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## **Serum ferritin in Nigerian patients with Burkitt's lymphoma and other malignant diseases**

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### **Summary**

Serum ferritin was studied in 4 patients with abdominal Burkitt's lymphoma, 6 with facial Burkitt's lymphoma, 10 with primary hepatocellular carcinoma, 6 with secondary hepatic cancer, 8 with primary breast cancer, 4 with Hodgkins's disease, 3 with chronic lymphocytic leukaemia and 6 with other neoplastic diseases. Control values were determined for 23 apparently healthy Nigerians. Serum ferritin was significantly elevated in patients with Burkitt's lymphoma (facial and abdominal combined), primary hepatocellular carcinoma, secondary hepatic cancer, chronic lymphocytic leukaemia ( $p < 0.00001$ ), Hodgkin's disease and in other neoplastic diseases as compared to the control ( $p < 0.0004$ ). Serum ferritin levels were significantly elevated ( $p < 0.00001$ ) in abdominal Burkitt's lymphoma but less dramatically elevated values or even values within the reference range (mean + 2 Standard Deviations of the controls) were seen in the values of serum ferritin in the patients with facial Burkitt's lymphoma. The assay of serum ferritin may be of some value in the diagnosis and classification of patients with Burkitt's lymphoma, and in monitoring the treatment provided.

**Key words:** serum ferritin; Burkitt's lymphoma; malignant diseases.

### **Introduction**

Ferritin is primarily an intracellular iron-storage protein with a high molecular weight of approximately 450,000 and it is found in all tissues, but in particularly high concentrations in the livers, spleen and bone marrow (Harrison et al., 1974; Tomada et al., 1982). With the development of sensitive immu-

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noradiometric assays for ferritin it has become possible to detect small amounts of ferritin in normal serum (Jacobs et al., 1972), and to record changes in the serum ferritin concentrations in patients with a variety of pathological conditions. The serum ferritin levels closely reflect the size of the iron stores in the body (Miles et al., 1974; Jacobs, 1977; Nelson et al., 1978). High serum ferritin concentrations have been found in anaemia of chronic diseases (Mazza et al., 1978), acute as well as chronic liver damage (Prieto et al., 1975), in haematological malignant diseases (Matzner et al., 1980) and in solid tumours (Tappin et al., 1979; Jones et al., 1980; Grail et al., 1982). The cause of increased serum ferritin in the neoplastic state is still uncertain. The report that circulating leukocytes in acute myeloblastic leukaemia contain increased amounts of ferritin (Worwood et al., 1974) has led to the suggestion that the high serum ferritin concentrations in this condition reflect increased ferritin synthesis by the leukaemic cells. In cases of Hodgkin's disease and other solid tumours, it has been suggested that ferritin may represent a tumour-associated antigen or a tumour marker (Siimes et al., 1977; Tomada et al., 1982), and its serum level may reflect the activity of the malignant disease.

Although there have been a number of studies dealing with serum ferritin in various clinical and experimental conditions (Mori et al., 1975; Pany et al., 1975; Lipschitz et al., 1974; Zuyderhoudt et al., 1978; Jones et al., 1980; Grail et al., 1982), no data have been reported to our knowledge on the status of ferritin in serum and lymphomatous tissues or cells of African or Nigerian patients with Burkitt's lymphoma. This work sets out to study whether there are distinct changes in serum ferritin in facial and abdominal Burkitt's lymphoma. The changes in these subgroups of Burkitt's lymphoma are compared with those occurring in some other malignant diseases of high incidence in Nigeria.

## **Materials and Methods**

### *Patients and control subjects*

Sera were obtained from 23 apparently healthy Nigerian control subjects, 12 males and 11 females. Their ages ranged from 15 to 60 years with a mean of 32 years. There were 47 patients with various malignant diseases, 10 with Burkitt's lymphoma (facial and abdominal subgroups) 7 males and 3 females, mean age 9 years (range 5–14 years); 10 with primary hepatocellular carcinoma, 6 males and 4 females, mean age 39 years (range 25–50 years); 6 with secondary hepatic cancer, 1 male and 5 females, mean age 45 years (30–50); 8 with breast cancer with no evidence of liver metastases, all were females, mean age of 38 years (30–45); 3 with chronic lymphocytic leukaemia, all females, mean age 39 years (20–60); and 6 with other malignant diseases with no evidence of liver metastases, 4 males and 2 females (25–60). All the patients had been admitted to various wards of the University of Ife Teaching Hospitals.

The Burkitt's lymphoma group included 4 patients with only abdominal Burkitt's lymphoma, 3 males and 1 female, mean age 10 years (range 6–14 years) (see Table 1). The diagnosis of Burkitt's lymphoma was based on a sufficient number of diagnostic criteria, such as histological, cytological and clinical findings (Berard et al., 1969; Ziegler, 1981). Tumour site was determined on the basis of pretreatment evaluation, with involvement being assessed on clinical examination. Since this study focused on serum ferritin concentrations in pretreated patients, necropsy results were not used to

Table 1

Group	n	Sex		Age <sup>2</sup>	Ferritin <sup>2</sup> ( $\mu\text{g/l}$ )	p <sup>3</sup>
		♂	♀			
Controls . . . . .	23	12	11	32 $\pm$ 14	105.78 $\pm$ 73.90	
Burkitt's lymphoma (BL) <sup>1</sup>	10	7	3	9 $\pm$ 3	729.00 $\pm$ 561.00	<0.00001
a) Facial BL . . . . .	6	4	2	8 $\pm$ 3	332.50 $\pm$ 260.00	<0.0004
b) Abdominal BL . . . . .	4	3	1	10 $\pm$ 3	1323.80 $\pm$ 216.00	<0.00001
Primary hepatocellular carcinoma . . . . .	10	6	4	39 $\pm$ 8	1233.00 $\pm$ 700.00	<0.00001
Secondary hepatic cancer	6	1	5	45 $\pm$ 8	2970.00 $\pm$ 1661.00	<0.00001
Primary breast cancer . . .	8	—	8	49 $\pm$ 10	686.88 $\pm$ 245.00	<0.00001
Hodgkin's disease . . . . .	4	3	1	38 $\pm$ 6	3960.00 $\pm$ 5051.00	<0.0004
Chronic lymphocytic leukaemia . . . . .	3	—	3	39 $\pm$ 20	7233.30 $\pm$ 6653.00	<0.00001
Other malignant diseases .	6	4	2	50 $\pm$ 14	782.50 $\pm$ 841.00	<0.0004

<sup>1</sup> Calculation is for combined facial and abdominal BL

<sup>2</sup> Mean  $\pm$  S.E.

<sup>3</sup> Statistical significance of the difference in serum ferritin when compared with the controls (Student's t test)

determine tumour site. The four patients in our study had very advanced abdominal Burkitt's lymphomas that were clinically obvious, and were histologically and cytologically confirmed. The primary hepatocellular carcinoma group included patients with various stages, but in most cases it was advanced. The diagnosis had been confirmed in each case by histological examination of a hepatic specimen obtained either by percutaneous needle biopsy or by laparotomy. The secondary hepatic cancer group likewise had their diagnosis confirmed in each case by histological examination and any patient in whom the primary site could not be determined were excluded. The primary neoplasm was located in the ovary (in 4 patients), breast (1) and stomach (1). All the patients with primary breast cancer had distinct histological findings in biopsy specimen. The patients with Hodgkin's lymphoma and chronic lymphocytic leukaemia were diagnosed, using conventional diagnostic criteria such as clinical, laboratory and histological findings. The group of other malignant diseases consisted of 2 patients with cancer of the colon, 1 in the pancreas, 1 in the stomach and 2 in the skin (one squamous-cell and one basal cell carcinoma). All these diagnoses were confirmed by histological examination of the biopsy specimens.

#### *Serum samples*

Since this study focused on pretreatment serum ferritin concentration in the groups of patients, blood samples were drawn prior to any form of treatment. The sera were separated after allowing the blood samples to coagulate at room temperature and stored at  $-20^{\circ}\text{C}$  until assayed for ferritin.

#### *Assay*

Serum ferritin concentration was measured by a two-site immunoradiometric assay (IRMA) (Miles et al., 1974), using a commercially available IRMA kit (Nordiclab Ltd., Oulu, Finland). The

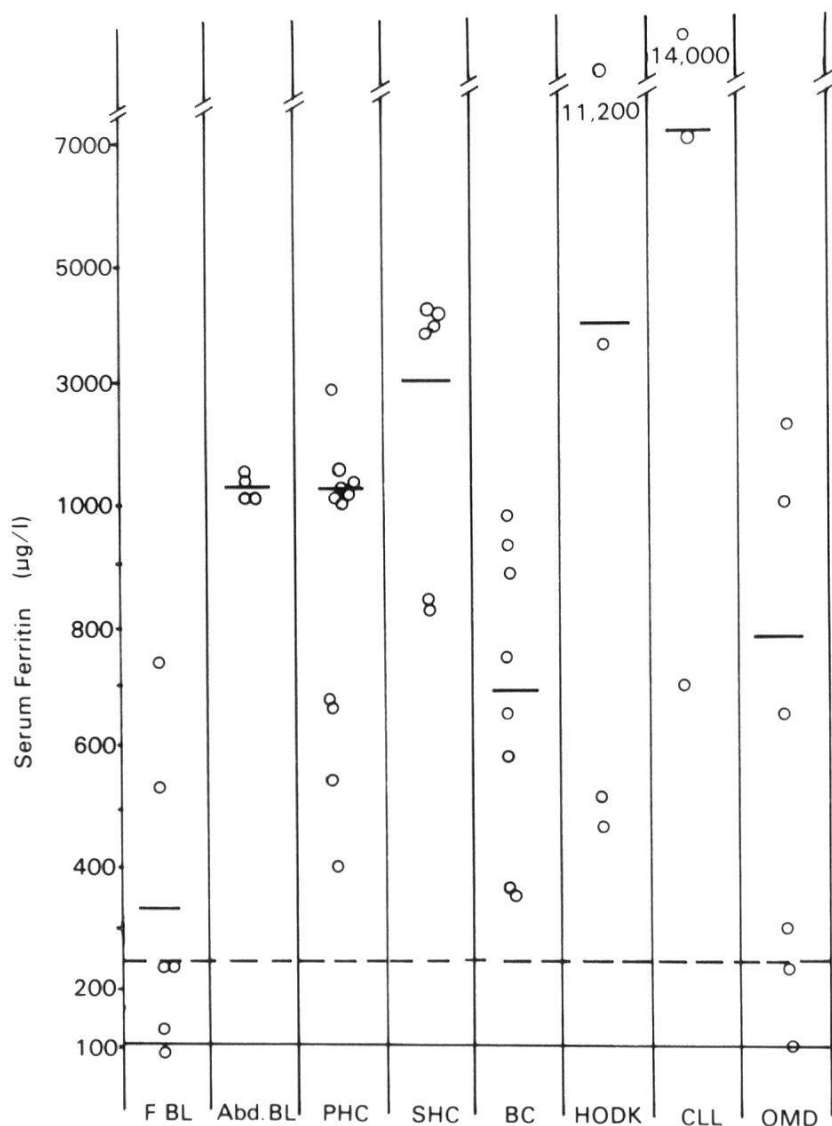


Fig. 1. Serum ferritin in patients with facial Burkitt's lymphoma (FBL), abdominal Burkitt's lymphoma (Abd. BL), primary hepatocellular carcinoma (PHC), secondary hepatic cancer (SHC), primary breast cancer (BC), Hodgkin's disease (HODK), chronic lymphocytic leukaemia (CLL) and other malignant diseases (OMD). The horizontal dashed line indicates the limit of the + 2 S. D. of the controls, the horizontal solid line indicates the mean of the controls and the short solid lines the means for the various patient groups.

assays were performed on three different dilutions of the patient's sample to avoid the risk of falsely low results (Green et al., 1977). Results are expressed as  $\mu\text{g/l}$ .

The statistical significances of the differences between two means were calculated by Student's t test.

## Results

Table 1 summarizes the mean values for serum ferritin in 23 healthy Nigerian subjects, patients with Burkitt's lymphoma, Hodgkin's disease, chronic lymphocytic leukaemia, primary hepatocellular carcinoma, secondary hepatic cancer, primary breast cancer and other malignant diseases. The mean serum

concentration was significantly elevated in Burkitt's lymphoma (combined facial and abdominal), primary hepatocellular carcinoma, secondary hepatic cancer, breast cancer, chronic lymphocytic leukaemia ( $p < 0.00001$ ), Hodgkin's disease, and in other malignant diseases ( $p < 0.0004$ ). The elevation in serum ferritin was most marked in Hodgkin's disease, secondary hepatic cancer, chronic lymphocytic leukaemia, and primary hepatocellular carcinoma. There was a marked difference in the mean serum ferritin concentrations between the two Burkitt's lymphoma subgroups (facial and abdominal, see Table 1 and Fig. 1). The mean serum ferritin concentration was highly significantly elevated ( $p < 0.00001$ ) in the abdominal Burkitt's lymphoma subgroup (Table 1). All 4 patients in this subgroup had serum ferritin values which exceeded the upper normal limit (i.e. mean + 2 S.D. of the controls). Less dramatically elevated values, or even values within the reference range (mean + 2 S.D. of the controls) were seen in the values of serum ferritin in the patients with facial Burkitt's lymphoma (Fig. 1). The change seen in the mean serum ferritin in the abdominal Burkitt's lymphoma patients was highly significant ( $p < 0.00001$ ) when compared with that of the facial subgroup.

## Discussion

The results indicate that serum ferritin is above the normal upper limit (mean + 2 S.D. of control) in about 60% of all the patients with Burkitt's lymphoma (i.e. facial and abdominal combined) studied here, but it is below this (about 33%) in patients with only facial Burkitt's lymphoma. All 4 patients with abdominal Burkitt's lymphoma had very high serum ferritin values that were highly elevated above the normal upper limit (Fig. 1). These data thus provide a parameter pointing to distinct differences in serum ferritin concentrations in the two subgroups of Burkitt's lymphoma.

High serum ferritin concentrations have previously been reported in patients with primary hepatocellular carcinoma, secondary hepatic cancer, breast cancer, Hodgkin's disease, chronic lymphocytic leukaemia and in other malignant diseases (Niitsu et al., 1975; Jones et al., 1973; Jacobs et al., 1976; Hazard and Drysdale, 1977; Gropp et al., 1978; DiMartino et al., 1982; Grail et al., 1982). Our data not only confirm these findings but also indicate that elevated serum ferritin concentration may be associated with tropical malignant diseases.

On the basis of our finding of significant elevation of serum ferritin in patients with abdominal Burkitt's lymphoma, assays of serum ferritin may be potentially useful in the diagnosis, classification into such subgroups (Biggar et al., 1981) and follow-up care of patients with Burkitt's lymphoma.



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