

## Estimating Steatosis Prevalence in Overweight and Obese Children: Comparison of Bayesian Small Area and Direct Methods

Hamid Reza Khalkhali<sup>1</sup>, Shahsanam Gheibi<sup>2</sup>, Rasool Gharaaghaji<sup>3</sup>, \*Alireza Didarloo<sup>4</sup>

<sup>1</sup>Associate Professor in Biostatistics, Inpatient's Safety Research Center, Department of Biostatistics and Epidemiology, Urmia University of Medical Sciences, Urmia, Iran. <sup>2</sup>Associate Professor of Pediatric Gastroenterology, Maternal and Childhood Obesity Research Center, Urmia University of Medical Sciences, Urmia, Iran. <sup>3</sup>Associate Professor in Biostatistics, Department of Health and Preventive Medicine, Urmia University of Medical Sciences, Urmia, Iran. <sup>4</sup>Associate Professor in Health Education and Promotion, Solid Tumor Research Center, Department of Health and Preventive Medicine, Urmia University of Medical Sciences, Urmia, Iran.

### Abstract

#### Background

Often, there is no access to sufficient sample size to estimate the prevalence using the method of direct estimator in all areas. The aim of this study was to compare small area's Bayesian method and direct method in estimating the prevalence of steatosis in obese and overweight children.

**Materials and Methods:** In this cross-sectional study, was conducted on 150 overweight and obese children aged 2 to 15 years referred to the Children's digestive clinic of Urmia University of Medical Sciences- Iran, in 2013. After Body mass index (BMI) calculation, children with overweight and obese were assessed in terms of primary tests of obesity screening. Then children with steatosis confirmed by abdominal Ultrasonography, were referred to the laboratory for doing further tests. Steatosis prevalence was estimated by direct and Bayesian method and their efficiency were evaluated using mean-square error Jackknife method. The study data was analyzed using the open BUGS3.1.2 and R2.15.2 software.

**Results:** The findings indicated that estimation of steatosis prevalence in children using Bayesian and direct methods were between 0.3098 to 0.493, and 0.355 to 0.560 respectively, in Health Districts; 0.3098 to 0.502, and 0.355 to 0.550 in Education Districts; 0.321 to 0.582, and 0.357 to 0.615 in age groups; 0.313 to 0.429, and 0.383 to 0.536 in sex groups. In general, according to the results, mean-square error of Bayesian estimation was smaller than direct estimation ( $P < 0.05$ ).

#### Conclusion

The study suggests that estimation of prevalence using Bayesian estimation method via the logistic mixed model was more efficient and better than direct estimation method.

**Key Words:** Children, Iran, Obese, Overweight, Small Area Estimation, Steatosis.

\*Please cite this article as: Khalkhali HR, Gheibi Sh, Gharaaghaji R, Didarloo A. Estimating Steatosis Prevalence in Overweight and Obese Children: Comparison of Bayesian Small Area and Direct Methods. *Int J Pediatr* 2016;4(9):3391-97. DOI: **10.22038/ijp.2016.7377**

#### \*Corresponding Author:

Alireza Didarloo, Solid Tumor Research Center, Department of Health and Preventive Medicine, Urmia University of Medical Sciences, P. O. Box: 57561-15111, Urmia, IR Iran.

Email: didarloo\_a@yahoo.com

Received date Mar 20, 2016; Accepted date: Jul 22, 2016

## 1- INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is called the wide range of liver problems along with obesity in children and adults (1-3). Its microscopic analyses show the simple accumulation of fat (steatosis) or the accumulation of fat along with inflammation and fibrosis (steatohepatitis). The recent finding is called "non-alcoholic steatohepatitis" (NASH) (4). People with obesity, diabetes, hyperlipidemia, severe weight loss, alcoholism are susceptible to NAFLD (5).

For the first time in 1983, Maron et al. described and explained the steatosis and steatohepatitis in obese children.(6) It seems that steatohepatitis has been an increasing trend in parallel to rapid and severe increase of obesity and its related diseases in the last three decades (7).

Tominaga et al. reported fatty liver using ultrasonography at 3% of Japanese children with normal weight and 22% of obese children aged 4 to 12 years (8). Franzese and his colleagues found steatohepatitis at 52.8% of Italian obese children using ultrasonography and also, 13% of cases had high aminotransferase (9). Although fatty liver itself is non-progressive, but patients with Nonalcoholic steatohepatitis (NASH) may develop hepatic progressive disease and cirrhosis (10-11).

Evidence shows that 75% of obese people have NAFLD, and only a few numbers of them, are suffering from NASH (4). In 15% of people with NASH may occur cirrhosis (12). Like adults, NAFLD probably is the most common cause of chronic liver disease in puberty and adolescent groups (7). Although, the status of children's NASH is unclear, but there are different degrees of fibrosis in most of their biopsies. In addition, cirrhosis has been observed in 10-year children (13).

In prevalence studies, suitable sample size was previously determined for estimating prevalence of a disease in the given population. In these conditions, the obtained estimation is called direct estimation method. But researchers usually cannot access to enough sample size to estimate the prevalence of disease in subpopulations or small areas.

Small area can be a small geographical portion such as city, municipality region, etc. or sex and age groups within a large geographical area. It therefore seems that using indirect estimation methods to be helpful in small areas (14).

In this research, we used the logistic linear mixed model with Hierarchical Bayesian approach and direct method to estimate the proportion of steatosis in overweight and obese children. Estimation of prevalence of fatty liver in obese children by Ultrasonography in different areas can be an effective step in evaluating the health status of obese children, and be useful in health policies making.

## 2- MATERIALS AND METHODS

This cross-sectional study was conducted on 150 overweight and obese children referred to the children digestive clinic of Urmia University of Medical Sciences, North West of Iran, in 2013.

Inclusion criteria included:

- Children with 2-15 years old,
- Children had willing to participate to study,
- Children with overweight and obese.

Subjects without the above criteria were excluded from the study. In this study, subjects' weight was measured via the Tefal digital scale made in France (with an accuracy of 100 grams).

Students' height was measured using a tape measure with an accuracy of half a

centimeter. Overweight and obesity were determined in accordance with the criteria developed through the USA center for health statistics in collaboration with the US Chronic Disease Center (CDC) for prevention and health promotion: subjects with BMI > 85<sup>th</sup>, but ≤ 95th percentiles were considered overweight and those with BMI > 95th percentile were considered obese.

Primary tests of disease screening such as the Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) Thyroid Stimulating Hormone (TSH), C-reactive protein (CRP), Complete Blood Count (CBC), Cholesterol (Chol), Triglyceride (TG), Fasting Blood Sugar (FBS), Alkaline Phosphate (ALKP), and Hemoglobin A1c (HbA1c), were performed for overweight and obese children. To identify steatosis in overweight and obese children, a radiologist screened them via abdominal Ultrasonography, and reported subjects with steatosis.

According to residence, the selected samples were categorized into the three groups (District 1, District 2 and out of the city area) in terms in the Training and Education Districts (TED), the four groups (Low, Moderate, High and Out of the city area) in terms in Health Districts (HD). Age, gender and other auxiliary variables were utilized for fitting a logistic mixed model with hierarchical Bayesian approach. The obtained estimations from the mixed model and direct method were compared using Mean Squared Error (MSE) through Jack knife method.

Jackknife is a resampling method to estimate parameter and its standard error. Recently it has been proposed for small area estimation especially for MSE estimation and confidence intervals (15). In statistical approach, the estimation with lower MSE is efficient. The study data was analyzed using the open BUGS3.1.2 and

R2.15.2 software. In all analyses, confidence level was considered 95%. Ethical issues were also considered in all research stages.

### 3-RESULTS

In this study, about 54 and 46% of subjects were boys and girls respectively. Obese and overweight children aged 2-15 years old, had median of 8 and Mean± SD (7.79± 3.9) years.

The frequency distribution of subjects in the TED including: 26.7 % (District 1), 52.6 % (District. 2), and 20.7 % (out of the city area). Based on Health Districts (HD), 19.3%, 26.7%, 33.3%, and 20.7% of subjects were distributed in Low District, Moderate District, High District, and out of city area, respectively. Among 150 subjects, 45.3% of them had steatosis. The findings indicate that there was no statistically significant association between TED and HD with proportion of the disease (P=0.25, P=0.28).

The results also showed that the chance of steatosis in girls was high than boys [OR= 1.85, confidence interval (CI) 95%:1.01-3.75]. There was significant relationship between the age and fatty liver in children (P=0.015), as the chance of fatty liver in children aged 5-10 years was 1.08 (CI 95%: 0.47-2.37) times greater than children less than 5 years. This chance of fatty liver in children more than 10 years was 2.88(CI 95%: 1.24-6.69) times greater than under 5 year group.

**Table.1** portrays frequency distribution of sample size, disease number, and percentage of disease in terms of HD, TED, age and sex groups.

Estimation of disease prevalence was computed through Direct and Bayesian Small Area methods. MSE of estimations also was computed using Jack knife method (**Table.2**).

**Table-1:** The frequency of fatty liver in children according to Districts, Sex and Age Groups

Classification		Girl			Boy		
		Fatty Liver	Sample Size	Percent (%)	Fatty Liver	Sample Size	Percent (%)
Low health District	Less than or equal to 5 years	3	6	50	2	4	50
	Between 5-10 years	1	2	50	0	7	0
	More than 10 years	4	6	66.6	2	4	50
Moderate health District	Less than or equal to 5 years	3	3	100	0	2	0
	Between 5-10 years	1	4	25	5	12	41.6
	More than 10 years	2	10	20	6	9	66.6
High health District	Less than or equal to 5 years	2	5	40	2	7	28.6
	Between 5-10 years	9	13	69.2	1	7	14.3
	More than 10 years	3	5	60	11	13	84.6
Out of the city area	Less than or equal to 5 years	3	3	100	0	9	0
	Between 5-10 years	2	3	66.6	2	6	33.3
	More than 10 years	0	4	0	0	1	0
Education Districts	Less than or equal to 5 years	1	4	25	3	4	75
	Between 5-10 years	3	4	75	2	10	20
	More than 10 years	5	8	62.5	8	10	80
Education District 2	Less than or equal to 5 years	7	10	70	1	9	11.1
	Between 5-10 years	8	15	53.3	4	16	25
	More than 10 years	4	13	30.8	11	16	68.7
Out of the city area	Less than or equal to 5 years	3	6	50	0	9	0
	Between 5-10 years	2	5	40	2	6	33.3
	More than 10 years	4	4	100	0	1	0

**Table-2:** proportion of fatty liver using direct and Bayesian estimation and Jackknife's MSE in overweight and obese children

Classification		Estimation of proportion (Jackknife' CI)			
		Bayesian method		Direct Method	
		Proportion (CI%95)	Jackknife's MSE	Proportion (CI%95)	Jackknife's MSE
Health Districts	Low	0.401 (0.335,0.468)	0.0015	0.414 (0.235,0.605)	0.1214
	Moderate	0.403 (0.353,0.450)	0.0012	0.425 (0.270,0.591)	0.0992
	High	0.493 (0.445,0.547)	0.0013	0.560 (0.412,0.709)	0.0728
	Out of the city area	0.331 (0.255,0.405)	0.0074	0.355 (0.192,0.516)	0.1829
Educational Districts	Area 1	0.502 (0.415,0.589)	0.0022	0.550 (0.375,0.727)	0.0743
	Area 2	0.399 (0.348,0.450)	0.0010	0.443 (0.331,0.559)	0.0962
	Out of the city area	0.331 (0.255,0.405)	0.0074	0.355 (0.192,0.516)	0.1829
Age group (year)	Less than or equal to 5	0.321 (0.235,0.405)	0.0053	0.357 (0.216,0.501)	0.1799
	Between 5-10	0.329 (0.245,0.415)	0.0042	0.375 (0.229,0.524)	0.1853
	More than 10	0.582 (0.535,0.625)	0.0008	0.615 (0.491,0.747)	0.0529
Gender	Boy	0.313 (0.225,0.405)	0.0061	0.383 (0.257,0.509)	0.1883
	Girl	0.492 (0.442,0.542)	0.0008	0.536 (0.412,0.657)	0.0782

CI: confidence interval.

#### 4- DISCUSSION

In recent years, the use of small areas estimation methods to estimate parameters has been increased in studies with small sample size (16). The purpose of the study was to compare Bayesian Small Area and Direct Method in Estimating Steatosis prevalence in overweight and obese children. According to the results, MSE in estimating prevalence of steatosis in terms of TED, HD, age- gender groups using of Bayesian estimation was more effective than direct estimation. There were no studies to compare these two methods in estimating steatosis prevalence in children. Small area estimation methods were conducted on other health challenges in studies. The study of Tohidnejad et al. (2014) conducted in Bushehr province highlighted that synthetic method in estimating prevalence of symptoms of mental disorders in high school students was better than direct and post-stratified methods (17). Mohammadzadeh et al. (2013) was estimated the prevalence of

chronic pain on the 368 neighborhoods of Tehran. They reported that hierarchical Bayesian approach estimation was reliable in comparison with generalized linear mixed model (18). Schneider et al. (2009) used synthetic regression estimation technique to estimate county-level prevalence of recent mammography (past 2 years) for women aged 40 to 79 years, in the contiguous United States, in 2009. They found Small-area estimation is advantageous in comparison with direct estimates for surveillance of mammography (19). Lee et al. (2010) utilized a Bayesian multilevel regression model with bivariate outcomes to predict school-level prevalence of serious emotional disturbance in the sample of 282 schools that participated in the National Comorbidity Survey Replication Adolescent Supplement, in USA (20). Zhang et al. (2011) used a combination of hierarchical modeling and synthetic estimation techniques to estimate County-Level Prevalence of Obesity in

Mississippi. In this research, they used auxiliary variables (height, weight, age, race, gender, education level, employment status, household income and marital status) to estimate obesity prevalence. They pointed out that this model was capable to estimate prevalence of County-Level Prevalence of Obesity with good accuracy (21). Zarei et al. (2007) used two methods of Empirical hierarchical Bayesian and best linear unbiased prediction (as small areas estimators) with direct method to estimate the average household income in the province of Lorestan, Khorasan, Hamedan and Tehran. The results generally showed the hierarchical Bayesian approach in contrast with two empirical Bayesian approach and direct estimators (22). Direct and small areas estimation methods have showed various efficient in different health topics. Hence, it is not claimed the priority of one method in estimating parameters. In each study, one of estimation method is appropriate based on auxiliary variables, number of areas, the prevalence of event (23, 24).

#### **4-1. Limitations of the study**

This research like other investigations has a number of limitations. Firstly, of this study is that the results can be generalized only to similar samples and not beyond. Secondly, lack of similar studies for supporting and confirming the present study findings.

#### **5. CONCLUSION**

The study highlighted the importance of two estimation methods in estimating prevalence of steatosis in overweight and obese children. As, small area's Bayesian approach showed its predominant efficiency compared to direct estimation method. It is recommended that clinicians and researchers applied small area estimation methods for different subjects

with small the sample size in subpopulations.

#### **6- CONFLICT OF INTEREST**

The authors have no conflicts of interest to declare for this study.

#### **7-ACKNOWLEDGMENT**

This paper has been elicited from a research project and approved by research council of Urmia University of Medical Sciences. Hereby, the authors would like to thank the financial support of vice Chancellor for research and technology.

#### **8- REFERENCES**

1. Kinugasa A, Tsunamoto K, Furukawa N, Sawada T, Kusunoki T, Shimada N. Fatty liver and its fibrous changes found in simple obesity of children. *J Pediatr Gastroenterol Nutr* 1984; 3: 408–14.
2. Strauss RS, Barlow SE, Dietz WH. Prevalence of abnormal serum aminotransferase values in overweight and obese adolescents. *J Pediatr* 2000; 136:727–33.
3. Alison GH. Obesity. In: Walker WA, Sherman PM, Goulet O, et al (editors). *Pediatric Gastrointestinal Disease*. 4 th ed. Hilton (on): BC Decker; 2004. 311-30.
4. Baldrige AD, Perez-Atayde AR, Graeme-Cook F, Higgins L, Lavine JE. Idiopathic steatohepatitis in childhood: a multicenter retrospective study. *J Pediatr* 1995; 127:700-4.
5. American Gastroenterological Association Medical Position Statement: Nonalcoholic Fatty Liver Disease. *Gastroenterology* 2002; 123:1702–1704.
6. Moran JR, Ghishan FK, Halter SA, Greene HL. Steatohepatitis in obese children: a cause of chronic liver dysfunction. *Am J Gastroenterol* 1983; 78: 374-7.
7. Patton HM, Sirlin C, Behling C, Middleton M, Schwimmer JB, Lavine J. Pediatric Nonalcoholic Fatty Liver Disease: A Critical Appraisal of Current Data and Implications for Future Research. *Journal of*

8. Pediatric Gastroenterology and Nutrition 2006; 43(4): 413-27.
9. Tominaga K, Kurata JH, Chen YK, Fujimoto E, Miyagawa S, Abe I, et al. Prevalence of fatty liver in Japanese children and relationship to obesity. An epidemiological ultrasonographic survey. *Dig Dis Sci* 1995; 40: 2002-9.
10. Saviano M.C, Brunetti F, Rubino A, Franzese A, Vajro P, Argenziano A, et al. Liver involvement in obese children. Ultrasonography and liver enzyme levels at diagnosis and during follow-up in an Italian population. *Dig Dis Sci* 1997; 42:1428-32.
11. Matteoni CA, Younessi ZM, Gramlich T, et al. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. *Gastroenterology* 1999; 116:1413-19.
12. Powell EE, Cooksley W.GE, Hanson R, Searle J, Halliday JW, Powell LW. The nature of nonalcoholic steatohepatitis: a follow up study of forty-two patients for up to 21 years. *Hepatology* 1990; 11(1):74-80.
13. Fishbein MH, Miner M, Mogren C, Chalekson J. The spectrum of fatty liver in obese children and the relationship of serum aminotransferases to severity of steatosis. *J Pediatr Gastroenterol Nutr* 2003; 36: 54-61.
14. Rashid M, Roberts EA. Nonalcoholic steatohepatitis in children. *J Pediatr Gastroenterol Nutr* 2000; 30: 48-53.
15. Rao JNK. *Small Area Estimation*. Led. New Jersey: John Wiley & Sons; 2003.
16. Rao JNK. Jackknife and Bootstrap Methods for Variance Estimation from Sample Survey Data. *International Journal of Statistical Sciences* 2009; 9(Special Issue):59-70.
17. Rao JNK. Some New Developments in Small Area Estimation. *JIRSS* 2003; 2(2): 145-69.
18. Tohidnejad E, Soltanian A.R, Roshanaei G. Comparison of Small Area Techniques for Estimating Prevalence of Mental Disorder Symptoms among Iranian's Southern Adolescents. *J Res Health Sci* 2014; 14(2): 146-51.
19. Mohammadzadeh F, Faghihzadeh S, Baghestani AR, Asadi Lari M, Vaez Mahdavi MR, Arab Kheradmand J, et al. Epidemiology of Chronic Pain in Tehran; Small Area Estimation of its Prevalence in Tehran Neighborhoods by Bayesian Approach (Urban HEART-2 study). *Iranian Journal of Epidemiology* 2013; 9(1): 19-31.
20. Schneider KL, Lapane KL, Clark MA, Rakowski W. Peer Reviewed: Using Small-Area Estimation to Describe County-Level Disparities in Mammography. *Preventing chronic disease* 2009; 6(4):1-10.
21. Li F, Green JG, Kessler RC, Zaslavsky AM. Estimating prevalence of serious emotional disturbance in schools using a brief screening scale. *International journal of methods in psychiatric research* 2010; 19(S1):88-98.
22. Zhang Z, Zhang L, Penman A, May W. Peer Reviewed: Using Small-Area Estimation Method to Calculate County-Level Prevalence of Obesity in Mississippi, 2007-2009. *Preventing chronic disease* 2011; 8(4):1-11.
23. Zarei Sh, Gerami A, Jafari Khaledi M. Small Area Estimation of the Mean of Household's Income in Selected Provinces of Iran with Hierarchical Bayes Approach. *JSRJ* 2007; 4(1):71-90.
24. Ugarte Martinez MD, Goicoa Mangado T, Fernandez Militino A, Sagaseta Lopez M. Estimating unemployment in very small areas. *Sort: Statistics and Operations Research Transactions* 2009; 33(1):49-70.
25. Jia H, Muennig P, Borawski E. Comparison of small-area analysis techniques for estimating county-level outcomes. *Am J Prev Med* 2004; 26(5):453-60.