Henry Ford Hospital Medical Journal

Volume 30 | Number 1 Article 5

3-1982

# Racial Differences in the Incidence of Steroid Diabetes in Renal Transplant Patients

Francis Dumler

Hajime Hayashi

Jay Hunter

Nathan W. Levin

Henry Ford Hosp Med J
Vol 30, No 1, 1982

# Racial Differences in the Incidence of Steroid Diabetes in Renal Transplant Patients

**Francis Dumler, MD,* Hajime Hayashi, PhD,** Jay Hunter, BS,** and Nathan W. Levin, MD***

*We have studied the development of steroid-induced diabetes in a population of 143 renal allograft recipients who were nondiabetic before transplantation. Steroid-induced diabetes developed in 9.8% of patients. However, in blacks its incidence was significantly higher than in whites (17.3% vs 5.5% respectively; $p < .01$). The development of steroid-induced diabetes was not associated with a higher frequency of HLA-B8 or HLA-Bw15 in either race. In black graft recipients, HLA-B14 was significantly more frequent ($p < .001$) among those who developed steroid-induced diabetes than in insulin-dependent diabetic (Type I) and nondiabetic recipients. The clinical course of patients with steroid-induced diabetes has been similar to that of noninsulin-dependent diabetics (Type II).*

The occurrence of diabetes mellitus in renal allograft recipients who are not diabetic before transplantation has been well documented, the incidence varying from 6 to 25% (1-6). A greater frequency of HLA-B8 and Bw15 has been reported in renal transplant recipients with significant glucose intolerance which suggests the uncovering of a latent diabetic state by corticosteroid therapy (7). We have studied the development of steroid-induced diabetes in a racially mixed population of renal allograft recipients and have found a higher incidence of steroid diabetes in blacks than in whites.

## Patients and Methods

The population studied consisted of 171 patients who were transplanted at Henry Ford Hospital during the past seven years. Of these, 129 were nondiabetic, 28 were juvenile-onset, insulin-dependent diabetics (Type I diabetes) diagnosed before transplantation, and 14 developed diabetes after receiving a renal allograft and while they were on maintenance corticosteroid therapy (Table I).

Submitted for publication: February 25, 1981
Accepted for publication: June 5, 1981

* Department of Internal Medicine, Division of Nephrology, Henry Ford Hospital
** Department of Pathology, Henry Ford Hospital
Address reprint requests to Dr. Dumler, Division of Nephrology, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202

The diagnosis of steroid diabetes was made on the basis of a negative history for diabetes before transplantation, a normal fasting blood glucose up to the time of receiving renal allograft, and the presence of persistent fasting hyperglycemia in the post-transplant period while on chronic maintenance corticosteroid therapy. HLA typing was carried out on all patients as previously described (8). Fisher's exact probability test was used for statistical analysis (9).

## Results

Of 143 patients who did not have diabetes before transplantation, 14 (9.8%) developed steroid diabetes at varying times after surgery. Analysis by race of the population at risk indicated that 9 of 52 blacks (17.3%) developed steroid diabetes as compared to 5 of 91 (5.5%) whites, a highly significant difference ($p < .01$).

The frequency of the HLA antigens B8 and Bw15 in our patient population is shown in Table II. None of the white patients with steroid diabetes was positive for B8 or Bw15, and the frequency of Bw15 did not differ between blacks with steroid diabetes and nondiabetic blacks. Among blacks with steroid diabetes, the frequency of HLA B14 was significantly higher ($p < .001$) than for insulin-dependent diabetics (Type I) or nondiabetics (Table II). No differences were noted in the frequency of HLA-B7, B12, or B18 among black or white nondiabetic, insulin-dependent, or steroid-induced diabetic patients.

In our patients with steroid-induced diabetes, the mean age was 42 $\pm$ 12 years, and the mean duration of onset after

**TABLE I**

**Steroid-Induced Diabetes in Renal Transplant Recipients: Racial Distribution**

| Patient Groups | Number of Patients | | |
|---|---|---|---|
| | Blacks | Whites | Total |
| Nondiabetics | 43 | 86 | 129 |
| Insulin-dependent | 13 | 15 | 28 |
| Steroid-induced Diabetics | 9 | 5 | 14 |
| | 65 | 106 | 171 |

transplantation was 9 ± 5 months. A positive family history of diabetes mellitus was present in two of the 14 patients who developed steroid diabetes. Only one of the patients with steroid-induced diabetes was obese. There were no differences in mean body weights between blacks and whites or between patients with steroid-induced diabetes and nondiabetic recipients. The frequency of furosemide usage and its dosage were similar in blacks and whites and in patients with and without steroid-induced diabetes. All black patients have required insulin for control of blood glucose. Two of the five white patients were managed by diet alone and have a normal glucose tolerance at a lower steroid dose. No patient has developed ketoacidosis, and three patients who lost their grafts are no longer diabetic after corticosteroids were discontinued.

## Discussion

The 9.8% incidence of steroid-induced diabetes in our series agrees with that cited in previous reports (1-6). A greater frequency of steroid diabetes in blacks has been reported by David, et al (6), who found a higher frequency of HLA-A28 in blacks and attributed the greater incidence of steroid diabetes in blacks to this fact. In our series, even when we excluded patients who were HLA-A28 positive, the incidence of steroid diabetes in blacks (15%) was still higher than in whites (6%). It has recently been shown that HLA-A2 may be a marker for insulin-independent or insulin-requiring diabetes (Type II) in South African blacks (10). We thus evaluated the frequency of this particular phenotype among our patients but found no differences between nondiabetics and steroid diabetics.

We could not document a higher frequency of HLA-B8 or Bw15 in steroid diabetics, black or white, as has been reported previously (7). Others have also failed to reveal such an association (5). None of our black, insulin-dependent diabetic patients (Type I) was positive for B8 or Bw15. This finding agrees with reports that indicated no association between the HLA-B locus and Type I diabetes in black Americans (11,12). However, we did find in blacks an

**TABLE II**

**Frequency (%) of HLA A2, A28, B8, B14 and Bw15 Antigens in Renal Transplant Recipients**

| | HLA Antigen | Nondiabetics | Insulin-dependent Diabetics | Steroid Diabetics |
|---|---|---|---|---|
| Whites | | (N=86) | (N=15) | (N=5) |
| | A2 | 46 | 63 | 80 |
| | A28 | 8 | 5 | 0 |
| | B8 | 27 | 37 | 0 |
| | B14 | 10 | 0 | 20 |
| | Bw15 | 14 | 32 | 0 |
| Blacks | | (N=43) | (N=13) | (N=9) |
| | A2 | 33 | 46 | 44 |
| | A28 | 19 | 31 | 33 |
| | B8 | 9 | 0 | 0 |
| | B14 | 2 | 0 | 33* |
| | Bw15 | 2 | 0 | 10 |

* $p < .001$ when compared to nondiabetics and insulin-dependent diabetics (Type I)

association between the development of steroid diabetes and an increased frequency of HLA-B14.

The mechanisms for the development of steroid diabetes are not clear. Several effects of corticosteroids may be relevant, such as an increase in gluconeogenesis, impaired peripheral utilization of glucose, insulin resistance, and induction of hyperglucagonemia. It has been recently shown that steroid therapy, even in renal transplant recipients with a normal glucose tolerance test, results in a significantly enhanced insulin release and an increased number of insulin receptors in monocytes (13). In general, patients with steroid diabetes are older, are cadaver allograft recipients, have been treated several times for acute rejection episodes, and acquire their diabetes during the first three months after transplantation. A family history of diabetes mellitus is present in one third to one half of these patients, and hyperglycemia is usually controlled without insulin (1-6).

We could not find any differences in the type of transplant (cadaveric or living related), family history of diabetes, total dose of steroids, and mode of steroid administration (daily versus alternate day) between patients who developed steroid diabetes and those who did not. Others have also found no consistent effect of alternate day steroid therapy on the development of steroid-induced diabetes (14). Whether the lower dosages of steroids currently used in renal transplantation will lead to a decreased incidence of steroid diabetes remains to be determined. The mean follow-up of these patients is 33 ± 25 months, and complications attributable to steroid diabetes have yet to occur. In

this series, steroid-induced diabetic patients did not have an increase in mortality (10 per 1,000 patient months) when compared to insulin-dependent diabetics (16 per 1,000 patient months) or to nondiabetic renal transplant recipients (18 per 1,000 patient months).

We hypothesize that steroid-induced diabetes as seen in the renal transplant population is distinct from insulin-dependent diabetes (Type I) and that clinically it resembles maturity-onset, noninsulin-dependent (Type II) diabetes (15). Why blacks are more prone to developing steroid diabetes is not clear from this study. The population analyzed is a selected one, since all patients have developed end-stage kidney disease. Analysis of data from the Michigan Kidney Registry for Southeastern Michigan indicates that diabetes mellitus is more frequently associated with end-stage kidney failure in blacks than in whites. The data also suggest that in the black diabetic population renal failure is more commonly associated with noninsulin dependent (Type II) diabetes (Weller JW, personal communication). Many socioeconomic and genetic factors may not only make diabetes more severe in black patients, i.e., development of end-stage kidney disease, but may also predispose them to developing diabetes under certain stressful conditions, i.e., maintenance corticosteroid therapy.

In summary, these data allow the clinician involved in renal transplantation to identify a group of patients at particular risk for steroid-induced diabetes, the black renal transplant recipient. They also suggest that once diabetes occurs, its clinical course will be similar to that of Type II diabetes mellitus and that remission may occur if steroid therapy is withdrawn.

## References


1. Ruiz JO, Simmons RL, Callender CO, Kjellstrand CM, Buselmeier TJ, Najarian JS. Steroid diabetes in renal transplant recipients: Pathogenetic factors and prognosis. Surgery 1973;73:759-65.
2. Hill CM, Rajkumar KV, McGeown MC, Douglas JF, McEvoy J. Glycosuria and hyperglycemia after kidney transplantation. Lancet 1974;2:490-94.
3. Woods JE, Zincke H, Palumbo PJ, Johnson WJ, Anderson CF, Frohnert PP, Service J. Hyperosomolar nonketotic syndrome and steroid diabetes: Occurrence after renal transplantation. JAMA 1975;231: 1261-63.
4. Gunnarson R, Arner P, Lundgren G, Magnusson G, Ostman J, Groth CG. Steroid diabetes after renal transplantation: Preliminary report. Scand J Urol Nephrol Suppl 1977;42:191-94.
5. Gunnarson R, Arner P, Lundgren G, Magnusson G, Ostman J, Groth CG. Diabetes mellitus: A-more-common-than-believed complication of renal transplantation. Trans Proc 1979;9:1280-81.
6. David DS, Cheigh JS, Braun DW, Fotino M, Stenzel KH, Rubin AL. HLA-A28 and steroid-induced diabetes in renal transplant patients. JAMA 1980;243:532-33.
7. d'Apice AJF, Mathews JD, Tait BD, Kincaid-Smith P. Association of HLA antigens with glucose intolerance following renal transplantation. Tissue Antigens 1978;11:423-26.
8. Hayashi H, Hunter JB. Histocompatibility testing in renal transplantation. Henry Ford Hosp Med J 1978;26:13-18.
9. Swinscow TDV. Statistics at square one. London: British Med Assoc, 1977:54.
10. Briggs BR, Jackson WPU, DuToit ED, Botha M. The histocompatibility (HLA) antigen distribution in diabetes in Southern African blacks (Xhosa). Diabetes 1980;29:68-71.
11. Rodey GE, White N, Frazer TE, Duquesnoy RJ, Santiago JV. HLA-DR specificities among black Americans with juvenile-onset diabetes. N Engl J Med 1979;301:810-12.
12. Zeidler A, Loon J, Frasier SD, Kumar D, Penny R, Terasaki P. HLA-DRW antigens in Mexican-American and Black-American diabetic patients. Diabetes 1980;29:247-50.
13. Briggs W, Migdal, S, Mahajan S, McDonald F. Insulin release, insulin binding and glucose tolerance in renal transplant recipients (Abst). Kidney Int 1981;19:264.
14. Sampson D, Albert DJ. Alternate-day therapy with methyl-prednisolone after renal transplantation. J Urol 1973;109:345-48.
15. Fajans SS, Cloutier MC, Crowther RL. Clinical and etiologic heterogeneity of idiopathic diabetes mellitus. Diabetes 1978;27:1112-25.