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Original Research Article

Prevalence and Socio-Demographic Profile of Overfat and Obese Primary School Children in Mashonaland West Province, Zimbabwe

Kambondo George[1], Sartorius Benn[1], Mhlanga Maxwell[2]

[1]Discipline of Public Health, School of Nursing and Public Health, University of KwaZulu Natal, Durban, South Africa
[2]College of Health Sciences, University of Zimbabwe

Corresponding Author: Mhlanga Maxwell

ABSTRACT

Background: The growing burden of obesity is evident especially in developing setting. The major health consequences of childhood obesity are realised in adulthood as cardiovascular diseases (mostly heart disease and stroke); diabetes and musculoskeletal disorders at a younger age as examples. This has a major bearing in health and economic consequences for developing countries. The study was conducted to estimate the burden of overfat and obesity among primary school children and identify associated socio-demographic correlates in Mashonaland West Province, Zimbabwe.
Methods: A cross-sectional study was conducted in 30 randomly selected (with probability proportional to size) schools ("clusters") in 2015. The participants were primary school children aged 6-12 years. At least 30 children were selected per school resulting in 974 randomly participants with a response rate of 98%. Sample weights were used for the analyses to account for the multistage sampling design. Nutritional status was determined using the international obesity task force (IOTF) criteria and McCarthy body fat reference curves.
Results: The overall prevalence of overfat and obese among primary school children was 8% (95%CI: 6-10%) and 10% (95%CI: 6-17%) respectively. Females had a higher prevalence of overfat/obese 11% (95% CI: 7-17%) as compared with males 7% (95%CI: 4-10%) and this difference was statistically significant (p<0.012). The estimated population burden of obesity among primary school children was 23 971 (95%CI: 10 198, 37 742) with 14 823 (95%CI: 5 285, 24 359) females and 9 148 (95%CI:4 327, 13 969) males. Prevalence of overfat/obese was significantly higher among high-income families as compared to the low social class (p=<0.002).
Conclusion: Overfat/obese prevalence is high in primary school children, especially among females in urban areas and in higher income families. Primary preventive intervention strategies need to be implemented such as dietary education and physical activities to primary schools and regular obesity assessments.
Key Words: Prevalence; overfat; obese; school children; Zimbabwe

INTRODUCTION

Childhood obesity has increased rapidly in the developed and developing countries in the past decade [1-4] and has emerged as a major risk factor of non-communicable diseases in both developed and developing countries. Most developing countries have been undergoing a rapid economic growth and a life-style change which has contributed to increasing prevalence of obesity. WHO estimated that by 2030 up to 57.8% of the world's adults would suffer from being overfat or obese. [3] A study by Onis et al (2010) found that prevalence of childhood overweight and obese in Africa was 8.5% and was likely to

increase to 12.7% by 2020. [5] According to previous research it is indicated that childhood obesity continues into adulthood in approximately 70% of the cases and it is the major risk factor for various chronic problems such as cardiovascular diseases, hypertension, stroke, type 2 diabetes mellitus, osteoarthritis and certain cancers which develop in adults later in life. [1,6]

The major determinants of obesity have been indicated as the main contributors of childhood obesity as genetics, dietary pattern, sedentary activities and physical activity pattern. [7] Zimbabwe as a developing country has been undergoing a rapid nutrition transition in the past few decades, contributing to increasing of obesity. [5,8,9] There is no study which has assessed on the burden of overfat and associated socio-demographic profile among primary school children in Zimbabwe using body fat percentage. Furthermore many studies assessing the burden of childhood obesity were conducted more than 10 years ago. [10-14]

The present study aims to provide updated prevalence, population burden and associated socio-demographic profile of overfat and obesity among primary school children aged 6-12 years in Mashonaland West Province in Zimbabwe and this help inform local public health programming interventions.

METHODS

Study setting and population

A school based cross sectional study was conducted among school- going children aged 6 to 12 years in Mashonaland West Province of Zimbabwe in September 2015. The province which has seven administrative Districts, a population of 1 449 938, with 65% residing in the rural areas has a total of 707 primary schools including both government and private schools. The Provincial primary school enrolment is 310 308 children.

Sampling: Multi stage cluster sampling was utilised in the districts and the schools to represent all primary school children aged 6 to 12 years in the province. The first stage of sampling schools was selected with probability proportional to size (PPS). In the second stage schools were randomly selected with primary sampling units (PSUs) and included 30 schools in the province representing 15 rural schools and 15 urban schools which formed the five strata from the randomly selected districts. Thirty primary schools from the five strata were found having 238 931 primary school children aged 6-12 years. The schools were randomly selected from the five districts.

We aimed for a minimum sample size of 900 children based on the traditional 30x30 cluster survey design proposed by WHO for acute malnutrition surveys [15,16] i.e. thirty schools were sampled with probability proportional to size (PPS) and the 30 children were randomly selected within each school. It assumes a design effect of 2 and it estimates prevalence with ±5% precision at 95% confidence interval width of 10%.Assuming a non response rate of 10%, the total sample size was increased to 990. A total of 974 were enrolled at a response rate of 98%. One grade seven class from Karoi School was excluded as the consent forms were issued to children who were perceived to be obese only.

Data collection

Children's anthropometric measurements were precisely measured by specially-trained nurses, environmental health technicians and an Occupational Therapist. All were provided a two-day training prior to the study to insure competence and consistency. Anthropometric measurements, namely weight, height, body fat mass, mid-upper arm circumference, hip and waist circumference were collected. An interviewer administered questionnaire was also administered to the eligible child respondents to capture socio-demographic and other factors.

Weight was measured with the subject wearing light clothing and without shoes using a Bioelectrical Impedance

Analysis (BIA) scale, Tanita-SECA-250 four compartment models. Height was measured with shoes off, feet together and head being held on the sheen in the horizontal plane.

Obesity measures, especially in epidemiological studies among adults and children includes: waist circumference, skin fold thickness and bioelectrical impedance analysis. These methods measure indirect body fats that are not based on weight. [17] Body fat percentages can be measured by other research techniques including under water weighing (densitometry) and magnetic resonance imaging (MRI). Many researchers have found that use of BMI to identify overweight and obese children is somewhat ineffective on account of body fat percentage indicated high specificity (95-100%), but low sensitivity (36-66%). [5] Many studies recommended Bioelectrical Impedance Analysis (BIA) for large populations and clinical studies [18] which measures direct the percentage of body fatness which is recommended as an accurate research method in childhood obesity. [19]

Body fat mass in our study was measured using BIA (Tanita-SECA-250) scale and the body fat mass was recorded as a percentage. Body fat mass was measured during recess and during the lunch hour before food was consumed.

The Mid-Upper Arm Circumference (MUAC) was determined by using a flexible non-stretchable Tape. Two readings of height, weight and MUAC were taken and their mean was considered final. The IOTF reference data using the Excel BMI Calculator (Metric Version) [15] was used for the estimation of overweight and obesity in the study subjects.

Precision: Weight was recorded using BIA electronic weight scale to the nearest 0.1kg and height was measured by the use of a SECA stadiometer and recorded to the nearest 0.1cm. The MUAC was then measured and recorded to the nearest 0.1cm.

Definition and category

In the current study overfat and obese was classified using the McCarthy [20] body fat reference curves which are defined by gender and age. These are as follows:

Females: Under fat = <15.9%, Healthy = 16-28.9%, over fat = 29-32.9% and obese = 33%+;

Males: Under fat = <12.9%, Healthy = 13-22.9%, over fat = 23-27.9% and obese = 28%+.

The current study also used IOTF reference data to define overweight and obesity as the age and gender- specific BMI of 85^{th} -94^{th} percentile and equal or higher than the 95^{th} percentile, respectively. [21] The agreement between BMI for age and bodyfat methods were evaluated by Kappa (k) statistic and the agreement was very high at 86.55% [expected agreement under null 73.29%, $p<0.001$].

Statistical Analysis

Data were processed and analysed using Stata 13. [22] Sample weights were incorporated into the analyses to account for the sampling design. This allowed estimation of survey weighted 95% confidence intervals and projected population totals of overfat/obese children in the province. Differences in the prevalence of over fat and obese by district, gender and school location were assessed using a survey weighted chi-square (χ^2) test. Crude odds ratios with 95% confidence intervals (CI) were estimated to quantify the strength of association between overfat/ obese and demographic characteristics (age group, gender, district, and location (urban, rural).

Ethical approval: The study protocol was approved by Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BE074/15) and Medical Research Council of Zimbabwe (MRCZ/A/1972). Prior authority was obtained from the Ministry of Primary and Secondary Education and each school's administration. The parents or guardians of the participants provided prior informed consent and the selected children written informed ascent.

RESULTS

Table 1 presents summary of the demographic characteristics of our study population. The majority of participants, 734(75.4%), were in the 10-12 year age band, followed by 7-9 year age band [220 (22.6%)], the majority of children were ingrade three to five [471(48.3%)] with the fewest in grade 1-2 [144(14.8%)]. Gender was roughly distributed with 458 (47%) males and 513 (53%) females. The educational status of the mothers were generally high with 665(68.3%) having attended secondary level and 139(14.3%) tertiary level. A majority [670 (68.8%)] of the fathers had attained secondary or higher education, with very few [7%] having no formal education. The majority 433 (44.5%) of the respondents were from families earning an income less than $200 per month and very few 207 (21%) were from families earning more than $550 per month.

Anthropometric Measurements

A summary of the anthropometric characteristic of study population stratified by gender are presented in Table 2. The overall mean percentage of body fat (%BF) and BMI for age was18.39 % (±SD8.97%) and 48.85 % (±SD 30.69) In terms of gender, the mean % BF among males was 15.51% (95% CI: 14.06, 16.97) compared to 20.91% (95% CI: 19.07, 22.74), and this difference was highly statistically significant ($p<0.001$). The mean mid upper arm circumference (MUAC) [in centimetres] was significantly lower ($p=0.008$) among males [20.34±3.23 (95% CI: 19.89, 20.80)] compared to females [21.38±3.24cm (95%CI: 20.71, 22.04)]. The overall mean (± SD) hip circumference was 75.45cm (±9.9cm) and it was significantly higher in females compared to males, 77.31cm (±10.13cm) vs 73.34cm (±9.7cm) respectively ($p=0.018$).

The prevalence of overfat and obese among school children was 8% (95% CI: 6-10%) and 10% (95% CI: 6-17%) respectively with a significantly higher burden among females compared to males, namely; 11% (95% CI: 7-17%) vs 7% (95% CI: 4-10%) respectively ($p=0.012$) (Table 3a). The prevalence of overweight and obesity based on BMI for age was 7% (95% CI: 5-11%) and 10% (95% CI: 6-15%) respectively and did not differ significantly by gender ($p=0.921$).

The overall projected number of overfat/obese children in the province (based on our sampling design) was 42 930 (95% CI: 22 584, 63 274) (Table 3b). The projected overall obese children in the province was estimated at 23 971 (95% CI: 10 198, 37 742). The gender breakdown of this was 14 823 (95% CI: 5 285, 24 359) obese females and 9 148 (95% CI: 4 327, 13 969) obese males.

Table (1): Socio-demographic characteristics of school children in Mashonaland West Province in 2015

Characteristics	Number	Proportion(95%CI)i
Age Group		
6	20	0.02 (0.01,0.05)
7-9	220	0.23 (0.17,0.30)
10-12	734	0.75 (0.67,0.82)
Gender		
Males	463	0.47 (0.39,0.55)
Females	511	0.53 (0.45,0.66)
Grades		
1-2	144	0.15 (0.09,0.22)
3-5	471	0.48 (0.40,0.57)
6-7	359	0.37 (0.26,0.49)
Residence		
Urban	403	0.41 (0.25,0.60)
Rural/communal	65	0.07 (0.03,0.13)
Farming	237	0.24 (0.14,0.39)
Mining	269	0.28 (0.11,0.55)
Education level of Mother		
None	52	0.06 (0.02,0.11)
Primary	118	0.12 (0.07,0.20)
Secondary	665	0.68 (0.63,0.73)
Tertiary	139	0.14 (0.10,0.20)
Occupation of Mother		
Formally employed	245	0.25 (0.19,0.32)
Self employed	212	0.22 (0.18,0.26)
Unemployed	131	0.13 (0.09,0.20)
House wife	386	0.40 (0.33,0.47)
Education level of Father		
None	68	0.07 (0.04,0.11)
Primary	37	0.04 (0.02,0.06)
Secondary	670	0.69 (0.63,0.74)
Tertiary	199	0.20 (0.15,0.27)
Occupation of Father		
Formally employed	558	0.57 (0.49,0.65)
Self employed	275	0.28 (0.23,0.34)
Unemployed	141	0.14 (0.10,0.21)
Socio-economic index		
≤$200 Low	433	0.44 (0.32,0.57)
$201-$500 Medium	334	0.34 (0.27,042)
≥$501 High	207	0.21 (0.14,0.31)

Survey weighted proportions

Table (2): Survey weighted Means (SD) of anthropometric measurements of school children in Mashonaland West in 2015 by gender

Measurement	Males(N=463)	Females(N=511)	Overall(N=974)	P-Value
Survey weighted Mean, SD (95%CI)				
Body fat mass %	15.51(8.67) (14.06, 16.97)	20.91(8.47) (19.07, 22.74)	18.39(8.97) (16.85, 19.92)	<0.001
Body fat free mass%	84.52(8.62) (83.05, 85.99)	79.11(8.41) (77.31, 80.91)	81.64(8.93) (80.09, 83.19)	<0.001
Body water %	60.70(7.09) (59.22, 62.18)	56.98 (7.09) (55.27, 58.68)	58.72(7.3) (57.25, 60.19)	<0.005
BMI for age percentile	45.53(31.37) (39.81, 51.27)	51.76(29.78) (46.37,57.14)	48.85(30.69) (43.90, 53.80)	<0.005
Weight/kg	34.05(10.07) ((32.73, 35.37)	36.98(10.11) (35.14,38.83)	35.61(10.2) (34.08, 37.14)	0.097
Height/cm	137.51(10.81) (135.77,139.26)	140.29 (11.53) (137.20,143.39)	138.99(11.29) (136.55, 141.43)	0.103
MUAC/cm	20.34(3.23) (19.87, 20.80)	21.38(3.24) (20.71, 22.04)	20.89(3.28) (20.33, 21.45)	<0.008
Waist circumference/cm	63.35(8.21) (61.67, 65.03)	64.78(8.67) (63.13, 66.43)	64.11(8.49) (62.61, 65.66)	0.322
Hip Circumference/cm	73.34(9.17) (71.57, 75.11)	77.31(10.13) (75.32, 79.29)	75.45(9.9) (73.57, 77.32)	<0.010

Table (3a): Survey weighted proportions of prevalence for obese school children in Mashonaland West 2015

Survey weighted Proportions(95%CI)	Males(N=463)	Females(N=511)	Overall (N=974)	P-Value
Body Fat %				
Under Fat	0.20 (0.16, 0.25)	0.16 (0.12, 0.21)	0.36 (0.29, 0.44)	<0.012
Healthy	0.19 (0.14, 0.27)	0.26 (0.20, 0.37)	0.46 (0.40, 0.51)	
Over fat	0.03 (0.02, 0.04)	0.05 (0.04, 0.06)	0.08 (0.06, 0.10)	
Obese	0.04 (0.02, 0.06)	0.06 (0.03, 0.11)	0.10 (0.06, 0.17)	
BMI for Age Percentile Outcome				
Underweight[1]	0.02 (0.01, 0.03)	0.03 (0.02, 0.04)	0.05 (0.03, 0.06)	0.921
Healthy[2]	0.37 (0.30, 0.43)	0.41(0.33, 0.50)	0.78 (0.73, 0.83)	
Overweight[3]	0.03 (0.02, 0.05)	0.04 (0.03, 0.06)	0.07 (0.05, 0.11)	
Obese[4]	0.05 (0.03, 0.08)	0.05 (0.03, 0.08)	0.10 (0.06, 0.15)	

[1]Underweight – BMI - for - age = 0.0 – 4.9th percentile; [2]Healthy weight - BMI - for - age = 5th – 84.9th percentile; [3]Overweight - BMI - for - age = 85th – 94.9th percentile; [4]Obese - BMI - for - age = 95th – 100th percentile.

Table (3b): Estimated population level burden (absolute count) of obese for primary school children by gender in Mashonaland West Province in Zimbabwe, 2015

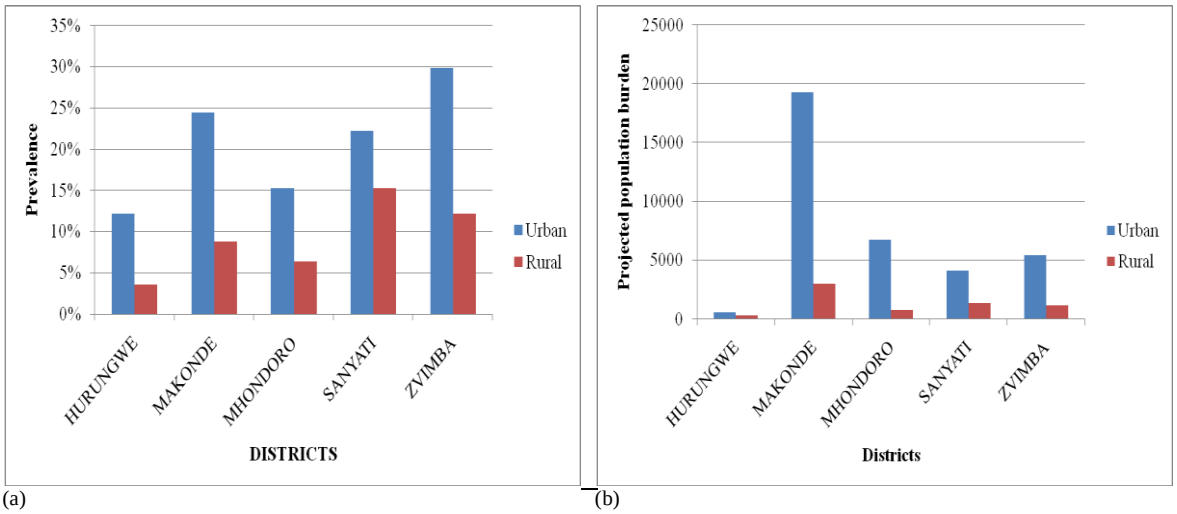
Population (95%CI)	Males(N=111747)	Females(N=127183)	Overall(N=238930)
Body Fat			
Under Fat	48 889 (38 303, 59 473)	38 119 (26 360, 49 879)	87 008(68 858, 105 157)
Healthy	46 346 (26 481, 66 210)	62 646 (38 876, 86 416)	108 992(76381, 141 603)
Over fat	7 364 (4 561, 10 166)	11 595 (7 124, 16 065)	18 959 (12 386, 25 532)
Obese	9 148 (4 327, 13 969)	14 823 (5 285, 24 359)	23 971 (10 198, 37 742)
BMI for Age			
Underweight	5 374 (3 178, 7 568)	6 097 (3 075, 9 118)	11 471 (7 570, 15 370)
Healthy	87 283 (65 434, 109 132)	98 642 (68 030, 129 253)	185925(144811, 226038)
Overweight	8 279 (3 951, 12 606)	10 693 (6 128, 15 258)	18 972 (10 866, 27 078)
Obese	10 811 (4 275, 17 346)	11 751 (4 841, 18 661)	22 562 (10 108, 35 015)

Fig (i) depicts the age specific prevalence and population level burden of overfat/obese by gender. The prevalence increased from age 7 to 9 years among females and significantly decreased at the age of 11 years, 18.6 % (95% CI: 17.5-19.5%) to 27.3% (95% CI: 26- 28.5%) respectively. The prevalence of obese was higher in girls than in boys in each age group except at the age of 10 years and 12 years (27.3% vs 9%).

Fig (i): Age prevalence and population level burden of overfat/obese by gender in Mashonaland West Province, Zimbabwe 2015

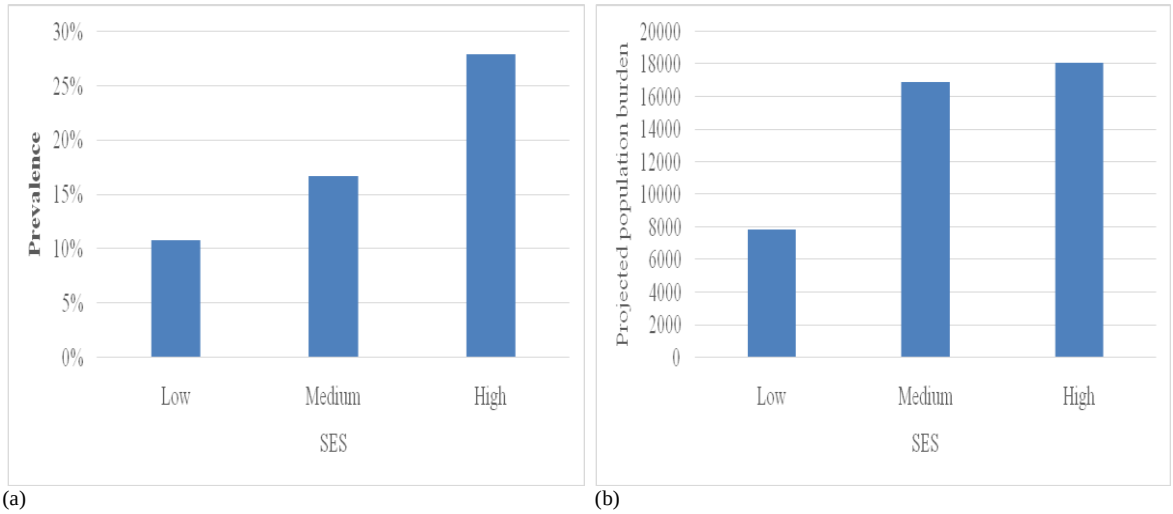
The overall projected number of overfat/obese children aged 8 years were 1 500male and 2 750 female. At the age of 12 years the projected burden significantly increased to 2 300 males and 4 000females.

The population burden of overfat/obese was higher in urban settings. Zvimba district had a high prevalence of overfat/obese in urban areas at 30% as compared to Hurungwe district with the least prevalence of 12% in urban areas and significantly low 4% in rural areas(Fig (ii) a & b). Makonde district had 25% prevalence in urban areas and 8% in rural areas. Makonde district had the highest absolute number of ovefat/obese children in urban area of 19 271 and very low numbers in rural area 3 039. The lowest estimate projected overfat/obese burden was observed in Hurungwe district urban and rural area 616 and 324, respectively. There was an association between prevalence of overfat/obese with socio-economic status of the families as those in high socio-economic status had the highest prevalence of 28%, as compared to 11% in low socio-economic status (p<0.002).The projected population burden of overfat/obese indicated that those in high socio-economic status were 18 110 children were at risk of obesity as compared low income earners with only 7 870 children being overfat/obese (Fig (iii) a & b).



(a) (b)

Fig (ii) District prevalence (a) and projected population burden (b) of overfat/obesity for primary school children in Mashonaland West Province in Zimbabwe, 2015



(a) (b)

Fig (iii): Prevalence (a) and projected population burden (b) of overfat/obese by Monthly income level of the family [P-value=0.002]

DISCUSSION

This was the first cross-sectional study in Zimbabwe to our knowledge to explore the prevalence of obesity among school children aged 6-12 years using the Body fat mass % classification and the Biological Impedance Analysis (BIA) scale. The previous studies conducted on prevalence of childhood obesity are now outdated as they were conducted in 2008or earlier. [11-14] Furthermore relevant studies are now more than 10 years old and may not reflect the rapidly changing nutritional profile and epidemiological transition taking place in developing settings such as Zimbabwe. This study suggests a high burden of overfat/obese in the Mashonaland West Province in Zimbabwe which also showed marked geographic heterogeneity within the province i.e. urban areas having higher burden. Gender difference in body fat mass, MUAC, waist circumference, BMI for age %, hip circumference was observed among the children. Females had higher burden of overfat/obese compared to males. Wealthier children especially in urban settings were significantly at higher risk of being overfat/obese.

The prevalence of overfat/obese found in this study was higher than the previous global prevalence reported for African countries. [5,23] This is probably due to the socioeconomic transitions which has taken place as these studies were conducted a decade ago. The prevalence of overfat/obese found in this study was comparable to that found in previous studies conducted in Tanzania [24] and slightly higher compared to that reported from South Africa. [25,26] Higher prevalence of childhood obesity has been reported from North Africa and other developing and developed countries. [23] Similar findings were reported by [27] in Egypt as they found an overall prevalence of obesity among children from 6-12 years was 13.5% while the overall prevalence of overweight was 17.7%, but using BMI for age classification.

If one extrapolates the projected obesity prevalence observed in the sample to the large provincial population (based on the sampling design/sample weights) there are an estimate 42 930 primary school children in the province who are obese. From a public policy perspective this is a massive problem especially if one considers that this projected absolute burden is one estimated in one province. New policies and more intensive interventions need to be implemented for primordial prevention of childhood obesity. The policy must include the continued assessment of obesity in schools and informing parents on the results on yearly basis for them to be involved on the health of their children.

In this study, prevalence of overfat/obese was higher among females than males. Other studies conducted among children in Africa [5,25] and outside Africa [21] have reported similar gender differences in the prevalence of childhood obesity. The gender difference in percent body fat mass has been reported in other studies, [28-30] and was attributed to the natural differences in distribution of fat between males and females mainly at adolescence stage. The findings are in line with what was found in South African children where there was higher prevalence of overweight and obese among female pupils (17.9% and 4.9% respectively) compared to boys (14% and 3.2% respectively). [25] This further highlight that females need to be targeted i.e. prevention strategies such as reduced dietary fat and energy intake and increased participation in physical activities and sport.

This study found an age-related decrease of obese. Similar findings were found in Zimbabwe and Africa by. [14,24,27,31-33] Monyeki (2008) reported hypertension patterning with obese in rural school children aged 6-13 years of which overweight raised from age 8 years to 9 years for both sexes. [34] A study in Egypt found an age related decrease in the prevalence of obesity the highest at the age 0f 7-8 years (grade 2) and decreased with increase in age, while overweight increased with an increase in age to be the highest at age of 9-10(grade 4) and 10-11 (grade 5).

Waters et al (2008) also found that younger children below 8 years had lower prevalence of overweight/obesity compared with children aged 9-13 years and the difference was statistically significant (p=0.003). [35] This study suggests that for Zimbabwean children at the age of 8 years for males and 9 years for females are crucial for targeting with prevention interventions. These results need to be interpreted with caution as there was considerable variation in the sample size among the age groups with highest at 12 years.

This study found a significant geographical heterogeneity prevalence as Zvimba district and Makonde district, especially in urban areas, had higher prevalence of overfat/obese and a high estimate projected burden of overfat/obese among school children (especially urban Makonde district). This may be due to presence of fast ("junk') food available at school tuck shops run by school development associations as income generating activities in urban school premises. This was supported by findings by [36] on his study on food items consumed by students in south Africa as 70% purchased no healthy food and 73% purchased two or more unhealthy items from school tuck shops. A study in South Africa indicated that urban areas are more obesogenic as many more fast food and street vending outlets are available to school children. [37] The interventions of childhood obesity in this province must be targeted to districts with high burden prevalence's especially in urban schools and policies to be formulated to regulate the selling and vending of unhealthy foods in schools.

Wealthier children especially in urban areas in this study were associated with increased prevalence of obesity. This is in consistent with studies conducted in developing countries [38-40] which demonstrated a strong association between obesity and high socioeconomic status. The results of several studies conducted in developed countries showed an association between low income and poorer families being overfat/obese in developed countries [41] while in developing countries it is opposite as high socioeconomic status of families is associated with increased overfat/obese prevalence, consistent with childhood obesity patterning in developing countries. [40,42-44] This shows the risk of obesity among the urban rich children as they can afford to buy foods with high content of fat, sugary drinks and beverages coupled with sedentary lifestyles of watching TV, using cars and buses going to school as compared to rural children. This makes this group to be a special group to be targeted with compulsory daily physical education.

Limitations

This study had some limitations that need to be taken into consideration. This was not a nationally representative study, but based on one of the ten provinces in Zimbabwe. Research incorporating prevalence's and estimated population level burden of overfat/obese across all provinces in Zimbabwe is recommended.

CONCLUSION

A high burden of overfat and obesity among primary school children was observed in Mashonaland West Province; especially among high income urban families which need planned intervention strategies. Currently childhood obesity prevalence and high risk socio-demographic groups are not being monitored in schools to delineate the magnitude and extent of childhood obesity in schools. More aggressive obesity tackling policies are needed in primary schools if this growing epidemic is to be curbed. We further recommend a similar national wide study be conducted to delineate the full extent of this silent epidemic in Zimbabwe.

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Competing Interests

The authors declare that they have no competing interests.

Authors' contributions

George Kambondo and Benn Sartorius conceived and designed the study. George Kambondo conducted field work and data collection. Benn Sartorius and George Kambondo analysed the data. George Kambondo wrote and compiled the manuscript. Benn Sartorius contributed in the writing of the paper and provided the overall guidance. All others read and approved the final manuscript.

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