

ROLE OF GLUCOSE 6 PHOSPHATE DEHYDROGENASE (G6PD) IN DIABETIC CATARACT

ABSTRACT

Introduction: Diabetes mellitus and its complications are spreading with increased rate in Asian population especially in Pakistan. Uncontrolled diabetes can lead to different micro vascular complications. Cataract is one of the complications of diabetes which may lead to lens degenerative changes and visual impairment. G6PD plays a vital role in preventive measurements from cataract development in normal population.

Objectives: This Study was designed to estimate G6PD levels in diabetic without ocular manifestations & diabetic cataract population.

Methodology: This cross sectional comparative study was done at the Department of Biochemistry LUMHS Jamshoro in collaboration with the Diabetic clinic, Institute of Ophthalmology & Diagnostic Research Laboratory LUMHS Jamshoro. 100 diagnosed subjects of diabetes were selected by Non-Probability type of sample technique with consent of subjects and they were divided in to two groups Group A as control 50 diabetic subjects with out ocular manifestation while Group B as case study group contain 50 subjects of diabetes with cataract. The fasting blood glucose level was estimated by Hexokinase Method while G6PD level was measured by kit method on SD Biosensor while HbA1c(%) was estimated by TTAB methodology. The data was statistically analyzed by SPSS 21.

Results: The mean level of G6PD in Group A was 15.63 ± 2.45 u/Hb while in group B it was 9.01 ± 3.11 u/G HB. This result finally concluded that there was significantly (<0.05) decline of G6PD diabetic cataract as compared with diabetic without cataract.

Conclusion: This study concluded that there was significant decline in G6PD level in diabetic cataract. It is also concluded that the estimation of G6PD level in diabetic population will be beneficial to take early preventive measurements against diabetic vascular complications.

Key Words: Diabetes Mellitus, Diabetic Cataract, G6PD

Introduction

The Diabetes Mellitus is one of the leading cause of morbidity and mortality of Pakistani population.¹The Pakistan included in top ten countries of the world with leading diabetes mellitus as mortal and morbid clinical syndrome.²The International Diabetic Federation (IDF) estimated that more than 4 millions people are suffered with diabetes mellitus all over the world.³ The different pathological, metabolic and micro vascular disorder can occur as complications of diabetes mellitus.⁴ Uncontrolled and prolonged duration with diabetes can be one of the leading cause of visual impairment and ocular complications like diabetic cataract, diabetic retinopathy etc.^{5,6} Visual impairment is one of the complaint of diabetic cataract.⁷ The diabetic patients are 5 to 7 times more prone to development of cataract as compared with non diabetic population.⁸ The incidence of diabetic cataract rising all over the world due to elevated prevalence of diabetes mellitus all over the world. Diabetic cataract is directly proportional with the duration of diabetes mellitus and poor glycemic control.^{6,9} The oxidative injury plays vital role in development of cataract in diabetic population.¹⁰ Glucose 6 Phosphate Dehydrogenase (G6PD) enzyme is the first enzyme of Hexose Monophosphate (HMP) shunt which produce redox pair potential which is preventable measurement against oxidative injury.^{11,12} So maintaining the normal concentration of G6PD is the key factor for prevention or delay development of cataract in diabetic population.¹³

In this study we evaluate the concentration or level of G6PD in the patients of Diabetic cataract.

Methodology:

This cross sectional comparative study was carried out at the Department of Biochemistry of LUMHS Jamshoro with collaboration of diabetic clinic LUMHS, Institute of Ophthalmology UMHS and Diagnostic & Research Laboratory LUMHS Jamshoro Sindh. Total 100 diabetic patients were recruited for this study which was divided in to two groups; group A which contained 50 diagnosed cases of type 2 diabetes mellitus without ocular manifestation consider as control group while group B contained 50 diagnosed cases of type-2 diabetes mellitus with development of cataract considered as case study group. Each subject was recruited by applying Non Probability type of sample technique with consent of the subjects. The diabetic patients with in age between 40 to 50 years with history of diabetes at least from last five years both males and females were included while patients of type-1 diabetes mellitus, below age of 40 years or above 50 years, patients of senile cataract and renal disorder were excluded from this study. Total 10 ml of venous blood was collected under aseptic measure for the estimation of fasting blood glucose level, G6PD level and HbA1c%. Serum fasting blood glucose levels was measured by hexokinase method applying at Hitachi Cobas C 501 analyzer D&R laboratory LUMHS while G6PD was analyze by kit method on SD Biosensor, Inc. Republic of Korea. Tetra-decyl-Tri-methyl-Ammonium Bromide (TTAB) methodology was used to analyze the HbA1c% on Hitachi Cobas analyzer. Data was statistically analyzed by SPSS version 21 by applying of Student pair t test and chi square test.

Results:

Total 100 diagnosed cases of type-2 diabetes mellitus recruited and divided in to two groups each group contained 50 diagnosed cases of type-2 diabetes mellitus, group A contained 33males and 17 females diabetic patients with out ocular manifestation, while group B contained 28males and 22 males diabetic patients with ocular manifestation means diagnosed cases of diabetic cataract. Three biochemical parameters (fasting blood glucose level, HbA1c% and G6PD) were analyzed. The mean values of understudy variables are provided in Table No. 01, together with their significant values. In this table, there is no significant difference in fasting blood glucose levels or glycemc control index between the two groups, however the level of G6PD declines considerably ($p=0.05$) more in group B with diabetic cataract than in group A with diabetes without ocular manifestation.

Table: 1

Biochemical Parameters under study in Group A & Group B

Parameter	Control Group	Case Study Group	P. Value
FBS (mg/dl)	152.36±24.73	151.63±24.45	0.76
HbA1c%	10.55±2.14%	10.67±2.11	0.87
G6PD (U/gHb)	15.63±2.45	9.01±3.11	<0.05

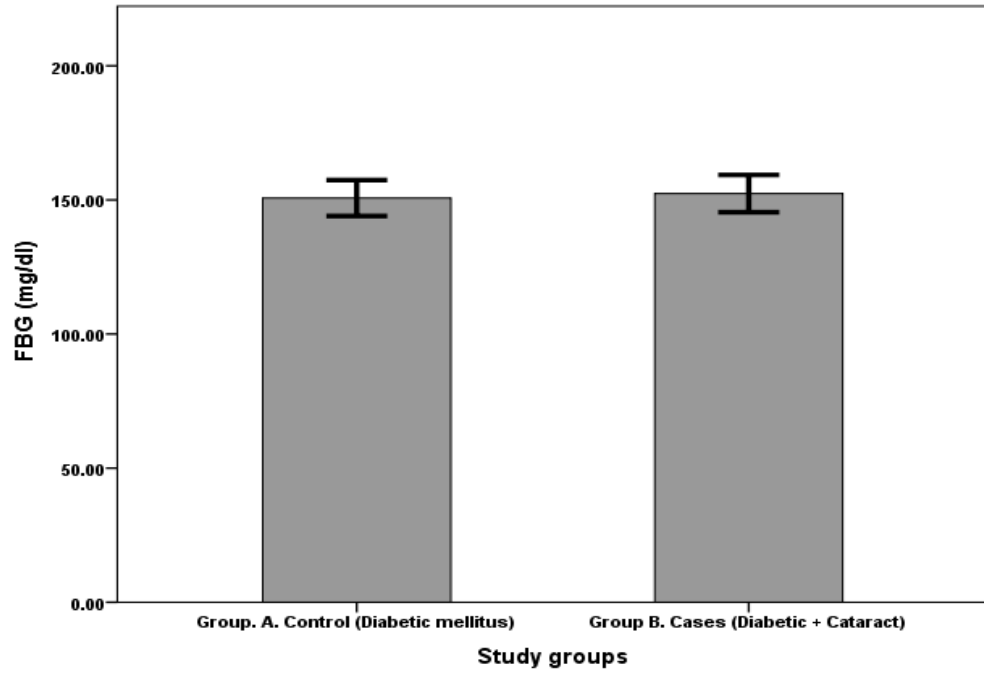


Figure: 1 FBS (mg/dl) Control & Case Study Groups

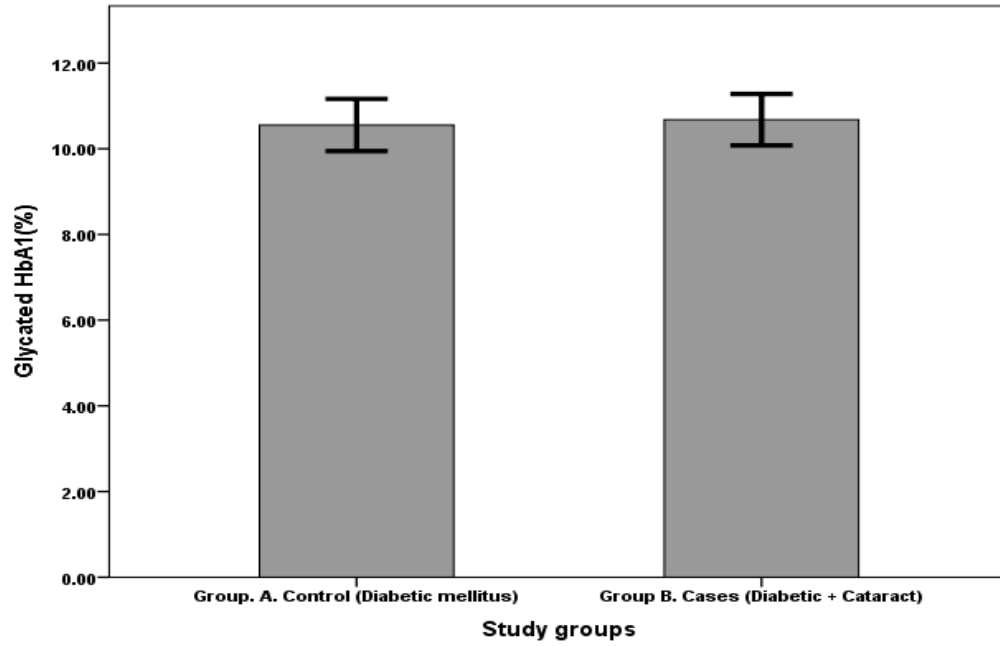


Figure: 2: HbA1c% Control & Case Study Groups

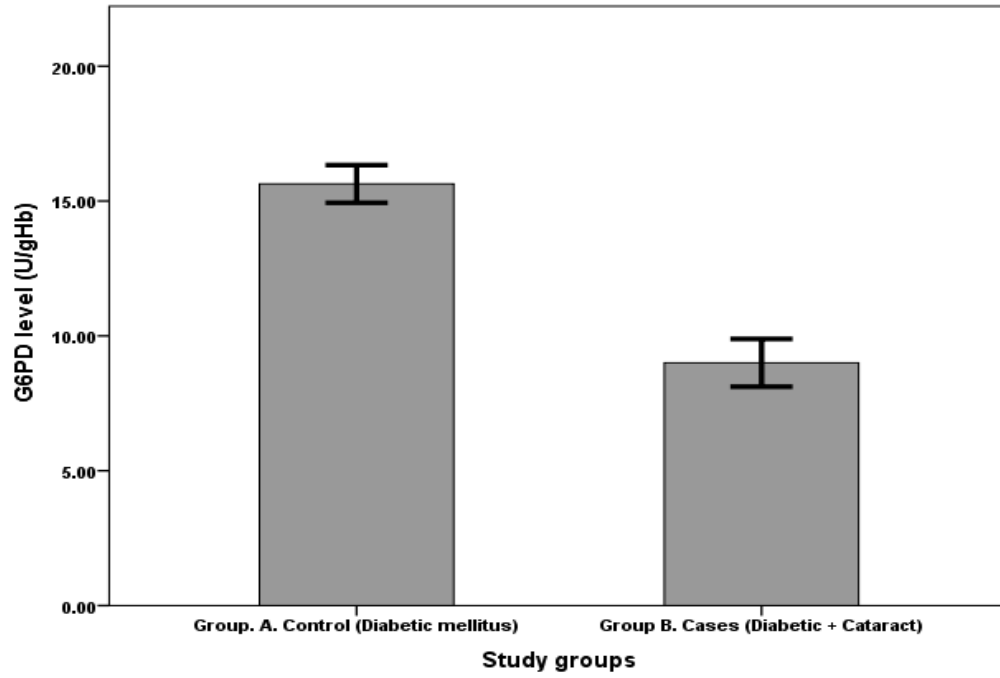


Figure: 3: G6PD (mg/dl) Control & Case Study Groups

Discussion

The development of cataract is earlier in diabetic population as compared to non diabetic population.¹⁴ Poor glycemic control and long duration of diabetes are the main risk factors for the development of diabetic cataract.⁵ The elder age cataract may be irreversible while the cataract developed in young diabetic patient can be reversible in nature.¹⁵ The reduction of glucose molecules into sorbitol by help of aldose reductase enzyme is the central mechanism for development of cataract this pathway also known as polyol pathway.¹⁶ In the polyol pathway there is degeneration of lens due to hyperosmotic effect due to intracellular accumulation of sorbitol at membrane.¹⁷ This mechanism stronger in diabetic population because there is quick conversion of sorbitol in to fructose by help of sorbitol dehydrogenase enzyme so diabetic population more prone to development of cataract as compared to general population. Another explanation for cataract formation in diabetics occurring sooner owing to early degenerative alterations in lens protein is this process.^{14,16,17} Glucose 6 Phosphate Dehydrogenase (G6PD) is the main regulatory enzyme for this function. G6PD provides redox potential which maintain the normal structure of lenticular proteins.

Our study shown that there is statistical significant ($P < 0.05$) decline in G6PD levels in diabetic cataract group as compared to diabetic without cataract group.

G6PD deficiency in diabetic cataract first observed by Orsalezi et al (1981)¹⁸ they reported that there was significant decline in G6PD compared with general population.

Our study also supported by the study of Lee et al (2016)¹⁹ they also concluded that G6PD level decline ($P < 0.001$) in diabetic cataract compared with non diabetic population.

Oleniyan et al (2019)²⁰ also reported that there was significant decline in G6PD level in diabetic population with vascular complications as compared with diabetic population without vascular complications. This study also suggested that when blood glucose level increased it causes phosphorylation of G6PD enzyme by activation of Protein Kinase A which reduces the level of G6PD in diabetic population.

Conclusion: This study concluded that there was significant decline in G6PD level in diabetic cataract. It is also concluded that the estimation of G6PD level in diabetic population will be beneficial to take early preventive measurements against diabetic vascular complications.

Future Recommendation: We believe that in the future, a bigger sample size will be required to ensure the veracity of the results.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References:

1. Naveed S, Nageen A, Ahmed SM, Ali Z, Fatima M, Khan ZA. Diabetes Lipidus-A persistent problem. Frequency and patterns of dyslipidemia among the diabetic adults of Pakistan. *The Professional Medical Journal*. 2021 Mar 10; 28(03):293-9.
2. Basit A, Fawwad A, Qureshi H, Shera AS. Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016–2017. *BMJ open*. 2018 Aug 1;8(8): e020961.
3. Lovic D, Piperidou A, Zografou I, Grassos H, Pittaras A, Manolis A. The growing epidemic of diabetes mellitus. *Current vascular pharmacology*. 2020 Mar 1;18 (2):104-9.
4. Forbes JM, Fotheringham AK. Vascular complications in diabetes: old messages, new thoughts. *Diabetologia*. 2017 Nov; 60 (11):2129-38.
5. Kiziltoprak H, Tekin K, Inanc M, Goker YS. Cataract in diabetes mellitus. *World journal of diabetes*. 2019 Mar 15;10 (3):140.
6. Bilen NB, Saricaoğlu MS. Assessment of cataract forming effect of diabetes in young adults by lens densitometer. *International Ophthalmology*. 2020 Dec;40(12):3357-62.
7. Zhu B, Ma Y, Lin S, Zou H. Vision-related quality of life and visual outcomes from cataract surgery in patients with vision-threatening diabetic retinopathy: a prospective observational study. *Health and quality of life outcomes*. 2017 Dec;15 (1):1-7.
8. Islam SM, Pahuja M, Mirza A, Mahesar ML, Maree GK, Bhatti U. Early postoperative complications of cataract surgery in diabetic patients. *Pakistan Journal of Physiology*. 2021 Mar 31; 17(1):12-4.
9. Kelkar A, Kelkar J, Mehta H, Amoaku W. Cataract surgery in diabetes mellitus: a systematic review. *Indian journal of ophthalmology*. 2018 Oct;66 (10):1401.
10. Ahmad A, Ahsan H. Biomarkers of inflammation and oxidative stress in ophthalmic disorders. *Journal of Immunoassay and Immunochemistry*. 2020 May 3; 41 (3):257-71.
11. Ge T, Yang J, Zhou S, Wang Y, Li Y, Tong X. The role of the pentose phosphate pathway in diabetes and cancer. *Frontiers in Endocrinology*. 2020 Jun 9; 11:365.
12. Jain SK, Parsanathan R, Levine SN, Bocchini JA, Holick MF, Vanchiere JA. The potential link between inherited G6PD deficiency, oxidative stress, and vitamin D deficiency and the racial inequities in mortality associated with COVID-19. *Free Radical Biology and Medicine*. 2020 Dec 1; 161: 84-91.

13. Heruye SH, MaffofouNkenyi LN, Singh NU, Yalzadeh D, Ngele KK, Njie-Mbye YF, Ohia SE, Opere CA. Current trends in the pharmacotherapy of cataracts. *Pharmaceuticals*. 2020 Jan;13(1):15.
14. Foote BC, Michau TM, Welihozkiy A, Stine JM. Retrospective analysis of ocular neuropathies in diabetic dogs following cataract surgery. *Veterinary ophthalmology*. 2019 May; 22 (3):284-93.
15. Bikbov MM, Kazakbaeva GM, Zainullin RM, Gilmanshin TR, Nuriev IF, Zaynetdinov AF, Yakupova DF, Uzianbaeva YV, Panda-Jonas S, Mukhamadieva SR, Khikmatullin RI. Prevalence and causes of vision impairment and blindness in the Russian rural eye and medical study. *Scientific Reports*. 2020 Jul 24; 10 (1):1-9.
16. Chitra PS, Chaki D, Boiroju NK, Mokalla TR, Gadde AK, Agraharam SG, Reddy GB. Status of oxidative stress markers, advanced glycation index, and polyol pathway in age-related cataract subjects with and without diabetes. *Experimental Eye Research*. 2020 Nov 1; 200: 108230.
17. Niimi N, Yako H, Takaku S, Chung SK, Sango K. Aldose Reductase and the Polyol Pathway in Schwann Cells: Old and New Problems. *International Journal of Molecular Sciences*. 2021 Jan; 22 (3):1031.
18. Orzalesi N, Sorcinelli R, Guiso G. Increased incidences of cataract in male subjects deficient in G6PD. *Arch Ophthalmol* 1981; 99: 69-70.
19. Lee JK, Qureshi S, Kurochkin P. Prevalence of cataracts in patients with G6PD deficiency. *Invest Ophthalmol Visual Sci* 2016; 57 (12):1540-5.
20. Olaniyan OO, Osadolor HB. Erythrocyte G6PD activity and GSH level as risk factors for vascular complications among type 2 diabetics in Osogbo, Nigeria, Alexandria. *J Med* 2019; 55(1):95-99.