SHORT REPORT

Prevalence of underweight, overweight, and obesity at diagnosis in UK patients with childhood Acute Lymphoblastic Leukaemia 1985-2002

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Abstract

Background: Underweight, overweight, and obesity at diagnosis may all worsen prognosis in childhood acute lymphoblastic leukaemia (ALL) but no studies have estimated prevalence of unhealthy weight status at diagnosis in large representative samples using contemporary definitions of weight status based on BMI for age.

Methods: Retrospective study which aimed to estimate prevalence of underweight, overweight, and obesity at diagnosis for patients with childhood ALL on three successive UK treatment trials: UKALL X (1985-1990, n 1033), UKALL XI (1990-1997, n 2031), UKALL 97/ 99 (1997-2002, n 898) .The BMI for age was used to define weight status with both UK 1990 BMI for age reference data and the Cole-International Obesity Task Force (IOTF) definitions.

Results: Prevalence of underweight was 6% in the most recent trial for which data were available. Prevalence of overweight and obesity was 35% in the most recent trial when expressed using Cole-IOTF definitions; 41% when expressed relative to UK 1990 reference data.

Conclusions: Even with highly conservative estimates >40% of all UK patients with ALL were underweight, overweight, or obese at diagnosis in the most recent trial for which UK data are available (UKALL 97/99, 1997-2002).

Keywords: Obesity; Overweight; Underweight; Child; ALL.

Introduction

Underweight, overweight, and obesity have adverse short and long-term health effects for children and adolescents (Reilly et al 2003; Reilly and Kelly 2011; Pelletier et al 2003). Moreover, both underweight and obesity at diagnosis of childhood acute lymphoblastic leukaemia (ALL) appear to have disease-specific adverse effects in that they can increase risk of relapse (Lobato-Mendizabal et al 2003; Butturini et al 2007; Gelelete et al 2011), with similar findings in some other childhood malignancies (Lange et al 2005). In addition, in a number of childhood malignancies, including ALL, obesity is a common consequence of the disease or its treatment (Reilly 2009).

Despite the clinical importance of weight status during and after diagnosis of ALL, prevalence estimates of weight status at diagnosis have usually been made with small samples, typically from samples of patients from single centres. Prevalence estimates for underweight, overweight, and obesity are not available for large nationally representative samples of patients. In addition, older studies generally did not base their prevalence estimates on well- established definitions of weight status (Reilly 2010) using the BMI for age (Cole et al 2000; Cole et al 2007; Cole et al 1995; Reilly et al 2010), some of which became available only recently, e.g. the definition of underweight from Cole et al (2007). Anonymised national trial data are available for patients with childhood ALL in the UK, and almost all patients enter these trials, so trials provide an excellent opportunity to estimate prevalence of underweight, overweight, and obesity for the entire patient population. The primary aim of the present study was therefore to describe weight status at diagnosis of ALL (typical age

of diagnosis is around age 4 years), using contemporary and recently-established definitions.

Methods

Study participants

The present study was based on clinic measures of weight and height of all patients at entry onto the trial protocol from successive UKALL national treatment trials, which covered the period 1985-2002: UKALL X (1985-1990), UKALL XI (1990-1997), and UKALL 97/99 (1997-2002). Since 2002, patient weight and height have no longer been routinely measured and recorded at diagnosis of ALL in the UK: no national estimates of the prevalence of unhealthy weight status are possible beyond 2002. The Clinical Trials Service Unit, Oxford, provided the data used in the present study, in anonymised form.

Definitions of weight status categories

Clinic measures of weight and height were recorded to 0.1kg and 0.1cm respectively. These measures were used to calculate the body mass index, BMI. Internationally accepted definitions of child and adolescent underweight (‘thinness’; Cole et al 2007), overweight, and obesity (Cole et al 2000) were used: these are conceptually equivalent to adult BMI cut-offs for underweight, overweight, and obesity. International definitions of weight status were chosen for the present study because they are widely used in research, and are particularly suitable for between-study and international comparisons. Prevalence estimates for overweight and obesity were also generated using UK BMI population reference data from 1990 (Cole et al 1995; Reilly 2010), with overweight defined as a BMI between the 85th and 94th percentiles and obesity $\geq$95th percentile. The BMI for age definitions of overweight and obesity

based on UK 1990 population reference data are used widely in the UK, and can be applied to a wider age range than the Cole et al definitions based on BMI for age, though no clear, evidence-based, definition of underweight exists with the UK 1990 BMI reference data. Use of UK national reference data for BMI has higher diagnostic accuracy for obesity (higher sensitivity for the detection of excessively fat children) than use of the international definitions (Reilly et al 2000; Reilly et al 2010), and has equal sensitivity for detection of excessive fatness in boys and girls (in contrast to use of Cole et al definitions in UK children; Reilly et al 2000).

Statistical analysis

Distributions of weight status variables were not normal, and so non-parametric tests were used, and non-parametric summary statistics are provided. Differences in the prevalence of underweight, overweight, and obesity between boys and girls were not significant, and so prevalence estimates have been presented with data combined. Secular trends in median BMI Z score across the three trials were tested for significance using a Kruskal Wallis test. Secular trends in the prevalence of underweight, overweight, and obesity across the three trials were tested for significance using a Chi Square Test for Trend. Minitab software version16.1.1 and Medcalc software version 11.5.0.0 were used for these statistical analyses.

Results

Characteristics of study samples are shown in Table 1.

Prevalence of underweight was 19.4% in UKALL X (1985-1990), 16.0% in UKALL XI (1990-1997), and 5.8% in UKALL 97/99 (1997-2002). The secular trend in prevalence of underweight between the three trials was statistically significant ($p < 0.0001$). Prevalence of overweight and obesity (combined) using the Cole-International Obesity Task Force definitions (table 2) was 10.2% in UKALL X, 13.1% in UKALL XI, and 34.5% in UKALL 97/99.The secular trend in prevalence of overweight and obesity between the three trials was statistically significant ($p < 0.0001$).

Prevalence of overweight and obesity (combined) using UK population reference data was 13.3% in UKALL X, 18.2% in UKALL XI, and 40.9% in UKALL 97/99 (Table 2). The secular trend in prevalence of overweight and obesity between the three trials was statistically significant ($p < 0.0001$).

Discussion

The present study demonstrates that in the UK >40% of all patients with ALL were underweight, overweight, or obese at diagnosis using the most recent UK dataset available (from the trial which ended in 2002) . No estimates of the prevalence of underweight, overweight, and obesity have previously been available from nationally representative samples of patients using the currently recommended definitions of weight status based on BMI for age. It is important to note that our prevalence estimates were conservative. The BMI-based definitions of obesity, at best, have moderate sensitivity for detection of excessively fat individuals, with a low false positive rate but a moderately high false negative rate, both in the general population of children (Reilly 2010) and in those with malignancy (Warner et al 1997; Aldhafiri et al 2012). The Cole-IOTF definitions are particularly conservative (Reilly 2010; Reilly et al 2010). In addition, children with ALL in the UK experience substantial excessive weight gain during and after therapy (Reilly 2009), so the estimates of prevalence of obesity made in the present study are also conservative because they are based on measures made at diagnosis rather than after therapy.

The implications of the age of the data available to the present study are worth considering. The last data used in this retrospective study are now ten years old, and routine measurement and recording of patient weight and height at diagnosis (before induction therapy) in the UK was abandoned a decade ago when the algorithm to estimate body surface area (to calculate drug dosage) was changed. This means that no more recent prevalence data from national samples are available in the UK.

Continued national surveillance of weight status of patients with ALL, with anonymised central data collection as used in the present study, has become impractical. The extent to which the prevalence estimates from the present study 'matter' today will depend to a large extent on secular trends in underweight, overweight, and obesity in the last 10 years. A dramatic increase in the prevalence of childhood obesity occurred in the general population in the UK between the mid-1980's until the late 1990's (Reilly and Dorosty 1999), and the present study findings were consistent with these population-wide trends. Childhood obesity prevalence in the UK has continued to increase over the past 10 years, but the rate of increase seems to have slowed recently (Stamatakis et al 2010). It seems probable that the prevalence of obesity from more contemporary samples of patients with ALL at diagnosis would be at least as high as those reported in the present study. Secular trends in underweight are not available for the UK as far as we are aware, and the definition of underweight used in the present study has emerged only relatively recently (Cole et al 2007).

In the absence of formal anthropometric screening for unhealthy weight status, few patients who have unhealthy weight status are identified by experienced paediatricians, paediatric dietitians, paediatric nurses (Cross et al 1995; Smith et al 2008) and parents (Parry et al 2008). Identification of both underweight and overweight/obesity at diagnosis of ALL should be relatively straightforward using the BMI in conjunction with widely available centile charts (Reilly 2010), but there remains resistance to using such charts routinely in paediatric practice, for reasons which have not been explored fully (Flower et al 2007). There is increasing evidence that paediatric nutritional screening tools are valid, reliable, and practical

(Gerasimidis et al 2010; Secker and Jeejeebhoy 2007; Hulst et al 2010) and these could also be considered in future management of ALL. Further research will be required to identify how and whether to establish nutritional assessment within routine management of childhood ALL.

In summary, the present study suggests that underweight, overweight, and obesity are likely to be very common at diagnosis in childhood ALL in the UK.

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Table 1 Characteristics of study participants at diagnosis in three UK ALL trials, 1985-2002, median (IQR)

	UKALLX n= 1033 (774 boys)	UKALL XI n= 2031 (1153 boys)	UKALL 97/99 n= 898 (488 boys)
Age y	4.5 (2.9, 8.1)	4.5 (2.5, 7.5)	4.5 (3.5,7.5)
BMI Z score*	-0.28 (-1.06, 0.47)	-0.10 (-0.82, 0.77)	0.78 (-0.18, 1.52)†
Height Z score*	0.10 (-0.67, 0.78)	0.17 (-0.66, 1.01)	0.24 (-0.66, 1.02)

*Z scores expressed relative to UK 1990 reference data using open access software.

† Significant difference in median BMI Z score across the three trials (Kruskal-Wallis test, P< 0.0001)

Table 2 Prevalence % (n) of weight status categories at diagnosis in three UKALL trials , 1985-2002

Definition and Reference Data	Weight status	UKALLX % (n)	UKALL XI % (n)	UKALL 97/99 % (n)

Cole et al/ IOTF* International Definitions	Underweight†	19.4 (178)	16.0 (301)	5.8 (49)
	Healthy weight†	70.3 (645)	70.9 (1330)	59.7 (506)
	Overweight and obese†	10.2 (94)	13.1 (246)	34.5 (293)
Definition based on national reference data				
UK 1990	Healthy weight†	86.6 (895)	81.6 (1657)	59.1 (531)
	Overweight and obese†	13.3 (138)	18.2 (374)	40.9 (367)

* IOTF; International Obesity Task Force. † Test for secular trend across the three trials significant ($p < 0.0001$)