Complications of early-onset insulin-dependent diabetes mellitus in Blacks and Indians

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Summary

Blacks and Indians with early-onset insulin-dependent diabetes mellitus (IDDM) were studied in order to assess the prevalence of acute and chronic complications. Of the 92 Blacks almost 70% developed keto-acidotic coma on one or more occasions, whereas 50% of the 41 Indians manifested this complication. Most of the chronic complications were related to duration of IDDM. Retinopathy was found in 14% of the Black and 22% of the Indian patients, nephropathy in 3% and 7% and neuropathy in 22% and 32% respectively. Compared with findings in other studies, IDDM in these population groups is not associated with a particularly high prevalence of chronic complications.

The discovery of insulin more than 50 years ago has brought about profound changes in the natural history of insulin-dependent diabetes mellitus (IDDM) in man. Today because of insulin and advances in the management of infection, shock and electrolyte imbalance, keto-acidosis rarely results in death. Instead, the chronic complications of the disease, such as microvascularity and macroangiopathy, are major causes of morbidity and mortality in these patients. Recent evidence suggests that optimal control of diabetes mellitus may prevent or at least delay some of these debilitating sequelae.

Previously it has been shown that metabolic control in Blacks and Indians with IDDM was far from satisfactory. This study was undertaken to assess the prevalence of acute and chronic complications of the disease in young patients from these population groups.

Patients and methods

A total of 133 patients with onset of IDDM before the age of 35 years was studied. The 92 Blacks and 41 Indians were all patients of the King Edward VIII Hospital in Durban. Diagnosis of IDDM was based on the criteria recommended by the WHO. Clinical characteristics are shown in Table I. Their case records were examined to obtain details of age at onset, duration of diabetes and episodes of keto-acidosis. Each patient underwent a thorough physical examination. Peripheral neuropathy was diagnosed on the basis of symptoms (pain, paraesthesiae, hyperesthesia, foot drop) and signs (loss of touch, pain, position or vibration sense, absent reflexes). Criteria used to diagnose autonomic neuropathy included impotence, heart rate response to standing, and postural hypotension, which was deemed to be present if the difference between the lying and standing systolic pressure was greater than 30 mmHg. Fundal examination was carried out by first instilling a mydriatic in each eye and then examining each fundus for at least 2 minutes. Nephropathy was deemed to be present if albuminuria was found in three consecutive urine samples taken on different occasions. If either of these abnormalities was detected the glomerular filtration rate (GFR) was determined using $^{51}$Cr-labelled EDTA.

Peripheral vascular disease was assessed by palpation of all the peripheral pulses, and ischaemic heart disease by the presence of angina or resting ECG changes such as ST-segment depression or T-wave inversion.

Results

These are shown in Tables II and III.

<table>
<thead>
<tr>
<th>TABLE I. CLINICAL CHARACTERISTICS OF PATIENTS WITH IDDM</th>
<th>Blacks</th>
<th>Indians</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>92</td>
<td>41</td>
</tr>
<tr>
<td>Male : female ratio</td>
<td>21 : 25</td>
<td>17 : 24</td>
</tr>
<tr>
<td>Mean age at onset (range)</td>
<td>17 yrs (8 mo. - 35 yrs)</td>
<td>23.5 yrs (1.5 - 35 yrs)</td>
</tr>
<tr>
<td>Mean duration of disease (range)</td>
<td>3.8 yrs (1 - 27)</td>
<td>5.4 yrs (1 - 22)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE II. PREVALENCE OF COMPLICATIONS IN PATIENTS WITH IDDM</th>
<th>Blacks</th>
<th>Indians</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keto-acidosis</td>
<td>53 (58%)</td>
<td>22 (54%)</td>
<td>75 (50%)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral</td>
<td>20 (22%)</td>
<td>13 (32%)</td>
<td>33 (25%)</td>
</tr>
<tr>
<td>Autonomic</td>
<td>4 (4%)</td>
<td>2 (5%)</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>13 (14%)</td>
<td>9 (22%)</td>
<td>22 (17%)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>3 (3%)</td>
<td>3 (7%)</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Triopathy</td>
<td>1 (1%)</td>
<td>2 (5%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (4%)</td>
<td>2 (5%)</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Cataracts</td>
<td>5 (5%)</td>
<td>2 (5%)</td>
<td>7 (5%)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>6 (7%)</td>
<td>1 (2%)</td>
<td>7 (5%)</td>
</tr>
</tbody>
</table>
Keto-acidotic coma. There were 75 patients who developed keto-acidotic coma on one or more occasions. This complication was the presenting feature of the disease in almost 30% of such patients, and omission of insulin was the precipitating factor in 44% of all cases. Almost 60% of the Black patients and just over 50% of the Indian patients manifested keto-acidotic coma on one or more occasions. Omission of insulin was a contributory factor in 56% of the Black patients and in only 26% of the Indian patients.

Peripheral neuropathy. The duration of IDDM was less than a year in 50% of the Black patients manifesting this complication. One Black patient and 4 Indian patients had symptoms of peripheral neuropathy. Absent ankle jerks were found in 20% of the patients and in 40% of these patients IDDM had been present for less than 2 years. Vibration sense and joint position were impaired in 3 patients. Abnormalities of these modalities of sensation were always associated with absent reflexes.

Autonomic neuropathy. Impotence was present in 6 patients, of whom 2 manifested this complication at the onset of the disease. Four patients showed evidence of autonomic neuropathy on the basis of the screening tests used. One of them also showed other florid features of autonomic neuropathy, viz. gastric and oesophageal atony, impotence, bladder atony and intractable diarrhoea. As expected, he had peripheral neuropathy which has been shown to be an invariable accompaniment of autonomic neuropathy.

Retinopathy. The incidence of background retinopathy was more common in the Indian than in the Black patients. The mean duration of the disease was similar in both racial groups. Of the 7 Black patients who had had IDDM for more than 10 years, all showed evidence of retinopathy, but only 5 of the 8 Indian patients with a similar duration of disease were affected. In patients who had had IDDM for less than 10 years only 7% of the Black and 12.5% of the Indian patients showed evidence of retinopathy. Only 1 patient had proliferative retinopathy.

Nephropathy. Based on the criteria used in this study, 6 patients were found to have nephropathy. Two patients had persistent albuminuria in the presence of a normal creatinine concentration. One of them, who died of acute suppurrative pyelonephritis and renal papillary necrosis, had typical features of diabetic nephropathy on histological examination of autopsy tissue. All 6 patients with nephropathy also had retinopathy, which has been found to be invariably associated with this complication. The mean GFR was 50 ml/minute (range 35 - 75 ml).

Triopathy. Nephropathy, retinopathy and nephropathy were associated in 3 patients. The mean duration of disease in these patients was 11.3 years.

Macrovascular disease. None of the patients had peripheral vascular disease or ischaemic heart disease.

Hypertension. Hypertension was seen in 6 patients. It was associated with nephropathy in both the Indian patients, but this relationship was found in only 2 of the 4 Black patients.

Cataracts. Cataracts of gradual onset, the usual form seen in diabetes of long duration, were seen in 3 patients, all of whom had had the disease for at least 10 years. Another 4 patients presented with dense subcapsular cataracts after a short history of symptoms of diabetes.

Tuberculosis. Active pulmonary tuberculosis was present in 6 of the Black patients with IDDM, but only 1 Indian patient had this complication.

Discussion

Despite the fact that the use of the term complications to describe the pathological manifestations of diabetes has now been challenged, this term has been retained in this study since the traditional term has not yet been generally discarded.

Diabetic coma due to keto-acidosis is today a largely preventable disorder in which social, economic, administrative and medical factors play a role. While improved public education has reduced the frequency with which diabetic keto-acidosis marks the onset of previously undiagnosed diabetes mellitus, about 8 - 20% of cases of keto-acidosis in various series still appear in new cases.

In this study, however, almost 30% of those who developed keto-acidosis presented with this complication at the onset of the disease. Inadequate public education and primary health facilities are probably responsible for the high rate.

Discontinuation of insulin therapy and infection used to be the most important causes of keto-acidosis in both developed and underdeveloped countries. Now, however, infection appears to be the main precipitating factor in most of the patients with diabetic keto-acidosis seen in developed countries, omission of insulin accounting for only 4 - 7% of cases. Among the patients reported in this study both omission of insulin and infection were equally important in precipitating keto-acidosis. Again inadequate education, poor socio-economic conditions and lack of primary health care facilities are to a large extent responsible for this high frequency.

The slight but significant difference in the incidence of keto-acidosis between the two racial groups may be related to the relatively better socio-economic status and educational background of the Indian patients.

Studies of the prevalence of diabetic neuropathy based on clinical criteria have yielded varying results because of inadequate standardization of criteria and methods of investigation. A prevalence of 40% has been reported by Goodman and one of 12% by Pirart. It is rare in children and uncommon in adolescents, occurring more frequently with increasing age. Peripheral neuropathy appears to be fairly common in both groups with IDDM. Studies in other Black and Indian population groups have also revealed a fairly high incidence of diabetic neuropathy.

In the majority of the Indian patients the duration of IDDM was more than 5 years, but in 50% of the Black patients the disease had been present for less than a year. It appears that in addition to duration of diabetes, as suggested by Gregersen, other factors play a role in the development of neuropathy. An association with hyperglycaemia has been noted by others.

Symptoms such as paraesthesiae and numbness are the least sensitive indices of neuropathy. Thus the rarity of symptomatic manifestations of this complication is not at all surprising. Nilsson et al. studied the significance of the ankle reflex in a group with no diabetes. Reflexes were absent in 25% of those over the age of 60 and in none under this age. Of their young diabetic patients (age 20 - 39), 34% had absent or partly absent ankle jerks. In our study 20% of the patients had absent ankle jerks.
jerks and in over 40% of these patients the disease had been present for less than 2 years. In the young diabetic patients studied by Nilsson et al., 21 34% of the patients with neuropathy had had diabetes for a short period (mean 1,5 years).

Some workers have considered an impaired vibration sense to be the earliest sign of peripheral neuropathy, 22 but only 2% of the patients reported in our study had impaired vibration sense. None of the young diabetic patients in the group studied by Nilsson et al. 21 showed impaired vibration sense. Although motor function abnormalities such as weakness of the legs and foot drop do occur, they are much less common. 23 None of the patients in this study showed any evidence of a motor neuropathy.

Although autonomic neuropathy depends on the duration of diabetes, 23 it has also been reported in the early stages of juvenile-onset diabetes. 24 The commonest manifestation of this form of neuropathy in adult males reported in this study was impotence, which is probably the most common symptom related to autonomic neuropathy. It has been found to be prevalent in up to 50% of men in various series. 23,33 It may be present without other features of autonomic neuropathy. 25 When other signs of autonomic neuropathy are present, impotence is an invariably sign. 25

Although the prevalence and natural history of diabetic autonomic neuropathy have not yet been clearly elucidated 23 it is still considered relatively uncommon. 26 Its rare occurrence in this study is therefore not unexpected.

Retinopathy is a major cause of morbidity in many diabetic patients. Although clinically detectable lesions of the retina eventually develop in most patients, impairment of vision of varying degrees occurs in about 50% of patients with longstanding diabetes. 1 The prevalence of retinopathy appears to vary in different population groups. 3 In young White diabetic patients seen at Joslin Clinic, Boston, retinopathy was rare (2%) if the duration of the disease was less than 10 years, 26 whereas it was common (48%) in young Kenyans also falling into this category. 37 The Black and Indian patients in this study also did not appear to be particularly prone to this complication when IDDM had been present for less than 10 years, although the frequency (7% and 12.5% respectively) was somewhat higher than in Joslin Clinic patients (2%) with a similar duration of disease.

IDDM of more than 10 years' duration was very commonly associated with retinopathy in the Black and Indian patients reported in our study. Comparison with other groups with similar disease duration shows a prevalence of 80% in young Kenyan diabetics, 31 14% in Nigerian 32 and 22% in Ugandan diabetics. 33 In Sweden a frequency of 35.7% was found in young diabetics who had had the disease for 8 - 15 years and in 100% of those who had had it for more than 18 years. 21

The rarity of proliferative retinopathy in our study may be due to the relatively short duration of disease in the vast majority of patients (mean 4.3 years). Nevertheless, this form of retinopathy has been found to be uncommon in other studies. 34,35 Knawels et al., 35 however, estimate that almost 50% eventually develop this complication during the course of 30 years of diabetes.

Diabetic nephropathy is the major cause of death in IDDM patients, accounting for up to 40% of deaths. 28 Although the prevalence of nephropathy varies, it has been found to be present in up to 30% of patients who have had the disease for more than 15 years. 35

Proteinuria is a useful but not very sensitive index of diabetic nephropathy. 1 The rarity of nephropathy in this study may therefore be due to the relatively insensitive method of detecting this complication, although the relatively short duration of IDDM in most of the patients may also play a part.

The 6 patients with nephropathy constitute 10% of those with a disease duration of more than 7 years. Nilsson et al. 21 found a similar frequency of proteinuria in their young diabetic patients with disease duration of more than 7 years. All 6 patients had retinopathy, which has also been found to be invariably associated with nephropathy. 3

In the majority of cases cataracts complicating diabetes mellitus are of gradual onset. 3 Such lesions have been found in 50% of young diabetic patients after 11 years of disease. 4 In this study, however, only 20% of the patients who had IDDM for more than 10 years manifested with cataracts, and all those with this complication had had the disease for more than a decade. Dense subcapsular cataracts which are rare and develop in some young patients who have had diabetes for a short time 11 were the more common type of cataract seen but were only observed in the Black patients.

An association between hypertension and diabetes has been found in many studies. 3,15,34 Obesity and diabetic glomerulosclerosis probably account for the increased frequency of hypertension in diabetic patients. 1 In IDDM hypertension is rare at the onset of the disease, with the frequency rising precipitously after 10 years of diabetes, to such an extent that about 50% of patients have hypertension after 30 years. 16

In our study, of the 6 patients who had hypertension only 3 patients had nephropathy as indicated by proteinuria. Nevertheless, the other patients would probably have shown evidence of nephropathy had a more sensitive method to estimate urinary protein been used. All the patients except 1 had had IDDM for a long time. Such a finding is in keeping with Christlieb's observation. 37

The increased frequency of tuberculosis in diabetic patients was observed by Avicenna as long ago as the 10th century. 38 Since the incidence of tuberculosis in Blacks is very high even in the general population, it is not surprising that this infection should manifest itself in Black diabetic patients more commonly than in populations in non-endemic areas. The frequency rate of 6.5% for active pulmonary tuberculosis is much higher than that in Jamaican diabetic patients (0.9%) and in a group of American patients (2%). 39,40

Conclusions

The data presented have shown that keto-acidotic coma is still a major cause of morbidity in young Blacks and Indians with IDDM and that chronic complications are in part related to duration of disease, as has been shown in numerous studies. 1 Although the role of poor metabolic control in the pathogenesis of microvascular complications cannot be denied it does appear that in spite of the relatively poor metabolic control in these patients, complications are not significantly commoner than in other population groups. Prolonged poor control may well be the major determinant in hastening the development of complications.

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REFERENCES

Inpatient cardiac rehabilitation

N. F. GORDON

Summary

Documentation of the deleterious effects associated with prolonged bed-rest provided the physiological basis for recommending more aggressive and earlier mobilization of the acute myocardial infarction patient. The 1 Military Hospital inpatient cardiac rehabilitation programme is discussed, together with the importance of the predischarge graded exercise test.


The 40 years after Herrick's description of acute myocardial infarction (MI) in 1912 were characterized by a classic approach to therapy which included between 4 and 8 weeks of enforced bed-rest in hospital. Mallory et al. seemed to support this concept when in 1939 their studies on the pathological changes occurring after acute transmural MI demonstrated that active scar tissue formation does not commence until towards the end of the 2nd week, mature scar tissue is not evident for at least 6 weeks after the initial event, and scar maturation may not be complete until 12 weeks after an extensive MI. It was generally believed that any exertion before the completion of scar maturation would place an increased mechanical strain on the damaged myocardium, and thus might result in extension of the infarcted area, ventricular aneurysm formation and even ventricular rupture.

The initial challenge to this dictum of prolonged bed-rest and an extended period of inactivity was provided in 1952 by Levine and Lown when they reported on acute MI patients who were seated in an armchair by the 3rd day after MI without any apparent adverse effects. On the contrary, they suggested that their regimen reduced the risk of thrombo-embolism, improved cardiac function in patients suffering from failure and had a beneficial psychological effect. Since their report, documentation of the deleterious effects associated with prolonged immobilization at bed-rest has provided the physiological basis for recommending more aggressive and earlier mobilization of the acute MI patient. Furthermore, a policy of early mobilization after MI has been supported by a number of retrospective studies and controlled trials which have shown no adverse effects.

This changing pattern of care for the patient with acute MI has been characterized by earlier discharge from hospital and earlier return to work. Furthermore, a policy of early mobilization after MI has been supported by a number of retrospective studies and controlled trials which have shown no adverse effects.