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Prevalence of Hepatitis B Surface Antigen and Antibody in White and Black Patients with Diabetes Mellitus

M. C. KEW,* M. E. MACKAY, A. MINDEL, B. I. JOFFE, B. KUSMAN, G. M. MACNAB, AND H. C. SEFTEL

Department of Medicine and Diabetic Clinic, Johannesburg Hospital and University of the Witwatersrand, and School of Pathology of the South African Institute for Medical Research and University of the Witwatersrand, Johannesburg, South Africa 2001*

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The prevalence of hepatitis B surface antigen (HB_sAg) and antibody (anti-HB_s) was determined in 531 white and 519 black diabetic outpatients and in appropriate white and black control populations. There was no difference between the prevalence of either HB_sAg or anti-HB_s in either the white or black diabetics and that in the white and black controls. These findings make it unlikely that the vast majority of patients with diabetes mellitus have either an increased susceptibility to infection by the hepatitis B virus or an impaired ability to clear the virus once they are infected.

During recent years evidence has accumulated that in patients with untreated or poorly controlled diabetes mellitus phagocytosis by polymorphonuclear leukocytes is impaired (1, 2, 6, 12) and disturbances in cell-mediated immune responses can be demonstrated (5, 9, 14). These observations may explain why diabetic patients with marked hyperglycemia with or without ketoacidosis are prone to mycobacterial and fungal infections (4). Cell-mediated immunity is involved in the defense against viruses as well as in that against mycobacteria and fungi. No increased incidence of viral infections has as yet been reported in patients with diabetes, either in the stable or in the uncontrolled state. There is, however, a study from Czechoslovakia (11) in which an increased prevalence of the hepatitis B (Australia) surface antigen (HB_sAg) was found in 788 diabetics. If confirmed, this finding would indicate that patients with diabetes have an impaired ability to eliminate the hepatitis B virus (HBV) once they have been infected, although it would not necessarily imply an enhanced susceptibility to HBV infections. To prove the latter, a finding of an increased prevalence of antibodies against HB_sAg (anti-HB_s) would be required. This prompted us to examine the sera of a group of diabetics for the presence of both anti-HB_s and HB_sAg. We have related our findings to the effectiveness of the control of the diabetes. Because this virus is often transmitted by the parenteral route and because the syringes and needles used by diabetics could possibly become contaminated by the virus, we have also related our findings to whether the patients were receiving insulin by injection. South African whites have a low prevalence of the HBV carrier state (0.1%), whereas the blacks have a prevalence that ranges from 2% in urban dwellers to 16% in some rural populations (3). Diabetics from both population groups were therefore studied.

MATERIALS AND METHODS

Sera from 531 white and 519 black diabetic outpatients were tested for the presence of HB_sAg and anti-HB_s. The control group for the black diabetics comprised 230 age- and sex-matched black inpatients and outpatients attending the same hospitals as the diabetics and suffering from diseases other than diabetes mellitus. Patients having a history of previous blood transfusion and those with diseases know to be associated with an increased carrier rate of HBV (liver disease, chronic renal failure, leukemia, lymphoma, cancer, and patients receiving corticosteroids or immunosuppressive drugs) were specifically excluded. All of the controls had random blood sugar levels of less than 8.9 mmol/liter (160 mg/100 ml). As the carrier rate of HBV in the white population is low, the white control group would have to be large in order to be meaningful. Because of the difficulty in finding sufficient numbers of white inpatients and outpatients who satisfied the criteria for a control group, we examined sera from 2,460 white voluntary blood donors. None of these donors was known to be diabetic although blood sugar levels were not specifically checked. In addition, we tested sera from 212 age- and sex-matched nondiabetic white outpatients (all of whom had random blood sugar levels of less than 8.9 mmol/liter (160 mg/100 ml), excluding the same categories of patients as was done for the black controls. An assessment of the effectiveness of diabetic control was based on clinical symptoms and on blood and

urinary sugar levels during the 6-month period prior to the investigation, except for those patients (less than 5% of the black and white diabetics studied) who were known to be diabetic for a shorter time than this. Control was regarded as "good" if the majority (more than two-thirds) of postprandial blood sugar levels were less than 9.7 mmol/liter (175 mg/100 ml) and the majority of urine specimens contained were not more than 1+ sugar, "fair" if the majority of blood sugar values were between 9.7 and 14 mmol/liter (250 mg/100 ml) and glucosuria was not more than 3+, and "poor" if the majority of blood and urine specimens contained more sugar than 14 mmol/liter and 3+, respectively.

HB_sAg was detected in the serum by solid-phase radioimmunoassay using the Austria II-^{125}I kit (8). All positive results were confirmed by using the neutralizing antibody technique (13). Anti-HB_s was detected by both passive hemagglutination (15) and radioimmunoassay (7). Blood sugar levels were measured in the diabetics and control subjects with Dextrostix and a Reflectance Meter (Ames Co.) or, in some cases, with an Auto-Analyzer. These methods are known to give comparable results.

RESULTS

The clinical features of the black and white diabetics are summarized in Table 1. The duration of diabetes was longer in the white patients, and a large proportion of them were receiving insulin.

The prevalence of HB_sAg and anti-HB_s in the white and black diabetics and controls is shown in Table 2. There was no significant difference between the prevalence of HB_sAg in white diabetics and that in white blood donors. The one white diabetic found to have HB_sAg in the serum was a 40-year-old Greek woman who had been known to be diabetic for 7 years and whose disease was well controlled by chlorpropamide and diet. Three HB_sAg-positive individuals were detected among the 212 white controls. The prevalence of HB_sAg in black diabetics was the same as that in black controls. Further, there was not a significant difference in the prevalence of anti-HB_s between white diabetics and white blood donors or controls, or between black diabetics and black controls. There was no relation between the prevalence of HB_sAg or anti-HB_s and the duration of disease in either the white or black diabetics.

The duration of diabetes, its mode of therapy, and the degree of control in white patients positive for anti-HB_s and in black patients positive for anti-HB_s or HB_sAg are shown in Table 3. Only a minority of the black diabetics with either HB_sAg or anti-HB_s were receiving insulin, and in only a small proportion was control of diabetes considered to be poor. The percentage of white diabetics with anti-HB_s who were receiving insulin was the same as for the white group as a whole. Control of diabetes was either good or fair in all of the white diabetics with anti-HB_s.

DISCUSSION

We have not found an increased prevalence of either anti-HB_s or HB_sAg in the sera of large groups of white and black diabetics, most of whom were satisfactorily controlled. These findings make it unlikely that the vast majority of patients with diabetes have either an in-

TABLE 1. *Summary of relevant features in white and black diabetic patients*

Patient group[a]	Ratio of male/female	Age (years)		Duration of diabetes (years)		% Receiving insulin
		Mean	Range	Mean	Range	
White diabetics (531)	1.5:1	56.3	14–85	12.6	0.25–26	42
Black diabetics (519)	1.5:1	49.5	14–76	4.6	0.25–34	24

[a] The number of patients is indicated in parentheses.

TABLE 2. *Prevalence of HB_sAg and anti-HB_s in white and black diabetic patients and controls*

Group	Whites		Blacks	
	HB_sAg (%)	Anti-HB_s (%)	HB_sAg (%)	Anti-HB_s (%)
Diabetics	0.19 (1/531)	6.4 (34/531)	4.6 (24/519)	44.7 (232/519)
Controls	0.16	5.3		
Blood donors	(4/2,460)	(131/2,460)		
Hospital patients	1.4 (3/212)	8.4 (17/202)	4.3 (10/230)	44.4 (102/230)

[a] The number of positive results to the total number of individuals in each group is given in parentheses.

TABLE 3. *Type of treatment received and degree of control of diabetes in black diabetic patients with HB$_s$Ag in the sera and white and black diabetics with anti-HB$_s$ in the sera*

Patient group	Treatment (%)			Control (%)		
	Insulin	Oral agents	Diet	Good	Fair	Poor
HB$_s$AG						
Black diabetics (24 patients)	13	83	4	29	58	13
Anti-HB$_s$ positive						
White diabetics (34 patients)	42	48	10	66	34	0
Black diabetics (232 patients)	24	73	3	56	34	10

creased susceptibility to infection by HBV or an impaired ability to clear the virus once infected. It is, therefore, not surprising that in the patients positive for either anti-HB$_s$ or HB$_s$Ag we could find no relation to the duration of diabetes, the effectiveness of control of the disease, or the mode of treatment. A negative result for anti-HB$_s$ is especially significant in the black patients, who have a high carrier rate of HBV in the general population (3), in whom the risk of exposure to the virus is great, and who often do not enjoy ideal facilities for sterilizing their syringes.

In the majority of our patients the diabetes was satisfactorily controlled. The in vitro studies reported to date have demonstrated impaired phagocytosis and cell-mediated immune responses only in the poorly controlled diabetic state (1, 2, 5, 6, 9, 10, 12, 14). Our findings do not exclude the possibility that these defects may be present in severely uncontrolled diabetics.

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LITERATURE CITED

1. **Bagdade, J. D., K. L. Nielson, and R. J. Bulger.** 1972. Reversible abnormalities in phagocytic function in poorly controlled diabetic patients. Am. J. Med. Sci. 263:451-456.
2. **Bagdade, J. D., R. K. Root, and R. J. Bulger.** 1974. Impaired leucocyte function in patients with poorly controlled diabetes. Diabetes 23:9-15.
3. **Bersohn, I., G. M. Macnab, J. Pyzikowska, and M. C. Kew.** 1974. The prevalence of hepatitis-B (Australia) antigen in Southern Africa. S. Afr. Med. J. 48:941-944.
4. **British Medical Journal.** 1974. Infection and diabetes. Br. Med. J. 3:76.
5. **Brody, J. I., and K. Merlie.** 1970. Metabolic and biosynthetic features of lymphocytes from patients with diabetes mellitus. Similarities to lymphocytes in chronic lymphatic leukemia. Br. J. Haematol. 19:193-201.
6. **Bybee, J. D., and D. E. Rogers.** 1964. The phagocytic activity of polymorphonuclear leucocytes obtained from patients with diabetes mellitus. J. Lab. Clin. Med. 64:1-13.
7. **Ginsberg, A. L., M. E. Conrad, W. H. Bancroft, C. M. Ling, and L. R. Overby.** 1973. Antibody to Australia-antigen: detection with a simple radioimmunoassay. Incidence in military populations, and role in the prevention of hepatitis-B with gamma globulin. J. Lab. Clin. Med. 82:317-325.
8. **Ling, C. M., and L. R. Overby.** 1972. Prevalence of hepatitis-B virus antigen as revealed by direct radioimmunoassay with ^{125}I antibody. J. Immunol. 109:834-841.
9. **MacGuish, A. C., S. J. Urbaniak, C. J. Campbell, L. J. P. Duncan, and W. J. Irvine.** 1974. Phytohemagglutinin transformation and circulating lymphocyte subpopulations in insulin-dependent diabetic patients. Diabetes 23:708-712.
10. **Mahmoud, A. A. F., H. M. Rodman, M. A. Mandel, and K. S. Warren.** 1976. Induced and spontaneous diabetes mellitus and suppression of cell-mediated immunologic responses. Granuloma formation, delayed dermal reactivity, and allograft rejection. J. Clin. Invest. 57:362-367.
11. **Meluzin, F., F. Kubecova, and J. Spicka.** 1974. Australia antigen in medical personnel and diabetic patients. Cas. Lek. Cesk. 113:1387-1389.
12. **Mowat, A. G., and J. Baum.** 1971. Chemotaxis of polymorphonuclear leucocytes from patients with diabetes mellitus. N. Engl. J. Med. 284:621-627.
13. **Prince, A. M., B. Brotman, D. Jass, and H. Ikram.** 1973. Specificity of the direct solid phase radioimmunoassay for detection of hepatitis-B antigen. Lancet i:1346-1350.
14. **Ragab, A. H., B. Hazlett, and C. H. Cowan.** 1972. Response of peripheral blood lymphocytes from patients with diabetes mellitus to phytohemagglutinin and Candida albicans antigen. Diabetes 21:906-907.
15. **Vyas, G. H., and H. R. Shulman.** 1970. Haemagglutinin assay for antigen and antibody associated with viral hepatitis. Science 170:332-333.