

A Case Report on Gilberts Syndrome Associated With both Denovo Hypertension and Denovo Type-2 Diabetes Mellitus

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Abstract: An unusual case was reported in 50 years male patient associated with dual conditions. He came to hospital with chief complaints of mild chest pain, excessive thirst, stress and also severe headache. He is overstressed due to his office work. His abnormal reports were with elevated blood pressure and sugar levels. His urine examination appears pale yellow colour, cloudy and with the presence of sugar, pus cells and epithelial cells. He was treated with amlodipine 5 mg OD, Tab rosuvastatin 20mg HS, Inj IV pantoprazole 40mg OD for his diagnosed conditions. After 4 days under observation patient again reported elevated levels of indirect bilirubin with no hepatic symptoms. So it was understood that type-2 diabetes and hypertension became the factors to cause Gilberts syndrome. There were previous studies that Gilbert's syndrome has a more prevalence with diabetes and hypertension individually. This case was reported with both denovo conditions of diabetes and hypertension.

Keywords: Gilbert's Syndrome, diabetes, hypertension, bilirubin, G6PD

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I. Introduction

Gilbert's syndrome is a harmless genetic condition which occurs due to hepatic enzyme abnormality which leads to mild elevations of bilirubin. The liver doesn't properly process bilirubin and it is produced by the breakdown of red blood cells [1]. The condition has also been referred to as constitutional hepatic dysfunction and familial nonhemolytic jaundice [2]. The gene normally controls an enzyme UGT1A (called Uridine Diphosphate Glucuronosyltransferases that are important for bilirubin metabolism) which locates on chromosome II [3-5]. Gilberts Syndrome is due to results of genetic mutation in the promoter region of a gene. An ineffective gene (inherited from parent) leads to excessive bilirubin build up in the blood [6]. Gilbert's syndrome has a higher prevalence in diabetes and hypertension.

Several studies showed that oxidative stress may act as a common pathway for diabetes, it seems that oxidative stress predisposes to Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency and impairs in the synthesis of nitric oxide. It leads to a type- 2 diabetes mellitus but its relationship with G6PD is unclear (7, 8). The causative factor to occur a Gilbert's syndrome is genetic mutation in the promoter region of a gene. This G6PD deficiency makes the genetic mutation over the promoter region of a gene UGT1A [9]. This gene (UGT1A) makes a hepatic enzyme abnormality leads to hyperbilirubinemia.

Some studies showed that in persons with hypertension, there was a trend toward higher mean total bilirubin level in the intermediate creatinine group when compared with high creatinine group [10]. In an animal model (using Gunn rats, which have a genetic deficiency in UGT), blood vessels isolated from hyperbilirubinemic rats exhibited reduced levels of superoxide production and a blunted tonic response to angiotensin II infusion [11, 12].

Poor glucuronidation is also a risk factor for drug-induced liver injury the main concern is cholestatic liver injury by inhibiting UGT activity which may leads to Gilberts Syndrome.

People with Gilberts syndrome may appears with mild yellowing of the eyes (jaundice) [13] or entirely normal with no signs and symptoms. Some of the conditions and situations that can cause Gilberts syndrome like cold, dehydration, fasting [14], menstruation, stress, strenuous exercise, lack of sleep. Gilbert syndrome is mostly diagnosed after puberty, when alterations in sex hormone levels cause the blood bilirubin levels to rise. It has an increased risk factor when both parents ineffective or abnormal gene and in male gender [15].

The combination of normal blood and liver function tests and elevated bilirubin levels is an indicator to diagnose Gilbert's syndrome. No other tests are needed. Genetic tests can confirm the diagnosis. Gilbert's syndromes don't require a treatment, usually it resolves with no ill effects. It can be managed by avoiding stress, fasting and eating high calorie diet [16].

II. Case Presentation

An unusual case report in India with Gilberts Syndrome associated with combination disorders like denovo Hypertension and denovo type II Diabetes Mellitus (DM) was reported in a male patient aged 50 years. Patient admitted in Omni hospital, Hyderabad with a sudden onset of chief complaints of mild chest pain, excessive thirst, stress and also severe headache. His social was history with heavy stress for his office work.

On physical examination his blood pressure reveals 150/90 mmHg. He also went with biochemical tests and complete blood picture tests, where these tests reveals abnormal results like Gross Random Blood Sugar's (GRBs) levels – 218 mg/dl, Neutrophils - 79%. His urine examination appears pale yellow colour, cloudy and with the presence of sugar, pus cells and epithelial cells but his urobilinogen and other things in urine were normal. He was prescribed with the drugs like Inj Insulin T1D, Tab amlodipine 5 mg OD, Tab rosuvastatin 20mg HS, Inj IV pantoprazole 40mg OD for his diagnosed conditions.

After 4 days of under observation his urine examination revealed- elevated levels of indirect bilirubin, HbA1c tests- 50mmol/mol and BP- 140/90 mmHg. These parametes diagnosed with Gilbert's syndrome with diabetes and hypertension.

III. Discussion

This is unusual case because Gilbert's syndrome with both diabetes and hypertension in India. A male patient aged 50 years admitted to hospital with chief complaints of mild chest pain, excessive thirst, and severe headache. His history was known with heavy stress due to office work. His investigations reveal elevated blood pressure, increased blood sugar levels. His appears to be like pale yellow colour, cloudy and with the presence of sugar, pus cells. He treated with the drugs like insulin, amlodipine, rosuvastatin and pantoprazole. After 4 days his urine reveals with elevated levels of indirect bilirubin with no hepatic symptoms.

The previous studies proved that diabetes and hypertension has a higher prevalence with Gilbert's syndrome, but both done its studies individually. The patient was diagnosed with diabetes and hypertension for a very first time. His social history known with heavy stress, this makes G6PD deficiency. Genetic mutation over the promoter gene UGT1A occurs due to G6PD deficiency. This abnormal gene can't metabolise dead RBCs, so bilirubin levels increased moderately. G6PD deficiency leads to type-2 diabetes but its link is unknown.

Hypertension was a trend toward higher mean total bilirubin level in the intermediate creatinine group. In animal studies it understood due to UGT gene abnormality, but in human studies is unclear. Specific treatment for Gilberts is no required and it can cure on its own or by staying fasting, but regular bilirubin levels should be monitored.

IV. Conclusion

Gilbert's association with 2 different disorders is an unusual and rare case in India; Specific treatment for Gilbert's syndrome is not so required and can be managed by fasting or eating low calorie diet. Simultaneously both diabetes and hypertension should be treated and regular monitoring of bilirubin levels required.

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References

- [1] Powell LW, Hemingway E, Billing BH, Sherlock S, Idiopathic unconjugated hyperbilirubinemia (Gilbert's syndrome): a study of 42 families, *N Engl J Med*, 277, 1967,1108-1112.
- [2] Foulk WT, Butt HR, Owen CA, Jr, Whitcomb FF, Mason HL, Constitutional hepatic dysfunction (Gilbert's disease): its natural history and related syndromes, *Medicine (Baltimore)*, 38, 1959, 25-46.
- [3] Clarke DJ, Moghrabi N, Monaghan G, Cassidy A, Boxer M, Hume R, Genetic defects of the UDP-glucuronosyltransferase-1 (UGT1) gene that cause familial non-hemolytic unconjugated hyperbilirubinemias. *Clin Chim Acta*, 266, 1997, 63-74.
- [4] Bosma PJ, Roy Chowdhury J, Bakker CTM, Gantla S, de Boer A, Oostra BA, The genetic basis of the reduced expression of bilirubin UDP-glucuronosyltransferase 1 in Gilbert's syndrome, *N Engl J Med*, 333, 1995, 1171-1175.
- [5] Sampietro M, Lupica L, Perrero L, Romano R, Molteni V, Fiorelli G, TATA-box mutant in the promoter of the uridine diphosphate glucuronosyltransferase gene in Italian patients with Gilbert's syndrome, *Ital J Gastroenterol Hepatol*, 30, 1998, 194-198.
- [6] Monaghan G, Ryan M, Seddon R, Hume R, Burchell B, Genetic variation in bilirubin UDP-glucuronosyltransferase gene promoter and Gilbert's syndrome, *Lancet*, 347, 1996, 578-581.
- [7] Gwo-Hwa Wan, Shu-Chen Tsai, and Daniel Tsun-Yee Chiu, Decreased Blood Activity of Glucose-6-Phosphate Dehydrogenase Associates with Increased Risk for Diabetes Mellitus, *Endocrine*, 19(2), 2002, 191-195.
- [8] TK Saeed, HA Hamamy, AAS Alwan, Association of Glucose-6-Phosphate Dehydrogenase Deficiency with Diabetes Mellitus, *Diabetic Medicine*, 2(2) 1985, 110-112.
- [9] Maurizio Sampietro, Loredana Lupica, Luca Perrero, Alessia Comino, Franco Martinez di Montemuros, Maria Domenica Cappellini, Gemino Fiorelli, The expression of uridine diphosphate glucuronosyltransferase gene is a major determinant of bilirubin level in heterozygous β -thalassaemia and in glucose-6-phosphate dehydrogenase deficiency, *British Journal of Hematology*, 99(2) 1997, 437-39.

- [10] Vitek L, Jirsa M, Brodanova M, Gilbert syndrome and ischemic heart disease: a protective effect of elevated bilirubin levels, *Atherosclerosis*, 160, 2002, 449–456.
- [11] Prasanna Santhanam MD, Zeid Khitan MD, Rodhan Khthir MD, Association Between Serum Total Bilirubin and Serum Creatinine and the Effect of Hypertension, *Journal of Clinical Hypertension*, 17(1), 2015, 61-62.
- [12] Schwertner HA, Vitek L, Gilbert syndrome, UGT1A1*28 allele, and cardiovascular disease risk: possible protective effects and therapeutic applications of bilirubin, *Atherosclerosis*, 198, 2008, 1–11.
- [13] Bancroft JD, Kreamer B, Gourley GR, Gilbert's syndrome accelerates development of neonatal jaundice, *J Pediatr*, 132, 1998, 656-660.
- [14] Perona G, Cellerino R, Casaril M, Cetto GL, Cappellaro O, de Sandre G, Fasting bilirubinaemia in haemolytic and Gilbert's patients, *Haematologica*, 60(4), 1975, 422-39.
- [15] Hauser SC, Gollan J, Bilirubin metabolism and hyperbilirubinemic disorders, In Millward-Sadler GH, Wright R, Arthur MJP, *Wright's liver and biliary disease*. 3rd Ed. London, W.B. Saunders Company, 1992, 317-70.
- [16] Gollan JL, Bateman C, Billing BH, Effect of dietary composition on the unconjugated hyperbilirubinemia of Gilbert's syndrome, *Gut*, 17, 1976, 335-340.

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