

# Clinical presentation and biochemical abnormalities in Black (Zulu) patients with cirrhosis in Durban

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## Summary

A retrospective study was designed to analyse the mode of presentation, clinical signs and haematological and biochemical abnormalities in 225 consecutive Black (Zulu) patients who were admitted to a general medical ward between the years 1970 and 1981 and in whom cirrhosis was later diagnosed. The most common presenting complaint was swelling of the body (60% of the patients), followed by abdominal pain (32%) and episodes of bleeding, mainly from the gastrointestinal tract (19%). On examination, hepatomegaly was encountered in 66% of the patients, with moderate to massive enlargement in 40%. Ascites was detected in 56%, with tense abdominal distension in 34%. Jaundice was present in 38% and emaciation, mental disturbance and splenomegaly in over 25%. Spider naevi (found in 2 patients) and Dupuytren's contracture (found in 1) were very rare. Thrombocytopenia and a high ESR were common. Over 90% of patients had low albumin and high globulin concentrations (albumin < 20 g/dl and globulin > 60 g/dl in 25%). Bilirubin and alkaline phosphatase levels and the prothrombin index were found to be within normal limits in 32%, 24% and 52% of cases respectively. Histologically the lesion was most commonly micronodular (73%) with variable deposits of fat and iron. Peritoneoscopy was the most useful special investigation in the diagnosis of cirrhosis, leading to a correct diagnosis in 77% of cases.

In conclusion, the clinical signs, biochemical abnormalities and histological features suggest that the factors causing cirrhosis in the community studied are mixed; it may result from the combined effects of alcohol abuse, malnutrition and chronic viral (e.g. hepatitis B) infections.

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Cirrhosis may by definition only be diagnosed after histological evidence has been obtained, but the way in which cirrhosis affects the rest of the body, producing various clinical signs and biochemical abnormalities, should lead the clinician to suspect diagnosis before biopsy is undertaken. However, these

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abnormalities are not constant and may vary with the cause of the cirrhosis.<sup>1</sup>

Cirrhosis is common in the Black population in Natal and is the eighth most common disease encountered at the King Edward VIII Hospital, Durban.<sup>2</sup> The exact aetiological process is controversial, but it could involve alcohol abuse, chronic viral infections and/or malnutrition. Traditionally alcohol has been taken in the form of 'home brews'; the alcohol level is not high, but the quantity taken often results in intoxication. The iron content is very high and is probably responsible for the known association between cirrhosis and siderosis in Black patients.<sup>3</sup> The incidence of hepatitis B virus antigenaemia is very high in the Black population of Natal, varying from 4% to 5.4% (compared with the figure of 0.09%<sup>4</sup> for the White population). Such a state has been shown to predispose towards the later development of cirrhosis.<sup>5</sup> Malnutrition and cirrhosis are associated,<sup>5</sup> but the mechanism involved is unknown and may well be indirect, possibly related to reduced immunocompetence<sup>6</sup> resulting in greater susceptibility to the infections and toxins that may induce cirrhosis. Examination of the associated clinical and biochemical abnormalities in our population group may provide indirect evidence of the main aetiological factor involved. In addition, the study should help the clinician in deciding which tests are helpful in the work-up of patients with suspected cirrhosis.

## Patients and methods

The admission summaries of 225 consecutive Black (mainly Zulu) patients hospitalized in the Professorial Medical Unit between the years 1970 and 1981 were studied. Special attention was paid to presenting complaints, clinical signs, and the results of biochemical and haematological tests and specialized investigations. Normal values were supplied by the routine pathological laboratories.

## Results

### Age and sex

The mean age at presentation was 45.5 years, and breakdown into decades is shown in Fig. 1 (paediatric patients were not included). The male/female ratio was 3:1.

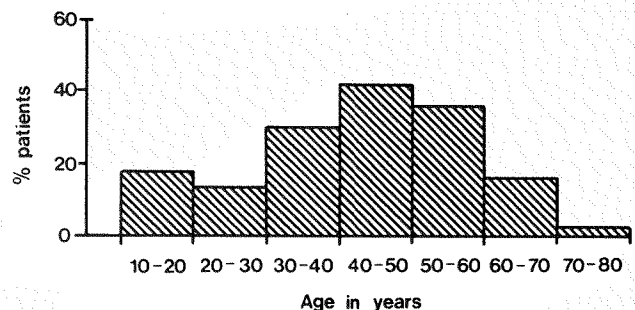


Fig. 1. Patients' ages.

## Aetiology

The precise aetiological processes were often obscure, but 42% of the men gave a history of heavy alcohol consumption (intoxication more than 3 times a week), while a further 16% admitted to occasional (e.g. weekend) abuse of alcohol. The figures for women were similar (40% and 15% respectively).

## Histological findings

The great majority (73%) of biopsy specimens showed evidence of micronodular cirrhosis. Frequent additional findings were siderosis and fat deposits. Macronodular cirrhosis was identified in only 8% of specimens, while evidence of post-viral infection, such as 'post-necrotic scarring' and 'chronic active hepatitis', was seen in 20% (12% and 8% respectively). Biliary cirrhosis was very uncommon (1%).

## Presenting complaints

Fig. 2 shows the common presenting complaints in order of frequency. By far the most common was 'swelling of the body' (60% of the patients). Abdominal pain, often vague in nature but commonly related to the right upper quadrant, was surprisingly common (32%). Jaundice was infrequently noted, either by the patient or by relatives.

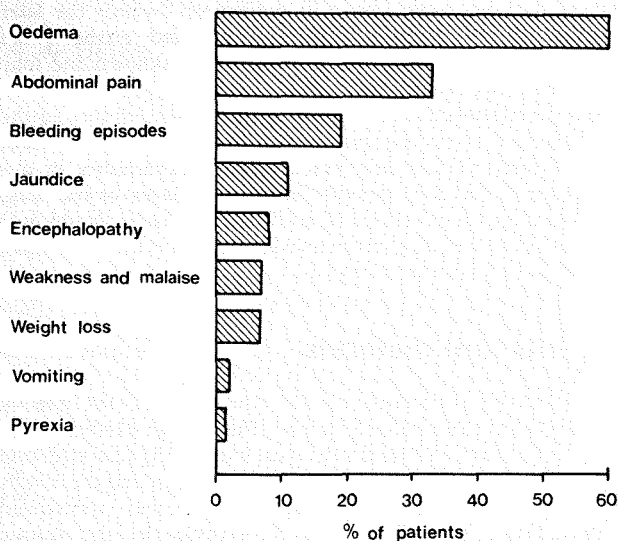


Fig. 2. Presenting complaints.

## Clinical signs

Fig. 3 indicates that, in keeping with the presenting complaints, ascites and oedema were observed in over half the patients (56%); hepatomegaly was even more common (66%). The incidence might even have been higher, since 34% of the patients had massive ascites which would have interfered with clinical assessment. Hepatomegaly greater than 3 fingerbreadths below the costal margin was noted in 40% of the patients. Splenomegaly was less frequently observed (24%), with increases greater than 3 fingerbreadths in only 7%. Clinical jaundice was noted in 38% of the patients.

Classic signs of chronic liver disease such as white nails, clubbing or spider naevi (2 patients), Dupuytren's contracture (1 patient), gynaecomastia (6 patients) and testicular atrophy were infrequently observed.

## Haematological findings (Table I)

Mild anaemia was common (mean haemoglobin concentration

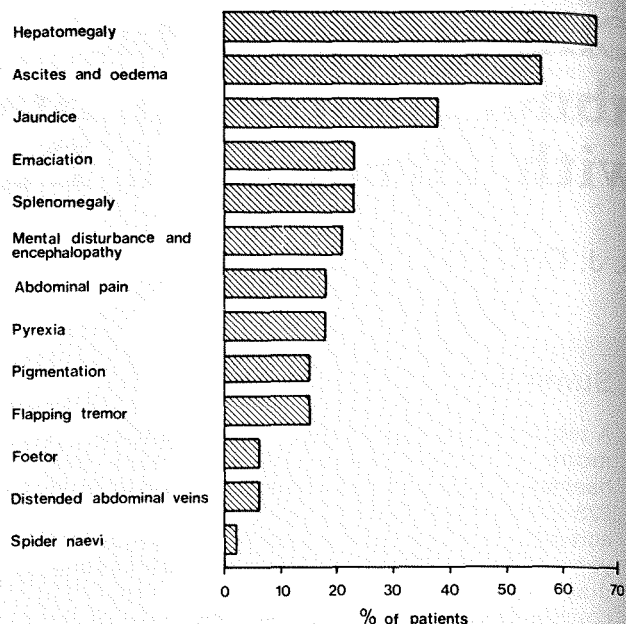


Fig. 3. Clinical signs.

TABLE I. HAEMATOLOGICAL FINDINGS

Parameter	Mean $\pm$ SD	Within normal limits	Abnormal
<b>Haemoglobin (g/dl)</b>	<b>11,7 <math>\pm</math> 2,2</b>	<b>46%</b>	<b>54% &lt; 12</b>
<b>White cell count (<math>\times 10^3/\mu\text{l}</math>)</b>	<b>8,4 <math>\pm</math> 4,3</b>	<b>76%</b>	<b>3% &lt; 3,5</b> <b>21% &gt; 11</b>
<b>Platelet count (<math>\times 10^3/\mu\text{l}</math>)</b>	<b>126 <math>\pm</math> 50</b>	<b>29%</b>	<b>71% &lt; 150</b> <b>43% &lt; 100</b> <b>10% &lt; 50</b>
<b>ESR (mm/1st h)</b>	<b>46 <math>\pm</math> 27</b>	<b>3%</b>	<b>97% &gt; 5</b> <b>38% &gt; 50</b>
<b>Prothrombin index (%)</b>	<b>79 <math>\pm</math> 13</b>	<b>52%</b>	<b>48% &lt; 80</b> <b>18% &lt; 70</b>

11,7  $\pm$  2,2 g/dl), although 46% of the patients had values higher than 12 g/dl (Fig. 3). Only 18% had values below 10 g/dl.

The white cell count was normal in 76% of the patients, the mean figure being 8,4  $\pm$  4,3  $\times 10^3/\mu\text{l}$ , while elevations above 11  $\times 10^3/\mu\text{l}$  were noted in 21%.

Platelet counts were normal in only 29% of cases; 43% of the patients were found to have thrombocytopenia (< 100 000/ $\mu\text{l}$ ) and 10% severe thrombocytopenia (< 50 000/ $\mu\text{l}$ ). All the patients in the latter group had a large spleen.

The ESR was normal in only 3% of the patients; the elevation was marked (above 50 mm/1st h) in 38%. The mean prothrombin index was 79  $\pm$  13%, being within normal limits (> 80%) in 52%.

## Biochemical values (Table II)

Hypo-albuminaemia was extremely common, only 6% of the patients having levels higher than 35 g/dl. Severe hypo-albuminaemia (< 20 g/dl) was demonstrated in 27% of cases (Fig. 4). Elevation of globulin values was even more dramatic, 95% of the patients being found to have values exceeding the normal range. Furthermore, 24% had values exceeding 60 g/dl, i.e. twice the normal level.

While nearly all the patients were found to have some elevation in liver enzyme values, only 50% had aspartate

TABLE II. BIOCHEMICAL FINDINGS

Parameter	Mean $\pm$ SD	Within normal limits	Abnormal
Albumin (g/l)	24 $\pm$ 6	6%	94% > 35 82% > 30 27% > 20
Globulin (g/l)	53 $\pm$ 12	5%	95% > 32 28% > 40 33% > 50 24% > 60
Bilirubin ( $\mu$ mol/l)	46 $\pm$ 49	32%	68% > 17 31% > 40
Alkaline phosphatase (IU/l)	167 $\pm$ 100	24%	76% > 95 27% > 200
Aspartate transaminase (IU/l)	62 $\pm$ 73	5%	95% > 16 50% > 40
Lactic dehydrogenase (IU/l)	375 $\pm$ 195	49%	51% > 340 13% > 600

transaminase concentrations greater than twice normal. The lactic dehydrogenase level was less commonly elevated. In general, correlation between levels of lactic dehydrogenase and clinical evidence of liver disease or aspartate transaminase levels was poor ( $r = 0,34$ ). Major abnormalities of the bilirubin and alkaline phosphatase levels were less common than abnormalities of the aspartate transaminase level, with 31% and 27% of patients respectively having levels more than twice normal. Alpha-fetoprotein levels were measured in only 25 patients; in 18 patients the test was positive (mean value  $13 \pm 9$  mg/dl).

The ascitic protein concentration was measured in 32 patients; the mean value was found to be  $21 \pm 9,5$  g/dl (range 5 - 40 g/dl).

### Special investigations

**Isotope liver scan.** Forty-three patients underwent scanning of the liver, but a specific diagnosis of cirrhosis was correctly made in only 11 (26%). In most of the remaining cases the report read 'increased irregular uptake with possible space occupying lesions'.

**Peritoneoscopy.** This was found to be the more useful of the special investigations in aiding the diagnosis of cirrhosis. The diagnosis was confirmed histologically in 77% of 35 patients who were suspected of having cirrhosis on peritoneoscopy. Misdiagnosis was common in the presence of hepatic fibrosis and macronodular cirrhosis.

### Miscellaneous associations

**Bacterial infections.** Twenty-five per cent of the patients were shown to have acute bacterial infections of sputum (11%), ascitic fluid (4%), urine (5%) and blood (5%).

**Tuberculosis.** Sixteen patients were proved to have active pulmonary tuberculosis during their stay in hospital.

**Porphyria.** This was noted most often in the years 1970-1975, when 15 patients were found to have porphyrins in the urine.

### Discussion

From the present analysis it is possible to construct a picture of the typical presenting features of a patient with cirrhosis at the King Edward VIII Hospital. The patient would be of middle age and male. He would give a history of alcohol abuse and would complain of swelling of the ankles and abdominal distension. On examination he would be found to have a large liver, ascites and

peripheral oedema. Spider naevi and Dupuytren's contractures would be absent. Blood tests would show that he was mildly anaemic with a normal white cell count, mild thrombocytopenia and a moderately elevated ESR. Liver function tests would demonstrate a low plasma albumin level, with inverse elevation of globulins. Bilirubin and alkaline phosphatase levels would be mildly elevated, while more significant increases in aspartate transaminase enzymes would be seen. The prothrombin index might well be normal. A liver isotope scan would demonstrate increased irregular uptake in the liver together with increased splenic uptake. Space-occupying lesions might be suggested. Laparoscopy would show an enlarged micronodular liver, and liver biopsy would confirm the diagnosis of micronodular cirrhosis with increased deposits of iron and fat.

In comparison with similar surveys in Boston and London<sup>7</sup> our patients had more ascites, a larger liver and spleen and a higher incidence of encephalopathy, were more jaundiced and had significantly lower albumin and higher globulin levels. These differences could be explained by their late referral to specialized hospitals and the later stage of their illness; however, it must be remembered that the liver generally becomes smaller in advanced cirrhosis. Hepatomegaly has been found to be more common in alcoholic liver disease, presumably owing to the frequently increased fat deposition.<sup>1</sup> Fat deposits were common in our patients, but other histological markers of alcoholic liver disease such as Mallory's hyaline were absent. Another factor in favour of alcohol ingestion as a major cause of cirrhosis in our patients was the male/female ratio of 3 : 1. The ratio for alcoholic cirrhotics in Boston was 2 : 1, while a similar study in Australia gave a ratio of 4 : 1. In cryptogenic cirrhosis there is usually a preponderance of females<sup>1</sup> or the sexes are equally distributed.<sup>8</sup>

Powell *et al.*<sup>8</sup> published results from a very similar survey in Australia, dividing their cirrhosis patients into four major aetiological subgroups (alcoholic, cryptogenic, biliary and chronic active hepatitis). In general, our observations most closely matched those in their cryptogenic group with regard to presentation with gastro-intestinal bleeding, splenomegaly, hypo-albuminaemia, reversed albumin/globulin ratios and thrombocytopenia. However, the remaining abnormalities of liver function (i.e. bilirubin, aspartate transaminase and alkaline phosphatase levels) and in the blood (i.e. haemoglobin concentration and white cell count) were more like those in their patients with alcoholic cirrhosis. Overall, our patients had more ascites, more abdominal pain, fewer spider naevi, lower albumin and higher globulin levels and lower platelet counts.

To summarize, the high incidence of ascites, the sex ratio, the mean age, the hepatomegaly, the low albumin levels and the micronodularity of the liver suggest that alcohol was a major factor in the causation of cirrhosis in our patients, whereas the hyperglobulinaemia and splenomegaly would suggest that it was infective or 'cryptogenic'.<sup>1</sup> The severity of the hypo-albuminaemia, the clinical evidence of malnutrition and the fatty liver may also point towards nutritional causes.<sup>6</sup> The complexity of the situation is in keeping with Conn's<sup>5</sup> statement that 'multiple factors, acting individually or in concert, may be responsible for cirrhosis'. It was not possible to distinguish the effects of alcohol from those of viral infection or malnutrition, as the classic histological markers of alcoholic liver disease were absent. For this reason, some are sceptical about the role of home-brewed beers as a cause of cirrhosis. However, one cannot ignore the strong history of alcohol abuse given by our patients, even though accurate estimation of alcohol intake is often difficult because of translation and variable concentration problems. The form in which alcohol is taken may be important, since Isaacson<sup>9</sup> has recently noted a change in histological findings from siderotic micronodular cirrhosis to a more classic micronodular picture with alcoholic hyaline and fat deposits. He related the change to the substitution of hard spirits for traditional brews in Johannesburg. This explanation was based on Christofferson *et al.*'s<sup>10</sup> observation of the association

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54% < 12  
18% < 10  
3% < 3,5  
21% > 11  
71% < 150  
43% < 100  
10% < 50  
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between prolonged abuse of spirits and alcoholic hyaline deposition. It is interesting that we have not noticed this in Durban. Possibly for financial reasons 'Zulu beer' remains the most popular alcoholic beverage. It is important to note that Isaacson did not associate the change in the histological picture with an alteration in the incidence of cirrhosis. Consequently, the possibility remains that cirrhogenic factors other than alcohol may be contained within traditional beer, the most likely candidate being iron.<sup>11</sup> Viral infection is probably as important as alcohol in the causation of cirrhosis. Unfortunately identification was not possible during the years of the study reported, but it is the subject of a prospective study. Initial results have shown that 21 of the 42 patients with cirrhosis identified so far this year have immunological markers of present or past hepatitis B virus infection (I. M. Windsor — personal communication). Finally, the high incidence of severe chronic malnutrition in our patients (about 80% of our male patients are below the 5th percentile for triceps skinfold thickness and weight/height ratios) probably predisposes the alcoholic or infected patient towards the later development of cirrhosis.<sup>5</sup> It remains possible that toxic dietary factors (including herbal

medicines, which are widely used by our patients) may form additional predisposing factors.

We are very grateful to Professor E. B. Adams for establishing a comprehensive record system from which the data could be collected.

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## Transurethral prostatectomy — studies with different intravesical pressures

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### Summary

In an attempt to study the safety of transurethral prostatectomy in our unit, the use of a low-pressure continuous-flow water irrigation system was compared with our routine method of intermittent bladder emptying during transurethral prostatectomy in 14 patients. The products of haemolysis and parameters of haemodilution were studied, and no significant differences were noted. However, a simple suprapubic shunt provided significant surgical advantages.

*S. Afr. med. J.* 61, 778 (1982).

Since McCarthy's resectoscope became available in 1935, transurethral prostatectomy (TUP) has become increasingly popular. In our unit we perform 200-300 prostatectomies annually, 86% by the transurethral route. We routinely employ

sterile water as an irrigant, with intermittent emptying of the bladder by removing the working element of the resectoscope.

The well-known and documented dangers of transurethral prostatectomy are thought to be the result of intravasation of irrigation fluid into the systemic circulation. These dangers are haemolysis due to increased red cell fragility in hypo-osmotic surroundings and the 'TUP syndrome' characterized by hyponatraemia and hypervolaemia. Both may occur concurrently and lead to gross fluid overload with cardiac failure, acute renal failure, haemolytic jaundice and death.

Factors incriminated in this regard are the intravesical pressure during resection, the tonicity of the irrigant, and the time required for the resection. Several workers have advised methods to lower intravesical pressure.<sup>1-3</sup> Other studies have examined the movement of irrigant into the general circulation and its effect on blood tonicity and red cell integrity.<sup>4-7</sup> The use of continuous-flow systems during resection has also been suggested and employed by several workers.

In an attempt to study the safety of TUP in our unit, we measured electrolyte changes and the products of haemolysis. We performed a pilot study comparing a continuous-flow low-pressure system of irrigation with our routine method of intermittent bladder emptying during TUP.

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### Patients and methods

Fourteen unselected patients were randomly allocated to two groups. The decision to proceed with TUP was made at