EDITORIAL

SPONTANEOUS BACTERIAL PERITONITIS

Spontaneous bacterial peritonitis (SBP) frequent]y occurs in patients with liver cirrhosis and ascites. It is defined as an infection of previously sterile ascitic fluid without any demonstrable intrabdominal source of infection. It is now internationally agreed that a polymorphonuclear (PMN) cell count in the ascitic fluid of over 250 cells/mm^3 is diagnostic of this condition(1).

Colonisation of the ascitic fluid from an episode of bacteraemia is nowadays the most accepted hypothesis in pathogenesis of SBP. Several factors have been postulated as leading to bacterial migration from the alimentary tract via the blood stream into the ascitic fluid. The skin, urinary tract and upper respiratory tract can also be sources of primary infection. Once bacteria gain access to the blood stream (bacteraemia), they can then easily pass on to the ascites because of the common fluid exchange between these two compartments(2). Cirrhotic also tend to have bacterial overgrowth in the gut leading to an increase in aerobic gram-negative bacilli. These can easily gain access to ascitic fluid due to altered gut permeability resulting from portal hypertension or compromised circulation which causes decreased mucosal blood flow.

Patients with cirrhosis also have diminished reticuloendothelial system capacity to prevent microorganisms crossing over from the bowel lumen to the systemic circulation via the portal vein. There is also increased bacterial translocation via the mesenteric nodes into the blood stream. Once microorganisms have colonised the ascites, the development of peritonitis depends on the defensive capacity of the ascitic fluid which is greatly compromised in most cirrhotics.

Clinically SBP may be asymptomatic. Where symptomatic, abdominal pain and fever are the most characteristic symptoms. Generalised tenderness occasionally with rebound may be elicited. Vomiting, ileus and diarrhoea due to altered gastric motility, hepatic encephalopathy, GIT bleeding, renal impairment, septic shock and hypothermia may be present in a high number of patients but are rather non specific.

The diagnosis depends on a high index of suspicion and careful clinical evaluation together with a few confirmatory laboratory tests. Ascitic fluid analysis is of great importance, and a PMN count of greater than 250 cells per mm^3 is diagnostic. Where the fluid is haemorrhagic allowance should be made using 1 PMN cell to 250 red blood cells; anything higher that this being significant.

New techniques that have led to more rapid diagnosis have been described. Castellote with others(3) described use of urine “dipsticks” to detect neutrophils in ascitic fluid, thereby reducing the time from paracentesis to presumptive diagnosis of SBP to seconds. Sensitivity was 96% with specificity of 89%.

Secondary bacterial peritonitis is suspected when ascitic lactic dehydrogenase levels are higher than serum levels, protein greater than l0g% and glucose levels are less than 50mg%(4).

Gram stain of centrifuged sediment normally yields gram negative bacteria although bacterial concentration is normally low with one organism per ml or less. Culture of ascitic fluid (aerobic and anaerobic) is positive between 50-70% of patients with SBP and blood cultures are positive in an equally significant number of patients.

Most common organisms encountered both locally and internationally are gram negative with *E. Coli* and *Klebsiella.* Gram positive organisms also occur and these include *Streptococci* and *Staphylococcal* species. In up to 30% of cases the culture might be negative for various reasons including prior use of antibiotics.

The prognosis of SBP has improved in recent years with the advent of effective antibiotics and quick intervention. Mortality remains high ; in some cases up to 30-50%. Known severe complications that often lead to fatal outcomes include renal impairment, gastrointestinal bleeding and hepatic encephalopathy.

Antibiotic therapy is the mainstay of treatment and this may be empirical while awaiting the results of culture. Third generation cephalosporins such as cefatoxime are the gold standard. In poor resource settings amoxycillin with clavulinic acid has been shown to be highly effective but quinolones and aminoglycosides such as gentamicin(5) are also equally effective. Oral antibiotic administration is effective and where possible, should be encouraged. Treatment with albumin infusions in addition to an antibiotic reduces the incidence of renal impairment and improves survival.

There is also room for antibiotic prophylaxis in those cirrhotic patients likely to develop SBP, for example, those with gastrointestinal haemorrhage, low ascitic total protein, or patients with established liver failure. However, evidence on the cost-effectiveness and efficacy of long term prophylaxis in patients with cirrhosis and ascites is still controversial and requires more study.

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PATTERN OF TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER AS SEEN AT KENYATTA NATIONAL HOSPITAL, NAIROBI
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PATTERN OF TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER AS SEEN AT KENYATTA NATIONAL HOSPITAL, NAIROBI

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ABSTRACT

Objective: **To highlight the pattern of patients with transitional cell carcinoma of the urinary bladder with regards to age, sex, ethnic origin and histopathological classification.**
Design: **A ten year retrospective study.**
Setting: **Kenyatta National Hospital, Nairobi, Kenya.**
Subjects: **Fifty two patients who presented at Kenyatta National Hospital over the ten year period with histologically proven transitional cell carcinoma of the urinary bladder. There were 41 males and 11 females aged 27 to 84 years. The mean age was 57 years.**
Results: **The peak incidence was in the 60-69 years age group. The male to female ratio was 4:1. The regional (provincial) distribution revealed Central and Eastern had 77%, Rift valley had 6%, Nairobi, North Eastern, Western and Coast provinces had 2% each. In the ethnic distribution; Kikuyus, Kambas and Merus were 77% while others were 17.3%. Transitional cell carcinoma was found in 67% of the patients, 60% had advanced disease. Twenty nine percent were smokers while 25% consumed alcohol. The main occupation was farming in 65%. The most Common clinical presentations were haematuria 98% and lower abdominal pains in 71%. A total of 99,028 patients were admitted to the surgical wards,transitional cell carcinoma patients represented only 0.6%.**
Conclusion: **Transitional cell carcinoma is a rare disease. At Kenyatta National Hospital it only represented 0.6% of all surgical admissions during the study period. It accounted for 67% of all bladder tumours an increase in incidence compared to previous studies. It is common in males more than females, with a peak in the seventh decade. Majority of the patients were from central Kenya. Alcohol, smoking and farming were the most important risk factors. Haematuria was the most important presenting clinical feature. Poor record keeping may have contributed to the low number of patients enrolled into the study. There is need for a thorough prospective study to find out the actual prevalence of bladder tumours.**

INTRODUCTION

Urinary bladder cancer represents a significant proportion of urologist's caseload because of its ubiquity and in the superficial disease long natural history. It is more common in men than women (2.3: 1). In men it is the fourth most common cancer after prostate, lung and colorectal tumours(1).

Carcinoma arising from the bladder may be of three cell types; transitional, squamous and adenocarcinoma. Bladder cancer is the most common cancer of the urinary tract and transitional cell carcinoma accounts for more than 90% of bladder tumours in western countries(2). In areas where *Schistosoma haematobium* is endemic the proportions are different. Ndaguatha in a review of urinary bladder cancers in Kenyatta National Hospital found 53.3% were transitional cell, 17.3% were anaplastic, 13.3% were squamous cell carcinomas and others were 16.1%(3).

This tumour features the entire range of aggressiveness from low-grade superficial to high-grade invasive cancers. The incidences are higher in whites than blacks, ratio 2:1(4,5), however the increased risk in whites appears to be limited to patients with non-invasive tumours(6). The observation suggests that some superficial tumours in blacks may go undetected.

The tumour can occur at any age even in children but it is generally a disease of the elderly with the median age of diagnosis being approximately 67 to 70 years. The aetiology of urinary bladder cancer remains unknown, but there are several predisposing factors. These include chemicals, cigarette smoking, radiotherapy and chemotherapy, chronic cystitis and schistosomiasis and bowel interposition.

Increase in understanding of the genetics of the bladder cancer has provided insights into the basis of the clinical behaviour of the tumours(5). The first suspicion of a chemical cause of bladder tumours was

raised by Rehn in 1894 when he recorded a series of tumours in workers in aniline dye factories(7). Aniline dyes were introduced in the mid-1800s to colour fabrics. Other such chemicals (e.g. 1-naphthylamine, xenylanine and benzidine) have since been identified(8).

There is a strong correlation between incidence of bladder cancer and cigarette smoking, with a four fold higher incidence of the disease in smokers(9-11). The risk correlates with the number of cigarettes smoked, the duration of smoking and the degree of inhalation of the smoke. This risk has been observed in both sexes. Ex-cigarette smokers have a reduced incidence of bladder cancer compared with smokers(l2). Other forms of tobacco are associated with only a slight higher risk for bladder cancer(9,13). An estimated one third of bladder cancer patients may be related to cigarette smoking(14).

The specific chemical carcinogen has not been identified but nitrosamines as well as 2- naphthylamine are known to be present. Increased urinary tryptophan metabolites also have been demonstrated in cigarette smokers(15). A significantly higher incidence of bladder cancer has been seen in-patients previously treated with pelvic irradiation or the chemotherapeutic drug cyclophosphamide(5).

Chronic cystitis due to infections and bladder calculi have been associated with increased incidence of urinary bladder cancer. In African patients, schistosomiasis appears to be related to a high incidence of not only squamous cell carcinoma but also other histological types. In a recent study by Groeneveld *et al.* schistosomiasis of the bladder was found in 85% of patients with squamous cell carcinomas, 50% of those with undifferentiated tumours and adenocarcinoma, in 17% of those with mixed tumours or sarcomas and in 10% of the patients with transitional cell carcinoma(16).

The resurgence in the use of bowel in bladder augumentation, and orthotopic replacement of the bladder has led to an increase of reports of patients with bladder cancer arising in the interposed bowel. All patients with interposed bowel in the urogenital system need life long follow-up because of the potentially greater risk of neoplasia caused by increased formation of nitrites and nitroso compounds in the bladder hence the need for regular check cystoscopies.

Molecular genetics have a role to play. It is thought that tumour development and progression is driven by accumulation of multiple genetic alteration by the normal cell. Many phenotypic changes in tumour cell events that are secondary to primary genetic alterations and some of these may have been caused by changes in the environment. The genetics of the bladder carcinogenesis is thought to be multifactorial, involving the action of proto-oncogenes through mutation of gene amplification. Several proto-oncogenes are over-expressed in bladder cancers, these include HRAS (ERBBI), EGFR (ERBB2), MYC and SRC. Their precise role is yet to be defined.

It is still unclear, however, how these alterations and deletions may be integrated in the development of bladder cancer(17). Pathologically, bladder cancer appears to progress from carcinoma *in situ* to a fixed mass (T4b) with worsening of prognosis in successive stage of the disease.

Further more carcinoma *in situ* may represent a parallel rather than a continuous form of the disease.

MATERIALS AND METHODS

The study was carried out at Kenyatta National Hospital. This was a retrospective study covering a period of ten years from January 1990 to December 1999. Only those patients with histologically confirmed diagnosis of transitional cell carcinoma of the urinary bladder treated at KNH during the study period were included. The sample size was determined by the study period. The relevant records of the patients with TCC were reviewed after approval of the study proposal by the KNH Research Committee. Data were collected using tally sheets and analysed using statistical computer programme (SPSS).

RESULTS

During the period of 1990 to 1999, 92,028 patients were admitted to all surgical units of Kenyatta National Hospital. Of these 224 patients were clinically diagnosed to have urinary bladder cancer. Of these 127 (57%) files were traceable from which 79 had histologically proven bladder cancer. Fifty two, patients of these were transitional cell carcinoma and were enrolled into the study.

The patients were from all parts of the country some seen primarily, others as referrals from provincial, district and mission hospitals. The number of patients recorded from 1990 to 1999 varied from one to ten each year with an average of five patients per anum. The highest number of patients were seen and recorded in the period 1996 to 1998 constituting 69.2% of all the patients. The 1990 to 1994 figures were low and accounted for 21.1 %.

Age/sex: The 52 patients of transitional cell carcinomas were analysed according to the age at presentation. Incidence increased with age. The youngest recorded age was 27 years and the oldest was 84 years. The mean age at presentation was 57.19 years and the median age was 60 years. The range was 57 years. The peak age group was 60 to 69 years accounting for 16 (30.8%) of the recorded patients. The other age groups had the following distribution, 20 to 29 years two patients (3.8%), 30 to 39 years; four patients (7.7%), 40 to 49 years; 11 patients (21.2%), 50 to 59 years; eight patients (15.4%), 70 to 79 years; seven patients (13.5%), 80 years and above had four patients (7.7%) (Table 1). Gender distribution revealed 78.8% were males and 21.2% were females. The male: female ratio was 3.7:1.

Table 1

Patients characteristics

Characteristic	No	%	Cumulative %
Yearly characteristics in number of patients seen			
1990	3	5.8	5.8
1991	2	3.8	9.6
1992	4	7.7	17.3
1993	1	1.9	19.2
1994	1	1.9	21.1
1995	7	13.5	34.6
1996	10	19.2	53.8
1997	9	17.3	71.1
1998	10	19.2	90.3
1999	5	9.6	100
Age characteristics (mean age 57.19 years: Range years 27-84)			
20-29	2	3.8	3.8
30-39	4	7.7	11.5
40-49	11	21.2	32.7
50-59	8	15.4	48.1
60-69	16	30.8	78.9
70-79	7	13.5	92.9
80 and Above	4	7.7	100
Gender characteristics			
Sex			
Male	41	78.8	78.8
Female	11	21.1	100

Table 2

Regional and ethnic characteristics

Characteristic	No.	%
Region		
Nairobi	1	1.9
Central	24	46.2
Eastern	16	30.8
Nyanza	5	9.6
North Eastern	1	1.9
Rift Valley	3	5.8
Western	1	1.9
Coast	1	1.9
Ethnic distribution		
Kikuyu	27	51.9
Kamba	9	17.3
Meru	4	7.7
Luo	3	5.8
Other tribes	9	17.3
Total	52	100

Table 3

Occupation and risk factors characteristics

Characteristic	No.	%
Occupation		
Farmers	34	65.4
Self employed	7	13.5
Salaried employment	5	9.6
Unemployed	1	1.9
Missing data	5	9.6
Total	52	100
Smoking		
Non-smokers	31	59.6
Smokers	15	28.8
Tobacco Snuff	1	1.9
Missing Data	5	9.6
Total	52	100
Alcohol		
Alcohol use	13	25.0
No alcohol	34	65.4
Missing data	5	9.6
Total	52	100

Table 4

Tumour characteristics and clinical features

Characteristic	No.	%
Signs/Symptoms		
Haematuria	51	98.1
Lower abdominal pain	37	71.2
Pelvic mass	19	36.5
Dysuria	17	31.7
Histological types		
Transitional cell	52	67
Squamous cell	12	15
Adenocarcinoma	6	8
Anaplastic	5	6
Rhadomyosarcoma	3	4
Total	78	100

Regional and ethnic distribution: The provincial distribution was central province, 24 patients (46.2%), Eastern province, 16 patients (30.8%), Nyanza, five patients (9.6%), Rift Valley three patients (5.8%), Nairobi, North Eastern, Western and Coast had one patient each (1.9%). (Table 2). The ethnic distribution was as follows Kikuyu, 27 (51.9%), Kamba, nine (17.3%), Meru, four (7.7%), Luo three (5.8%) and other tribes nine (17.3%) (Table 2).

Risk factors: Smoking was found in 28.8% of the patients. One patient was using tobacco snuff. There were 13 patients (25%) who consumed alcohol, information of five patients was missing from the records (Table 3). The amount consumed and durations were not recorded in most of the files.

Clinical presentation: Patients presented with various signs and symptoms, namely haematuria; 51 patients (98.1%), low abdominal pains; 37 patients (71.2%), pelvic mass; 19 patients (36.5%), dysuria; 17 patients (32.7%). Haematuria was the most common presenting symptom (Table 4).

Histological diagnosis: There were a total of 78 patients seen in the hospital with histologically confirmed urinary bladder cancers for the ten year period. Fifty two (67%) of the patients had transitional cell carcinoma, 12 (15%) of the patients had squamous cell carcinomas, six (8%) had adenocarcinomas, five (6%) had anaplastic and three (4%) had rhabdomyosarcomas (Table 4). The commonest stage of TCC was muscle invasive in 22

patients (42.3%), superficial in 20 patients (38.5%), metastatic in nine patients (17.3%) and carcinoma *in situ* one patient (1.9%). Overall majority of the patients had invasive disease (59.6%) as compared to superficial (40.4%). Carcinoma *in situ* was only recorded at the peak age of 60 to 69 years. Metastatic disease was more common in the age group 30 to 59 years than in older patients.

DISCUSSION

Transitional cell carcinoma of the urinary bladder is a rare malignancy. In this study covering ten years only 52 patients of histologically proven transitional cell carcinoma patients were seen at Kenyatta National Hospital. This accounts for 67% of all bladder tumours. Over the same period of time total surgical admissions to the hospital were 99,028. Thus transitional cell carcinoma formed 0.06% of all surgical admissions in the hospital. The average annual incidence of this condition over the ten year period was 5.2 patients. These figures reveal that there is an increase in the incidence of transitional cell carcinoma from 53% to 67%(3).

The highest number of patients were seen and recorded in the period 1995 to 1998 constituting 69.2% of all the patients. The 1990 to 1993 period figures were low. This may be explained by the poor social economic situation prevailing in the country in this period, where most patients could not afford medical services and opted to stay away or seek medical advice from alternative sources. In the period of 1993 to 1994 there was a national doctors and university lectures strike and this affected the provision of medical services.

In 1995 to 1998, introduction of cystoscopy as a routine diagnostic tool and transient improvement of the country's economy explains the increase in the number of patients at this time. In the year 1999 the number of patients reduced due to falling social-economic status (Table 1). It is possible that there was better record keeping in the year l996 to 1998.

Peak age incidence of transitional cell carcinoma occurs between 67 to 70 years. In this study, overall peak incidence occurred between 60 to 69 year age group accounting for 16 patients (30.8%). This compares with the peak incidence of 67 to 70 in the existing literature. The youngest patient was 27 years and the oldest was 84 years with a mean of 57.19 and a median of 60 years. The majority of the patients were between 40 and 69 years (67.4%).

In this study 78.8% of the patients were males and 21.1% were females giving a male to female ratio of 3.7:1 compared to 2.3:1, reported elsewhere(4,5). There was a variation in provincial representation with 46.2% of patients coming from central province, 30.8% from Eastern province, 9.6% from Nyanza, 5.8% from Rift Valley while Nairobi, North Eastern, Western and Coast provinces had 1.9% each. The possible reason for this pattern is that KNH is in close proximity to patients from Central province and therefore easily accessible on logistic grounds. The other possible reason is because Central, Nyanza and Eastern provinces are areas where rice is grown and schistosomiasis is endemic (note that schistosomiasis is responsible for 10% of TCC)(16). In this study the ethnic distribution were Kikuyu 51.9%, Kamba 17.3%, Meru 7.7%, Luo 5.8% and other tribes 17.3%. The reason for this distribution is most likely as stated in the regional distribution.

About 28.8% were smokers, this account for about a third of all patients with transitional cell carcinoma and is similar to existing literature(14). One of the patients was using tobacco snuff and this is a known risk factor(9,13). None of the patients had a past history of surgery (ureterosigmoidostomy or bladder substitution), chemotherapy or abdominal irradiation which are known risk factors in developing TCC(5).

Farmers constituted 65.4 % of all the patients. It was not specified in the records the type of farming they were engaged in, but it is known that rice farming where schistosomiasis is endemic increases the risk of TCC(16). Haematuria was found in 51 patients (98.1%), lower abdominal pain in 37 patients (71.2%), pelvic mass in 19 patients (36.5%) and dysuria in 17 patients (32.7%). Pelvic mass was a sign of advanced disease.

Presentation of transitional cell carcinoma depend on the clinical stage of the disease, presence or absence of metastases, haematuria being the most common presentation(31). Transitional cell carcinoma was the most common urinary bladder malignancy accounting for 67% of the patients followed by squamous cell 15%, adenocarcinoma 8%, anaplastic 6% and rhabdomyosarcoma 8%. This revealed an increase in transition cell carcinoma incident compared with figures from other studies(3).

Of the various stages of transitional cell carcinoma, muscle invasive was the most common accounting for 22 patients (42.3%) followed by superficial in 20 patients (38.5%) metastatic in nine patients (17.3%) and carcinoma *in situ* in one patient (1.9%). Many early stage tumours could be missed and many patients presented late(6). Muscle invasive histological stage account for the majority of patients of transitional cell carcinoma across the age spectrum.

In conclusion, transitional cell carcinoma is a rare disease in Kenyatta National Hospital. It accounts for 67% of all bladder tumours, an increase in incidence compared to previous studies. It is common in males more than females, with a peak incidence in the seventh decade. Majority of the patients were from central Kenya. Alcohol, smoking and farming were the most important risk factors. Haematuria was the most important presenting clinical feature. Poor record keeping may have contributed to the low number of patients enrolled into the study. There is need for a thorough prospective study to find out the actual prevalence of bladder tumours.

Transitional cell carcinoma is a rare disease at Kenyatta National Hospital, common in males than in females, and it is a disease of the elderly. Majority of the patients were from central Kenya. Alcohol, smoking and farming were important risk factors. Haematuria was the most important presenting clinical feature. Poor record keeping may have contributed to the low number of patients enrolled into the study.

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KAPOSIS SARCOMA IN A NAIROBI HOSPITAL
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KAPOSIS SARCOMA IN A NAIROBI HOSPITAL

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ABSTRACT

Background: **Kaposi's sarcoma (KS) is associated epidemiologically with HIV infection and a number of countries have reported a dramatic increase in the incidence of KS with the advent of AIDS. Although AIDS is prevalent in Kenya, no studies on the impact of AIDS on the pattern of KS has been carried out.**
Objective: **To determine any changes in the pattern of KS that might have occurred since the advent of AIDS in the country.**
Design: **Retrospective descriptive study.**
Setting: **Kenyatta National Hospital (KNH).**
Method: **Pathology records of cases of KS diagnosed at KNH from 1968 to 1997 were analysed with respect to relative frequency, age, sex and site distribution; and trend. The period was divided into the pre and post AIDS era from 1983, which is the time the first AIDS patient was reported in the country.**
Result: **A total of 1108 cases of KS consisting of 911 males and 197 females were recorded. The relative frequency of KS ranged between 2% to 5% of the total malignancies. There was a gradual decline in the male to female ratio from about 10:1 in the sixties to about 2:1 in 1997. There was no dramatic difference in the age distribution in the pre- and post AIDS era, although a large number of cases were recorded as adults without age specification in the post AlDS era. Site distribution was characteristic of the disease with most of the cases having the lesions occurring in the lower limbs and involving the skin.**
Conclusion: **Although these findings do not demonstrate a dramatic alteration in the pattern of KS in the post AIDS era there were indications that such changes may have been obscured by under-reporting. The fall in the male:female ratio is a strong indication of a rise in KS among female patients. A further study is necessary to elucidate the true impact of AIDS on the pattern of KS in the country.**

INTRODUCTION

Kaposi's sarcoma (KS) is the most common AlDS-associated malignancy(1,2) and a number of countries have reported a dramatic increase in the incidence of KS as a consequence of the increased incidence of AIDS. While AIDS has led to a dramatic increase in the rate of KS, the pattern of the disease shows variation with location and time(3,4). For example the pattern of AlDS-associated KS (AIDS-KS) in the west differs significantly from that in sub-Saharan Africa in terms of the relative risk, sex and age distribution as well as trend (5-14). Even within the same country the incidence of AIDS-KS is not uniform(3).

In spite of the high prevalence of AIDS in Kenya the pattern of KS in the country has not been studied so far. While it might be assumed to conform to that seen in other sub-Saharan countries, it is still necessary to get accurate information on the disease within the country if meaningful strategies for treatment and prevention are to be made. This study therefore aimed at assessing the impact of the AIDS pandemic on the incidence of KS in Kenya by comparing the rates and pattern of KS before and after the advent of AIDS.

MATERIALS AND METHODS

The materials for this study were derived from pathology records in the Histopathology Department at KNH. All records of histologically confirmed cases of KS from 1968 to 1997 were analysed for age, sex, and site distribution. The relative frequency of the tumours was calculated relative to all malignancies diagnosed in the same period.

RESULTS

Relative frequency, gender and age distribution: The relative frequency is shown in Table 1. The yearly relative frequency of KS ranged between 2% and 5% of all malignancies recorded. This Table also shows a general decline in all malignancies recorded over the study period. The proportion of KS has however, remained relatively unchanged. The age of patients presenting with KS ranged from the 1st to the 8th decades (Figure 1). By far KS was predominantly a disease of the male in all age categories. A large number of adult cases, however, did not have their ages specified. Site distribution for KS is shown in Table 2. Most of the cases of KS involved the lower limbs followed by the upper limbs. The head and neck region was less commonly involved.

Figure 1

Age and sex distribution

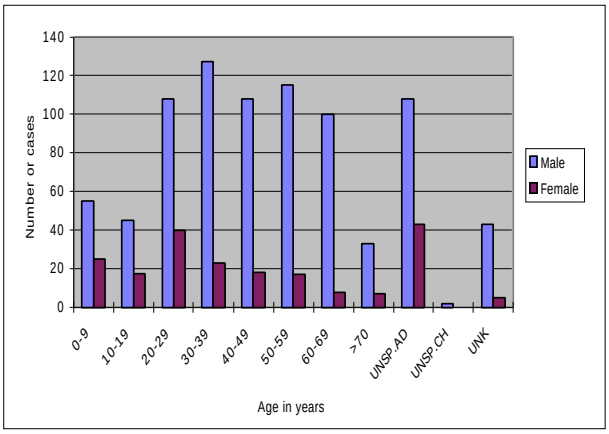

Figure 2

Age distribution of KS before and after the AIDS era

Table 1

Relative frequency of KS

Year	Total Malignancies	KS	%
1968	1434	37	2.58
1969	1469	43	2.93
1970	1505	37	2.46
1971	1559	47	3.01
1972	1514	37	2.44
1973	1700	45	2.65
1974	1691	45	2.66
1975	1761	35	1.99
1976	1745	47	2.69
1977	1730	34	1.97
1978	1659	39	2.35
1979	1925	42	2.18
1980	1645	31	1.88
1981	1550	26	1.68
1982	1790	45	2.51
1983	1704	37	2.17
1984	1757	42	2.39
1985	1246	30	2.40
1986	939	22	2.34
1987	808	28	3.47
1988	734	25	3.41
1989	656	35	5.34
1990	867	44	5.07
1991	907	48	5.29
1992	734	35	4.77
1993	980	49	5
1994	598	29	4.85
1995	790	28	3.54
1996	829	37	4.46
1997	670	26	3.88
Total	38896	1105	2.84

Table 2

Distribution of KS lesions according to site

Site	No.	%
Lower limb	543	45
Upper limb	117	10
Torso	28	2
Groin	7	1
Genito-inguinal	22	2
Head and Neck	85	7
lntra oral	49	4
Visceral	9	1
Unspecified skin	243	20
Unspecified lymph node	76	6
Unknown	17	1
Total	1196	100

Table 3

Distribution of KS lesions according to gender

Year	Total	Male	Female	Unknown	M: F Ratio
1968	37	35	2	–	18:1
1969	44	41	3	–	14:1
1970	37	34	3	–	11:1
1971	47	36	11	–	3:1
1972	37	31	6	–	5:1
1973	45	36	9	–	4:1
1974	45	41	5	–	8:1
1975	36	32	4	–	8:1
1976	47	44	3	–	15:1
1977	34	29	5	–	6:1
1978	39	33	6	–	6:1
1979	44	37	7	–	5:1
1080	31	29	2	–	15:1
1981	26	20	6	–	3:1
1982	45	36	9	–	4:1
1983	37	33	4	–	8:1
1984	42	33	9	–	4:1
1985	30	26	4	–	7:1
1986	22	17	5	–	3:1
1987	28	22	6	–	4:1
1988	25	16	8	1	2:1
1989	35	29	6	–	5:1
1990	44	37	7	–	5:1
1991	48	39	9	–	4:1
1992	35	27	8	–	3:1
1993	49	37	12	–	3:1
1994	29	19	10	–	2:1
1995	28	17	11	–	2:1
1996	36	28	8	–	4:1
1997	26	17	9	–	2:1
Total	1108	911	197	1	5:1

Comparison between the pre and post AIDS era: It can be seen from Table 1 that the relative frequency of KS before and after 1983 does not vary significantly although there is a gradual decline in the number of malignancies recorded. From Table 3 it is seen that the male to female ratio falls dramatically to stand at about 2:1 by 1977. The distribution before and after the AIDS pandemic shows no dramatic differences in the age distribution between the two periods (Figure 2).

DISCUSSION

With the advent of the AIDS pandemic there has been a dramatic increase in the incidence of KS in a number of countries(3). However, the pattern of occurrence and trend of the disease has differed from one country to another. In the west, the AIDS associated KS has been seen most commonly among homosexual or bisexual men. It is rarely seen among patients who have acquired HIV infection through heterosexual contact, intravenous drug use or vertical transmission. This pattern contrasts sharply with that seen in Africa. Here, both males and females; and paediatric patients are equally affected. Indeed with the advent of AIDS the incidence of KS among females and children has more than doubled in some African series(5,12,16).

The presentation of the AIDS associated KS in the Kenyan population has not been studied so far although it may be assumed to conform to that seen in other African countries with which it shares geographic location and similar AIDS statistics. In Kenya the HIV/AIDS disease was first reported in 1983 among prostitutes(15) and has since spread to involve all strata of the society. By 1997 the overall national AIDS prevalence was estimated at 15% and was considered as one of the highest in the world(17). It would, therefore, be expected that the incidence of KS would be correspondingly high.

This study, however, does not support such expectations. Over the thirty-year study period the relative frequency of KS has not changed significantly, ranging between 2% to 5% of the total malignancies recorded. For a region where endemic KS has been reported to constitute between 3% to 9% of total malignancies(18,19) these figures do not reflect any impact of AIDS on the incidence of KS in this hospital population. This finding differs markedly from those reported from Uganda(6,12), Zimbabwe(14,20), Zambia(11,13), Rwanda(9,10) and South Africa(5,21) where there has been a dramatic increase in the incidence of KS with the advent of AIDS. Similarly there is no evidence of a dramatic rise in the incidence of KS among children in the post AIDS era in comparison with the pre AIDS era. The only significant change in this study is the gradual drop in the male to female ratio, which had previously stood at approximately 10:1 in the sixties but had dropped to 2:1 by 1997.

A number of hypotheses could be advanced to explain this rather unexpected presentation of KS in our study. However, our favoured view is that this study, which is hospital based, rather than a population-based survey, might have failed to give a true picture of KS in the country due to under-reporting. One can see the gradual decline of reported malignancies from a figure of 1434 in 1968 to less than one half; thirty years later in 1997. Clearly this cannot be taken as an indication of a decline of cancers in Kenya. If anything this figure should go up in keeping with population growth and improvement in health services. Furthermore the gradual fall in the male to female ratio is a fairly reliable indication of the rise of incidence of KS among female patients.

Under-reporting may occur for a number of reasons. First there may be a decline of biopsies being taken in the hospital. This is particularly true for KS, which is easily diagnosed on clinical grounds. Also when faced with the possibility of self injury and contraction of the AIDS disease a number of clinicians may be reluctant to carry out biopsies in AIDS patients. Secondly there may be a referral bias where patients

who are severely sick may not be referred for treatment from peripheral health facilities to a tertiary facility like KNH. Thirdly, due to the cost sharing programme introduced in government facilities recently many patients may fail to access healthcare due to financial problems. Fourthly, with the recent development of several alternative private health care facilities a number of cases may seek attention at these facilities and therefore be lost to a study such as this. Lastly, multiple pathology and rapid mortality associated with HIV infection may hide some cases of the AlDS-associated KS. Therefore, although this study does not show a dramatic rise in the incidence of KS in this selected population there is a strong indication of a dramatic rise of KS among female patients, which may have been obscured by under-reporting. However, while we strongly suspect that under-reporting is the reason for the unusual pattern of KS in view of the high rate of HIV infection in the country other reasons may well exist and warrant further study. A population-based study would be necessary to define the pattern of the disease in the population.

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MISSED OPPORTUNITIES AND INAPPROPRIATELY GIVEN VACCINES REDUCE IMMUNISATION COVERAGE IN FACILITIES THAT SERVE SLUM AREAS OF NAIROBI
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MISSED OPPORTUNITIES AND INAPPROPRIATELY GIVEN VACCINES REDUCE IMMUNISATION COVERAGE IN FACILITIES THAT SERVE SLUM AREAS OF NAIROBI

P. K. BORUS

ABSTRACT

Objectives: **To quantify missed opportunities for immunisation, document reasons for their occurrence and evaluate the extent of inappropriately given vaccine doses.**
Design: **A cross sectional study of children under two years of age attending health facilities.**
Setting: **Six health facilities predominantly serving the slums of Nairobi.**
Methodology: **Information on vaccination was extracted from child immunisation cards as well as from mothers or guardians of children.**
Results: **Effective immunisation coverage for Bacille-Callmette Guerin (BCG) was 91%. Coverage for the birth dose, first, second, and third doses of oral polio vaccine (OPV0, OPVI, OPV2, and OPV3) was 44%, 83%, 79% and 75% respectively. Effective coverage for first, second and third doses of diphtheria-pertusis-tetanus (DPTI, DPT2 and DPT3) vaccine was 88%, 87% and 85% respectively. Measles coverage was 80%. Immunisation coverage for all antigens except OPV0 and OPV3 would have been increased to over 90% had missed immunisation opportunities and inappropriately administered vaccination been avoided. There would have been an 11% increase in OPV3 coverage to 86%. Increases in coverage for OPVI and OPV2 would have been 16% and 18% respectively. Coverage would have increased by 10% for diphtheria pertusis-tetanus (DPT) doses DPTI and DPT2, and 7% for DPT3. Measles immunisation coverage would have increased by 19% had missed immunisation opportunities and inappropriately administered vaccinations been avoided. The overall missed opportunities rate was 3%. The proportions of missed opportunities were higher for the OPV series than DPT series.**
Conclusion: **Missed immunisation opportunities among clinic attendees in Nairobi occur and routine supervision should be strengthened in these health facilities in order to minimise such missed opportunities and inappropriately administered vaccines.**

INTRODUCTION

The World Health Organisation's Expanded Programme on Immunization (EPI) recommends that children be vaccinated at every contact with a health facility(1). Failure to vaccinate a child who attends immunisation or curative clinics with vaccine(s), for which he/she is eligible in the absence of any known contra-indication, constitutes a missed immunisation opportunity.

Missed immunisation opportunities arise because of system factors such as non availability of vaccines, failure by facilities to immunise on all days of the week, or negative parental beliefs that prevent them from allowing their children to be vaccinated. When there is a true or absolute contraindication to vaccination, failure to immunise does not, by definition, constitute a missed immunisation opportunity. True contraindications of vaccination include complications arising from use of vaccines. Although the rate of occurrence of these complications is very rare, convulsions may, for example, follow DPT or measles immunisation(2). DPT vaccination should not be given if a previous dose resulted in severe reactions such as shock, high fever, convulsions, neurological conditions or anaphylactic shock. It is recommended for sick children whose conditions require hospital admission, that immunisation is deferred so that the decision to immunise is made by the admitting hospital. This is to avoid difficulties in subsequent diagnosis should a child's condition worsen after immunisation(3). The EPI recommends that children who had not received relevant doses are eligible for immunisation even if they present in health facilities with low-grade fever, mild respiratory illness, diarrhoea and other minor illnesses that are considered as false contraindications.

The routine immunisation schedule in developing countries aims to avail vaccines before ages when

children are at risk of disease and includes administration of BCG and OPV at birth. During recommended visits at 6, 10 and 14 weeks, DPT and OPV are given whereas measles is given at nine months(4). The interval between attenuated live vaccine doses in this schedule should be four weeks. The basis for the selection of the primary immunisation schedule has been extensively reviewed(5). Inappropriate doses as referred to in this study are those given either earlier than the recommended time, or for attenuated live antigen doses, when the intervals between doses were less than four weeks.

Determination of the extent and reasons for missed immunisation opportunities gives an estimate of the magnitude of the opportunity that exists for the direct increase of immunisation coverage. On the other hand, inappropriately given doses could be less effective due to viral interference. Thus, these could be discounted in a 'worst-case' scenario when calculating vaccine coverage levels. The proportion of missed immunisation opportunities and inappropriately given doses has been calculated during coverage surveys and through exit interviews of mothers as they leave health facilities with their children(6).

A large amount of literature exists on the extent and reasons for missed opportunities. Most of these come from surveys in developing countries and poor inner cities in developed countries, reflecting on the emphasis attached to improving coverage in underserved populations. In a review of missed opportunities in developing and developed countries, Hutchins and colleagues(7) found the reasons for missed opportunities to be similar in both settings, variations being in their prevalence. This variation is understandable because there is bound to be differences in EPI infrastructure and provider-clientele characteristics in both settings. Failure to immunise for vaccines that are given on a single visit in the routine schedule i.e. OPV and DPT at 6, 10 and 14 weeks, was reported as a common reason for missed immunisation opportunities. Other reasons were false contraindications of immunisation as well as improper health worker practices including failure to open a multi-dose vial for a small number of children. Other reasons included weaknesses in logistics that lead to vaccine shortage, poor clinic organisation and inefficient scheduling of vaccination. Parental refusal to let a child be vaccinated was not a common reason. A small study involving 23 children in the first decade of the existence of the Kenya Expanded Programme on Immunisation (KEPI) reported 4% of children were missed for immunisation when they attended an outpatient clinic(8).

This study was primarily designed to calculate the rate of and reasons for missed immunisation opportunities. The number of inappropriate doses given by facilities were assessed to determine the increase in immunisation coverage that would be achieved if these were correctly given.

MATERIALS AND METHODS

The study was a cross-sectional assessment of missed immunisation opportunities in six health facilities in Nairobi. These facilities were four health centres (African Medical and Research Foundation - AMREF, Baba Dogo, Kayole, Mukuru), one hospital (Mbagathi) and one clinic (Pangani). The study was carried out between April and May 2001. The choice of facilities was made purposively to reflect on facilities that serve slum areas of the city.

Children under two years of age attending these health facilities were included in the study and their mothers or adult carers of children were interviewed. The reference population of these children for each facility for use in sample size calculation was determined using figures available from the facilities or from census data. A minimum sample size of 51 children was required for each facility as determined using EPI INFO software. The calculation assumed missed opportunities rate of 16% (for the primary objective), a precision of 10% and 95% confidence level.

The KEMRI ethical committee approved the study and written permission was given by the medical officer/ administrator in-charge of facilities. Informed consent was sought from the mother or guardian of participating children. A questionnaire was used to collect information on documented immunisation as well as reasons for a child's visit, mother's knowledge of and attitudes towards immunisation, as well as information on costs relating to immunisation, and in particular on supplies such as syringes and needles. The timing of vaccination as well as intervals between doses of the same antigen were noted in order to determine inappropriately administered vaccines.

Whenever possible, interview days in the facilities were planned for the same days of the week or were synchronised to take place on days when the same antigens were given across facilities. The days spent on a facility were minimised to avoid influencing clinic practice and routines.

RESULTS

Four hundred and eighteen children participated in the study. Routine immunisation coverage for the primary EPI series was assessed by extracting information from child immunisation cards and by maternal recall of vaccination. Four hundred and fourteen (99%) of respondent mothers claimed a child they came with had an immunisation card. This was confirmed in 409 (98%) children by physical inspection.

The proportion of children who were validly vaccinated for each antigen was determined. Valid vaccine doses are those administered at or after the recommended age of vaccination i.e. 42 days for OPVI/ DPTI, 70 days for OPV2/DPT2, 98 days for OPV3/ DPT3 and 274 days for measles vaccine and within two weeks of birth for OPV0. Coverage ror DPTI, DPT2 and DPT3 was 88%, 87% and 85% respectively compared to 83%, 79% and 75% for OPV1, OPV2 and OPV3. Measles immunisation coverage was 80%. The median ages for DPT1, DPT2 and DPT3 immunisation were 47, 80 and 115 days respectively. The median age of measles immunisation was 290 days.

Table 1

Vaccine coverage and missed opportunities

Antigen	Vaccinated at correct age				Missed Opportunities			Early or inappropriate doses		Potential coverage by avoiding MIO & ID	
	N	n	%	Median age	n	%	PC-MIO	n	%	n	%
BCG	418	384	91.9	17	20	4.8	96.7	0	0	404	96.7
OPVO	392	173	44.1	4	3	0.7	45.7	0	0	179	45.7
OPV1	340	282	82.9	47	15	4.4	87.3	41	12	338	99.4
OPV2	289	228	78.9	82	16	5.5	84.4	30	10	274	94.8
OPV3	247	186	75.3	117	14	5.7	81.0	14	6	214	86.6
DPT1	340	298	87.6	47	2	0.6	88.2	33	10	333	97.9
DPT2	289	249	86.2	80	2	0.7	86.9	26	9	277	95.8
DPT3	247	210	85.0	115	1	0.4	85.4	15	6	226	91.5
Measles	107	86	80.4	290	4	3.7	84.1	16	15	106	99.1

N= Denominator or number of children eligible for immunisation, n= Numerator, PC-MIO= Coverage by avoiding missed opportunities, MIO and ID=Missed immunisation opportunities and early/inappropriately administered vaccination

The proportion of children aged 12-23 months old who were fully immunised was assessed. The median age of these children was 455 days (15 months). Of 23 children who were aged over one year old, 19 were fully immunised, that is, each had received one dose of BCG, three valid doses of OPV, three valid doses of DPT and one valid dose of measles vaccine.

Missed immunisation opportunities were assessed as a proportion of age-eligible children who were attended to at surveyed health facilities for various reasons over interview days. The overall missed opportunities rate was 3% (77/2659). Missed immunisation opportunities were more common for oral polio vaccines. The proportion of missed opportunities for OPV1, OPV2 and OPV3 was 4.4%, 5.5% and 5.7% respectively (Table 1). In contrast, the proportion of missed immunisation opportunities for the DPT series was 0.6%, 0.7% and 0.4% for DPT1, DPT2 and DPT3 respectively. The proportion of missed opportunities to immunise for measles was 3.7%.

Had all opportunities to immunise been utilised, immunisation coverage for BCG would have increased to 97%. Similarly coverage for OPV0, OPV1, OPV2 and OPV3 would have increased to 46%, 87%, 84% and 81% respectively. For the DPT series, coverage would have increased only marginally. Measles immunisation coverage would have increased to 84%.

Immunisation coverage for all antigens except OPV0 and OPV3 would have been increased to over 90% had missed immunisation opportunities and inappropriately given vaccines been avoided. There would have been 16%, 18% and 11% increase in coverage for OPVl, OPV2 and OPV3; whereas DPTl and DPT2 coverage would have increased by 10%. DPT3 and measles coverage would have increased by 7% and 19% respectively.

Missed immunisation opportunities were also assessed by health facility (Table 2). The proportion of missed immunisation opportunities varied according to facility. Baba Dogo and Kayole had high proportions of missed immunisation opportunities for OPV. AMREF had only missed opportunities for BCG and not other antigens. Mbagathi, Mukuru and Pangani never had missed opportunities for the majority of antigens. Mukuru had the highest proportion (11%) of missed opportunities for BCG vaccination. Missed opportunities for OPVl and OPV2 occurred only in Baba Dogo and Kayole where the proportions were 7.4% and 18%, and 9.6% and 23.9% respectively. In addition, the proportion of missed opportunities for OPV3 in Baba Dogo, Kayole and Mukuru were 19%, 10% and 3% respectively.

Table 2

Missed immunisation opportunities according to health facility

Health facility	BCG	OPVO	OPVI	OPV2	OPV3	DPTI	DPT2	DPT3	Measles	Total
AMREF	4 (5.1)	0	0	0	0	0	0	0	0	4
Baba Dogo	1 (1.8)	0	4 (7.4)	5 (9.6)	9 (18.8)	0	2 (3.8)	1 (2.1)	1 (4)	23
Kayole	1 (1.2)	1	11 (18.0)	11(23.9)	4 (10.3)	1 (1.6)	0	0	0	29
Mbagathi	2 (3.1)	0	0	0	0	1 (1.7)	0	0	1 (12.5)	4
Mukuru	8 (11.3)	1	0	0	0	0	0	0	0	10
Pangani	4 (6.1)	1	0	0	0	0	0	0	2 (14.3)	7
Total	20 (4.8)	3	15 (4.4)	16 (5.5)	14 (5.7)	2 (0.6)	2 (0.7)	1 (0.4)	4 (4.1)	77

Parantheses show missed opportunities for immunisation as proportion of children eligible for each antigen who attended the health facilities.

Missed immunisation opportunities for the DPT series were fewer than for the OPV series. Missed opportunities for DPT1 occurred in Kayole and Mbagathi only where the proportions were similar at 1.6% and 1.7% respectively. Only Kayole had missed to immunise children who were eligible for DPT2 and DPT3, and the proportion of missed immunisation opportunities in Baba Dogo were 4% and 2% respectively. There were two children who were missed for measles immunisation in Pangani, representing 14% of eligible children who had presented at the facility for measles vaccination. The missed measles immunisation opportunities for Mbagathi and Baba Dogo were 13% and 4% respectively.

Missed immunisation opportunities were assessed according to reason for visit to the health facility (Table 3). Eighty four percent of missed opportunities occurred while children were brought to clinics for vaccination. Only 4% of missed opportunities occurred while child came to the clinic for curative services.

Table 3

Missed immunisation opportunities by reason of visit

Reason for visit	BCG	OPV0	OPV1	OPV2	OPV3	DPT1	DPT2	DPT1	Measles	Total	%
Vaccination	19	1	15	15	8	2	2	0	3	65	84.4
Treatment	1	0	0	0	1	0	0	0	1	3	4.0
Other	0	2	0	1	5	0	0	1	0	9	11.6
Total	20	3	15	16	14	2	2	1	4	77	100

Other - Includes weighing, accompanying other child and normal check up.

Mothers were asked the reasons why their children were not vaccinated. Only 20 mothers enumerated reasons they claimed health workers gave for not vaccinating children who came for immunisation (Table 4).

Table 4

Reasons given for non-vaccination

Reason for failure to immunise	No. of Observations	Proportion (%)
Vaccine was out of stock	4	20
Vaccine scheduled not to be given that day	7	35
Child was sick or under-weight	4	20
Child not yet of age	3	15
BCG syringe out of stock	2	10
Total	20	100

Of the 20 responses mothers gave, scheduling of immunisation to other days was the most common reason (35%). The refusal to immunise ill or under-weight children was the reason given by four mothers, including not immunising because a child had a rash. Four mothers claimed children were not immunised because BCG vaccine and OPV were out of stock.

DISCUSSION

In the facilities covered by this study, immunisation coverage was higher for the DPT series (all above 85%) compared to the OPV series (83% and below). There were more incorrectly administered OPVI and OPV2 vaccine doses, compared to corresponding doses of DPT. This partly explains the relatively lower coverage for the OPV series compared to the DPT series.

The lower immunisation coverage for OPV doses, had also to do with missed immunisation opportunities arising from a shortage of OPV that was reported in the period preceding to and during the survey. Interestingly, the 80% immunisation coverage for measles was higher than that for OPV3.

The overall missed immunisation opportunities rate in this study was 3%. Compared to one recent and several old studies from Africa, this was similar to rates found in preventive settings in Zimbabwe (4%) and Comoros (5%) (9,10). However, it was lower than findings in Congo (13%), South Africa (11% and 16%), Ethiopia (41%), and Egypt (30%) (11-15). Eighty four percent of the missed immunisation opportunities occurred when a child was brought for vaccination. Most missed opportunities for OPV immunisation occurred in Baba Dogo and Kayole health centres. This was mainly because these facilities had a shortage of OPV stocks, which was more pronounced in Kayole during the survey period. Of the 33 children who came for treatment as a primary reason for visiting the facilities, only three of those eligible for vaccination were not immunised at those health facilities. The 4% missed opportunities rate for measles in this study was lower than estimates recorded elsewhere which ranged from 9.8% to 80% (16-20).

Avoidance of inappropriately administered doses of vaccine and missed immunisation opportunities would have increased immunisation coverage for all antigens, with an increase of measles immunisation coverage by 19%. Inappropriately administered immunisation and missed opportunities points to a gap in health worker training and systems of supply of vaccines that requires health policy to address. This would call for a reappraisal of routine supervision and training within relevant city facilities so that the primary schedule is understood and practiced by health providers.

Inappropriately timed or early vaccination is a main issue that came out of this study. We used the cut-off recommended by KEPI to determine ages of vaccination and intervals between doses, so that the age cut-off for, for example, OPV1/DPT1 administration was six weeks (42 days), and the interval between doses in a series was four weeks (28 days). What arises then is whether routine KEPI supervision or practitioners stress the exactness of immunisation timing. It is conceivable that EPI service providers at the facility level take the age cut-off in approximate rather than absolute terms so that 42 days would be "about 42". If the latter is practised it opens the way for different provider interpretations and a variation in practice by creating a "best judgement" scenario, which is not ideal from a programmatic point of view. The dilemma with absoluteness of age cut-offs to the health professional would, of course be choosing between turning back a child who is say 37 days old, without giving OPV1/ DPT1 and risking the mothers never bringing back that child for vaccination on the appropriate date.

A strengthened routine supervision during which EPI personnel are updated on the need to follow the recommended schedule may result in fewer inappropriate doses. As the policy of vaccinating children at all contacts is in place in all facilities country wide, the issue on the existence of missed immunisation opportunities points to some instances in practice where EPI workers do not check for children who are eligible for vaccination. The change here would be for managers or matrons of facilities to ensure that all contacts with children eligible for vaccination are utilised to increase vaccine coverage. Social mobilisation through community based organisations (CBOs) and other groups involved in health within the slums should be strengthened in order to impart more knowledge to mothers regarding the importance of routine vaccination.

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MORPHOLOGICAL STUDY OF THE UNCOMMON RECTUS STERNI MUSCLE IN GERMAN CADAVERS
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MORPHOLOGICAL STUDY OF THE UNCOMMON RECTUS STERNI MUSCLE IN GERMAN CADAVERS

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ABSTRACT

Objective: **The present investigation has been designed to study the incidence of the rectus stern muscle in German human cadavers dissected in the Kingdom of Saudi Arabia, trying to find a postulation for the development of such muscle when present.**
Design: **Gross dissection of 130 cadavers, of both sexes, was performed throughout a period of 10 years.**
Setting: **Department of Anatomy College of Medicine, King Faisal University, Dammam, Saudi Arabia.**
Intervention: **Investigation of the origin and insertion of the rectus sterni and measurements of its length and width.**
Results: **Two adult cadavers, one of each sex, had shown well-developed bilateral rectus stern muscles. All muscles identified were parasternal in position, being superficial to the medial portion of the pectoralis major muscle. Minor morphological differences were observed among the four muscle masses concerning their length, breadth, origin and insertion.**
Conclusion: **The current study has determined the incidence of the rectus sterni muscle, in German cadavers to be 1.54% per bodies examined compared to 4% in cadavers from Saudis. Such a frequency is compared to that reported in different geographic populations. The rectus sterni muscle is innervated by the anterior cutaneous branches of the intercostal nerves. The description of the rectus sterni muscle and its incidence determined in the present study, might be of a great help for clinicians radiographing or tackling the pectoral region.**

INTRODUCTION

The rectus sterni muscle has been identified as an infrequent mass of striated musculature in front of the human chest(1). The muscle, when present, received other names as the sternalis, the episternalis, the rectus thoracis and the superficial rectus abdominis(2). The prevalence of the rectus sterni muscle has been reported to vary widely among different nationalities, from 1% in Taiwanese(3) to 23.5% in Chinese(4). Certain morphological and mammographic studies, determined the incidence of this muscle to be 4% in the Kingdom of Saudi Arabia(5).

The laterality of the rectus sterni muscle has been also investigated by many authors. It is twice unilateral than bilateral(6). The rectus sterni muscle has been classified into unilateral and bilateral with four subtypes for each type group(7).When identified, the muscle is described as thin, flat and long arising from the anterior chest wall, below the clavicle, running parallel to the sternum but superficial to the medial part of the rectus abdominis muscle, and finally gaining insertion into the costal cartilages, the lower end of the sternum or the external oblique aponeurosis of the abdomen(1,8).

It has been phylogenetically suggested that there is a longitudinal ventral paramedian muscle sheet that disappears leaving the hyoid muscles in the neck and the rectus abdominis muscle as representatives. The rectus sterni muscle is a remnant of this longitudinal muscle in the anterior thoracic wall although it has been always demonstrated to be superficial to but not continuous with the rectus abdominis muscle(9).

In certain mammographic studies the rectus sterni muscle appeared as an irregular focal density along the medial aspects of the mammograms, giving a false perception of a breast mass(10,11). The aim of the current study was to determine the incidence of the German rectus sterni muscle dissected in Saudi Arabia and to describe, in details, the morphology of this muscle when identified. The results of this study might highlight the reported postulations concerning its development. Furthermore, the exact location and extension of this muscle would be of a great concern to clinicians when interpreting mammograms.

MATERIALS AND METHODS

One hundred and thirty formalin fixed adult German cadavers, of both sexes over a period of 10 years, were utilised in this study. They were used for teaching the medical students in the Anatomy Laboratory, College of Medicine, King Faisal University, Dammam, Saudi Arabia. Fine dissection of the pectoral region was carefully performed. Any muscular variant in the paramedian region of the anterior chest wall was looked for and followed for its origin, insertion, nerve supply and morphological features. The length and breadth of the muscle, along its whole extension, were determined using a thread that was then applied to a ruler.

RESULTS

Two cadavers, one of each sex, out of 130 formalin-fixed German human cadavers over a 10 year period, were observed to exhibit bilateral rectus sterni muscles.

Two well-demarcated masses of an asymmetrical bilateral rectus sterni muscle were observed in a male adult cadaver. Each muscle mass was located on the anterior chest wall, in a paramedian position, just deep to the skin and superficial fascia of the pectoral region, but superficial to the pectoral fascia and the pectoralis major muscle. The left muscle measured 11 cm long and 2 cm broad. It arose from the left part of the front of the manubrium sterni and from the sternal tendon of the left sternocleidomastoid muscle. This left rectus sterni muscle descended vertically to gain insertion into the left 5th and 6th costal cartilages and the aponeurosis of the left external oblique muscle of the abdomen taking share in the formation of the anterior wall of the left rectus sheath (Figures 1-3).

Figure 1

Morphological types of the rectus sterni muscle as described by Jelev et al. (2001)

Figure 2

A photograph (A) and a schematic diagram (B) of an asymmetrical bilateral rectus sterni muscles (RS) of specimen I, showing their location and extension. The right muscle is larger than the left one. Note the sternocleidomastoid (SM) and pectoralis major (PM) muscles

Figure 3

A photograph (A) and a schematic diagram (B) of the magnified proximal parts of the rectus sterni muscles (RS) shown in figure 2, revealing the origin of each muscle from the corresponding sternal tendon of the sternocleidomastoid muscle (SM). The rectus sterni muscles are located superficially to the pectoralis major muscles (PH)

The right rectus sterni muscle, demonstrated in the same cadaver, was larger than the left one. It measured 12cm long and 2.5cm at its broadest part. It had an origin similar to that of its left counterpart but it slightly inclined to the right near its lower end to gain insertion into the right 5th, 6th and 7th costal cartilages and the right external oblique aponeurosis.

As regards the arterial supply and innervation of the left rectus sterni muscle, it was found that the perforating branches of the left internal thoracic artery and the anterior cutaneous branches of the left 2nd, 3rd and 4th intercostal nerves were noticed to it. The left pectoral nerves were observed to give no branches to the left rectus sterni muscle. The superficial and deep relations of the right rectus sterni as well as its arterial supply were exactly similar to those of the left muscle. The right muscle was innervated by the anterior cutaneous branches of the right 3rd and 4th intercostal nerves.

The pectoralis major muscle, on each side, was morphologically normal without presenting any anomaly or variation.

Figure 4

A photograph (A) and a schematic diagram (B) of the asymmetrical bilateral rectus sterni muscles (RS) of specimen II, showing the right muscle is larger than the left one. The left rectus sterni muscle occupies an infraclavicular position without any apparent continuity with the left sternocleidomastoid muscle (SM). Note the pectoralis major muscles (PM)

Figure 5

A photograph (A) and a schematic diagram (B) of the magnified proximal parts of the rectus sterni muscles (RS) shown in figure 4, revealing their asymmetry in origin and size. The sternocleidomastoid (SM) and pectoralis major (PM) muscles are also shown

Another asymmetrical bilateral rectus sterni muscle was demonstrated in a female adult cadaver . The left rectus sterni muscle, in this specimen, was relatively smaller measuring 8cm long and 1.5cm broad. It extended from the left margin of the sternal angle down to the left 5th costochondral junction.

The right muscle mass had a proximal tendinous part (7cm) and a distal fleshy part (5cm) with a maximal breadth of 2.5 cm. It also arose from the sternal tendon of the sternocleidomastoid muscle, and gained insertion into the right 5th and 6th costal cartilage and the right external oblique aponeurosis.

As regards to the arterial supply and innervation of the left rectus sterni, it was found that this muscle was supplied by the perforating branches of the left internal thoracic artery and innervated by the left 3rd and 4th intercostal nerves. The right rectus sterni received supply from perforating branches of the right internal thoracic artery and innervation from the anterior cutaneous branches of the right 4th and 5th intercostal nerves.

Both muscles, in specimen II, assumed the same vertical position, relation and location as the rectus sterni muscles of specimen I (Figures 4-5).

DISCUSSION

The rectus sterni muscle has been investigated by many authors in different populations. It is assumed that this muscle is developed from one or more of the neighbouring muscles such as the pectoralis major muscle (12,13) the sternocleidomastoid muscle(l4), or the rectus abdominis muscle(l5). Furthermore, the previous authors suggested that the rectus sterni muscle has the same innervation as the muscle of origin. Some authors agreed that the rectus sterni muscle is innervated by the pectoral nerves while other investigator demonstrated its nerve supply from the intercostal nerves and sometimes the muscle had dual innervation indicating dual origins(13).

The rectus sterni muscle has been demonstrated, in the present study, to be supplied by the anterior cutaneous branches of the intercostal nerves and the perforating branches of the internal thoracic artery. Such findings are not consistent with the old reports which suggested that the rectus sterni muscle is supplied by the pectoral nerves(16-18) but the findings of the present study run in accordance with the recent reports of other workers(3,7,19).

The present study has demonstrated two specimens with bilateral rectus sterni muscles innervated solely by the intercostal nerves. Communicating twigs were not observed between the pectoral and intercostal nerves, in the specimens investigated. The present work, therefore, supports the opinion that the rectus sterni muscle is derived from the rectus abdominis muscle as the two muscles have the same innervation. The results of this study also run in accordance to the proposal that a ventral longitudinal paramedian muscular sheet is represented, in human being, by the hyoid muscles in the neck, the rectus abdominis muscle in the abdomen, and occasionally the rectus sterni muscle in the thorax(9,19).

Based on a previous classification(7), the current first specimen represents subtype while the second specimen represents subtype of the bilateral group of the rectus sterni muscles.

The present work determined the incidence of the rectus sterni muscle is 1.54% per German cadavers dissected in Saudi Arabia. The frequency however, has been reported to vary widely from 1% in Taiwanese (3,16) to 23.5% in Chinese(4). This muscle has been previously reported to have an incidence of 4% in the cadaveric specimens in Saudi Arabia(5).

The present investigation provides a detailed morphology of the rectus sterni muscle. The incidence of such uncommon muscle is determined to be 1.54% amongst German cadavers compared to 4% in Saudis. Moreover, this work suggests that the rectus sterni muscle is derived from the rectus abdominis muscle as the two muscle masses are supplied by the segmental intercostal nerves. The results of the present study might be of great concern to radiologists and surgeons dealing with the pectoral region.

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COMPARATIVE EFFICACY OF ALBENDAZOLE AND THREE BRANDS OF MEBENDAZOLE IN THE TREATMENT OF ASCARIASIS AND TRICHURIASIS
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COMPARATIVE EFFICACY OF ALBENDAZOLE AND THREE BRANDS OF MEBENDAZOLE IN THE TREATMENT OF ASCARIASIS AND TRICHURIASIS

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ABSTRACT

Objective: **To evaluate the comparative efficacy of 400 mg albendazole (Smith Kline Beecham) as a single dose and three brands of mebendazole (Janssen, Unibios and East African Pharmaceuticals) at doses of 100 mg twice a day for three consecutive days in the treatment of single or mixed infections with *Ascaris lumbricoides* and or *Trichuris trichiura* in four treatment groups of school children.**
Design: **Randomized trial.**
Setting: **Wondo-Genet, southern Ethiopia.**
Subjects: **School children, aged six to nineteen years.**
Results: **The percentage cure rate and egg reduction rate obtained with albendazole and mebendazole from the three brands were not significantly different in the treatment of ascariasis. However, significant differences were found among the percentage cure rates and egg reduction rates of the four treatment groups in the treatment of trichuriasis. Comparatively, high cure rate (89.8%) and egg reduction rate (99.1%) were observed in vermox (Janssen) treated group followed by Unibios (India) treated group (53.3% and 96.53% cure and egg reduction rates, respectively), whereas low cure rate (17.1%) and egg reduction rate (69.8%) were seen in the albendazole treated group.**
Conclusion: **The results of this study suggest that in areas of single or mixed infections with *Trichuris trichiura* and/or *Ascaris lumbricoides* are common public health problems and where laboratory facilities are not available to make parasite identification, mebendazole (particularly vermox, a product of Janssen laboratory) would be the drug of choice to treat trichuriasis and ascariasis. However, either mebendazole from the different brands or albendazole is effective in the treatment of ascariasis in areas where trichuriasis is not prevalent.**

INTRODUCTION

Infection with intestinal helminths is one of the most common health problems of children in developing countries. Moreover, chronic intestinal helminthic infections have been identified as one of the possible risk factors that contribute to the pathogenesis as well as the widespread of other infectious agents such as HIV and mycobacterium in the tropical countries(1-4).

In developing countries, it is difficult to prevent infection with geo-helminths because improvements in environmental sanitation are not easily achievable. However, treatment of infected individuals with effective and broad-spectrum anthelminitics can minimise problems that arise from intestinal helminthic infections(5,6).

Several studies have shown that albendazole and mebendazole from different brands are drugs of choices for the treatment of single or mixed infections with intestinal helminths(7-10). In contrast, others have reported that these drugs are not equally effective in curing all intestinal helminthic infections(11-15). Few studies have directly compared the efficacies of mebendazole from different brands or efficacy of albendazole to that of mebendazole from different brands in the treatment of intestinal helminths using the recommended dosages by the manufacturers (12,16).

In the present study, comparative efficacy of three brands of mebendazole (i.e. Janssen, Unibios and East African Pharmaceuticals) and albendazole (Smith Kline Beecham) was assessed in Wondo-Genet, southern Ethiopia, against the most common geo-helminths, *Ascaris lumbricoides* and *Trichuris trichiura.*

MATERIALS AND METHODS

Study Area: The trial was conducted in Wondo-Genet, southern Ethiopia, in March 2003. Wondo-Genet is a district located some 270 km south of Addis Ababa at an altitude of about 1800 m above sea level. Majority of inhabitants of Wondo-Genet belong to the Sidama ethnic group and chiefly earn their living as farmers practicing settled mixed agriculture. Enset and maize are the principal food crops produced while

sugar cane and chat *(Catha edulis)* are the principal cash crops of the area. *Ascaris lumbricoides, Trichuris trichiura* and *Schistosoma mansoni* are the three most prevalent intestinal helminths in the area (Berhanu Erko, Institute of Pathobiology, personal communication).

Study population: A cross-sectional parasitological survey was conducted in two schools (Shesha Kekel and Wondo Wosha) to identify positive subjects to be randomised into four treatment arms. In the survey, stool specimens were collected from 730 children (387 males and 343 females) age ranged from six to nineteen years. After examining the stool specimens all subjects positive for *Ascaris lumbricoides* and/ or *Trichuris trichiura* infections were randomised into four groups.

Sample size determination: Sample size for this trial was estimated in such a way that the study would attain power of 80% to 85% and estimation of effects with 90% to 95% confidence levels. The following additional assumptions were also used as inputs to sample size calculation(1). In the treatment of trichuris infection cure rate of each brand of mebendazole was assumed to be 37% while cure rate of albendazole was assumed to be significantly less than 37% taking 15% as minimum detectable difference(2). That each drug to be used in this trial would result in at least 94% cure rate with minimum detectable difference of 6% in the treatment of ascaris infection. Hence, about 148 students positive for each of the two target parasites (i.e. Ascaris and Trichuris) per treatment group (i.e. about 608 students in total) were sufficient for the trial.

Stool collection and examination: After giving adequate instruction on how to provide stool samples, small pieces of plastic sheets were distributed to the study subjects to provide sizeable fresh stool specimens of their own. The specimens were processed using Kato technique employing a template delivering a plug of 41.7mg of stool as previously described(17) and microscopically examined for eggs of intestinal helminths by two senior laboratory technicians. Egg count was performed for *Ascaris lumbricoides* and *Trichuris trichiura.*

Drugs: Albendazole (Smith Kline Beecham, France), vermox (Janssen, South Africa) and mebendazole (Unibios, India) were purchased from local pharmacies. Mebendazole, a product of East African pharmaceuticals (Ethiopia), was kindly donated by Dr. A.R. Hashim, Manager of East African pharmaceuticals in Addis Ababa.

Treatment allocation: A sequentially numbered list of students positive for at least one of the two helminth infections (ascariasis or trichuriasis) was prepared and randomly divided into four treatment groups using random numbers obtained from a random number table. Following randomisation, the students were informed the date of treatment through their school teachers. Hence, 661 children showed up on treatment day. On the basis of the random assignment prepared before hand, 197 children were treated with 400 mg of albendazole as a single dose while 144 children, 166 children and 154 children were treated with 100 mg of mebendazole from Unibios, Janssen and East African pharmaceuticals, respectively, twice a day for three consecutive days. The single-dose treatment of albendazole and the first dose of mebendazole were administered under the supervision of a local nurse and the research team. The remaining mebendazole tablets were given to the parents or guardians of the children after giving adequate instruction on the dosage of the drugs. The parents or guardians of the children as well as school teachers verified that the drugs were taken properly. During the initiation of treatment, all children were interviewed whether or not they had received any anthelminthic drugs in the past three months and none of them reported to receive drug treatment during the period in question. Twenty-one days after treatment, faecal samples were collected for efficacy determination.

Ethical considerations: The objective of the study was explained to school teachers and the students at the time of baseline data collection. The stool sample was then collected after obtaining verbal consent. Positive individuals for *S. mansoni* infection were treated with praziquantel at the time of stool collection for efficacy determination.

Statistical analysis: The egg reduction and cure rates of each drug were compared based on their percent of egg count reduction and cure rate using Stata Version 6. Fisher's exact test was used to compare proportions among the study groups. The intensity of infection was determined for *Ascaris lumbricoides* and *Trichuris trichiura* and expressed as egg per gram (epg) of faeces for each individual. Geometric mean egg count was estimated as exp [1n (c+1)/n], -1 where c was the egg counts (epg) for a particular individual and n is the number of individuals. Intensity of infection was compared using ANOVA. Changes in egg counts within individuals were compared by calculating $D_i = \ln (c_o+1)-\ln (c_1+1)$ for each individual, where 1n is natural logarithm, c_o is the egg count before treatment, c_1 is the egg count after treatment and Di is the difference for the i^{th} individual. Differences among the four treatments were compared using ANOVA and the percentage of egg count reduction induced by the treatment was estimated as 100[1-exp(-D)]%, where D was the mean difference for a particular treatment.

RESULTS

Of the 730 stool specimens collected, 13 (1.8%) specimens were not examined because of mislabeling. Of the remaining 717 specimens, 703 (98.0%) were positive for one or more helminth infections. The most prevalent parasite was *Trichuris trichiura* (91.0%) followed by *Ascaris lumbricoides* (81.4%), and then by *Schistosoma mansoni* (55.2%). Prevalence of taeniasis and entrobiasis was not high (3.1% and 2%, respectively). Since stool examination was not performed within one hour of sample collection(12), prevalence of hookworm infection was not determined.

Stool specimens were collected from 534 children, 130 albendazole and 404 mebendazole treated (123 Unibios, 138 Janssen and 143 East African pharmaceuticals) 21 days post-treatment to determine the efficacy of each drug on cure and egg reduction rates in ascariasis and trichuriasis. From those who received treatment, 127 children (34.0%) from albendazole treated group, 11(7.1%) from East African mebendazole treated group, 21(14.6%) from Unibios mebendazole treated group and 28(16.9%) from vermox treated group] did not appear during stool collection for efficacy determination.

Table 1

Baseline characteristics of the study subjects as randomised into different treated groups

Variable	Alb (n=130)	EA-meb (n=143)	Meb (n=123)	Vermox (n=138)	p-value
Sex (%)					
Male students	55	53	47	54	0.715
Age mean(SD)	10.5(2.2)	10.1(2.0)	10.9(2.1)	11.1(2.2)	0.000
Prevalence					
Ascariasis	82.3	80.4	78.9	81.9	0.919
Trichuriasis	94.6	90.9	92.7	85.5	0.084
Intensity (G. mean)					
Ascariasis	290.9	258.3	288.6	341.2	0.676
Trichuriasis	18.6	21.8	15.7	17.3	0.396

Alb= albendazole, EA-meb = East African mebendazole, Meb = Indian mebendazole (Unibios), and vermox = South African mebendazole (Janssen)

Table 2

Percentage of egg reduction and cure rates obtained with different brands of mebendazole (Janssen, Unibios and East Africa) and albendazole in ascariasis and trichuriasis 21 days post-treatment

Helminth	Treatment	No. of individuals	No. execrating Bef. treat.	Aft. tret	Cure rate(%)	Geom Bef. tre.	Mean Aft. tret.	Egg Reduction (%)
Al	vermox	138	113	4	96.5a	8188.9	1833.2	99.9
	Meb	123	97	1	99.0b	6925.5	384.0	99.9
	EA-meb	143	115	8	93.0c	6198.2	1295.9	99.9
	Alb	130	107	89	92.5	6982.2	305.1	99.9
Tt	vermox	138	118	14	89.8a*	414.1	91.4	99.1*
	Meb	123	114	55	53.5b*	376.4	118.1	96.5*
	EA-meb	143	130	97	27.9c*	522.3	171.6	88.5*
	Alb	130	123	107	17.1*	445.7	258.0	69.8*

a = Vermox compared versus Meb, EA-meb & Alb, b = Meb compared versus EA-meb and Alb, c = EA- meb compared versus Alb. * there were statistically significant differences in cure rates and egg reduction rates of the drugs ($P<0.05$). Al = *Ascaris lumbricoides,* Tt = *Trichuris trichiura,* Alb= albendazole, EA-. meb = East African mebendazole, Meb = Indian mebendazole (Unibios) and vermox = South African mebendazole (Janssen).

The effect of withdrawal from different treatment groups on baseline data (sex composition, mean age, intensity and prevalence of ascariasis and trichuriasis) was assessed (Table 1). Significant difference was found in the prevalence of *trichuriasis* among mebendazole (Unibios) treated subjects (76.2% among absent versus 92.7% among present; $p < 0.05$) and in the percentage of absent and present female students in the albendazole treated group (27.3% of females in the absent versus 44.6% of the females in the present, $p = 0.02$).

The number of children excreting eggs of *Ascaris lumbricoides* and *Trichuris trichiura* pre-and post-treatment, geometric mean egg count and the overall percentage of egg reduction and cure rates are shown in Table 2. Percentage cure and egg reduction rates obtained with albendazole and mebendazole from the three brands were not significantly different in ascariasis. Significant differences were found among the percentage cure rates as well as egg reduction rates of the four treatment groups in trichuriasis. Comparatively, high cure rate (89.8%) and egg reduction rate (99.1%) were observed in vermox (Janssen) treated group followed by Unibios (India) treated group (cure and egg reduction rates, 53.3% and 96.5%, respectively), whereas low cure rate (17.1%) and egg reduction rate (69.8%) were seen in the albendazole treated group.

DISCUSSION

In the present study, the comparative efficacy of mebendazole from three brands and albendazole was evaluated against ascariasis and trichuriasis at the dosages recommended by the manufacturers. The results indicated that mebendazole from the three brands (Janssen, Unibios and East African Pharmaceuticals) at doses of 100 mg twice a day for three consecutive days and 400 mg of albendazole (Smith Kline Beecham) as

a single dose were highly effective against *Ascaris lumbricoides* and did not differ in egg reduction rates as well as in cure rates. However, they did differ significantly both in egg reduction rates and cure rates in the treatment of trichuriasis although there were no differences among the four treatment groups in the intensity of *Trichuris trichiura* infection before treatment as determined by egg counts. A previous study in Ethiopia has shown that Indian brand of mebendazole (Unibios) is more effective than albendazole (Smith Kline Beecham, France) in the treatment of single or mixed infections with *Ascaris lumbricoides* and *Trichuris trichiura*(16). In the present study, 400 mg single dose of albendazole brought about low egg reduction and cure rates in trichuriasis as compared to multiple doses of mebendazole from the three brands.

The egg reduction rate of 69.8% obtained with a single dose of 400 mg albendazole in the present study in the treatment of trichuriasis is almost comparable to the previous report from Ethiopia(16), but slightly lower than the egg reduction rates (73.3% to 87%) observed elsewhere with the same dose of albendazole 21 days post-treatment in children infected with *Trichuris trichiura*(12,18). Cure rate of 17.1% observed in trichuriasis in this study is somewhat higher than the cure rates observed in previous studies(12,16). However, it is lower than cure rate reported by Rossignol and Maisonneve(18).

A dose of 100 mg mebendazole (vermox a product of Janssen laboratory) twice a day for three consecutive days resulted in cure rates of 70%-75% and egg reduction rates of 97.9% to 99.3% in trichuriasis(7,8). Comparable to these pervious reports, treatment of trichuriasis with mebendazole (vermox) resulted in a cure rate of 89.9% and egg reduction rate of 99.1%, which is significantly higher than the cure and egg reduction rates obtained with mebendazole either from Unibios (India) or East African pharmaceuticals (Ethiopia). In contrast to our observation, Albonico *et al. (12)* have reported the absence of difference between generic mebendazole (Pharmamed) and original mebendazole (Janssen) at a single dose of 500 mg in curing ascariasis, trichuriasis and hookworm infection. However, generic mebendazole has been reported to be less effective than the original product in the treatment of trichuriasis and hookworm infection(19), which is in agreement with our results.

In conclusion, the present study provides useful information on the comparative efficacy of albendazole and mebendazole from three brands in the treatment of ascariasis and trichuriasis. Nevertheless, the comparative efficacy of these drugs was not assessed against hookworm infection. In areas of single or mixed infections with *Trichuris trichiura* and *Ascaris lumbricoides* are common public health problems and where laboratory facilities are not available to make parasite identification, mebendazole (particularly, vermox a product of Janssen laboratory) would be the drug of choice to treat trichuriasis and ascariasis. In areas where trichuriasis is not prevalent, either mebendazole from the different brands or albendazole would be effective in the treatment of ascariasis.

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OBSTETRIC PERFORMANCE OF WOMEN AGED OVER FORTY YEARS
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OBSTETRIC PERFORMANCE OF WOMEN AGED OVER FORTY YEARS

E. O. ORJI and V. I. NDUBUBA

ABSTRACT

Background: **Advanced age and parity constitute two major factors in the outcome of pregnancy and labour management both in the developed and developing countries.**
Objective: **To examine pregnancy outcomes in women aged 40 years and above with the view of proffering solution to some of the problems encountered.**
Design: **A case control retrospective study.**
Setting: **Obafemi Awolowo University Teaching Hospital, lle-lfe, Nigeria from 1st January, 1995 to 31st December, 1999.**
Subjects: **Three hundred and three women who delivered at 40 years of age or above. The control group comprised of 303 women who delivered between 20 and 29 years during the five years period.**
Main outcome measures: **Gestational age at delivery, birth weight, mode and type of delivery, pregnancy and birth outcome.**
Results: **This showed a significant increase in prematurity, low birth weight, medical complications, operative deliveries (Caesarean section, vacuum and forceps), birth asphyxia and perinatal deaths all at $P<0.05$.**
Conclusion: **There is a poor pregnancy outcome at fourty years and above. Patients need to be counselled for care in a specialised centre.**

INTRODUCTION

Childbearing after the age of 40 years continues to be prevalent because of the high incidence of grand multiparity in our environment and the tendency to delay childbearing in pursuance of professional careers(1-4). Pregnancy at advanced maternal age has been regarded as high risk because of the associated increase in both maternal and perinatal morbidity and mortality(2-5). However, recent literature suggests that when underlying maternal disease conditions such as hypertension and diabetes are taken into account the risks are minimal and the overall neonatal outcome do not appear to be significantly affected(6-10).

Primigravid women after the age of 40 years and above are often well-educated professionals who purposely have delayed childbearing and who want as little distraction as possible(3). They often require special counselling concerning their risks so that they can make informed decisions. Previous data on this topic is composed largely of multiparous patients who have many unique problems that often are unrelated to the problems of the nulliparous women. Thus the results from these studies may be unhelpful to physicians counselling primigravid women about pregnancy outcome at an advanced age. In our study the results were stratified by parity, which is an important confounder.

This study was undertaken to identify the problems of pregnant women aged 40 years or above during pregnancy and labour at the Obafemi Awolowo University Teaching Hospitals Complex (O.A.U.T.H.C.), lle-lfe and to identify the ways of improving the maternal and perinatal outcome.

MATERIALS AND METHODS

This retrospective analysis of the pregnancy outcome of women aged 40 years or above covered a five year period from 15th January, 1995 to 31st December, 1999 at the Obafemi Awolowo University Teaching Hospitals Complex (O.A.U.T.H.C.), lle-lfe. Case notes of 303 women aged 40 years or above and 303 controls, which comprised of women aged between 20 and 29 years who delivered during the study period were analysed. The information obtained included the age at delivery, literacy level, complications during pregnancy and labour, mode of delivery, maternal mortality and foetal outcome. In our study the results were stratified by parity, which is an important confounder.

RESULTS

During the study period there were 4,691 deliveries of which 303 were aged 40 years or above giving the study population an incidence of 6.5% of the total population. The control population consisted of 303 parity-matched women who delivered between 20 and 29 years during the study period. Two hundred and sixty five women (87.5%) were aged 40 years while 38 (12.5%) were aged 45-49 years. Twenty eight (9.3%) were nulliparas, 127 (41.9%) were para 1-4, 148 (48.8%) were para 5-7.

Table 1

Pregnancy and delivery characteristics

	Nulliparous			Multiparous		
	≥ 40 Years	20-29 Years	P-value	≥ 40 Years	20-29 Years	P-value
Mean Gestational Age (days)	273.4 ± 0.4	178.5 ± 0.1	0.002	274.9± 0.2	278.3 ± 0.1	0.004
Mean Birth Weight (g)	2901 ± 10	3197 ± 1	0.03	3211 ± 5	3387 ±1	0.008
Delivery Mode (%)						
Caesarean	47.0	22.5	0.02	29.6	17.8	0.02
Forceps	4.5	3.1	0.04	1.2	0.8	0.05
Vacuum	9.7	9.8	0.05	5.1	3.8	0.05

Table 2

Pregnancy outcome of older mothers

Outcome	Nulliparous			Multiparous		
(%)	≥ 40 Years	20-29 Years	P-value	≥ 40 Years	20-29 Years	P-value
Anaemia	5	6	0.22	14.3	7.1	0.03
Hypertension/Pre eclampsia	10.6	6.8	0.03	5.3	2.3	0.06
Diabetes Mellitus	2.6	0.5	0.04	1.4	0.9	0.04
Placenta Praevia	16.0	18.8	0.05	9.2	5.7	0.03
Abruptio Placenta	3.6	2.5	0.04	3.3	0 4	0.04
Multiple Pregnancy	5.4	3.4	0.03	18.3	11.1	0.03
Malpresentations	1.6	0.3	0.06	6.5	4.0	0.04
Prematurity	1.4	0.9	0.04	5.7	2.9	0.04
Prolonged Pregnancy	7.0	8.7	0.03	2.5	1.6	0.02
Obstructed Labour	4.1	2.1	0 03	6.4	3.7	0.04
Prolonged Labour	7.2	6.1	0.06	9.9	5.1	0.05

Table 3

Neonatal complications in older mothers

	Nulliparous			Multiparous		
Apgar Score	≥40 Years	20-29 Years	P-value	≥ 40 Years	20-29 Years	P-value
<7 at 1 Minute	79	60	0.04	64	44	0.02
< 7 at 5 Minutes	61	35	0.03	23	19	0.04
Perinatal Deaths	1.3	0.9	0.15	3.0	1.1	0.04

In Table 1, the distribution by gestational characteristics is given for both the nulliparous and mutiparous in each age group. The most significant finding is that the Caesarean rate is significantly higher in the older nulliparous and older multiparous groups compared with their respective control groups. More nulliparous women aged 40 years had Caesarean section (47%) compared to 29.6% among the older multiparous. Table 2, shows the various complications observed in pregnancy and labour. There were statistically significant increases in the medical, pregnancy and labour complications among the nulliparous aged 40 years or older compared with control groups. In Table 3, the rate of birth asphyxia (low 5-minute Apgar scores) was increased in the older nulliparous and multiparous group compared with their respective controls - the same was also true of perinatal mortality rate. More of the older nulliparous had lower Apgar scores both at 1 and 5 minutes respectively compared to older multiparous.

DISCUSSION

The older women in this study had a lower mean gestational age (273.4 ± 0.4) compared with the control population. This may reflect the tendency towards earlier delivery because of the anxiety of still birth in older nulliparous women who often have a long history

of infertility and in whom the chances of subsequent pregnancy is reduced due to diminishing fertility(1-4,6). The lower mean birth weight in the older mothers may also reflect lower mean gestational age at delivery, but the associated increased pregnancy complications discussed below may also be a contributory factor(2,3).

In this study, the incidence of Caesarean section and operative vaginal delivery in nulliparous women aged 40 years or above (Caesarean 47.0%, operative vaginal delivery 12.9%) is significantly higher than younger nulliparous controls (Caesarean 22.5%, operative vaginal delivery 12.9%). A similar finding is also observed in older multiparous group (caesarean 26.9%, operative vaginal delivery 6.3%) compared with their younger counterpart (Caesarean 17.8%, operative vaginal delivery 4.6%). The increased rate of operative delivery observed in older mothers can be attributed to the associated increase in pregnancy complications such as malpresentations and abnormal forces of labour. However malpresentation are common in older multiparous compared to older nulliparous as shown in Table 2. The higher caesarean section rate of 47% among older mothers while in agreement with reports from other centres(5-10), was markedly higher than 9.7% reported in Sagamu, Ogun State, Nigeria(4). However within the same parous group there is no significant difference in the operative vaginal delivery.

This may de due to the fact that conditions likely to necessitate operative vaginal delivery may be more influenced by parity after controlling for age.

Though pregnancy complication such as hypertension, malpresentations, premature labour and prolonged labour were increased in the older women compared with control patients the number of these complications were small to make a categorical statement on this. These findings are however consistent with studies from other centres(5-8). However, complications such as anaemia and placenta praevia were not significantly increased in the older nulliparous group compared with control, but it is increased in the older multiparous. This would suggest that parity play an important role in the occurrence of anaemia and placenta praevia in the older mothers and agree with previous findings. The incidence of prolonged pregnancy is less in the older mothers and may reflect earlier intervention in view of the increased associated complication.

The Apgar scores at 1 and 5 minutes were better for the younger controls of both parous group compared to women aged 40 years and above but this did not show a very strong statistical significance. Similarly the elderly multiparous women had better Apgar scores than their nullliparous counterpart but this did not also show strong statistical significance. Also the younger multiparous women also had better Apgar scores than their nulliparous counterpart. In general the neonatal complications noted in the study were increased in the older patients compared with the younger controls but the increase in perinatal death was more noticeable in the multiparous groups. These results are consistent with previous reports(7-9). The lack of significant increase in perinatal mortality in the older nulliparous group over the nulliparous control could be attributed to the increased rate of elective Caesarean section performed in the former group so that the foetuses are not subjected to the labour complications mentioned before.

In conclusion, pregnant women aged 40 or over have a higher risk of caesarean section; not operative vaginal deliveries which are the same. This data highlights the need for proper counseling of such patients about their pregnancy expectations and possible outcomes as well as the need for delivery in specialised centres.

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MALIGNANT TUMOURS OF FEMALE GENITAL TRACT IN NORTH EASTERN NIGERIA
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MALIGNANT TUMOURS OF FEMALE GENITAL TRACT IN NORTH EASTERN NIGERIA

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ABSTRACT

Objective: **To ascertain the pattern and frequency of malignant tumours of female genital tract in North Eastern Nigeria.**
Design: **A retrospective analysis of surgical biopsy materials.**
Setting: **University of Maiduguri Teaching Hospital, the only teaching hospital in the North Eastern region of Nigeria.**
Subjects: **Three hundred and eighty-two cases of female genital malignancies histologically confirmed between January 1st 1991 and December 31st 2000.**
Results: **The age range of patients whose specimens were received during the ten year period was three to eighty years. Mean age of presentation was 44.2 years, (SD$\pm$13). Cancer of the uterine cervix was the most common (70.5%), followed by ovarian cancer (16.3%), then cancer involving the uterus (8.5%). There was a steep rise in reported cases within the period of study especially for cancer of the cervix. Ovarian tumours were the most common tumours in the teenage group.**
Conclusion: **The high incidence of cancer of the uterine cervix and the early mean age of presentation of all malignancies underlies the importance of screening programmes and awareness campaign in our community. The study also provides the basis for further analysis of female genital malignancies**.

INTRODUCTION

Most malignant female genital tumours have a worldwide distribution, but the distribution and frequency vary from one region to the other. Although four main reports from different parts of Nigeria(l-4), have attempted to focus on patterns of malignant tumours of female genital tract. To our knowledge none has dealt specifically with the tumours in Northern Nigeria.

Organised screening has contributed to a decline of cancer of uterine cervix incidence and mortality over the past 50 years in developed countries(5). However, women in developing countries are yet to profit from the benefits of screening programmes, and therefore, uterine cervical cancer rate remain high in Nigeria(4). Ovarian cancer is a major cause of death from gynaecological malignancies. About 75% of patients with the entity present with advanced disease as a result of failure to detect the tumour early(6).

Choriocarcinoma is the second most common female genital malignancy in Ibadan(4). Fifty percent of cases proceeded by molar gestation, 40% by normal pregnancy, 5% by abortion or ectopic pregnancy and 5% are of non-gestational origin(5).

Despite the high frequency of some malignant female genital tumours in our environment, there is a paucity of literature on the subject in Nigeria especially the northern part of the country. Therefore, this study aimed at increasing the knowledge on the subject and provide baseline data on the topic in North Eastern Nigeria. These findings could have a significant implication on health planning and clinical practice in our locality. Furthermore, the emergence of new diseases such as the Acquired Immune Deficiency Syndrome (AIDS) may conceivably alter the pattern of female genital malignancies(5).

MATERIALS AND METHODS

This retrospective investigation is based on a study of surgical biopsy materials received in the Histopathology Laboratory of University of Maiduguri Teaching Hospital (UMTH), Maiduguri, from January 1st 1991 through December 31st 2000. The sources of specimens were:

In-patients biopsy specimens and referrals from government and private health centres.

Demographic data, which included: Age of patients, site of tumour and diagnosis were extracted from the cancer registry, request forms and patients' cases files. These specimens were fixed in 10% formal saline embedded in paraffin wax. Sections were stained with routine haematoxylin and eosin. The results were analysed using simple statistical methods.

RESULTS

One thousand six hundred and eighty two cases of histologically confirmed cancers were recorded during the ten years period of study with a mean annual

total of 168 cases. During this period there were 887 registered cases of cancers of all sites among females, while 387 cases were female genital cancers. Thus, malignant tumours of female genital tract accounted for 23.0% of all the cancers diagnosed and 43.6% of all female cancers.

The age range of patients whose specimens were received was 3-80 years and a mean age of presentation of 44.2 years (SD±13). In this study choriocarcinoma accounted for only 4.1% of malignant tumours of female genital tract. Cancer of the uterine cervix accounted for the majority (70.5%) of all the female genital cancers, followed by the ovarian cancers (16.3%) and then uterine cancer (8.5%) (Table 1).

Table 1

Site distribution of malignant tumours of female genital tract

Site of tumour	No. of cases	(%)
Cervix	273	70.5
Ovary	63	16.3
Uterus	33	8.5
Choriocarcinoma	(16)	(4.1)
Others	(17)	(4.4)
Vagina	2	3.1
Vulva	6	1.6
Total	387	100

Table 2

Age distribution of malignant tumours of female genital tract

Age (years)	No. of cases	(%)
<20	13	3.4
20-29	24	6.2
30-39	77	19.9
40-49	104	26.9
50-59	87	22.5
≥ 60	56	14.5
Not specified	26	6.7
Total	387	100

Table 3

Age distribution of individual malignant tumours female genital tract

Age (years)	Cervix	Ovary	Cancers of Uterus	Vagina	Vulva
<20	1	8	3	1	-
20-29	15	3	6	-	-
30-39	57	12	5	3	-
40-49	83	10	3	7	1
50-59	64	13	8	-	2
≥ 60	36	12	5	-	3
Unspecified	17	5	3	1	-
Total	273	63	33	12	6

Figure 1

Yearly distribution of malignant tumours of female genital tract

Figure 2

Age distribution of malignant tumours of female genital tract

About 49.4% of cancer cases presented at the 5th and 6th decades of life (Table 2), and rarely below the age of 30 years. Figure 1 demonstrates the yearly distribution of the gynaecological malignancies within the study period. There were declines of reported cases in 1993/1994 and 1998/1999 periods. It should however, be noted that those periods were disrupted by health workers national industrial disputes, steep economic decline and fuel crises that probably affected hospital attendance.

The frequency of carcinoma of the cervix increased sharply during the period of study (except for the periods of the declines), while ovarian and uterine cancers remained constant (Figure 2). Absence of screening programmes, increase awareness and change in life styles (increase unprotected sexual activities) might have been responsible for the increased frequency and diagnosis of the cancers of the uterine cervix. Ovarian cancers are the common malignancies of the teenage group, followed by uterine cancers (Table 3).

DISCUSSION

The UMTH serves as a referral center for the north eastern sub-region of Nigeria, and quite a number of patients are also seen from the neighbouring countries of Niger, Chad and Cameroon Republics.

Malignant tumours of female genital tract accounted for 43.6% of all female cancers, while cancers of the uterine cervix accounted for the majority (70.5%), ovarian tumours (16.3%) and uterine tumours (8.5%). Although breast cancer is the most common tumour affecting women world wide, cancer of the uterine cervix is the most common in the developing countries(7). Babarinsa *et al.* in Ibadan found 62.7% of all female genital cancers to be cancers of the uterine cervix(4). Except an early report from Benin(8), all other incidences (from hospital-based records) in other parts of Nigeria(2-5) were lower than our findings. This could be attributed to early marriage and high number of live birth in our region(9).

Epidemiological studies have consistently indicated that the risk of cancer of the uterine cervix is strongly influenced by measures of sexual activity(5). Human papilloma virus (HPV) DNA is found in 99.7% of cervical cancers(10). Tobacco smoking has been a well-known risk factor for cervical cancer(11). Other factors include high number of live births, long-term use (12 years or more) of oral contraceptives, lack of food containing beta-carotene, vitamin C and to a lesser extent vitamin A(5). The risk of cervical intraepithelial neoplasm (CIN) in HIV sero-positive women is at least five fold higher than in their sero-negative counterparts, and CIN in sero-positive women is more likely to progress and recur after treatment(11). Unlike a study from Ibadan(4), the second common female genital cancers were ovarian tumours. which accounted for 16.3% of the cancers. Carcinoma of the ovary is now the most common malignant tumour found in gynaecology in the United Kingdom(12). Similar to our finding, Onuigbo found that ovarian tumours were the most common tumours in the teenage group in Enugu(13). Obed *et al.* in an earlier study found out that 20.7% of ovarian tumours in Maiduguri were matignant tumours(l4).

About 94% of ovarian tumours are said to arise from the surface epithelium of the ovary(6), but in UMTH only 40.5% were epithelial tumours(14). The events leading to malignant transformation within these cells are uncertain, but risk factors that appear to be related to the development of ovarian cancers include genetic, environmental and hormonal factors(15).

Choriocarcinoma was found to be the second most common malignant tumour of female genital tract in Ibadan(3,4), but in this study it accounted for only 4.1%. Considering that choriocarcinoma can complicate any conception and that its presentation may mislead clinicians(4), it is possible that the true frequency of this entity is much higher than is suggested from this study.

The data presented in this study were certainly not representative of community prevalence rates, they may be higher. More so cancer statistic go beyond hospital based data(4). But what do these figures imply for cancer prevention and diagnosis in our environment? Cancer of the uterine cervix rate is high in the catchment area of north eastern Nigeria, and affecting female of younger age. Other female genital tract malignancies are also a significant problem, especially when problems of diagnosis and management are concerned, therefore, cancer screening practice and increased physician awareness deserve prompt institution at all levels of health care.

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THE FIRST SIX MONTH GROWTH AND ILLNESS OF EXCLUSIVELY AND NON-EXCLUSIVELY BREAST-FED INFANTS IN NIGERIA
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THE FIRST SIX MONTH GROWTH AND ILLNESS OF EXCLUSIVELY AND NON-EXCLUSIVELY BREAST-FED INFANTS IN NIGERIA

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ABSTRACT

Objective: **To compare the growth and illness pattern of infants who were exclusively breast fed for six months with those of infants commenced on complementary feeding before the age of six months and ascertain reasons for the early introduction of complementary feeding.**
Design: **A comparative prospective study.**
Setting: **Urban Comprehensive Health Centre (UCHC), Obafemi Awolowo University Teaching Hospitals Complex, lle-lfe.**
Subjects: **Three hundred and fifty-two mothers and their normal birth weight babies, weighing 2.500kg or more, and aged less than 14 days were serially recruited into the study.**
Main outcome measures: **Mean/median monthly weights in the first six months of life, history/outpatient presentation for illnesses.**
Results: **Of the 352 mother-infant pairs recruited into the study, 345 (98%) were successfully followed up for the first six months of life. At six months, 264 (76.5%) were exclusively breast-fed, 45 (13.1%) were started on complementary feeding, between the ages of four and six months while 36 (10.4%) commenced complementary feeding before the age of four months. Infants who were exclusively breast-fed for six months had median weights above the 50th percentiles of the WHO/NCHS reference that is currently used in the national "road to health" (growth monitoring) cards. Furthermore, the mean weight of these babies at age six months was above those of babies who started complementary foods before six months. They also reported fewer symptoms and had fewer illness episodes (0.l episodes per child) compared to those who started complementary feeding before six months. Infants who commenced complementary feeding before four months reported more symptoms and had more illness episodes (1.4 episodes per child) compared to those that commenced complementary feeding between four and six months (1.2 episodes per child). Common symptoms/illnesses seen or reported during the study among the groups were fever, diarrhoea and cough. Reasons given for early introduction of complementary foods include insufficient breast milk, thirst and convenience.**
Conclusion: **It is concluded that exclusive breast-feeding supported adequate growth during the first six months of life for most of the infants studied. Early introduction of complementary foods did not provide any advantages in terms of weight gain in our environment, it was frequently associated with illness episodes and growth faltering. Many mothers however require support, encouragement and access to health care providers to breastfeed exclusively for the first six months of life.**

INTRODUCTION

The marked disparity in infant mortality between developed and developing countries is a cause of global concern and reduction of infant mortality remains a major challenge in developing countries including Nigeria where about 114/1000 children aged 0-12 months die yearly from various causes(1). Common causes of deaths among these infants include preventable conditions such as acute respiratory infection (ARI), diarrhoeal diseases, malaria, anaemia and other infectious diseases with malnutrition as a frequent and important underlying cause(2). In an effort to reduce the unacceptably high infant deaths in the developing countries, the United Nations Children's Fund (UNICEF) and World Health Organization (WHO) introduced the "Child Survival Strategies" in 1978. These strategies consisting of growth monitoring and promotion (GMP);

oral rehydration therapy (ORT); promotion of breast-feeding; immunization; family planning; food and appropriate nutrition and female education (GOBIFFF) have received strong national and international promotion as cheap, highly effective and sustainable strategies for developing countries(3).

Breast-feeding has been acknowledged as the most important of the child survival strategies as it is intimately related to all the other strategies. Globally, it is estimated that about one million infant deaths can be prevented annually by the adoption of correct breast-feeding practices(4). Thus, a world summit for children held in Florence, Italy, in 1990, adopted the Innocenti Declaration for the promotion, protection and support for breast-feeding through the Baby Friendly Hospital Initiative (BFHI). The two broad objectives of the initiative are: (a) the promotion of exclusive breast-feeding for the first six months of life and (b) continuation of breast-feeding with adequate and appropriate locally available complementary foods till the age of two years.

Evidence from several studies suggests that breast-feeding exclusively for the first six months of life supports optimal growth with the lowest risks of infection and ill health(5-9). The acquisition of the many anti-infective agents in colostrum and breast milk provides protection for the young infant against infective agents while the elimination of exposure of the young infant to contaminated foods and drinks provides added advantage(10). Exclusive breast-feeding for the first six months of life however conflicts with local knowledge in our environment and mothers frequently start complementary feeding before the age of six months. Furthermore, health workers who are expected to implement the policy have expressed reservations about the recommendation doubting the ability of many mothers from developing countries to provide sufficient breast-milk to support adequate growth during the first six months of life. To ascertain that normal birth weight infants (NBW), weighing 2.500 kg or more, are able to achieve adequate growth in the first six months of life on their mothers' breast milk alone irrespective of the mother's social, demographic or anthropometric status, and assess the advantages or otherwise of introducing complementary feeding before six months in our environment, this study therefore compared growth and illness pattern of exclusively and non-exclusively breast-fed infants during the first six months of life. To obtain a clearer understanding of the advantages or otherwise of complementary feeding before six months, infants introduced to complementary feeding before six months were sub-grouped into those commencing complementary feeding before four months and those commencing complementary feeding between four and six months.

MATERIALS AND METHODS

This prospective study was conducted at the Urban Comprehensive Health Centre (UCHC), Obafemi Awolowo University Teaching Hospitals Complex, lle-lfe. Mothers and their babies aged 14 days or less and who weighed 2.5 kg and above were recruited into the study from mission hospitals and immunization clinics of all the major government health facilities in Ile-lfe. All recruited mothers and their babies were followed up for a period of six months using UCHC as the base for the study. The mean ambient temperature in this part of Nigeria oscillates between 25°C and 40°C. In order to encourage participation in the study mothers were introduced to the study during the last trimester of pregnancy through formal health education sessions that were normally held in the antenatal clinics. The inclusion criteria were: (a) mothers whose babies weighed 2.5kg or more during the first two weeks of life and who consented to participate in the study. Excluded from the study were: (a) mothers who had multiple births, (b) babies with any form of congenital abnormality, (c) any mother who exclusively bottle-fed or who fed her baby exclusively on infant formula or breast-milk substitutes in the first six months of life, (d) pre-term and (e) low birth weight babies (weighing less than 2.5 kg).

Sample size for the study was determined using the highest standard deviation of 0.93kg as obtained by Zumrawi and Diamond(11) for infants aged six months in a study conducted in Sudan. Accepting a 90% confidence level and an error rate of 0.1, a minimum sample size of 235 subjects was determined. This figure was however increased to 350 to compensate for recruited mothers who would introduce complementary feeding before the age of six months and those who would voluntarily drop out of the study for one reason or another. Eligible mothers who accepted to participate were therefore recruited into the study serially until the desired sample size was attained.

Prior to data collection, ethical clearance for the study was obtained from the Ethical Committee of the Obafemi Awolowo University Teaching Hospitals Complex, lle-lfe. For ethical reasons, all mothers were encouraged to breast-feed exclusively for the first six months of life in line with our national guidelines. All mothers were thus counselled on the benefits of breast-feeding and mothers who accepted to participate in the study were also counselled on the purpose and demands of the study. In addition, consenting mothers were informed about the importance of providing correct and accurate information to the researchers during enrolment and follow-up on the mode of feeding and occurrence of symptoms of illnesses. Mothers were also informed that if they voluntarily decided to introduce complementary feeding at anytime before six months, their decision would be respected, and that they would not be removed from the study and would continue to enjoy all privileges provided in terms of follow-up. More importantly, no mother- suffered any disadvantages as a result of refusal to participate in the study. In this regard, all mothers and their babies aged 0-6 months were attended to as a matter of priority throughout the duration of the study by the researchers or other resident doctors in the department of Community Health who functioned as research assistants.

Information was collected from consenting mothers with the aid of a purpose-designed interview schedule. The schedule was administered at enrolment by the researchers or the research assistants. Follow-up information on weights, history of illnesses and other relevant pieces of information were recorded on the follow-up charts that were maintained for each enrolled child. To cross-check the authenticity of the pieces of information provided by mothers on mode of feeding, the researchers or assistants paid one or more unannounced home visits to every participating mother during the first three months of enrolment and at least once in the last three months.

Monthly weight measurements were made using a digital electronic solar weighing scale (Seca® Uniscale, Model 890, manufactured in Australia). Infants were weighed on the day of recruitment and subsequently monthly (every 27 to 33 days) by the researchers or research assistants. Babies were weighed nude and only one measurement was taken. Although the scale checks for zero error automatically, validation of measurements was achieved by regularly weighing two heavy metal objects that were kept for this purpose. All infants were managed for any reported illnesses by the researchers or research assistants. All had earlier received training concerning the weighing and recording of baseline and follow-up information.

Statistical analysis of the data was carried out with a personal computer using appropriate software and the results presented with tables and graphs. Comparison of continuous variables was by means of the students t-test while categorical variables were compared with the Chi-square test. For all tests, a P-value of less than 5% was accepted as statistically significant.

RESULTS

Three hundred and fifty two mother/baby pairs were recruited into the study; 68(19.3%) were recruited during the first week of life while 284(80.7%) were recruited during the second week of life. Of these, 345(98%) were successfully followed up until the infants were six months old while seven (2%) of the mothers were lost to follow up. Two hundred and sixty four (76.5%) of the 345 babies were breast-fed exclusively for the first six months of life while 81 (23.5%) were introduced to complementary feeding before the age of six months. Table 1 compares the social and demographic characteristics of the mothers who breastfed exclusively and those who introduced complementary feeding before six months. Mothers in the 30-39 year age group were more likely to breast-feed exclusively for the first six months of life compared to the other age groups (P=0.036). Concerning marital status, mothers who were married and living with their spouses were more likely to breast-feed exclusively for the first six months of life (P=0.009) while mothers who were unemployed (kept home) were more likely to introduce complementary feeding before six months (P=0.00l). Similarly, mothers who were nursing their first babies were more likely to start their infants on complementary feeding before six months compared to those who had had other babies (P=0.019).

Pertaining to the place of delivery of the babies, 144(40.9%) were delivered in government hospitals, 97 (27.3%) in mission houses, 68(19.3%) in private hospitals, 26(7.4%) at home, 14(4.0%) in primary health centres and three (0.9%) in the homes of traditional birth attendants.

Table 2 shows the main complementary feed introduced to the 81 babies by age. Eleven babies (13.5%) were introduced to complementary feeding during the first three months of life while the remaining 70 (86.5%) were introduced to complementary feeding from the fourth to the sixth month. Concerning the main form of complementary feeding introduced to the babies, water was the more frequently introduced feed in the first three months of life while local or prepackaged cereal and infant formula were more frequently introduced from the fourth to sixth month.

Table 3 explores the main reasons provided by the mothers for introducing complementary feeding. 'Thirst' was the more frequently given reason for introducing complementaly feeding during the first three months of life while inadequate growth due to insufficient breast-milk, "child old enough to start complementary feeding" and convenience were more cited for introducing complementary feeding from the fourth to sixth month of life.

With regard to the symptoms or illness episodes reported or seen among the babies during the first six months of life, the 36 babies introduced to complementary feeding before four months had a total of 50 illness episodes (1.4 episodes per child). Of these, 45(90%) episodes were due to fever, diarrhoea and ARI (cough or other respiratory symptoms). For the 45 babies introduced to complementary feeding between four and six months of life, 52 illness episodes (1.2 episodes per child) were recorded of which, 48 (92.3%) were due to fever, diarrhoea and ARI. Babies who were exclusively breast-fed for six months had fewer illness episodes, 41 episodes among the 345 babies (0.1 episodes per child). Of these episodes, 30(73.2%) were due to fever, ARI and diarrhoea. The relative risk (RR) for fever, diarrhoea and cough among babies commenced on complementary feeding before six months were: for diarrhoea, 44(95% C.I.=10.3-188.7) for those commenced on complementary feeding before four months and 46.9(95% C.I=l1.2-197.2) for those commenced on complementary feeding between four and six months. For fever, RR was 13.5 (95% C.l.=7.6-24.1) and 11.7(95% C.I.=8.5-21.1) for those commenced on complementary feeding before four months and those commenced on complementary feeding between four and six months respectively. For ARI, RR was 4.4 (95% C.l= 2.1-9.3) and 2.3 (95% C.l.=I-5.73) for the babies commenced on complementary feeding before four months and those commenced on complementary feeding between four and six months respectively.

Table 1

Social and demographic characteristics of the mothers successfully followed up for six months

Characteristic	Exclusively breast fed (n=264) n (%)	Commenced complementary feeding before six months (n=81) n (%)	Total (n=345) n (%)	Chi	DF	P-value
Age (years)						
Less than 20	13 (72.2)	5 (27.8)	18 (100)			
20-<30	140 (71.4)	56 (28.6)	196 (100)			
30-<40	108 (85.0)	19 (15.0)	127 (100)	8.56	3	0.0036
40 and above	3 (75.0)	1 (25.0)	4 (100)			
Marital status						
Single	1 (50)	1 (50)	4 (100)			
Married (living With husband)	249 (78.8)	67 (21.2)	316 (100)	9.37	2	0.009
Married (living separately)	14 (51.9)	13 (48.1)	27 (100)			
Level of education						
No formal education	2 (40)	3 (60)	5 (100)			
Primary	27 (71.1)	11 (28.9)	38 (100)	5.08	3	0.166
Secondary	167 (73.6)	52 (23.7)	219 (100)			
Post-secondary	68 (81.9)	15 (18.1)	83 (100)			
Maternal occupation						
Unemployed (Students)	14 (87.5)	2 (12.5)	16 (100)			
Unemployed (Kept home)	13 (44.8)	16 (55.2)	29 (100)	18.29	3	0.001
Self employed	191 (77.3)	56 (22.7)	247 (100)			
Employed in Formal sector	46 (86.8)	7 (13.2)	53 (100)			
Parity						
1	105 (70.0)	45 (30.0)	150 (100)			
2-3	125 (81.7)	28 (18.3)	153 (100)	7.88	3	0.019
4 and above	36 (85.70)	6 (14.3)	42 (100)			

Table 2

Main complementary feed introduced by age

Age (months)	Complementary feed				Total
	Local Cereal	Infant formula	Water	Pre-packaged cereal	
0-<1	1	0	3	0	4
1-<2	1	0	2	0	3
2-<3	1	0	3	0	4
3-<4	13	4	4	4	2.5
4-<5	12	15	5	6	38
5-<6	1	4	2	0	7
Total	29	23	19	10	81

Table 3

Main reasons offered by mothers for introduction of complementary feeding before six months by age

Age (months)	Reasons					
	Insufficient breast-milk or inadequate growth	Thirst	Convenience	"Child old enough"	Mother-in-law insisted	Total
0	2	2	-	-	-	
1	1	1	1	-	-	
2	2	2	-	-	-	
3	11	5	5	4	-	
4	20	6	5	6	-	
5	5	1	-	1	1	
Total (%)	41 (50.6)	17 (21.0)	11 (13.6)	11 (13.6)	1 (1.2)	81 (100)

Table 4

Mean monthly weights of the boys during the first six months of life

Age (months)	Mean weights (S.D.) Kg			P-values of differences between the groups		
	1	2	3	1vs	1vs3	2vs3
	Commmenced on complementary feeding before four months (n=l6)	Commenced on complementary feeding between four and six months (n=18)	Commenced on Exclusively breast-fed for six months (n=133)			
0	3.156 (0.388)	3.400 (0.460)	3.243 (0.406)	> 0.05	> 0.05	> 0.05
1	4.380 (0.466)	4.561 (0.581)	4.573 (0.613)	> 0.05	> 0.05	> 0.05
2	5.269 (0.357)	5.456 (0.721)	5.725 (0.754)	> 0.05	> 0.01	> 0.05
3	6.106 (0.475)	6.347 (0.734)	6.725 (0.754)	> 0.05	> 0.01	> 0.05
4	6.727 (0.550)	7.000 (0.704)	7.631 (0.826)	> 0.05	> 0.01	< 0.01
5	7.075 (0.676)	7.505 (0.765)	8.496 (0.883)	> 0.05	< 0.01	< 0.01
6	7.444 (0.677)	7.942 (0.888)	9.276 (0.995)	> 0.05	< 0.01	< 0.01

Table 5

Mean monthly weights of girls during the first six months of life

Age (months)	Mean weights (SD) Kg			P-values of differences between the groups		
	1	2	3	1vs	1vs3	2vs3
	Commenced on complementary feeding before four months (n=l6)	Commenced on complementary feeding between four and six months (n=l6)	Exclusively breast-fed for six months (n=133)			
0	3.030 (0.506)	3.252 (0.425)	3.203 (0.433)	> 0.05	> 0.05	> 0.05
1	3.960 (0.717)	4.404 (0.571)	4.408 (0.573)	> 0.05	> 0.05	> 0.05
2	4.728 (0.685)	5.400 (0.761)	5.484 (0.732)	< 0.01	< 0.01	> 0.05
3	5.537 (0.859)	6.263 (0.722)	6.418 (0.828)	< 0.01	< 0.01	> 0.05
4	6.105 (0.795)	6.881 (0.816)	7.289 (0.895)	< 0.01	< 0.01	> 0.05
5	6.579 (0.763)	7.233 (0.809)	8.062 (0.946)	< 0.05	< 0.01	< 0.01
6	7.215 (0.849)	7.567 (0.845)	8.764 (1.020)	< 0.05	< 0.01	< 0.01

Table 4 shows the mean monthly weights of boys during the first six months of life. Although the mean weights of the babies were comparable at birth and one month (P >0.05), from the age of two months through to six months, exclusively breastfed babies had mean monthly weights that were higher than those of babies that commenced complementary feeding before four months. For the babies commenced on complementary feeding between four and six months, the mean monthly weights of the babies were comparable for the first three months, subsequently, the mean monthly weights of exclusively breast-fed babies were higher from the fourth month to the sixth month (P< 0.05). In addition, from the third month, babies started on complementary feeding between four and six months were also heavier than those started on complementary feeding before four months (P<0.05).

Among the girls (Table 5), all the three groups had comparable mean birth weights (P >0.05), however from the age of one month, girls exclusively breast-fed for six months had higher mean monthly weights compared to those commenced on complementary feeding before four months (P< 0.05). Similarly, at five and six months girls who were breast-fed exclusively for six months were heavier than those that commenced complementary feeding between four and six months. In addition, from the age of two to six months, girls commenced on complementary feeding between four and six months were heavier than those commenced on complementary feeding before four months (P< 0.05). Also, infants (both sexes) who were exclusively breast-fed for six months had median weights above the 50th percentiles of the WHO/NCHS reference that is currently used on our national "road to health" (growth monitoring) cards.

DISCUSSION

Exclusive breastfeeding, feeding an infant on only breast milk and no other liquids or solids with the exception of drops or syrups consisting of vitamins, for the first 4 - 6 months of life is a key recommendation of the global Baby Friendly Hospital initiative (BFHI). There is strong agreement worldwide on the benefits of breast-feeding especially in environments where sanitation is poor(6,8,12,13), however, there is debate on the optimal time for the introduction of complementary foods(13,14). Currently, the Nigerian national BFHI recommends that complementary foods be introduced from the age of six months but doubts have been expressed locally as to the sufficiency of exclusive breast-feeding to support adequate growth during the first six months of life in our environment. Davies-Adetugbo(15), observed in a study conducted in this same local area that the concept of exclusive breast-feeding posed the greatest conflict between local knowledge and WHO/UNICEF breast-feeding recommendations. Locally, nursing mothers, particularly those from rural areas, are perceived as having borderline or poor nutritional status and their diet is inadequate in terms of nutrient intake. Concerns have therefore been expressed about the ability of such mothers to produce breast-milk of adequate nutritional quality and in sufficient quantity to support adequate growth of infants in the first six months of life. Concerns have similarly been expressed about the need for water supplementation though such concerns are not, however, limited to our environment as Sachdev *et al.*(16) reported that a significant proportion of health workers (doctors and nurses) in India believed that water supplementation was necessary under certain climatic conditions.

Several studies that related lactation performance of nursing mothers to their social, demographic or anthropometric status have concluded that these factors have limited impact on breast-milk output in terms of quantity or quality(l7-20). Nevertheless, determining an optimal timing for introduction of complementary feeding is important to achieve optimal growth and development in the first year of life.

The findings of this study agree with the observation of other workers(21-23), that exclusively breast-fed infants gained adequate weight during the first six months of life. The mean of monthly weights of exclusively breast-fed boys and girls increased from birth to six months and no faltering was observed. From one month, the mean monthly weights of these babies were either comparable or higher than for babies commenced on complementary feeding before four months and those that commenced complementary feeding between four and six months.

The mean weight of the babies who commenced complementary feeding before the age of four months was slightly lower at recruitment than those of the other groups. While it is not certain if the mothers of these babies commenced them on complementary feeding because they perceived them to be lighter than their peers, early introduction of complementary feeding probably only worsened the infants' condition by predisposing them to frequent illness episodes; it provided no advantages in terms of weight gain. If anything, these babies reported more symptoms and had more frequent illness episodes necessitating visits to the health centre compared to the other babies. This probably also contributed to the lower rate of monthly weight gain.

Infants commenced on complementary feeding between four and six months on the other hand were slightly heavier at recruitment compared to their exclusively breast-fed counterparts but their mean monthly weight gain from one month was below that of their exclusively breastfed counterparts. Again while it is not certain if the mothers of these infants commenced complementary feeding because they perceived them to be gaining weight at a lower rate compared to their exclusively breast-fed peers, the

introduction of complementary feeds was not really beneficial since the infants had more frequent illness episodes with the commencement of complementary feeding and the gap between their mean monthly weight compared to those of their exclusively breastfed counterparts continued to widen.

Complementary feeding in our environment includes the use of various food items such as infant formula, local cereal (pap), water and pre-packaged cereal (e.g. Cerelac, Babeena, Nutrend) with different energy contents. The mode of preparation of these foods would certainly not match the standards in developed countries in terms of nutritional quality and the level of hygiene observed in their preparation. This probably explains why the infants starting complementary feeding early in this study were worse off in terms of illness episodes and weight gain. Various reasons were given by mothers for starting complementary foods before the age of six months. In agreement with a study conducted in Jos by Ogbonna *et al.*(24) insufficient breastmilk was also the commonest reason given for introducing complementary feeding in this study; this is also consistent with finding from other parts of the world(5). Thirst, convenience, inadequate growth were the other common reasons given for early introduction of complementary feeding.

That the mean monthly weight of the infants in this study were consistently higher than those reported by other workers is probably due to the fact that not only were the mothers in this study encouraged to breastfeed exclusively but also on demand. Mothers were instructed to nurse the baby for any form of discomfort and the use of pacifiers was totally discouraged. Furthermore, all the mothers had improved access to health workers and health care including immunisation throughout the study period in addition to regular counselling and encouragement on breastfeeding. The contribution of these factors to the very favourable outcome concerning weight gain must have been significant though difficult to assess. Even mothers who introduced complementary feeding before six months were encouraged to continue breastfeeding inclusively and it is not certain to what extent this affected the breastfeeding practices or the number of mothers that would have stopped breast-feeding altogether without the support and encouragement provided.

The findings of this study agree with the observation by Juez *et al.*(5) and Cohen *et al.*(25) that hospitalisation, diarrhoea, anaemia and respiratory illnesses were rare events in infants exclusively breast-fed for six months. It is possible that infants introduced to complementary foods before six months of age reported more symptoms/ illnesses because of contamination of the food items including the use of unsafe water for food preparation and unhygienic handling of the foods. This in turn affected their weight gain, and resulted in a vicious cycle of early complementation, more illness and inadequate weight gain. The findings also support the conclusion by Cohen *et al.*(25) that there is no advantage in introducing complementary foods before six months in poor population and that there may be disadvantages if there is increased exposure to contaminated weaning foods.

In conclusion, exclusive breastfeeding for the first six months of life supported adequate growth for the infants studied. Early introduction of complementary feeding particularly before four months resulted in frequent illness episodes and growth faltering. Health workers are encouraged to continue to correct misconceptions concerning the sufficiency of exclusive breastfeeding for the first six months of life through antenatal and postnatal education about the physiology of lactation. Mothers should be supported and encouraged to breastfeed exclusively for as long as possible and preferably for the first six months of life. During this period efforts should be made to ensure that the mothers have better access to health services and information.

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COMPARISON OF CALCULATED AND DIRECT LOW DENSITY LIPOPROTEIN CHOLESTEROL DETERMINATIONS IN A ROUTINE LABORATORY
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COMPARISON OF CALCULATED AND DIRECT LOW DENSITY LIPOPROTEIN CHOLESTEROL DETERMINATIONS IN A ROUTINE LABORATORY

A. A. AMAYO and S. KIRERA

ABSTRACT

Background: **Low density lipoprotein cholesterol (LDL-C) concentrations form the basis for treatment guidelines established for hyperlipidaemic patients. LDL-C concentrations are commonly calculated using the Friedwald formula (FF) which has several limitations. Recently, direct methods for LDL-C estimation have been developed which are suitable for routine laboratories.**
Objective: **To compare serum LDL-C concentrations determined by a direct assay and the Friedwald formula.**
Design: **Cross-sectional study.**
Setting: **Mater Hospital Laboratory, Nairobi, Kenya. Methods: The clinical performance of the two methods was evaluated by analysing 211 fresh plasma samples from fasting adult patients. The samples were divided into four groups-normolipidaemic; and Types IIa, IIb and IV hyperlipidaemias.**
Results: **The Friedwald formula (FF) correlated best with the direct assay in the normolipidaemic samples (r = 0.879; y= 0.468 + 0.852x). Direct LDL-C values were significantly lower than the FF in the Type IIa hyperlipidaemia samples (paired differences 0.38 ± 0.62). There was only 65% agreement between the two methods in the borderline high LDL-C group of the National Cholesterol Education Program (NCEP) classification (LDL-C 3.36 - 4.14mmol/L).**
Conclusion: **There is lack of agreement between the FF and the Abbott direct LDL-C assay. If the two methods are used interchangeably, there may be confusion in the classification and control of lipid lowering medication for patients with hyperlipidaemia.**

INTRODUCTION

The association between increased concentrations of low-density lipoprotein cholesterol (LDL-C) and increased risk of coronary artery disease (CAD) has been clearly demonstrated in clinical and epidemiological studies(1-3), and intervention with dietary or drug therapy to lower LDL-C has been shown to decrease morbidity and cardiovascular mortality(4,6).

Because of the causal role LDL-C plays in the development of atherosclerosis, blood LDL-C concentration is an important criterion for diagnosis and treatment of patients with hyperlipidaemia (HPL). The accepted "gold" standard method for blood LDL-C estimation is the beta - quantification (BQ-LDL) which is an expensive, labour intensive method and not generally available in routine laboratories(7,8).

Most clinical laboratories have therefore depended on calculations of LDL-C using the Friedwald formula (FF) which is based on three independent measurements: total cholesterol (TC), HDL-cholesterol (HDL-C) and triglycerides (TG)(9). This equation assumes that the amount of cholesterol in very-low density lipoprotein (VLDL) can be estimated by dividing the serum TG by a factor of 5. The use of the FF has shortcomings: firstly, combining three measurements increases analytical variability; secondly, the formula has been shown to be invalid in samples with high triglyceride concentrations and can therefore only be used in fasting blood samples. Thirdly the assumption that the relationship between cholesterol and triglyceride in VLDL is constant has been shown to be inaccurate in some hyperlipidaemias(10,11).

Several direct assays for LDL-C estimation have recently been developed and the kits are available for use by routine laboratories. There are reports of differences between LDL-C values calculated using the FF and those obtained by direct assays(12-15). Since some laboratories continue to use the FF and others use the two methods interchangeably(16,17), significant variations in the LDL-C results obtained by the different methods may create confusion in the risk stratification of patients and treatment follow-up as the use of LDL-C measurements in routine laboratories increases. In this study LDL-C was calculated using the FF and the values were compared with those obtained from a direct LDL-C assay used routinely in this laboratory.

MATERIALS AND METHODS

Samples: Plasma samples from 211 adults received at the Mater Hospital Laboratory, Nairobi were used. Only those where a full fasting lipid profile was requested were considered. Sampies with fasting TG concentrations >4.5mmol/L were excluded from the FF calculations because the equation has been clearly shown to be invalid in hypertriglyceridaemic samples (10,11).

Quantification of lipids: All the lipid analyses were performed on the Alcyon 300i (Abbott Park IL). Total cholesterol and TG were measured enzymatically with the appropriate reagents from Abbott Diagnosis (Coefficients of variation (CV) 2.4% and 5.6% for TC and TG respectively). HDL-C: A homogeneous direct HDL-C method was used (Abbott reagent list 8D42-02). This assay utilizes a unique detergent to solubilise only the high density lipoptrotein particles, thus releasing HDL-C to react with cholesterol esterase and cholesterol oxidase in the presence of chromogens to produce colour. Analysis was done on the Alcyon 300i according to the manufacturer's protocol (CV 5.2%).

LDL-C: A homogeneous direct LDL-C method was used (Abbott reagent list 8D45-02). The assay uses two reagents. Reagent 1 solubilises only the non LDL particles. The cholesterol released is consumed by cholesterol esterase and cholesterol oxidase in a non colour forming reaction. Reagent 2 solubilises the remaining LDL particles and a chromogenic coupler allows for colour development. Analysis was done on the Alcyon 300i according to the manufacturer's protocol (CV 4.1%). All lipid analyses were performed within three hours of sample collection.

Friedwald calculation: LDL-C was estimated as follows LDL-C = TC - ($^{TG}/_{2.17}$) - (HDL -C)(8).

Comparison between methods: For this purpose, samples were classified into four groups according to their TC and TG concentrations (i) Normolipidaemia defined as TC ≤ 6.2 mmol/L and TG ≤ 2.66 mmol/L; (ii) Type II a hyperlipidaemia (HPL) as TC > 6.2 mmo/L and TG < 2.66 mmo/L; (iii) Type IIb HPL as TC > 6.2 mmol/L and TG>2.66 mmol/L and (iv) Type IV HPL as TC ≤ 6.2 mmol/L and TG >2.66 mmol/L.

Statistical analysis: All data were entered in a personal computer. Descriptive statistics (means, standard deviations (SD) and CVs) were calculated with Microsoft Excel (Microsoft). Mean values for LDL-C by the two methods were compared by paired student's t-tests. Linear relationships were determined from standard Pearson correlation coefficients by linear regression analyses using SPSS (VER 10.0). To assess the degree of agreement between the methods, the graphical procedure outlined by Bland and Altman(18) was used. A scattergram of the methods versus the difference between the two methods was prepared. Differences were considered significant at $p<0.05$.

RESULTS

The lipid and lipoprotein concentrations, and correlation results are summarised in Table l. The overall mean for direct LDL-C was 3.24 mmo/L which compared well with for the FF (3.30mmo/L). The correlation coefficient for this association was r = 0.891. However, when the four groups were analysed separately, differences were noted between the two methods in some groups. As in shown in linear regression analysis (Figure 1 Top panels), the best correlation between the two methods was seen with the normolipidaemic samples: r= 0.879, slope =0.82 (Figure lA). Good correlation was also found among the Type IIb HPL samples: r = 0.886, slope =0.758 but this was not statistically significant (Figure lC). Among Type IIa HP-L samples, results obtained by the two methods showed significant deviation from the line of identity: r =0.525, slope = 0.537 (Figure lB). Deviation was also seen in the Type IV HPL sample but it did not attain statistical significance (Figure lD).

Table 1

Summary of Cholesterol, TG's, HDL-C and LDL-C; and correlation between calculated and direct LDC-C among the groups(a)

	Normolipidaemia 152	Type IIa HPL 32	Type IIb HPL 15	Type IV HPL 12
Total cholestero(mmol/L)	4.9 ± 0.825	6.9 ± 0.675	5.2 ± 0.746	6.8 ± 0.611
TG mmol/L	1.28 ±0.541	1.63 ± 0.574	3.23 ± 0.483	3.46 ± 1.00
HDL mmol/L	1.28 ±0.343	1.40 ± 0.260	1.04 ± 0.273	1.22 ± 0.277
Direct LDL-C mmol/L	2.97 ± 0.766	4.40 ± 0.628	2.86 ± 0.670	4.28 ± 0.631
Calc. LDL-C mmol/L	3.0 ± 0.743b	4.78 ± 0.643b	2.66 ± 0.573	4.03 ± 0.602
Paired diff. mmol/L	0.03 ± 0.371	0.38 ± 0.62	0.20 ± 0.310	0.34 ± 0.526
Correlations calculated LDC-C.direct LDC-C				
Intercept	0.468	2.419	0.495	1.771
Slope0.852	0.537	0.758	0.527	
r	0.879	0.525	0.886	0.638
p	0.00	0	0.017	0.12

[a] Results are given as mean ± SD
P < 0.05 in relation to direct LDL-C

Table 2

Agreement in classification of LDL-C by the FF compared with the direct assay at the NCEP cutpoints of 3.37 and 4.14mmol/L

	Agreement (%)
<3.37 (n=119)	91
3..37-4.13 (n=61)	65
≥ 4.14 (n=31)	94

Figure 1

Correlations (top panels) and Bland-Altman plots (bottom panels)

1a: LDL-C in normolipidaemic

1b: Type IIa HP

1c: Type IIb HPL

1d: Type IV HPL samples

Agreement between the two methods was assessed using the Bland - Altman graphical technique(18). The degree of agreement is indicated by the bias, estimated by the mean and SD of the differences. The direct LDL-C values were significantly lower than those obtained by the FF in the type IIa HPL samples (paired differences -0.38 ± 0.62). Thus in the Bland - Altman plot, most of the points lie below zero on the x - axis (Figure lB, Bottom panel). There were also differences among the type IIb and IV HPL samples as most points on the Bland Altman plots lie on one side of the mean, but these were not statistically significant (Figure lC, lD). The good correlation in the normolipidaemic samples was verified by the Bland Altman plots which showed an equal distribution of the points around the mean (paired differences -0.03 ± 0.371) (Figure 1A, Bottom panel).

Classification of samples with the NCEP cut off points: The National Cholesterol Education Program (NCEP) Adult Treatment Program II (ATP II) of 1994 laid down LDL-C values of <3.36, 3.36 - 4.14, and ≥4.14 as cutoff points for classifying patients into normal, borderline and high LDL-C(8). We studied the agreement in classification by the two methods into the three categories with CLDL-C values obtained by the FF coinciding within 10% of the direct LDL-C values. As seen in Table 2, there is considerable lack of agreement among the samples in the borderline high category (35%). The level of agreement in the other two categories is high (>90%).

DISCUSSION

LDL-C is a key factor in the pathogenesis of premature coronary disease(1-3). Blood LDL-C concentration is used to assess cardiovascular risk and effectiveness of cholesterol lowering regimens(4,6). The accuracy and precision of the method used to estimate blood LDL-C is therefore very important. There is evidence that there is an increase in risk factors for CAD among Africans(19-21), which will increase the demand for blood lipid analyses in routine clinical laboratories. Until recently, most routine laboratories used the FF to calculate LDL-C concentrations. Several direct assays for LDL-C estimation have now been developed which are adaptable to automatic analyzers in routine laboratories.

The findings of this study show that there is good correlation between the Abbott direct homogeneous assay and the FF in the normolipidaemic samples. The two methods were however not in complete agreement as is shown by examination of the Bland Altman plots. Among the hyperlipidaemic samples, there were significant differences in the type ILA HPL samples, the paired differences indicating a positive bias in the Friedwald calculation as compared to the direct LDL-C assay. There were also differences among the type IIb and type IV HPL samples but these did not attain statistical significance possibly because of the comparatively small sample sizes in these two groups.

Previous studies have also reported differences between calculated LDL-C and other methods for LDL-C estimation in various hyperlipidaemias(12-14). Matas and colleagues found significant variation between calculated and measured LDL-C in a group of patients with liver cirrhosis (mean SD: 3.01+1.03 and 2.59 + 0.99; $p<0.001$ for direct and calculated LDL-C respectively), despite the fact that none of the patients had marked hypertriglyceridaemia(12). They attributed the discrepancy to an abnormal VLDL particle in which the cholesterol component was significantly decreased. The FF assumes that most of the circulating triglyceride is carried in VLDL, and that the relationship between the cholesterol and TG in this fraction is constant. This assumption has been demonstrated to be inaccurate in several hyperlipidaemias(22). The particles generally called VLDL are a heterogeneous mix of VLDL, chylomicron remnants and VLDL remnants. The percentage of cholesterol across this range of particles varies significantly depending on the TG concentration. Errors in calculating the cholesterol in the particles will ultimately reflect as an error in the calculated LDL-C(14). It has therefore been recommended that the FF should be used with caution in several conditions associated with hyperlipidaemia, including diabetes mellitus, nephrotic syndrome and hepatopathy, even if triglycerides are less than 4.5 mmol/L(14,23). The samples used in this study were from a heterogeneous adult population with various underlying disorders some of which may cause such alterations in the concentration and composition of the VLDL particles leading to the bias observed in the type IIa HPL samples. It is possible that with a larger sample size, lack of agreement between the two methods would also be found in the samples with types IIb and IV HPL.

While it is unlikely that different methods will agree exactly, the question is whether the magnitude of the differences will impact clinical judgment. The NCEP ATP II (1994) LDL-C cut-off concentrations of 3.36 mmo/L and 4.13 mmol/L are important parameters in therapeutic decision making. Reporting a patient's LDL-C above or below the conventional cut-off conveys a message about risk stratification and an incorrect classification could lead to inappropriate treatment. This study showed >90% agreement in classification for the <3.36mmol/L and >4.13 mmo/L groups but only 65% agreement in the middle 3.36 - 4.14 mmo/L group.

Previous LDL-C method comparison studies have also reported higher rates of disagreement in this borderline high risk group than in the other two groups(13-15). Esteban-Salan and colleagues reported that although the FF correctly classified 95% of patients with normolipidaemia, only 76% of the rest were correctly classified. Direct methods classified >90% of patients in both groups(14).These discrepancies in classification would be of concern to the physician who must interpret LDL-C measurements from different laboratories using different methods.

These findings invite the question as to which of the two methods is more reliable. The only way to answer this would be to compare the two methods against the reference BQ method. However, because the FF has several sources of error from several measurements but the direct assay has only one source of error from one measurement, it might be reasonable to question the reliability of the FF. Higher accuracy of direct LDL-C assays over FF in secondary hyperlipidaemias has also been reported(12-14,24).

In conclusion, this study shows lack of agreement between LDL-C estimated by a direct assay and the FF in HPL samples in a routine diagnostic laboratory. There were previous recommendations that direct LDL-C estimation and the FF should be used interchangeably to minimise laboratory costs(16,17), the FF for the initial classification as a full lipid profile is usually required and the direct LDL-C for treatment follow up. There should be caution about adopting this recommendation in a routine laboratory for two reasons. First the routine laboratory handles samples from patients with a wide range of clinical conditions some of which may affect the VLDL composition with attendant errors in the FF. Secondly the adequacy of the FF is governed by strict adherence to the NCEP criteria for TC, TG and HDL-C measurements(8).

Small routine laboratories may not always meet the NCEP performance standards and this may decrease the reliability of the FF. Interchanging of the methods may therefore be associated with discordant serial LDL-C results, which may cause confusion in risk assessment as well as follow-up of patients. This may ultimately lead to several repeat analyses and additional costs. Routine diagnostic laboratories should instead maintain one method of LDL-C estimation to ensure internal standardization . This will enable them to keep a constant vigilance on the quality of the results reported so that they are transferable across laboratories.

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SALICYLATE POISONING IN CHILDREN: REPORT OF THREE CASES
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SALICYLATE POISONING IN CHILDREN: REPORT OF THREE CASES

C.O. MUSUMBA, A.O. PAMBA, P. A. SASI, M. ENGLISH and K. MAITLAND

SUMMARY

To raise clinicians' awareness of chronic (therapeutic) salicylate poisoning as a common cause of admission in paediatric patients presenting to hospital with respiratory distress (a clinical manifestation of metabolic acidosis) and a history of 'over the counter' treatment with salicylate (Aspirin). We present two complex cases and provide a review of the literature on pathogenesis, clinical presentation and management of salicylate poisoning. A **complete history of the illness, including questions on drug use, is vital in assessing the cause of metabolic acidosis in children. Due to the limited options available in managing such patients in many developing countries, emphasis should be placed on prevention of poisoning by educating the community and health care providers.**

INTRODUCTION

Whereas the incidence has largely declined in the developed countries(1), the true extent of salicylate poisoning, especially chronic poisoning (repeated administration of therapeutic or excessive doses for longer than 12 hours) in developing countries is as yet undetermined. Aspirin and other salicylate containing medications are still widely available as over-the-counter (OTC) medications in many developing countries and are widely used at home as early treatments for childhood fevers. Their use, for this reason, is prevented by law in developed countries. In Kilifi district of Kenya, English and colleagues found 94% of mothers to have used a drug containing a salicylate preparation as first-line treatment for a febrile child, and 21% of these administered a dose exceeding the minimum daily dose recommended by manufacturers(2). As the clinical features of chronic salicylate poisoning are similar to those of a number of serious disorders in children it is likely that many cases go unnoticed, particularly as serum salicylate determination is almost never available. Management of patients with severe poisoning also poses unique problems, the laboratory back up so crucial in the monitoring of treatment is lacking, and therapeutic options may be limited.

We present two cases of salicylate poisoning (one with co-existent malaria) who provide good examples of the features of chronic severe intoxication and review the literature on the current recommended management. It is important to note the clear distinction between chronic, accidental overdosing (usually in young children) and the use of massive single doses of salicylates taken for the purpose of deliberate self-harm.

CASE REPORTS

Case 1: A four year-old boy admitted with a presumptive diagnosis of severe malaria presented in coma following a three day history of fever, cough and dyspnoea. At presentation he was in extreme respiratory distress with tachypnoea (54 breaths/min), deep ('acidotic' or 'Kussmaul's') breathing and lower chest wall indrawing. Blood pressure was 111 /54 mmHg (mean 74). Other clinical and laboratory findings and progress are summarised in Tables 1 and 2.

A presumptive diagnosis of severe malaria was made and the child was started on parenteral quinine (loading dose of 15 mg/kg and maintenance of 10mg/kg 12 hourly) and covered with broad-spectrum antibiotics. Shortly thereafter the child developed frothy white secretions from the mouth. Auscultation revealed bilateral coarse crepitations. The central venous pressure (CVP) was raised, heart sounds were normal and there was no hepatomegaly. Further enquiry into the history revealed the child had been given ten tablets of adult aspirin plus another two tablets of a salicylate-containing preparation over the preceding two days. A diagnosis of suspected chronic salicylate poisoning with pulmonary oedema was made and subsequently confirmed by serum salicylate level measurements. The only specific treatment available was administration of sodium bicarbonate (4mmol/kg of 8.4% sodium bicarbonate, diluted with dextrose to 2.1%, and given as an infusion over four hours) in an attempt to alkalinise the blood and urine. During the course of his admission, the child developed seizures, hypoglycaemia, hypercapnoea and impaired renal function with progressive oliguria, all of which were actively managed. He had a cardiopulmonary arrest 11 hours into admission and died.

Table 1

Clinical characteristics and laboratory parameters at admission in two children with suspected chronic salicylate poisoning

	Case 1	Case 2
Age (months)	41	33
Weight (kg)	11	10.7
Aspirin tablets ingested	10	Unspecified
Duration of salicylate ingestion (hrs)	48	24
Salicylate (mg/L)	740	404
Parasitaemia (per µL)	2000	Nil
WBC (per mm^3)	24000	28000
Haemoglobin (g/dl)	11.2	9.7
Urinalysis*: Ketones	+++	++++
Blood	+	++
Proteins	++	++
Outcome	Died	Alive

*:Urinalysis: Ketones +++ = 8mmol/1; ++++ = 16mmol/1
Blood: + = Small; ++ = Moderate
Proteins: ++ = 1 g/l

Table 2

Summary of physical findings and laboratory results of case one

Time (hrs)†	Rectal temp,ºC	CVP cmH_20	pH*	pCO_2	HCO_3	BE**	Na mmol/L	K mmol/L	Crt µmol/L	Urine pH	Glucose mmol	Salicylate mg/L
0	40.0	12.0	7.3	1.33	5.2	-21	140	4.4	99	6	3.0	740
1	40.8	12.5	7.2	1.82	6.2	-17	141	4.7	111		0.5	
2	40.0	9	6.7	12.8	13.6	-21	139	6.4	96	5	9.3	
3	40.3	15	7.2	3.2	11.2	-16	143	4.7	102		8.4	718
5	40.0	11.0					146	4.1	130	5	9.7	
8	39.7	12.0	7.1	3.6	10.3	-18	146	5.0	135	6		579
11	39.0	12.0	7.1	4.3	12.5	-13	148	5.7	138		9.4	592

†=Refers to time from admission, *= Blood gas analysis was done on venous blood
**=BE=Base Excess, Na=Sodium, K= Potassium, Crt=Creatinine

Table 3

Summary of physical finding and laboratory results of case two

Time (hrs)†	Rectal temp,ºC	CVP cmH_20	pH*	pCO_2	HCO_3	BE**	Na mmol/L	K mmol/L	Crt µmol/L	Urine pH	Glucose mmol/L	Salicylate mg/L
0	40.9	9	7.18	1.51	4.3	-21.4	135	4.9	120	5	2.8	404
8	39.6		7.34	2.04	7.6	-15.4	145	2.87	136			251
14	39.0	6	7.40	2.79	13.0	-9.4	147	2.64		6	11.4	231
24	37.5		7.39	3.23	14.7	-8.4	142	-3.4	73	6	6.6	161
31	37.9		7.36	3.61	16.3	-7.3	140	3.3	74	6	5.0	
40	36.9										4.6	57
54	37.9		7.37	4.6	20.1	-3.6	135	3.5	57		5.2	24

†=Refers to time from admission, *= Blood gas analysis was done on venous blood
**=BE Base Excess, Na=Sodium, K= Potassium, Crt=Creatinine

Table 4

Toxic effects of salicylate

Acid, base and electrolyte disturbances
Metabolic acidosis*
Metabolic alkalosis
Ketonuria/ketonaemia*
Hyponatraemia hypernatraemia
Central nervous system
Tinnitus, deafness, vertigo
Confusion, agitation, hallucinations
Seizures*
Coma (with response only to painful stimuli)*
Coagulation abnormalities
Gastrointestinal
Nausea, vomiting*, decreased motility
Hepatic
Impaired liver function
Hypoglycaemia/Hyperglycaemia*
Hypermetabolic state
Vasodilatation
Sweating
Hyperthermia*
Hyperpnoea*
Dehydration*
Hypersensitivity (anaphylaxis)
Pulmonary
Non-cardiogenic pulmonary oedema*
Renal
Decreased urine output*
Tubular damage
Proteinuria*
Salt (sodium chloride) and water retention
Hypouricaemia hyperuricaemia

* Noted in our patients
Data are from (references 1 and 4)

Table 5

Classification of severity of salicylate overdose

Classification	Symptoms
Asymptomatic	No obvious clinical features
Mild	Nausea and vomiting, lethargy, mild hyperventilation, sweating, metabolic alkalosis
Moderate	Hyperventilation, metabolic alkalosis, marked agitation hyperglycaemia, dehydration, metabolic acidosis, tinnitus, deafness, hypokalaemia
Severe	CNS toxicity, coma, convulsion, hypoglycaemia

Data are from (reference 6)

Table 6

Guidelines on treatment of chronic salicylate toxicity

Proven benefit	Unproven benefit/dangerous
Possible in district hospital setting	Forced alkaline diuresis
Fluid replacement	Activated charcoal
Alkalinisation	Whole bowel irrigation
Serum electrolyte correction	
Vitamin K (in cases of haemorrhage)	
Drugs for specific symptoms (e.g.) anti-convulsants, dextrose)	
Possible in specialised setting	
Haemodialysis	
Haemoperfusion	

Sources of information; References, 1,6,9-11

Table 7

Factors to be monitored in severely poisoned patients

Volume status / level of dehydration*
Neurological status - Depth of coma*
Urinary pH/output*
Blood glucose*
Serum electrolytes (potassium, sodium, creatinine, calcium)
Plasma pH
Prothrombin time

* Can be done in a district hospital setting.

Case 2: A three year old boy presented with a two day history of fever followed by dyspnoea and vomiting on the day of admission. He had been given an unspecified number of aspirin tablets on the day preceding admission for fever accompanying an abscess on the left thigh. He was fully conscious on admission but developed a convulsion and lapsed into coma shortly thereafter. On examination, he had severe respiratory distress with deep breathing and nasal flaring. He was clinically dehydrated and had haemodynamic features of shock with a blood pressure of 67/36mmHg (mean 38), a delayed capillary refill time of three seconds and severe tachycardia (pulse rate of 208). Other clinical and laboratory findings and progress are summarised in Tables 1 and 3.

A diagnosis of suspected salicylate poisoning was made and confirmed by serum salicylate level. After the initial bolus of 20mls/kg of 0.9% (normal) saline, sodium bicarbonate (20mls/kg) was administered initially over one hour, followed by a slower infusion over the next 24 hours. The child regained consciousness 15 hours later. He was discharged well after three days.

DISCUSSION

Chronic salicylate poisoning is serious and is associated with more frequent signs and symptoms than salicylate overdosing as a form of self-harm(3), although it is much less well recognised. The exact amount of salicylate ingested and over what duration required to produce chronic poisoning is unknown. It has been suggested that toxicity is likely to occur when more than 100mg/kg/day has been ingested over at least two days(4). This is equivalent to giving a three year old child weighing 14kg five tablets of adult aspirin daily for two or more days. However, daily doses as low as 32mg/kg may cause this complication (reducing the potentially toxic dose to less than two tablets a day for a 14kg child) (5).

Salicylate metabolism following administration of normal therapeutic doses is a saturable process, meaning levels can rise rapidly once this capacity is exceeded(6). The primary pathophysiologic effects of intoxication are of a complex nature and include direct stimulation of the central nervous system (CNS) respiratory centre, unecupling of oxidative phosphorylation, inhibition of Krebs cycle enzymes, stimulation of gluconeogenesis, increased tissue glycolysis, stimulation of lipid metabolism, inhibition of amino acid metabolism and interference with homeostatic mechanisms. The clinical picture at presentation arises from the secondary and tertiary effects, which include respiratory alkalosis with excretion of base initially followed by metabolic acidosis with excretion of acid, impaired glucose metabolism, and water and electrolyte loss(4). Children frequently do not exhibit respiratory alkalosis but tend to progress directly to metabolic acidosis. They are also more prone to CNS and metabolic toxicity which develop more rapidly and are more pronounced due to the greater uptake of salicylate from plasma into vital organs and tissues. Clinical features of salicylate intoxication are protean and affect almost all organ systems in the body(6). (Table 4).

Pulmonary oedema is well described in severe poisoning and correlates with high plasma salicylate concentration and anion gap(7). It is usually seen in chronic poisoning and may be caused by alveolar capillary leakage, fluid overload during treatment or left ventricular failure due to myocardial dysfunction(8). Small reductions in plasma pH produce large increases in free unionised salicylate, which penetrates brain tissue enhancing cerebral toxic effects. Oliguria usually follows dehydration but may be due to acute renal failure or a syndrome of inappropriate anti-diuretic hormone (ADH) secretion with fluid retention and concentrated urine despite adequate hydration, leading to cerebral oedema(4). Bleeding from the gastrointestinal tract may be seen in severe cases and may be caused by gastric erosions or decreased platelet adhesiveness and hypothrombinaemia secondary to inhibition of vitamin K dependent synthesis of factor VII. Death can result from pulmonary oedema and respiratory failure, cerebral oedema, haemorrhage, severe electrolyte imbalance or cardiovascular collapse.

An assessment of the severity of toxicity is useful as a guide on what treatment to institute and should be accomplished by clinical observation of the patient combined with plasma salicylate concentrations where available (Table 5). The clinical findings in both acute and chronic poisoning reflect severity of intoxication, but there is poor correlation between plasma salicylate concentration at admission and clinical severity based on observed symptoms in chronic intoxication(6). The clinical condition of the patient is therefore of paramount importance in chronic poisoning, and not their-salicylate level. The Done normogram, is useful as a predictor of severity after an acute ingestion but is not useful in cases of chronic poisoning(3).

The goals of treatment are to correct volume deficit in severely dehydrated or hypovolaemic patients, to minimise CNS salicylate accumulation and to facilitate salicylate excretion. Treatment is directed at raising the blood pH to between 7.45 and 7.50, and the urinary pH to between seven and eight by administering sodium bicarbonate either orally, by infusion or intermittent bolus. At these pH values, the salicylate is predominantly ionised hence less is available to enter the brain and other tissues, and maximum renal excretion occurs. Each one unit rise in urinary pH causes a four fold increase in salicylate clearance. Potential hazards of alkalinisation include hypernatraemia, hypokalaemia and precipitation of fluid overload and congestive heart failure(3). It is contraindicated in patients with cardiac or renal disease, and in those with cerebral oedema. Alkalinisation should be considered at plasma salicylate levels of greater than 350mg/L in acute poisoning, but even at levels lower than these in children with chronic salicylism exhibiting moderate to severe intoxication(1,6). Therapy should only be terminated once the patient's overall clinical condition progressively improves and the salicylate level drops to the therapeutic level(4). Severely poisoned patients frequently do not generate sufficient alkaline urine even after high doses of bicarbonate(3,4). Forced alkaline diuresis is no longer recommended, being potentially hazardous and not very beneficial(3). There is inconclusive evidence in support of methods that have been employed to minimise absorption or promote excretion such as multi-dose activated charcoal and whole bowel irrigation(9-11). Table 6 summarises the various methods used in management of chronic salicylate poisoning.

Supportive care includes correction of hypoglycaemia and electrolyte disturbances and control of seizures. Hyperthermia should be treated with external cooling using fans or tepid sponging. A prolonged prothrombin time should be treated with vitamin K. Close monitoring of the patient's course during treatment is mandatory, ideally hourly. Table 7 lists what should be monitored, and suggests what can be done in a district hospital setting.

Haemodialysis is the method of choice in patients who do not respond to alkalinisation or where this is contraindicated, since it allows for rapid correction of fluid and electrolyte abnormalities and acid-base imbalances. Generally, it is indicated in severely poisoned patients exhibiting salicylate injury to vital organs (CNS impairment, pulmonary oedema), renal/ hepatic dysfunction, clinical deterioration despite supportive care and urinary alkalinisation or severe acid-base disturbances despite appropriate supportive measures(3). It cannot be over emphasised that though helpful, the serum salicylate level should not be the sole determinant in the decision to dialyse. Case one was a definite candidate for early haemodialysis, which is not available in our unit.

These cases adequately highlight the many practical problems faced in managing a severely ill child with severe acidosis in a district hospital in many developing countries. Most of these children do not in fact have salicylate poisoning, with causes such as gastroenteritis and malaria, especially with anaemia being much more common. The history is therefore critical and the cornerstone of management initially is adequate fluid replacement or transfusion if in respiratory distress and very pale. However, it is important to remember that some of these children may have chronic salicylate poisoning, and it is these who pose a special management problem. A helpful discriminating point is that pulmonary oedema is rarely seen in children with severe malaria(12) and when found in combination with severe malaria and metabolic acidosis, one should consider salicylate poisoning in the differential diagnosis.

The initial diagnosis may be delayed due to the underlying illness (as in case 1), as well as the inability to obtain plasma salicylate levels for confirmation of diagnosis. Treatment is initiated blindly without knowing the acid-base or serum electrolyte status of the patient. The laboratory facilities that are crucial for monitoring treatment are lacking in most cases. Extracorporeal methods for eliminating the drug such as haemodialysis are not widely available, and are confined to a few specialist centres.

The best approach lies in prevention of poisoning by educating the community on the hazards of using salicylates as home remedies in children. One problem is the availability, in the local shops of multiple products containing aspirin, but under different names. Health care providers need to be trained to be able to advise parents of sick children on the dangers of purchasing multiple products, which contain aspirin, as well as have a high index of suspicion when faced with the severely ill, acidotic patient, even in the face of another obvious diagnosis.

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LETTER TO THE EDITOR-IN-CHIEF

RE: LAPAROSCOPIC APPENDICECTOMY

Dear Editor

At a time when indications for laparoscopic surgery are broadening(1,2), it was surprising to read your editorial of September 2003, which suggested otherwise. Even here in Kenya, where the technology had a relatively late arrival, the fact that at least four hospitals in Nairobi have purchased laparoscopic equipment is proof that usage is on the increase and we are fast catching up with other countries where operations like laparoscopic cholecystectomy have long surpassed the open method for elective removal of the gall bladder(3). Although the digestive tract best lends itself to this technology, where anti reflux surgery, groin hernia repair(4), appendicectomy are routine and resection of the colon is fast becoming a laparoscopic procedure(5,6). Other branches of surgery have taken advantage of the technology to dissect or excise organs previously thought to be inaccessible, and the advantages are regularly reported.

The problem with the reasoning in your editorial stems from earlier laparoscopists' obsession with keyhole surgery, but we must remember that the two are not synonymous(7). Today laparoscopists are less concerned with the size of the wound and more with the advantages the method provides for safe and accurate surgery with minimal trauma(2,8). The smaller wound is only an icing on the cake, and of course generally means less trauma and better cosmesis, but this is no longer necessarily the main consideration.

While it is true as your author states that initial costs for laparoscopy are high, these are rapidly dropping both for the hardware and software. As to the duration of surgery, laparoscopy takes longer only during the learning phase, or where surgery is relatively complicated. An expert laparoscopist with the right equipment will remove the appendix or gall bladder in a shorter time than open laparotomy because entry and exit times are much shorter.

As a surgeon who has recently taken interest in this type of surgery my scepticism has not only melted away but I have been impressed by its versatility. The most immediate advantage of the laparoscope is the clarity of the operating field in comparison to open surgery. This is of benefit not just to the surgeon but also to non-surgical staff who can see just as clearly what the surgeon is doing and assistance is enhanced. Moreover, any students in theatre can follow the procedure without just taking the surgeon's word for it.

In our team, which consists of six surgeons and gynaecologists, we regularly operate together, and although only two or three are scrubbed at a time, the rest give valuable advice during surgery. In this way the quality of surgery is improved and the "touchline" comments instill confidence in the lead surgeon. Many are times when a difficult decision has been overcome or a dilemma solved because there was extra expertise visualising the operation. Even relatively low ranking onlookers can give helpful suggestions. This is not possible with open surgery without the assistant scrubbing.

Laparoscopic surgery is routinely recorded on video giving the patient a chance to view the surgery afterwards, which is much appreciated. In some countries, it is a legal requirement to do so. For our team, the most important advantage of the videotape is that it can be played later, even at home, over and over again and forms an important component of learning and audit. We point out to areas of risk, ways of improvement, better performance and we note manoeuvres which waste time.

Your editorialist attributes to whole countries or even continents statements quoted from writers who hold similar views to his. No author, no matter the status can speak for a whole community. In fact laparoscopy has been nurtured and developed fastest in many of the countries quoted.

What about the future? Well, we may say it is already here. Surgeons have used robots to perform computer-enhanced laparoscopic surgery from a remote location(9-11).

The potential for robotics is enormous, as it will enable surgical and anatomical teaching without cadavers and without students having to huddle in theatres. Who knows, soon we may have tele-surgery where a specialist in say Europe assists a surgeon in trouble in Bungoma. It is likely that introduction of robotics will be the next revolution in surgery. The author may be right in saying that excitement about keyhole surgery is waning, but surely excitement about laparoscopic surgery is only beginning.

Yours Sincerely

R. Baraza FRCS., Nairobi Hospital, P.O Box 20713, Nairobi, Kenya

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LETTER TO THE EDITOR-IN-CHIEF

Dear Sir

RE: COMMENTS ON SEPTEMBER 2003 EDITORIAL

We the authors of Laparoscopic appendicectomy at the Aga Khan Hospital, Nairobi published in the September issue (Vol. 80 No. 9 2003) of the East African medical Journal, strongly object to the editorial views on “laparoscopic appendicectomy” by Mr. I.J.P. Loefler, published in the same issue. In our opinion, Mr. I.J.P. Loefler has never done any laparoscopic procedure in his life and therefore he is not qualified to give editorial comment on this particular subject.

Without doing his homework properly, for various and different laparoscopic procedures, he has given an average of four days of stay in the hospital. He should have only compared the stay in hospital for laparoscopic versus open appendicectomy, only then is his comment valid, otherwise it is misleading.

Similarly he has also misled the readers about the cost of the procedure, (very much exaggerated).

Chronic appendicitis is a distinct pathological entity. He is questioning the removal of 47 such chronic appendicitis done in our series. Majority of them had faecoliths and obstructive appendicitis and each case is documented in the hospital file as per the histopathological findings.

Because of no technical know how and total inexperience in laparoscopic surgery, his opinion is biased and therefore we strongly condemn his editorial.

S. C. Patel, FRCS, FICS, EITS, Consultant Surgeon and G. F. Jumba, MD, PhD, Consultant Surgeon, Aga Khan Hospital, P.O Box 30270, Nairobi, Kenya

LETTER TO THE EDITOR-IN-CHIEF

Dear Editor,

RE: RESPONSE TO LETTERS BY S. C. PATEL AND G. F. JUMBA AND R. BARAZA

Messrs. S.C. Patel, and G.F, Jumba take exception with what I have written.

The gentlemen hold the view that, as I have not performed any laparoscopic procedure, I am not qualified to have opinions on the matter.

I anticipated such reaction, hence the first sentence of my editorial. I have emphasised that perusal of the literature indicates a waning of enthusiasm for laparoscopic appendicectomy. I stand to this statement. I further suggest that one could become an expert in the aerodynamics of parachutes by virtue of studying the matter without ever jumping from an aeroplane.

With regard to the four days stay and the cost of Kshs.140,000 (US$1866) per patient, I have made it quite clear that these data refer to a mixed bag of laparoscopic surgery and not to appendicectomy alone, hence on these two points the gentlemen accuse me altogether mistakenly. Nevertheless here I have the opportunity to emphasize what I have written: that, except for a Mayo Clinic Paper, every publication confesses laparoscopic appendicectomy to be more expensive than the open variety.

This leaves us with the problem of "chronic appendicitis" Is there such a thing?

The Oxford Textbook of Surgery does not recognise its existence, neither do most textbooks. A Medline search yields but a few papers on the subject, some claiming that scarring, fibrosis, adhesions, represent chronic inflammation.

Indeed pathologists often describe scarred, fibrotic specimens as chronic appendicitis. This diagnosis would however be only permissible if there was an inflammatory infiltration consisting of immune cells, for that is the essence of chronic inflammation. It is extremely unlikely that half of the patients referred to in the paper under discussion had such pathology. I challenge Messrs. S. C. Patel and G. F. Jumba to ask their pathologist to re-examine the 47 slides. If 47 of 94 appendices are genuinely found to be chronically inflamed, the finding would be sensational and should be published. Until I see a publication explaining, satisfactorily, this remarkable epidemic of chronic appendicitis occurring in The Aga Khan Hospital, I shall maintain that perhaps as many as half of the appendices reported in the paper under discussion were removed unnecessarily.

I find it much more difficult to reply to R. Baraza's letter, for it is rather diffuse and does not focus on the gist of my editorial. Mr. Baraza's argument that laparoscopic surgery must be good thing otherwise the four larger hospitals in the Nairobi would not have purchased the equipment, is rather quaint. In my career, spanning fifty years, I have seen the rise and fall of many procedures, most of them associated with specific equipment. The common denominators in all these instances were initial enthusiasm fostered and nursed by the makers of the equipment, slow disillusionment, disuse of procedure and transfer of equipment to the hospital junkyard.

Fortunately the fate of laparoscopic surgery is not as bleak as that.

I have no doubt that laparoscopic surgery, whether "keyhole" or "assisted" has great future. This does not detract from the fact that laparoscopic appendicectomy does not offer great advantages over open appendicectomy except when the diagnosis is uncertain, particularly so in young women.

This is the central thesis of my editorial and the comments made by the laparoscopic surgery enthusiasts do not persuade me to change that opinion.

Yours faithfully,

I. J. P. Loefler, FRCS
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INFORMATION FOR CONTRIBUTORS

The East African Medical Journal (EAMJ) aims to improve the practice of all aspects of medicine and health care in general. To achieve these objectives, the journal publishes original scientific articles, reviews, clinical case reports and letters dealing with any factor impacting on health. EAMJ in published monthly since 1923 and is quoted in many authoritative databases including Index Medicus (med-line), SCISEARCH, EMBASE, Current contents clin. med., Sci Cit. Index. Communications should be addressed to the Editor-in-Chief, P.O. Box 41632, 00100, GPO Nairobi, Kenya, Telephone: +254-020-2712010: Facsimile +254-020-2724617; E-mail: eamj@wananchi.com.

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