year incidence of cataract. The outcomes of this longitudinal find out about carried out by way of the identical crew of investigators as the Blue Mountains Eye Study verified a twofold greater 5-year incidence of cortical cataract in individuals with impaired fasting glucose. Statistically tremendous associations have been proven between incident posterior subcapsular cataract and the range of newly identified diabetic patients75. The Visual Impairment Project evaluated threat elements for the improvement of cataracts in Australians. The find out about confirmed that diabetes mellitus was once an impartial threat aspect for posterior subcapsular cataract when existing for extra than 5 years76. A purpose of the Barbados Eye find out about was once to consider the relationship between diabetes and lens opacities amongst 4314 black participants[77]. The authors discovered that diabetes records (18% prevalence) used to be associated to all lens changes, at youthful ages. There is a opportunity that hypertension may additionally exacerbate the terrible have an effect on of diabetes mellitus in the development of diabetic cataract. Initially in diabetes mellitus, the excessive stage of glucose in the aqueous humor diffuses into the lens and is metabolized to superior glycation cease merchandise which accumulate inside the lens and play an essential function in cataract formation[78]. Intraocular strain and systemic blood stress have been observed to correlate. [79] intraocular stresses may additionally lead to quicker accumulation of glucose inside the lens from the aqueous humor due to the accelerated stress gradient, hence accelerating cataract formation in instances of diabetes mellitus with comorbid hypertension. Regarding dyslipidemia, the preliminary findings of statins related with cataract genesis are reversed in scientific exercise considering a current meta-analysis has discovered a clinically applicable defensive impact of statins in stopping cataracts[80].

CONCLUSION:

diabetes mellitus, hypertension, and dyslipidemia have been the primary hazard elements for cataract development. More lookup might also be warranted in the blended impact of hypertension and diabetes mellitus in the etiopathology of cataract. Early detection and prevention of hypertension, a cardiovascular situation can extend the development of cataract.

REFERENCES:

1. Adler, A.I.; Stratton, I.M.; Neil, H.A.W.; Yudkin, J.S.; Matthews, D.R.; Cull, C.A.; Wright, A.D.; Turner, R.C.; Holman, R.R.

Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (ukpds 36): Prospective observational study. BMJ 2000, 321, 412–419. [CrossRef] [PubMed]

2. Holman, R.R.; Paul, S.K.; Bethel, M.A.; Neil, H.A.W.; Matthews, D.R. Long-term follow-up after tight control of blood pressure in type 2 diabetes. N. Engl. J. Med. 2008, 359, 1565–1576. [CrossRef] [PubMed]
3. Yu, X.; Lyu, D.; Dong, X.; He, J.; Yao, K. Hypertension, and risk of cataract: A meta-analysis. PLoS ONE 2014, 9, e114012. [CrossRef] [PubMed]
4. Tan, J.S.; Wang, J.J.; Mitchell, P. Influence of diabetes and cardiovascular disease on the long-term incidence of cataract: The blue mountains eye study. Ophthalmic Epidemiol. 2008, 15, 317–327. [CrossRef] [PubMed]
5. Wang, S.; Xu, L.; Jonas, J.B.; Wang, Y.X.; You, Q.S.; Yang, H. Dyslipidemia, and eye diseases in the adult chinese population: The Beijing eye study. PLoS ONE 2012, 7, e26871. [CrossRef]
6. Klein, B.E.; Klein, R.; Lee, K.E.; Grady, L.M. Statin use and incident nuclear cataract. JAMA 2006, 295, 2752–2758. [CrossRef]
7. Sabanayagam, C.; Wang, J.J.; Mitchell, P.; Tan, A.G.; Tai, E.S.; Aung, T.; Saw, S.-M.; Wong, T.Y. Metabolic syndrome components and age-related cataract: The singaporemalay eye study. Investig. Ophthalmol. Vis. Sci. 2011, 52, 2397–2404. [CrossRef]
8. Chylack, L.T.; Wolfe, J.K.; Singer, D.M.; Leske, M.C.; Bullimore, M.A.; Bailey, I.L.; Friend, J.; McCarthy, D.; Wu, S.-Y. The lens opacities classification system III. Arch. Ophthalmol. 1993, 111, 831–836. [CrossRef] [PubMed]
9. Beaney T, Schutte AE, Tomaszewski M, Ariti C, Burrell LM, Castillo RR, Charchar FJ, Damasceno A, Kruger R, Lackland DT, et al.. May Measurement Month 2017: an analysis of blood pressure screening results worldwide.**Lancet Glob Health**. 2018; 6:e736–e743.CrossrefMedlineGoogle Scholar
10. Hypertension in adults: diagnosis and management. NICE guideline [NG136].August

2019. https://www.nice.org.uk/guidance/ng136. Google Scholar

11. Nerenberg KA, Zarnke KB, Leung AA, Dasgupta K, Butalia S, McBrien K, Harris KC, Nakhla M, Cloutier L, Gelfer M. Hypertension Canada's 2018 guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults and children.**Can J Cardiol**. 2018; 34:506–525.CrossrefMedlineGoogle Scholar
12. Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, Horio T, Hoshide S, Ikeda S, Ishimitsu T, et al.. The Japanese Society of Hypertension Guidelines for the management of hypertension (JSH 2019).**Hypertens Res**. 2019; 42:1235–1481.CrossrefMedlineGoogle Scholar.
13. Felner EI, Klitz W, Ham M, Lazaro AM, Stastny P, Dupont B, White PC. Genetic interaction among three genomic regions creates distinct contributions to early- and late-onset type 1 diabetes mellitus. Pediatr Diabetes. 2005 Dec;6(4):213-20. [PubMed]
14. Writing Group for the SEARCH for Diabetes in Youth Study Group. Dabelea D, Bell RA, D'Agostino RB, Imperatore G, Johansen JM, Linder B, Liu LL, Loots B, Marcovina S, Mayer-Davis EJ, Pettitt DJ, Waitzfelder B. Incidence of diabetes in youth in the United States. JAMA. 2007 Jun 27;297(24):2716-24. [PubMed]
15. Gale EA, Gillespie KM. Diabetes and gender. Diabetologia. 2001 Jan;44(1):3-15. [PubMed]
16. Mamoulakis D, Galanakis E, Bicouvarakis S, Paraskakis E, Sbyrakis S. Epidemiology of childhood type I diabetes in Crete, 1990-2001. Acta Paediatr. 2003 Jun;92(6):737-9. [PubMed]
17. Tuomilehto J. The emerging global epidemic of type 1 diabetes. Curr Diab Rep. 2013 Dec;13(6):795-804. [PubMed]
18. Patterson CC, Dahlquist GG, Gyürüs E, Green A, Soltész G., EURODIAB Study Group. Incidence trends for childhood type 1 diabetes in Europe during 1989-2003 and predicted new cases 2005-20: a multicentre prospective registration study. Lancet. 2009 Jun 13;373(9680):2027-33. [PubMed]
19. Vehik K, Hamman RF, Lezotte D, Norris JM, Klingensmith G, Bloch C, Rewers M, Dabelea

D. Increasing incidence of type 1 diabetes in 0- to 17-year-old Colorado youth. Diabetes Care. 2007 Mar;30(3):503-9. [PubMed]

20. Rush T, McGeary M, Sicignano N, Buryk MA. A plateau in new onset type 1 diabetes: Incidence of pediatric diabetes in the United States Military Health System. Pediatr Diabetes. 2018 Aug;19(5):917-922. [PubMed]
21. Bautista LE, Vera LM, Arenas IA, Gamrara G (2005) Independent association between inflammatorymarkers (C-reactive protein, interleukin-6, and TNF-alpha) and essential hypertension. J HumHypertension 19: 149–154. doi: 10.1038/sj.jhh.1001785.
22. Ridker PM, Buring JE, Cook NR, Rifai N (2003) C-reactive protein, the metabolic syndrome, and risk ofincident cardiovascular events: an 8-year follow-up of 14,719 initially healthy American women.Circulation 107: 391–397. doi: dx.doi.org/10.1161/01. CIR.0000055014.62083.05.
23. Schaumberg DA, Ridker PM, Glynn RJ, Christen WG, Dana MR, et al. (1999) High levels of plasma c-reactive protein and future risk of Age-Related Cataract. Ann Epidemiol 9: 166–171. doi: 10.1016/S1047-27 97(98)00049-0.
24. Klein BE, Klein R, Lee KE, Knudtson MD, Tsai MY (2006) Markers of inflammation, vascularendothelial dysfunction, and age-related cataract. Am J Ophthalmol 141: 116–122. doi: 10.1016/j.ajo.2005.08.021.
25. Lee SM, Lin SY, Li MJ, Liang RC (1997) Possible mechanism of exacerbating cataract formation incataractous human lens capsules induced by systemic hypertension or glaucoma. Ophthalmic Res 29:83–90. doi: 10.1159/000268001.
26. Schaumberg DA, Glynn RJ, Christen WG, Ajani UA, Sturmer T, et al. (2001) A prospective study ofblood pressure and risk of cataract in men. Ann Epidemiol 11: 104–110. doi: 10.1016/S1047-2797(00)00178-2.
27. Tan JS, Wang JJ, Mitchell P (2008) Influence of diabetes and cardiovascular disease on the long-termincidence of cataract: the Blue Mountains eye study. Ophthalmic Epidemiol 15: 317–327. doi: 10.1080/09286580802105806.
28. Cumming RG, Mitchell P (1998) Medications and cataract: the Blue Mountains Eye Study.

Ophthalmology 105: 1751–1758. doi: 10.1016/S0161-6420(98)99049-2.

29. Ye JJ, Zadunaisky JA (1992) Ca2+ /Na+ exchanger and Na+ K+ 2Cl- cotransporter in lens fiber plasma membrane vesicles. Exp Eye Res 55: 797–804. doi: 10.1016/0014-4835(92)90006-E.
30. Kanthan GL, Wang JJ, Rochtchina E, Mitchell P (2009) Use of antihypertensive medications and topical beta-blockers and the long-term incidence of cataract and cataract surgery. Br J Ophthalmol 93: 1210–1214. doi: 10.1136/bjo.2008.153379.
31. Klein BE, Klein R, Jensen SC, Linton KL (1995) Hypertension and lens opacities from the Beaver Dam Eye Study. Am J Ophthalmol 119: 640–646.
32. Ireland ME, Shanbom S (1991) Lens beta-adrenergic receptors. Functional coupling to adenylate cyclase and photoaffinity labeling. Invest Ophthalmol Vis Sci 32: 541–548.
33. Spector A, Chiesa R, Sredy J, Garner W (1985) cAMP-dependent phosphorylation of bovine lens alpha-crystalline. Proc Natl Acad Sci USA 82: 4712–4716. doi: 10.1073/pnas.82.14.4712.
34. Klein BE, Klein R, Lee KE, Danforth LG (2001) Drug use and five-year incidence of age-related cataracts. Ophthalmology 108: 1670–1674. doi: 10.1016/S0161-6420(01)00656-X.
35. Sagent CR, Cangiano JL, Caban GB, Marrero E, Maldonado MM (1987) Cataracts and hypertension in salt-sensitive rats: a possible ion transport defect Hypertension. 9: 304–308.
36. Sargent CR, Estape ES, Fernandez N, Irizarry JE, Cangiano JL, et al. (1996) Altered lens short-circuit current in adult cataract-prone dahl hypertensive rats. Hypertension 28: 440–443.
37. O¨ rnek K, Karel F, Buyukbingol Z (2003) May nitric oxide molecule have a role in the pathogenesis of human cataract? Exp Eye Res 76: 23–27.doi: 10.1016/S0014-4835(02)00268-3.
38. Johnson AC, Lee JW, Harmon AC, Morris Z, Wang XX, et al. (2013) A mutation in the start codon of ccrystallin D leads to nuclear cataracts in the Dahl SS/Jr-Ctr strain. Mamm Genome 24: 95–104. doi: 0.1007/s00335-013-9447-1
39. Sabanayagam C, Wang JJ, Mitcbell P, Tan AG, Tai ES, et al. (2011) Metabolic syndrome components and age-related cataract: the

Singapore Malay Eye Study. Invest Ophthalmol Vis Sci 52: 2397–2404. doi: 10.1167/iovs.10-6373.

40. Richter GM, Torres M, Choudhury F, Azen SP, Varma R (2013) Risk factors for cortical, nuclear, posterior subcapsular, and mixed lens opacities: The Los Angeles Latino Eye Study. Ophthalmology 119: 547–554. doi: 10.1016/j.ophtha.2012.05.001.
41. Screenivas V, Prabhakar A, Badrinath SS, Fernandes T, Roy IS, et al. (1999) A rural population based case-control study of senile cataract in India. J Epidemiol 9: 327–326. doi: 10.2188/jea.9.327.
42. Mukesh BN, Le A, Dimitrov PN, Ahmed S, Taylor HR, et al. (2006) Development of cataract and associated risk factors. Arch Ophthalmol 124: 79–85. doi: 10.1001/archopht.124.1.79
43. J. H. Kinoshita, S. Fukushi, P. Kador, and L. O. Merola, "Aldose reductase in diabetic complications of the eye," Metabolism, vol. 28, no. 4, pp. 462–469, 1979.
44. J. H. Kinoshita, "Mechanisms initiating cataract formation. Proctor lecture," Investigative Ophthalmology, vol. 13, no. 10, pp. 713–724, 1974.
45. J. H. Kinoshita, "Cataracts in galactosemia. The Jonas S. Friedenwald memorial lecture," Investigative Ophthalmology, vol. 4, no. 5, pp. 786–799, 1965.
46. P. F. Kador and J. H. Kinoshita, "Diabetic and galactosaemic cataracts," Ciba Foundation Symposium, vol. 106, pp. 110– 131, 1984.
47. S. K. Srivastava, K. V. Ramana, and A. Bhatnagar, "Role of aldose reductase and oxidative damage in diabetes and the consequent potential for therapeutic options," Endocrine Reviews, vol. 26, no. 3, pp. 380–392, 2005.
48. Y. Takamura, Y. Sugimoto, E. Kubo, Y. Takahashi, and Y. Akagi, "Immunohistochemical study of apoptosis of lens epithelial cells in human and diabetic rat cataracts," Japanese Journal of Ophthalmology, vol. 45, no. 6, pp. 559–563, 2001.
49. W.-C. Li, J. R. Kuszak, K. Dunn, et al., "Lens epithelial cell apoptosis appears to be a common cellular basis for non-congenital cataract development in humans and animals," Journal

of Cell Biology, vol. 130, no. 1, pp. 169–181, 1995.

50. P. Huang, Z. Jiang, S. Teng, et al., “Synergism between phospholipase D2 and sorbitol accumulation in diabetic cataract formation through modulation of Na,K-ATPase activity and osmotic stress,” Experimental Eye Research, vol. 83, no. 4, pp. 939–948, 2006.
51. M. E. Wilson Jr., A. V. Levin, R. H. Trivedi, et al., “Cataract associated with type-1 diabetes mellitus in the pediatric population,” Journal of AAPOS, vol. 11, no. 2, pp. 162–165, 2007. [18] M. B. Datiles III and P. F. Kador, “Type I diabetic cataract,” Archives of Ophthalmology, vol. 117, no. 2, pp. 284–285, 1999.
52. N. Oishi, S. Morikubo, Y. Takamura, et al., “Correlation between adult diabetic cataracts and red blood cell aldose reductase levels,” Investigative Ophthalmology and Visual Science, vol. 47, no. 5, pp. 2061–2064, 2006.
53. Y. Kumamoto, Y. Takamura, E. Kubo, S. Tsuzuki, and Y. Akagi, “Epithelial cell density in cataractous lenses of patients with diabetes: association with erythrocyte aldose reductase,” Experimental Eye Research, vol. 85, no. 3, pp. 393–399, 2007.
54. S. S. M. Chung, E. C. M. Ho, K. S. L. Lam, and S. K. Chung, “Contribution of polyol pathway to diabetesinduced oxidative stress,” Journal of the American Society of Nephrology, vol. 14, no. 3, pp. S233–S236, 2003.
55. M. L. Mulhern, C. J. Madson, A. Danford, K. Ikesugi, P. F. Kador, and T. Shinohara, “The unfolded protein response in lens epithelial cells from galactosemic rat lenses,” Investigative Ophthalmology and Visual Science, vol. 47, no. 9, pp. 3951– 3959, 2006.
56. A. J. Bron, J. Sparrow, N. A. P. Brown, J. J. Harding, and R. Blakytny, “The lens in diabetes,” Eye, vol. 7, no. 2, pp. 260– 275, 1993.
57. K. Ornek, F. Karel, and Z. B ¨ uy¨ ukbing ¨ ol, “May nitric oxide ¨ molecule have a role in the pathogenesis of human cataract?” Experimental Eye Research, vol. 76, no. 1, pp. 23–27, 2003.
58. S.-H. Chiou, C.-J. Chang, C.-K. Chou, W.-M. Hsu, J.-H. Liu, and C.-H. Chiang, “Increased nitric oxide levels in aqueous humor of diabetic

patients with neovascular glaucoma," Diabetes Care, vol. 22, no. 5, pp. 861–862, 1999.

59. A. W. Stitt, "The Maillard reaction in eye diseases," Annals of the New York Academy of Sciences, vol. 1043, pp. 582–597, 2005.
60. S.-B. Hong, K.-W. Lee, J. T. Handa, and C.-K. Joo, "Effect of advanced glycation end products on lens epithelial cells in vitro," Biochemical and Biophysical Research Communications, vol. 275, no. 1, pp. 53–59, 2000.
61. T. Ookawara, N. Kawamura, Y. Kitagawa, and N. Taniguchi, "Site-specific and random fragmentation of Cu,Znsuperoxide dismutase by glycation reaction. Implication of reactive oxygen species," Journal of Biological Chemistry, vol. 267, no. 26, pp. 18505–18510, 1992.
62. A. Behndig, K. Karlsson, B. O. Johansson, T. Brannstr ¨ om, ¨ and S. L. Marklund, "Superoxide dismutase isoenzymes in the normal and diseased human cornea," Investigative Ophthalmology and Visual Science, vol. 42, no. 10, pp. 2293– 2296, 2001.
63. J. M. McCord and I. Fridovich, "Superoxide dismutase. An enzymic function for erythrocuprein (hemocuprein)," Journal of Biological Chemistry, vol. 244, no. 22, pp. 6049– 6055, 1969.
64. A. Behndig, K. Karlsson, A. G. Reaume, M.-L. Sentman, and S. L. Marklund, "In vitro photochemical cataract in mice lacking copper-zinc superoxide dismutase," Free Radical Biology and Medicine, vol. 31, no. 6, pp. 738–744, 2001.
65. E. M. Olofsson, S. L. Marklund, K. Karlsson, T. Brannstr ¨ om, ¨ and A. Behndig, "In vitro glucose-induced cataract in copper-zinc superoxide dismutase null mice," Experimental Eye Research, vol. 81, no. 6, pp. 639–646, 2005.
66. E. M. Olofsson, S. L. Marklund, and A. Behndig, "Enhanced diabetes-induced cataract in copper-zinc superoxide dismutase-null mice," Investigative Ophthalmology & Visual Science, vol. 50, no. 6, pp. 2913–2918, 2009.
67. B. E. K. Klein, R. Klein, and S. E. Moss, "Prevalence of cataracts in a population-based study of persons with diabetes mellitus," Ophthalmology, vol. 92, no. 9, pp. 1191– 1196, 1985.

68. N. V. Nielsen and T. Vinding, “The prevalence of cataract in insulin-dependent and non-insulin-dependent-diabetes mellitus,” Acta Ophthalmologica, vol. 62, no. 4, pp. 595–602, 1984.
69. W. E. Benson, “Cataract surgery and diabetic retinopathy,” Current Opinion in Ophthalmology, vol. 3, no. 3, pp. 396–400, 1992.
70. F. Ederer, R. Hiller, and H. R. Taylor, “Senile lens changes and diabetes in two population studies,” American Journal of Ophthalmology, vol. 91, no. 3, pp. 381–395, 1981.
71. B. E. K. Klein, R. Klein, and S. E. Moss, “Incidence of cataract surgery in the Wisconsin epidemiologic study of diabetic retinopathy,” American Journal of Ophthalmology, vol. 119, no. 3, pp. 295–300, 1995.
72. B. E. K. Klein, R. Klein, and K. E. Lee, “Diabetes, cardiovascular disease, selected cardiovascular disease risk factors, and the 5-year incidence of age-related cataract and progression of lens opacities: the Beaver Dam Eye Study,” American Journal of Ophthalmology, vol. 126, no. 6, pp. 782–790, 1998.
73. B. E. Klein, R. Klein, Q. Wang, and S. E. Moss, “Older-onset diabetes and lens opacities. The Beaver Dam Eye Study,” Ophthalmic Epidemiology, vol. 2, no. 1, pp. 49–55, 1995.
74. N. Rowe, P. Mitchell, R. G. Cumming, and J. J. Wans, “Diabetes, fasting blood glucose and age-related cataract: the Blue Mountains Eye Study,” Ophthalmic Epidemiology, vol. 7, no. 2, pp. 103–114, 2000.
75. S. Saxena, P. Mitchell, and E. Rochtchina, “Five-year incidence of cataract in older persons with diabetes and prediabetes,” Ophthalmic Epidemiology, vol. 11, no. 4, pp. 271– 277, 2004.
76. B. N. Mukesh, A. Le, P. N. Dimitrov, S. Ahmed, H. R. Taylor, and C. A. McCarty, “Development of cataract and associated risk factors: the Visual Impairment Project,” Archives of Ophthalmology, vol. 124, no. 1, pp. 79–85, 2006.
77. M. C. Leske, S.-Y. Wu, A. Hennis, et al., “Diabetes, hypertension, and central obesity as cataract risk factors in a black population: the

Barbados Eye Study," Ophthalmology, vol. 106, no. 1, pp. 35–41, 1999.

78. Sayin, N.; Kara, N.; Pekel, G. Ocular complications of diabetes mellitus. World J. Diabetes 2015, 6, 489–499. [CrossRef] [PubMed]
79. Klein, B.E.K.; Klein, R.; Knudtson, M.D. Intraocular pressure and systemic blood pressure: Longitudinal perspective: The beaver dam eye study. Br. J. Ophthalmol. 2005, 89, 284–287. [CrossRef] [PubMed]
80. Kostis, J.B.; Dobrzynski, J.M. Prevention of cataracts by statins: A meta-analysis. J. Cardiovasc. Pharmacol. Ther. 2014, 19, 191–200. [CrossRef] [PubMed].