Kwashiorkor – is it a dying disease?

O A Oyelami, T A Ogunlesi

Objective. To review the occurrence of kwashiorkor before and after the establishment of the Diarrhoea Training Unit at a Nigerian tertiary hospital in 1992.

Design. A retrospective hospital-based analytical study was undertaken. Groups of subjects were compared using odds ratios (95% confidence intervals) and regression analysis.

*Setting***.** The paediatric wards of the Wesley Guild Hospital, Ilesa, Nigeria.

Subjects. The number of children admitted with kwashiorkor, measles, gastroenteritis and marasmus between 1983 and 1991 (group I) was compared with similar data for the period 1993 - 2002 (group 2).

Results. There was a 30.4% reduction in the total admissions between these periods, while incidences of kwashiorkor, measles, gastroenteritis and marasmus fell by 70%, 55%, 57.4% and 55.8% respectively. Reduction in number of kwashiorkor cases between groups 1 and 2 was significantly related to the reduced incidence of measles ($p = 0.000002$) and gastroenteritis ($p = 0.000003$). The total number of admissions was correlated with the number of measles ($r = 0.623$ and 0.573 for group 1 and 2) and kwashiorkor cases ($r = - 0.412$ and 0.233 for groups 1 and 2).

Conclusion. The incidence of kwashiorkor has fallen in Ilesa, Nigeria. Given the relatively low HIV prevalence rate in the country during the study period, better management of diarrhoeal diseases, including measles, may have accounted for this drastic fall.

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The term protein-energy malnutrition (PEM) describes a spectrum of pathological conditions ranging from kwashiorkor to marasmus. The risk factors and clinical features of these two forms of PEM may be similar, but the cardinal feature of kwashiorkor is oedema.[1] Infection often precedes the development of kwashiorkor, with Morley[2] reporting that measles preceded the development of kwashiorkor in about 25% of cases. Various hypotheses have attempted to explain the differences between kwashiorkor and marasmus and to account for the confusing clinical features of kwashiorkor, but the most recent emphasised an imbalance between the production of free radicals and their safe disposal.[3]

Free radicals that destroy body tissues are also generated during infections.[4] The free radicals are disposed of by a protective mechanism that includes glutathione peroxidase. More recent developments in the pathogenesis of oedematous malnutrition include the role of oxidant stress in reducing the activities of glutathione. Depleted glutathione, characteristic of kwashiorkor, results in the enhancement of intracellular sodium pump activities and high intracellular sodium content, unlike in marasmus where glutathione levels are normal. [5]

The Wesley Guild Hospital in Ilesa was originally a missionary hospital; it was founded about 100 years ago but in 1975 became a unit of the Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) in Ile-Ife, Nigeria. It serves about 6 of the 36 states of the federation. In 1992, the World Health Organization (WHO) trained physicians and other senior health workers in the hospital on case management of diarrhoea. A Diarrhoea Training Unit (DTU) was then established at the hospital to train mothers on the prevention and treatment of dehydration.

The aim of this article was to ascertain the admission pattern for kwashiorkor following the establishment of the DTU and to determine its relationship to the pattern for other ailments traditionally associated with kwashiorkor, viz. measles, gastroenteritis and marasmus.

Methods

This was a retrospective analytical study. All cases of kwashiorkor, gastroenteritis, measles and marasmus admitted to the hospital as documented in the hospital's records between 1982 and 1991 (group 1) before the establishment of the DTU were compared with similar data for the period 1993 - 2002 (group 2) following the establishment of the DTU. The total number of children admitted over these periods was also recorded.

Statistical analysis of the data was done with odds ratios (ORs) and 95% confidence intervals (CIs), regression analysis and bivariate correlation using the Computer Programme for Epidemiologists (PEPI) software. *p*-values less than 0.05 in two-tailed tests were accepted as significant.

Results

The total admissions for group 1 were 18 895 compared with 13 157 for group 2, therefore representing a fall of 30.4% over

Department of Paediatrics, Obafemi Awolowo University, Ile-Ife, Nigeria
O A Oyelami, MB BS, FWACP

Department of Paediatrics, Olabisi Onabanjo University, Sagamu, Nigeria
T A Ogunlesi, MB ChB, FWACP

Corresponding author: *T A Ogunlesi (tinuade_ogunlesi@yahoo.co.uk)*

Table III. Relationship between total admissions and individual diseases in groups 1 and 2

Variables		Group 1			Group 2		
Independent	Dependent	r*	*p*-value	ß+	r*	*p*-value	ß+
Total admissions	Kwashiorkor	-0.412	0.242	-0.05	0.233	0.526	0.025
Total admissions	Marasmus	-0.257	0.484	-0.012	-0.057	0.879	-0.004
Total admissions	Gastroenteritis	0.557	0.092	0.101	-0.047	0.900	-0.005
Total admissions	Measles	0.623	0.055	0.135	0.573	0.081	0.150
Gastroenteritis	Kwashiorkor	-0.359	0.316	-0.241	-0.05	0.895	-0.052
Gastroenteritis	Marasmus	-0.308	0.396	-0.079	0.041	0.912	0.027
Measles	Kwashiorkor	-0.013	0.908	-0.017	0.045	0.904	0.019
Measles	Marasmus	-0.574	0.080	-0.088	0.176	0.636	0.044
Marasmus	Kwashiorkor	-0.089	0.812	-0.034	0.812	0.002	0.496

*Pearson's correlation coefficient.
+Regression coefficient.

these two periods (Table I). The number of kwashiorkor cases fell from 938 (group 1) to 276 (group 2), representing a fall of 70.6%. The number of cases of gastroenteritis, measles and marasmus admitted over these two periods also fell by 57.4%, 55.5% and 55.8% respectively (Table II). The number of kwashiorkor cases fell from 120 in 1992 when the diarrhoea management training was instituted to 61 cases in 1993. In 2001, only 9 cases of kwashiorkor were admitted (Table I).

Comparison of the other diseases in groups 1 and 2 showed a significant drop, but the most dramatic fall was noted for kwashiorkor (Table II). The fall in the total admissions between groups 1 and 2 was significantly related to the drop in incidence of kwashiorkor (30.4% v. 70.6%, OR 0.42, 95% CI: 0.37 - 0.49, p = 0.000000), measles (30.4% v. 55.5%, OR 0.64, 95% CI: 0.57 - 0.71, p = 0.000000), marasmus (30.4% v. 55.8%, OR 0.63, 95% CI: 0.52 - 0.77, p = 0.0000013) and gastroenteritis (30.4% v. 57.4%, OR 0.61, 95% CI: 0.56 - 0.67, p = 0.000000). The drop in the number of kwashiorkor cases between groups 1 and 2 was significantly related to reduced incidence of measles (70.6% v. 55.5%, OR 1.51, 95% CI: 1.27 - 1.80, p = 0.000002) and gastroenteritis (70.6% v. 57.4%, OR 1.45, 95% CI: 1.23 - 1.70, p = 0.000003). However, there was no significant relationship between the reduced number of marasmus cases and the drop in the number of measles (55.8% v. 55.5%, OR 1.01, 95% CI: 0.81 - 1.25, p = 0.947) and gastroenteritis cases (55.8% v. 57.4%, OR 0.96, 95% CI: 0.78 - 1.19, p = 0.721).

Table I. Distribution of children admitted between 1982 and 2002 by disease types

Year	Total	Gastro-enteritis	Measles	Marasmus	Kwashior-kor
1982	2 009	264	167	24	50
1983	2 187	237	146	35	75
1984	1 386	178	76	34	148
1985	2 110	249	272	24	101
1986	1 604	154	68	39	80
1987	1 825	199	121	56	92
1988	1 955	200	88	42	75
1989	1 919	189	35	53	94
1990	2 054	176	143	26	137
1991	1 846	122	28	35	86
1992*	1 726	99	102	49	120
1993	1 247	93	16	32	61
1994	1 143	76	51	27	33
1995	1 428	47	11	16	37
1996	1 422	99	97	17	38
1997	1 377	83	18	0	13
1998	1 419	87	87	27	31
1999	1 210	76	44	11	14
2000	1 580	92	121	14	28
2001	1 177	100	50	11	9
2002	1 154	85	14	8	12

*Year of intervention.

Table III shows the regression and correlation analysis for the total admissions and the individual diseases over these two periods. The total admissions showed a strong correlation with measles and kwashiorkor in both groups 1 and 2. Kwashiorkor was correlated with gastroenteritis in group I and marasmus in group 2. Except for the correlation between kwashiorkor and marasmus in group 2, these correlations lack statistical significance but their directions (positive/direct and negative/inverse) are also indicated in Table III.

Discussion

Reduction in the traditional catchment area of our hospital and the higher fees charged by the hospital may explain the global reduction in paediatric admissions over the periods studied. Improved home management of childhood diarrhoea may explain the drop in number of admitted gastroenteritis cases. Following the establishment of a DTU at the hospital in 1992, health education on home management of childhood diarrhoea was emphasised, both in the hospital and in the community by health visitors from the hospital. Thus, a recent study of childhood diarrhoea in the hospital showed very high use of oral rehydration therapy (ORT) and a very low incidence of severe dehydration among the subjects.[6] High ORT use had reduced the severity of the disease and thus lessened hospitalisation.

Table II. Pattern of admissions between group 1 (1982 - 1991) and group 2 (1993 - 2002)

	Group 1 (*N*)	Group 2 (*N*)	% drop
Total admissions	18 895	13 157	30.4
Kwashiorkor	938	276	70.6
Marasmus	369	163	55.8
Gastroenteritis	1 968	838	57.4
Measles	1 144	509	55.5

The persistence of childhood malnutrition in most parts of the developing world has been attributed to the lack of access to formal health services despite the availability of more efficient dietary plans.[1] Paradoxically, there has been a decline in the incidence of severe malnutrition cases seen in our hospital. However, the reduction in the number of kwashiorkor cases was more spectacular as it was disproportionate to the reduction in the total hospital admissions. Notably, there was a 50% reduction in kwashiorkor cases within a period of 1 year after the initiation of diarrhoea management training, while the cases of measles usually associated with diarrhoea and dehydration also fell by about the same proportion. Instructively, only complicated cases of measles were usually hospitalised, yet pulses of increment in measles admission produced similar increments in number of kwashiorkor cases. For instance, measles cases increased from 44 in 1999 to 121 in the year 2000 and there was a concomitant increase in the number of kwashiorkor cases from 14 to 28 during this same period.

The strong correlation between marasmus and kwashiorkor in the post-1992 period lent credence to the involvement of the former in the final pathway to the latter. This is not surprising since marasmus is known to lead to kwashiorkor in the presence of infections like gastroenteritis and measles. It is clinically important to infer that with better management of gastroenteritis the number of severe gastroenteritis cases requiring hospitalisation fell, but that there had been an even greater reduction in the number of kwashiorkor cases. It is difficult to attribute the fall in kwashiorkor cases in our hospital to deflection of such cases to other local under-5 clinics, which lacked the facilities and the personnel to manage them. In addition, the reduction in kwashiorkor cases was not likely to have been because of improved standard of living, improved dietary habits or other social changes in the community since the socio-economic conditions of most families in the community had not improved over the years in consonance with a progressively depressed national economy. Although hospital charges had increased, the increments were not prohibitive and other seriously ill children were still brought to the hospital for care. It was therefore not likely that children with kwashiorkor were no longer brought to the hospital on account of the increased hospital charges.

Lack of a positive relationship between the reduced incidence of marasmus and reduced incidence of measles and severe gastroenteritis further suggests that the aetiopathogenesis of marasmus probably differs from that of kwashiorkor. It appears that kwashiorkor results from infectious diseases, notably measles and gastroenteritis, while marasmus results from inadequate food intake arising from various causes.

Reduction in the number of kwashiorkor cases may be due to fewer cases of severe measles following widespread immunisation against measles. However, this cannot explain things entirely since the sharp reduction in number of kwashiorkor cases followed on the heels of better management of diarrhoea with ORT and nutrition. Like other infections, measles and gastroenteritis may provoke the generation of free radicals in the body and the accumulation of aflatoxins and free radicals may result in kwashiorkor.[5,7] Good hydration prevents the accumulation of free radicals and aflatoxins in the tissues, hence the likely prevention of kwashiorkor.

Nutritional management of diarrhoea is equally important. In the past, children with diarrhoea were traditionally given maize gruel known to be potentially contaminated with aflatoxins.[8] Currently, mothers are encouraged to give energy-dense, protein-rich food during episodes of diarrhoea. This enables the child to produce glutathione, the enzyme that metabolises aflatoxins and other noxiae that may be agents in the pathogenesis of kwashiorkor.[7]

However, a recent Malawian study[9] showed that anti-oxidants did not protect children with borderline nutritional status from developing kwashiorkor. This casts doubt on the oxidative stress theory in the pathogenesis of kwashiorkor. On the other hand, it has also been suggested that the lack of efficacy of antioxidants in the Malawian study may also have been due to the confounding effects of HIV in the children studied.[10]

There are suggestions that the incidence of severe childhood malnutrition may actually be rising in certain parts of the developing world, particularly Africa.[11,12] This rise has also been ascribed to the HIV pandemic.[12-14] It is therefore attractive to postulate that the decline in the incidence of kwashiorkor in Ilesa, Nigeria, may because of the relatively low prevalence of HIV in the country during the period studied. Even at present, Nigeria, has a low HIV prevalence rate (5.4%) compared with other African countries such as South Africa (21.5%) and Zimbabwe (24.6%).[15] Specifically, in more recent studies of hospitalised children with features of immunosuppression in OAUTHC, Ile-Ife (our sister hospital), the prevalence of HIV infection varied between 13% and 20%.[16,17] Interestingly, marasmus was the only form of severe malnutrition recorded.[17]

In conclusion, the declining incidence of kwashiorkor in Ilesa, Nigeria, may be attributed to improved management of diarrhoeal diseases, including measles, following the establishment of a DTU at the hospital, with bandwagon effect on the community. However, we hasten to add that the sustained decline in the incidence of kwashiorkor may also be because of the low prevalence of HIV infection in these communities during these periods.

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