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Special article

High levels of both serum gamma-glutamyl transferase and alkaline phosphatase are independent predictors of mortality in patients with stage 4–5 chronic kidney disease☆

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ABSTRACT

Introduction: High serum gamma-glutamyl transferase (GGT) levels are associated with increased mortality in the general population. However, this association has scarcely been investigated in patients with chronic kidney disease (CKD).

This study aims to investigate the clinical characteristics of CKD patients with abnormally elevated serum GGT, and its value for predicting mortality.

Material and methods: Retrospective observational study in a population cohort of adults with stage 4–5 CKD not yet on dialysis. Demographic, clinical, and biochemical parameters of prognostic interest were recorded and used to characterise CKD patients with high levels of GGT (>36 IU/L). Cox proportional hazard regression models were used to analyse the influence of baseline serum GGT and alkaline phosphatase (ALP) levels on mortality for whatever reason.

Results: The study group consisted of 909 patients (mean age 65 ± 15 years). Abnormally elevated GGT or ALP levels at baseline were observed in 209 (23%) and 172 (19%) patients, respectively, and concomitant elevations of GGT and ALP in 68 (7%). High GGT levels were associated with higher comorbidity burden, and a biochemical profile characterised by higher serum concentration of uric acid, triglycerides, alanine aminotransferase, ferritin, and C-reactive.

During the study period, 365 patients (40%) died (median survival time = 74 months). In adjusted Cox regression models, high levels of GGT (*hazard ratio* [HR] = 1.39; CI 95%: 1.09–1.78, $P = 0.009$) and ALP (HR = 1.31; CI 95%: 1.02–1.68, $P = 0.038$) were independently associated with mortality.

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Conclusion: High serum levels of GGT are independent predictors of mortality in CKD patients.

Niveles séricos elevados de gamma-glutamil transferasa y fosfatasa alcalina son predictores independientes de mortalidad en la enfermedad renal crónica estadio 4-5

Palabras clave:
Enfermedad renal crónica
Fosfatasa alcalina
Gamma glutamil-transferasa
Mortalidad

RESUMEN

Introducción: Los niveles séricos elevados de gamma-glutamil transferasa (GGT) se asocian con una mayor mortalidad en la población general, pero es desconocido si esta asociación también ocurre en pacientes con enfermedad renal crónica (ERC).

Los objetivos de este estudio fueron investigar las características clínicas de los pacientes con ERC y elevación de los niveles séricos de GGT, así como el valour de predicción de esta enzima sobre la mortalidad.

Material y métodos: Estudio retrospectivo de observación en una cohorte de pacientes con ERC estadios 4-5 prediálisis. Se recogieron los parámetros demográficos, clínicos y bioquímicos de interés pronóstico y se utilizaron para caracterizar a los pacientes con elevación de GGT (>36 UI/l). Mediante regresión de Cox se analizó la asociación de los valores basales de GGT y fosfatasa alcalina (FA) sobre la mortalidad por cualquier causa.

Resultados: Se incluyó a 909 pacientes (edad media 65 ± 15 años). Se observaron niveles elevados de GGT o FA en 209 (23%) y 172 (19%) pacientes, respectivamente, y elevación simultánea en 68 (7%) pacientes. Niveles elevados de GGT se asociaron con mayor comorbilidad y un perfil bioquímico con concentraciones más elevadas de ácido úrico, triglicéridos, transaminasa glutámico-pirúvica, ferritina, y proteína C reactiva.

Durante el seguimiento fallecieron 365 pacientes (40%). Niveles elevados de GGT (*hazard ratio* [HR] = 1,39; IC 95%: 1,09-1,78; p = 0,009), o de FA (HR = 1,31; IC 95%: 1,02-1,68; p = 0,038) se asociaron de forma independiente con la mortalidad.

Conclusiones: Niveles séricos elevados de GGT o de FA son predictores independientes de mortalidad en pacientes con ERC.

Introduction

Chronic kidney disease (CKD) is associated with high mortality, particularly of cardiovascular-related origin. However, the limited association between mortality and traditional cardiovascular risk factors in these patients is paradoxical. Only some markers related to inflammation or nutrition (e.g. C-reactive protein and serum albumin) have been shown to be consistent predictors of mortality in CKD.[1]

In recent years some observational studies have shown an association between elevated total serum alkaline phosphatase (ALP) concentrations and mortality in patients with CKD[2–5]; however, the biological and clinical significance of this finding remains unknown.

Gamma-glutamyl transferase (GGT) is an enzyme present in serum and on the outer surface of cells from different organs such as the liver, pancreas, intestine, lungs and kidneys.[6] Serum GGT is not only a traditional marker of alcohol consumption and hepatobiliary diseases, but several studies have also shown an association between elevated serum GGT levels and cardiovascular disease, diabetes mellitus, hypertension and metabolic syndrome.[7]

GGT levels is a predictor of mortality in the general population; in fact, this enzyme has recently been included as one of a set of biochemical parameters that predict mortality.[8] Furthermore, serum GGT levels could help to interpret high ALP values of unclear origin.

There are only few studies that have analysed the clinical and prognostic significance of serum GGT in CKD.[9,10] The aim of this study was to investigate the clinical characteristics of CKD patients with abnormally elevated serum GGT levels and their interaction with ALP, and to determine the value of this parameter as a predictor of mortality.

Materials and methods

This is a retrospective, observational study conducted on a cohort of adult patients being followed in the low clearance (advanced CKD) outpatients clinic of the Nephrology department of the Hospital Infanta Cristina, Badajoz, Spain, from January 2002 to October 2013. The study included all