Review Article

Malignant hypertension and its renal complications in black South Africans

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Summary

Malignant hypertension is an important cause of morbidity and mortality among urban black South Africans. Hypertension accounts for 15,9% of all patients and for 34,6% of blacks receiving treatment for end-stage renal failure. Malignant hypertension is more commonly diagnosed than benign hypertension and two-thirds of patients present in the age group 30 - 49 years. Together they are the most common preventable cause of end-stage renal failure in this country. Acute partially reversible renal failure occurs in 20% of patients with malignant hypertension who require dialysis. This is an important subgroup, who may be recognised by their younger age, female preponderance and fulminant presentation. Short-term peritoneal dialysis and effective control of blood pressure will result in satisfactory return of renal function. However, only adequate country-wide control of hypertension will prevent these costly renal complications.

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Two recent reviews have covered many of the clinical and management aspects of malignant hypertension among black South Africans,[1] and world-wide.[2] Demographic and epidemiological data suggest that this disease has been under-emphasised in the past in the RSA and that the medical profession should be made aware not only of the extent of the problem but also the serious complications and the important challenges for clinical and basic research. This article emphasises the renal complications of malignant hypertension seen in this country.

Demographic data

Malignant hypertension is now a rare disease in the Western world[3] but is more prevalent among black Americans than white.[4] The only published prevalence study in South Africa showed a hospital prevalence of 2,2% in Johannesburg during 1979/1980,[5] while Seedat and Reddy[6] in 1974 quoted a 7% incidence at a hypertension clinic in Durban. An unpublished survey of medical admissions to Hillbrow Hospital, Johannesburg, showed an average annual admission rate of 0,94% over the years 1985 and 1986 (S. H. James, M.Med. (Med.) dissertation, University of the Witwatersrand). There were 135 admissions for malignant hypertension from a total of 14 327 patients for the 2 years. This relatively common occurrence of malignant hypertension in blacks contrasts strikingly with its rarity in whites.

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Definition

The terms 'accelerated hypertension' and 'malignant hypertension' cause confusion, since they are sometimes used to describe the same syndrome and sometimes to imply different phases of the same syndrome. The term 'malignant' has been used to describe patients who in addition to high blood pressure have papilloedema, while the term 'accelerated' has been used when papilloedema is absent but there are fresh bilateral haemorrhages of the flame type with or without cotton wool spots. McGregor *et al.*[7] and Ahmed *et al.*[8] have convincingly shown that the prognosis of so-called 'accelerated' and 'malignant' hypertension is the same. Thus we prefer the term 'malignant' hypertension to describe all patients presenting with a diastolic pressure above 120 mmHg and bilateral fresh haemorrhages and/or exudates or papilloedema.

Aetiology

Malignant hypertension is rarely seen in whites unless there is an underlying secondary cause, usually bilateral renal parenchymal disease or renal artery stenosis. In blacks the majority of patients appear to have essential hypertension. The diagnosis is usually made on clinical grounds but has been supported histologically by tissue obtained either at autopsy[9] or from nephrectomy specimens obtained from patients on dialysis or at the time of transplantation.[10] Although no systematic angiographic study has been performed to exclude renal artery stenosis, which is commonly associated with malignant hypertension in white Americans,[11] this is an unlikely cause in black South Africans. Fibrous dysplasia and aortitis even of the Takayasu type is generally rare and, because atheroma of the aorta is still uncommon in blacks, renal artery stenosis is unlikely to be an important cause of malignant hypertension in this group. The endocrine causes of malignant hypertension are anecdotally as rare in blacks as whites and, apart from phaeochromocytoma, they seldom present in the malignant phase. Table I shows the distribution of malignant hypertension in three areas of the world and confirms not only the predominance of essential malignant hypertension (82%) in South Africa, but also the large numbers of patients that presented to a single medical unit in the space of 1 year.[5]

TABLE I. MALIGNANT HYPERTENSION AROUND THE WORLD

	Glasgow	Melbourne	Johannesburg blacks
Period of study	**1968-1983**	**1979-1985**	**1979-1980**
No. of patients	**139**	**83**	**62**
Essential (%)	**60**	**20**	**82**
Secondary (%)	**40**	**80**	**18**

Modified from Isles.[2]

Renal disease

The renal disease in malignant hypertension has been well described in a recent review.[12] Musculomucoid hyperplasia and fibrinoid necrosis of the smaller intrarenal arteries are characteristic lesions. Fibrinoid necrosis was considered to be the hallmark of the malignant phase of hypertension.[13] It is not clear whether this is simply a manifestation of malignant hypertension or whether it is pathogenetic. If, as suspected, fibrinoid necrosis is only a manifestation of extremely high arterial pressure, then musculomucoid hyperplasia is more likely to be the basic pathological lesion in malignant hypertension. Hyaline arteriosclerosis will only be present if there has been longstanding benign hypertension. Isaacson and Milne[14] have studied the nephropathology of malignant hypertension in blacks in Johannesburg. Unlike the findings in black Americans, they saw fibrinoid necrosis in a large proportion of their autopsy series, and also confirmed musculomucoid hyperplasia in all.

Diagnosis

The renal complications of malignant hypertension range from mild proteinuria to end-stage renal failure. The specific diagnosis of essential malignant hypertension is difficult when renal insufficiency is present. These patients commonly present with some blood and protein in the urine. Red blood cell casts or, rarely, frank haematuria may confuse the diagnosis with primary glomerulonephritis and superimposed malignant hypertension. In favour of essential malignant hypertension is the lack of past renal history, modest concentrations of protein in the urine (< 1 g/d) and normal to only slightly decreased renal size on ultrasonography. Confirmation of the diagnosis can only be obtained by renal biopsy. However, this may be hazardous in the setting of malignant hypertension. Many of the local studies quoted can be criticised on the grounds that there was no histological proof of essential malignant hypertension, but nephrologists have been reluctant to perform renal biopsies in the malignant phase.

Renal failure following malignant hypertension may present in three forms. These are acute, acute-on-chronic and chronic. Of great interest are the acute and the acute-on-chronic presentations. Complete recovery of renal function has been well documented provided the rise in serum creatinine level is modest.[15] Serum creatinine concentrations of less than 300 μmol/l frequently return to normal values once adequate control of the blood pressure has been obtained. Less well documented is a subgroup of patients who present with oliguric renal failure requiring dialysis but who later recover some renal function.[16] We have had a 20% recovery rate among black patients at Hillbrow Hospital, Johannesburg. It would appear that here acute renal failure occurs as a result of fulminant or intensified renal ischaemia following the occlusive vasculopathy of malignant hypertension. Acute tubular necrosis develops as well as cortical ischaemia as shown by glomerular basement membrane wrinkling on histological examination.[17,18] With stabilisation of the blood pressure and maintenance dialysis, resolution of the tubular and vascular lesions may occur with variable recovery of renal function. This process may take a few days to more than 1 year but the mean duration of dialysis of these patients is 2-3 months. This potential for recovery of renal function must question the practice of bilateral nephrectomy for the control of refractory hypertension, which was practised in local dialysis patients in the past.[19] In addition, these patients should be maintained on dialysis for up to 6 months before being referred for transplantation. The clinical profile of patients who may recover some renal function is characterised by the explosive onset of malignant hypertension. They tend to be younger (±37 years) than the average malignant hypertension patients (±47 years) and most are female. The known duration of hypertension is short, they present with very high blood pressures, many are anuric (urine volume $<$ 100 ml/d) and the majority show haematological evidence of micro-angiopathic haemolytic anaemia. Whether they represent an aetiological subset of patients needs to be established.

Gold *et al.*[10] showed in 1982 that essential malignant hypertension was the most common proven cause of end-stage renal failure in black patients accepted for long-term dialysis at Baragwanath Hospital. In their series a definite pathological diagnosis of essential malignant hypertension was made in 49% of 65 patients in whom renal histological examination was carried out. In patients in whom renal histological examination was not carried out malignant hypertension accounted for 33% on a clinical basis. At Johannesburg Hospital only 3% and 2% of whites during the period 1966 - 1973[20] and 1978 - 1982[21] respectively, had end-stage renal failure because of essential hypertension.

Data from the South African Dialysis and Transplantation Registry[22] provide a national perspective on hypertension as a cause of end-stage renal failure. During the period 1982 -1987, 3 632 patients with end-stage renal failure were treated at the various centres countrywide. Hypertension was the cause of end-stage renal failure in 577 patients or 15,9% of the total. It was the dominant cause of end-stage renal failure in blacks (34,6%) and the second commonest cause among coloureds (20,9%) while in only 4,3% of white patients was hypertension responsible for end-stage renal failure (Table II). Malignant hypertension was more commonly diagnosed than benign hypertension (57,0% v. 43,0%; $P < 0{,}001$) (Table III). It is, however, intriguing that in a significantly high proportion of patients in the SA Dialysis and Transplantation Registry, benign hypertension is incriminated as the cause of end-stage renal failure. It should be stressed, however, that these diagnoses are clinical and not pathological. Of 328 malignant hypertension patients, blacks comprised 59,6%, coloureds 27,7%, whites 10,3% and Asians 2,4%. The overall male to female ratio of 3:2 was similar to that in the group with benign hypertension. The age at onset of treatment for end-stage renal failure is younger in this group of patients with malignant

TABLE II. SOUTH AFRICAN DIALYSIS AND TRANSPLANTATION REGISTRY (1982 - 1987) — ESSENTIAL HYPERTENSION

	Black	White	Coloured	Asian	Total
No. of patients treated for ESRF	**952**	**1 771**	**640**	**269**	**3 632**
No. of patients with EHT causing ESRF	**329**	**77**	**134**	**37**	**577**
Occurrence (%)*	**34,6**	**4,3**	**20,9**	**13,8**	**15,9**

* 2/1 x 100.
ESRF = end-stage renal failure; EHT = essential hypertension.

TABLE III. HYPERTENSION CAUSING END-STAGE RENAL FAILURE

	All groups	Black	White	Coloured	Asian
Total No. of patients with essential hypertension	**577**	**329**	**77**	**134**	**37**
Malignant hypertension					
No. of patients	**328**	**195**	**34**	**91**	**8**
%	**57**	**59,6**	**10,3**	**27,7**	**2,4**
Benign hypertension					
No. of patients	**249**	**134**	**43**	**43**	**29**
%	**43**	**54,0**	**17,2**	**17,2**	**11,6**

hypertension than the mean age in other series of malignant hypertension quoted.[13] The greater number of patients (37,4% of all malignant hypertension patients) were started on treatment for end-stage renal failure during the decile 30 - 39 years, followed by 30,1% in the 40 - 49-year age group. This trend was found in all population groups. The survival of patients with hypertension and other causes of end-stage renal failure was similar. Furthermore, no significant difference in survival between end-stage renal failure patients with benign or malignant hypertension could be demonstrated. It is clear from the SA Dialysis and Transplantation Registry data that hypertension, both malignant and benign, is the most common preventable cause of end-stage renal failure in the RSA and the predominant cause of end-stage renal failure among South African blacks who constitute the major population group in the country.

We have found that after renal transplantation bilateral nephrectomy did not improve blood pressure control or graft survival in these patients. Our experience with survival of black transplant patients has been that there is no significant difference over 30 months comparing patients with malignant hypertension and other causes of renal failure. This is in broad agreement with the SA Dialysis and Transplantation Registry figures which show an 80% actuarial graft survival at 30 months of 1 072 patients of all race groups who received transplants without hypertension compared with a 75% survival of 113 patients, again of all race groups, who received transplants and who had a diagnosis of hypertension. The period of observation is short and it is possible that differences may develop as the number of black patients and the duration of follow-up increases.

Management

A comprehensive account of the management of malignant hypertension has been presented in the two recent reviews.[1,2] It is worth noting that in the past, when effective therapy was not available, the 1-year mortality rate was 80%. Advances in therapy have revolutionised the management of this disorder with reversal of the malignant state and prolonged patient survival.

Essential malignant hypertension may present in two forms: most commonly there is no immediate threat to life, but on rare occasions patients present in hypertensive crisis with either encephalopathy or severe pulmonary oedema. In this rare crisis situation the patient should ideally be admitted to an intensive care unit where the blood pressure can be rapidly controlled with intravenous sodium nitroprusside. If an intensive care unit is not available, oral or sublingual nifedipine (capsule bitten and the contents swallowed) will lower the pressure to safe levels within 30 minutes during which time other therapy may be instituted for a longer-term antihypertensive effect.[23]

The basic aim of active therapy in the non-crisis situation is to reduce the diastolic blood pressure gradually to 110 mmHg over a 48-hour period. It must, however, be remembered that autoregulation of cerebral and renal blood flow is set at a higher arterial pressure in patients with malignant hypertension. Should the pressure fall too rapidly and to too low a level, a significant reduction in renal and cerebral perfusion may occur and result in acute tubular necrosis or cerebral ischaemia. Renal function must be closely monitored by serial serum creatinine level estimations and when these stabilise or improve, then further attempts must be made to bring the blood pressure to within normal limits. In this non-crisis situation oral atenolol or slow-release nifedipine have been shown to be safe and effective within the first 24 hours in local black patients.[24]

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