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Haptoglobin genotype among patients with IgA nephropathy: Impact on disease progression and response to treatment

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Background: IgA nephropathy (IgAN) is the most common primary glomerulonephritis, with high incidence of progression to end-stage renal disease ESRD. Although the pace of decline in kidney function in IgAN is affected by proteinuria, hypertension and decreased estimated glomerular filtration rate (eGFR) at the time of diagnosis, exact mechanisms underlying the pace of deterioration is still largely unknown. In recent years, the role of genetic risk factors in pathogenesis of IgAN is being elucidated by genome-wide association studies, with multiple risk alleles has been described. However, the impact of haptoglobin (Hp) genotype on the progression of IgAN was not studied yet. Therefore, the current study examines whether Hp genotype influences disease progression and response to treatment.

Methods: The present study included 28 patients with IgAN (mean age of 42.5±2.5 years), 26 non-IgAN chronic kidney disease (CKD), 54 patients on hemodialysis, and 150 healthy subjects. Blood and urine samples were collected at baseline and 6 months after initiation therapy. Serum creatinine (SCr) and total proteinuria were determined in all IgAN patients. Blood analysis for Hp genotype was performed for all patients and healthy controls.

Results: 29% of IgAN patients were Hp 1-1, 36% Hp 2-1, and 36% Hp 2-2. In contrast, in patients with non-IgAN chronic kidney disease, the prevalence of Hp 1-1, Hp 2-1, and Hp 2-2 was 8%, 19%, and 73%, respectively. In hemodialytic patients, prevalence of Hp 1-1, Hp 2-1, and Hp 2-2 was 19%, 28%, and 54%, respectively. In healthy subjects, the distribution of Hp 1-1, Hp 2-1, and Hp 2-2 was 7%, 39%, and 54%, respectively. Interestingly, IgAN Hp 2-2 patients were more stable and responded better to treatment with routine therapy (RAS or inhibitors steroid) than other Hp genotype.

Conclusions: Hp 1-1 genotype is more common in IgAN patients as compared to the general population in Israel and even more than CK patients and subjects on HD. Patients with Hp 2-2 responded better to appropriate therapy. The mechanisms underlying this phenomenon remain to be explored.

Biography

Zaher Armaly, Clinical Lecturer in the Faculty of Medicine, Bar Ilan University has been a member of the faculty since 2009. He received his MD degree from Padua, Italy in 1989. After one-year Medical Training in Nahariya Medical Center, he moved to Rambam Medical Center for Residency & Specialization in Internal Medicine and subsequently sub-specialization in Nephrology and Hypertension. Since 2003, he serves as Director of the Department of Nephrology and Hypertension at Nazareth Hospital, Nazareth, Israel. He has received several awards for his research and clinical activity including Dangur Family Award from Bar Ilan University. He has over 30 original publications in peer review journals and text books. Besides his recent and past achievements in research, he had excellent achievements as a Lecturer, expressed by a wide variety of prizes that he received for (constantly) excellence in teaching including the best Bar Ilan Lecturer Award. He has extensive experience in Nephrology research. His main interest is anemia and the impact of carnitine on iron-induced oxidative stress in CKD patients. Over the last 10 years, his group has been studying the pathophysiology of inflammation and oxidative stress following IV iron administration. In addition, his research focuses on contrast-induced nephropathy and novel therapeutic approaches to this common disease state. Finally, he studies the incidence of depression in ESRD patients on hemodialysis and peritoneal dialysis and the factors underlying this phenomenon.

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