



Impact of Mannose-Binding Lectin and Mortality Rates in Type 2 Diabetes Patients under treatment in selected Hospitals in Indore

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Introduction

Diabetes type 2 is linked to much higher morbidity and mortality, primarily from cardiovascular and microvascular illness. New focused intensive treatment algorithms may considerably improve outcomes, but techniques to accurately anticipate the course of illness in specific patients are still required to make the most use of available resources.

The complement system has become an important part of the body's natural defences against pathogens. When activated, complement may harm innocent bystander cells by depositing the membrane attack complex and causing inflammation by releasing the anaphylatoxins C5a and C3a. Mannose-binding lectin (MBL) is a serum protein produced by the liver that activates complement through MBL-associated serine proteases. MBL levels are genetically determined and vary greatly from person to person, due mostly to commonly occurring genetic polymorphisms. Functional MBL deficiency affects up to 10% of the general population, and these people may be more susceptible to infections. In individuals with autoimmune disorders such as systemic lupus erythematosus, it may also raise the likelihood of harmful disease activity and thrombogenesis.

Cardiovascular disease is thought to be caused in part by low-grade inflammation that lasts for a long time. This is shown by high levels of the inflammatory marker C-reactive protein (CRP). C-reactive protein is a well-known way to measure cardiovascular and all-cause mortality in people with type 2 diabetes. It is also an independent predictor of changes in the amount of albumin that is excreted in urine over time. By turning on complement, mannose-binding lectin may make local and systemic inflammation worse. It has been shown that stopping the complement cascade at the MBL level and further down the line improves the prognosis of patients with acute myocardial infarction. High levels of MBL in the blood and genotypes that are linked to high MBL levels have been linked to type 1 diabetes patients getting diabetic nephropathy and cardiovascular disease.

The link between MBL levels, mortality, and the development of albuminuria in type 2 diabetic patients is uncertain. To address this problem, we evaluated MBL levels at baseline in a well-characterized cohort of type 2 diabetes patients who were followed for more than 15 years.

Methodology

The researcher conducted an observational study on all type 2 diabetes patients who attended the designated Indore hospitals. The study was approved by the ethics committee, and all participants supplied written informed consent before taking part. Two independent observers obtained the cause of death from death certificates, including information available from necropsy reports. An age- and gender-matched control group of 200 healthy adults drawn from blood donors was used to compare MBL levels in type 2 diabetes patients with healthy volunteers. At the outset of the trial, blood samples were collected without fasting and stored at 70°C. Haemoglobin, serum total cholesterol, and serum creatinine levels were measured using standard techniques. In 24-hour urine samples, the urinary albumin concentration was determined using radioimmunoassay. Serum MBL levels were evaluated utilising an in-house time-resolved immunofluorometric technique, as well as intra-assay and interassay CVs. Among healthy adults, the median day-to-day variability in MBL concentrations, denoted as CV, was 6%. CRP was tested using a very sensitive enzyme-linked immunosorbent method developed in-house. The data was analysed using descriptive and inferential statistics. All other information is presented as means standard deviations. To compare groups, the unpaired t test, Mann-Whitney U test, or Kruskal-Wallis test were employed, as appropriate. Spearman correlation with 2-tailed probability values was used to assess the degree of relationship between variables.

Results

The baseline features of the group were divided into survival and baseline MBL status. MBL levels in type 2 diabetes patients were not significantly different from those in healthy controls. The control volunteers had the same mean age (55.75 years) and gender distribution (male/female, 60%/39%) as the patients. MBL levels in diabetic patients were significantly higher in men than in women, and in ever smokers than in never smokers. MBL

concentrations were unaffected by age, diabetes duration, blood pressure, body mass index, serum total cholesterol levels, haemoglobin A1c levels, serum creatinine levels, urine albumin excretion, diabetic treatment, or antihypertensive medication.

MBL and CRP levels were not associated in the general population ($r = 0.021$) or in patient subgroups based on albuminuria, gender, or smoking status. Unlike MBL concentrations, CRP concentrations did not differ between men and women or between ever smokers and never smokers.

The median term of follow-up was 18.7 years, during which time 200 patients (30%) died. 70% of these people died from cardiovascular disease, 10% from end-stage renal failure, and 20% died from other causes such as cancer, infection, and unknown causes.

At baseline, the median blood MBL concentrations in patients who died subsequently were almost twice as high as in survivors.

A similar difference was seen when persons with normoalbuminuria at baseline were divided into nonsurvivors and survivors. To identify the appropriate discriminative cutoff value for MBL as a predictor of survival, a ROC curve was constructed using increments of 200 g/L of MBL. The MBL cutoff with the greatest sum of sensitivity and specificity was found to be 1000 g/L based on this investigation. A similar ROC curve investigation in patients with normoalbuminuria at baseline discovered the same optimal cutoff level of 1000 g/L. When the 200 patients were split according to this cutoff level, the mortality rate during follow-up was 28% in patients with MBL levels more than 1000 g/L and 16% in patients with MBL levels less than 1000 g/L. Normoalbuminuric patients with a baseline MBL level more than 1000 g/L had a 22% risk of mortality during follow-up, compared to 28% in normoalbuminuric patients with an MBL level less than 1000 g/L.

Conclusion

The study concluded that more than 200 million individuals worldwide suffer from type 2 diabetes mellitus. Improved risk classification is therefore essential for making the most use of available resources. Our data suggest that assessing MBL in white people with type 2 diabetes, either alone or in combination with CRP, provides independent prognostic information on all-cause mortality and albuminuria development. Our results are restricted by the small size of the study, the minor amplitude of the observed effects, and the unavailability of DNA samples for MBL genotype analysis.

Reference

- [1]. Best LG, Davidson MN, North KE et al. Prospective analysis of mannan-binding lectin genotypes and coronary artery disease in American Indians: the Strong Heart Study. *Circulation* 2004;109:471- 475.
- [2]. Dahl MT, Tybjaerg-Hansen A, Schnohr P, Nordestgaard BG. A population-based study of morbidity and mortality in mannan-binding lectin deficiency. *J Exp Med* 2004;199:1391- 1399.
- [3]. Hovind P, Hansen TK, Tarnow L et al. Mannan-binding lectin as a predictor of microalbuminuria in type 1 diabetes: an inception cohort study. *Diabetes* 2005;54:1523- 1527.
- [4]. Ohlenschlaeger T, Garred PM, Madsen HO, Jacobsen S. Mannan-binding lectin variant alleles and the risk of arterial thrombosis in systemic lupus erythematosus. *N Engl J Med* 2004;351:260- 267.
- [5]. Stehouwer CD, GallMA, Twisk JW, Knudsen EE, Meis JJ, Parving HH. Increased urinary albumin excretion, endothelial dysfunction, and chronic low-grade inflammation in type 2 diabetes: progressive, interrelated, and independently associated with risk of death. *Diabetes* 2002;51:1157- 1165.
- [6]. Saraheimo M, Forsblom CH, Hansen TK et al. Increased levels of mannan-binding lectin in type 1 diabetic patients with incipient and overt nephropathy. *Diabetologia* 2005;48:198- 202.
- [7]. Thiel S, Moller-Kristensen M, Jensen LJ, Jensenius JC. Assays for the functional activity of the mannan-binding lectin pathway of complement activation. *Immunobiology* 2002;205:446- 454.