

Original Article

Identification of emotional and behavior problems in obese children using Child Behavior Checklist (CBCL) and 17-items Pediatric Symptom Checklist (PSC-17)

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Abstract

Background Obesity can result in emotional and behavior problems in school-age children. Child Behavior Checklist (CBCL) is a standard instrument for evaluating behavior problems, however it is considered not practical. The 17-item Pediatric Symptom Checklist (PSC-17) is a more simple instrument but its diagnostic value has never been evaluated in obese children.

Objectives To evaluate the diagnostic value of PSC-17 compared to CBCL as the gold standard.

Methods This cross-sectional study was done in May - June 2009. Children aged 6-12 years with obesity were included. Parents filled the CBCL and PSC-17 questionnaires. Sensitivity, specificity, predictive values, and likelihood ratios were calculated for PSC-17.

Results Most subjects aged 6-9 years (83%). Boys outnumbered girls. Emotional and behavior problems detected by CBCL and PSC-17 were identified in 28% and 22% subjects, respectively. The most common problem was internalization (withdrawal, somatic complaints, anxiety/depression). The PSC-17 had sensitivity and specificity of 69.2% and 95.6% respectively. Positive and negative predictive values were 85.7% and 89%, whereas positive and negative likelihood ratios were 15.7 and 0.32.

Conclusions The prevalence of emotional and behavior problems detected using CBCL and PSC-17 in obese children was 28% and 22%, respectively. The PSC-17 has moderate sensitivity to screen emotional and behavior problem in obese children. [Paediatr Indones. 2010;50:42-8].

Keywords: obesity, emotional problem, CBCL, PSC-17

Obesity is a pandemic, with more than a billion people affected worldwide.¹ Data from The International Obesity Task Force (IOTF) indicated that 22 million of the world's children under 5 years of age are overweight or obese.² In Indonesia, as well as worldwide, there has been an increase in the number of obese children.³ Susanti reported that in 2007, 15.3% of school-age children in five districts in Jakarta were obese.⁴

Obesity has physical and psychosocial impacts, which can influence the growth and development.⁵ There is growing evidences addressing the psychological impact of obesity, especially among school-age children.⁵⁻⁷ Previous studies indicated that the process of stigmatization could explain an association between obesity with psychological disorders. A stigmatized person possesses some attribute or

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characteristic that conveys a social identity that is devalued in some particular context.⁶⁻⁷ Obesity that is not treated early will result in psychological distress in relationships with peers, parents, and teachers; emotional distress manifested as low self esteem, aggressive behavior, suicide, promiscuity, drug and alcohol abuse; and unhealthy behavior such as extreme dieting, skipping meals, and prolonged TV watching.⁸

The CBCL has been widely used as a standard measure of emotional and behavior problem in children, including those with obesity.⁹ Other screening tool is the 17-items Pediatric Symptom Checklist (PSC-17), designed specifically for use by pediatrician to screen for mental health problems in children. The PSC-17 is short, easy to use, and practical. However, to our knowledge, there has been no study evaluating the diagnostic value of PSC-17 in childhood obesity.⁹⁻¹⁰ Research of psychosocial impact of childhood obesity in Indonesia is limited. The purpose of this study was to evaluate the diagnostic value of PSC-17 compared to CBCL as the gold standard.

Methods

This was a cross-sectional study conducted in May-June 2009 at the Menteng 01 elementary school, Jakarta. Children aged 6-12 years old with obesity as defined by body mass index above the 95th percentile were included.

Each parent of the obese children completed a demographic questionnaire, the CBCL, and the PSC-17. Information gathered included child sex and age, parental education, family income, family size, history of parental mental illness, and parental divorce. The CBCL consisted of 118 items that described specific emotional and behavioral problems. Parents rated their children for how true each item was at that time or within the past 6 months using the following scale: 0, not true; 1, somewhat or sometimes true; 2, very true or often true. A syndrome score is the sum of scores on all items included in the syndrome scale as defined by Achenbach.⁹ The following syndromes were analyzed: withdrawn, somatic complaints, anxious/depressed, which form the internalizing group; social problems, thought problems, and attention problems, which are not part of either the

internalizing or externalizing grouping; and delinquent behavior and aggressive behavior, which form the externalizing group. Raw scores were converted to normalized T scores. T scores of 60 or higher were within the clinical referral range.

The PSC-17 was a 1-page, parent-completed questionnaire with 17 items that screened for childhood behavioral problems. The PSC-17 is a short form of the PSC with three subscales measuring common childhood attention, externalizing (i.e., "disruptive behavior"), and internalizing (i.e., depression and anxiety) problems. Parents rated the frequency of behaviors and symptoms listed as "never", "sometimes", or "often". This responses are given 0, 1, or 2 points, respectively. A total score is calculated by adding the individual values for each item. This total score then is compared with a cut off (internalization ≥ 5 , externalization ≥ 7 , attention ≥ 7 , and total score ≥ 15).¹⁰

Demographic characteristics of the study population were determined. Descriptive analyses were used to examine the association of demographic characteristic/risk factors with positive result of CBCL. The diagnostic value (sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio) of PSC-17 were calculated using the CBCL as the gold standard.

Results

During the study period, 94 eligible children were included. Most subjects aged 6-9 years (83%) and were male (61%) (**Table 1**). Most mother had moderate educational level (86.2%), but most father had high educational level (86.2%). More than two third (68.1%) of the respondents had moderate to high income. Most of the family size was less than 4 (80.8%). There was no history of parental mental illness or divorce among all subjects.

Table 2 presents the results of CBCL examination. Based on this instrument 26 of 94 (28%) children had emotional and behavior problems (24/26 and 8/26 on internalization and externalization scales, respectively). The proportion of male and female with emotional and behavior problems was 28% and 27% respectively.

The PSC-17 detected 21 of 94 (22%) children

had emotional and behavior problems (17/21 and 2/21 on internalization and externalization, respectively).

Table 1. Subjects' characteristics

Characteristic	n=94	%
Age, mean (range), years	8.9(6-12.6)	
Sex		
Male	57	61
Female	37	39
Age group		
6-9 years	78	83
10-12 years	16	17
Respondent		
Mother	91	97
Other	3	3
Father education		
Low	0	0
Moderate	13	14
High	81	86
Mother education		
Low	0	0
Moderate	15	16
High	79	84
Family income		
Low	0	0
Low moderate	30	32
High moderate	43	46
High	21	22
Family size		
< 4	76	81
≥ 4	18	19
Parent divorce		
Yes	0	0
No	94	100
History of parental mental illness		
Yes	0	0
No	94	100

The proportion of male and female with emotional and behavior problems by this questionnaire was 23% and 22% respectively (Table 3).

The most common emotional and behavior problems detected using the CBCL was somatic complaints (10 of 26) followed by withdrawal, anxiety/depression, social problems, and aggression (7 of 26). Attention and delinquency problems were found in five and one subjects, respectively.

The risk factors of emotional and behavior problem in obese children was evaluated. As shown in Table 4, based on bivariate analysis, age group, father and mother education, family income, and family size were significantly associated with emotional and behavior problems. However based on multivariate analysis, only age group and parents' education were significantly associated with emotional and behavior problem in obese children (Table 5).

The multistage multivariate analysis revealed the following regression equation:

$$y = -2.98 + 2.49 \text{ fathers' education} + 2.36 \text{ mothers' education} + 1.44 \text{ income} + 2.63 \text{ family size},$$

with "y" as the dependent variable (emotional and behavior problems in obese children); "a" as a constant. Independent variables was scored 1 for yes and 0 for no.

We calculated the diagnostic value of PSC-17 using the CBCL as the gold standard. The PSC-17 had sensitivity of 69.2% and specificity of 95.6%. Positive

Table2. Prevalence of emotional and behavior problems based on CBCL

Characteristics	Sex		Total	%
	Male n=57	Female n=37	n=94	
No problems	41	27	68	72
Emotional & behavior problems	16	10	26	28
Internalization (n=26)	16	8	24/26	-
Externalization (n=26)	5	3	8/26	-
Total score (n=26)	14	6	20/26	-

Table3. Prevalence of emotional and behavior problems based on the PSC-17

Characteristics	Sex		Total	%
	Male n=57	Female n=37	n=94	
PSC-17				
No problems	44	29	73	78
Emotional & behavior problems	13	8	21	22
Internalization (n=21)	10	7	17/21	-
Externalization (n=21)	1	1	2/21	-
Total score (n=21)	4	1	5/21	-

Table 4. Factors associated by emotional and behavior problems in obese children

Characteristics	Problems (+) n = 26	Problem (-) n= 68	Odds ratio	P	95%CI *
Sex					
Male (n = 57)	16	41	1.05	0.912	0.42-2.7
Female (n = 37)	10	27			
Age group					
10-12 years (n=16)	9	7	2.28	0.005	1.42-3.49
6-9years (n=78)	17	61			
Father education					
Low-moderate (n=13)	11	2	4.57	<0.001	2.91-7.17
High (n=81)	15	66			
Mother education					
Low-moderate(n=15)	13	2	5.26	<0.001	3.38-8.33
High (n=79)	13	66			
Family income					
Low - low moderate (n=30)	19	11	5.79	<0.001	3.67-9.02
High moderate – high (n=64)	7	57			
Family size					
≥ 4 (n=18)	14	4	9.15	<0.001	5.81-14.29
<4 (n=76)	12	64			
Parent divorce					
Yes (n=0)	0	0	-		-
No (n=94)	26	68			
History of parental mental illness					
Yes (n=0)	0	0	-		-
No (n=94)	33	61			

*CI 95% = confidence interval 95%

Table 5. Multivariate analysis of associated factors on emotional and behavior problems in obese children

Variables	b*	S.E. *	Wald	df*	P	OR*	95%CI
Fathers' education	2.49	1.07	5.44	1	0.020	12.1	1.5-98.1
Mothers' education	2.36	1.06	4.97	1	0.026	10.6	1.3-84.0
Family income	1.44	0.74	3.82	1	0.051	4.2	1.0-18.0
Family size	2.63	0.83	10.10	1	0.001	13.8	1.2-70.0
Constant	-2.98	0.55	29.32	1	0.000	0.1	

*b = regression coefficient

*SE = standard error

*df = degree of freedom

*OR = odds ratio

and negative predictive values were 85.7% and 89%, whereas positive and negative likelihood ratio were 15.7 and 0.32, respectively (Table 6).

Discussion

This was the first study in Indonesia evaluating the emotional and behavior problems in obese children using the CBCL and PSC-17 questionnaires. The prevalence of emotional and behavior problems detected by the CBCL was 28%, which was similar to that reported by Myers et al¹² (29%), although they only evaluated children aged 8-12 years. However the prevalence found in this study was lower than that was found by Rekk's¹³ study which reported a prevalence

of 46.6% among 30 subjects. The different result was probably caused by different sample size (they used only 30 subjects) so it may not represent the real condition. In this study, the prevalence detected by PSC-17 was 22% that was higher than that was found by a study in Solo (11.6%) using PSC-35 as the diagnostic tool.¹¹ It might be caused by difference type of tools and their interpretation. They used PSC-35 which defined that emotional and behavior problems only based on the total score, while PSC-17 is more detail because that consists of subscale internalization, externalization, and attention score to define the problem. One of the limitations of this study was that there was no control of non-obese children so that we could not conclude whether obesity increased the likelihood of emotional and behavior problems in children or not.

The most common type of emotional and behavior problems found in this study was the somatic complaints (10 of 26 children), followed by withdrawal, anxiety or depression, social problems and aggressive behavior. Similar findings were found by studies in Germany¹³ and French.¹⁴ This suggested that internalization problems were dominant, probably because at this school age, social cognitive process appears and children starts to have stigmatization as well as body dissatisfaction. The acceptance or internalization of a set of values (distortion of body image and stigmatization, for example) could result in withdrawal, anxiety, depression, and somatic problems. At this age, children also start to feel shame and develop pride that can affect how they value themselves.^{9,15}

In this study, externalization (delinquency and aggressive behavior) problems were only found in 8 children, which was similar to that was reported by Bradley et al¹⁶ Flodmark¹⁷ found an association between body mass index and externalization problems on obese children following a weight reduction program.

Depression can occur secondarily to obesity. Obese children tend to have a wish for ideal body proportion and feel frustrated because they can not achieve it. It also can occur due to body image distortion that they do not see themselves as the real they, so they do not realize how fat they are.¹⁸ A study reported that anxiety or depression is the most common problems found in obese children.¹⁸ Other emotional and behavior problems found are self-withdrawal which expresses lack of confidence and attention deficit disorders reflecting anxiety or missed expectation which results in confusion or difficulty to concentrate on a particular task.¹⁹

Previous studies reported several factors affecting the development of emotional and behavior problems in obese children, which are sex, age, low socioeconomic level, parental divorce, parental education, history of mental illness in parents, and family size.^{11,14,20-23} In a study on normal weight population, Garnezy et al²⁴⁻²⁵ found that males have greater risk of developing emotional and behaviour problems compared to females. However, studies on obese children reported various results. In this study, we did not found different prevalence of emotional and behaviour problems between boys and girls, which was similar to that reported by a study in French which evaluated obese children aged 5-17 years.¹⁴

On bivariate analysis, we found that age group of 10-12 years old was significantly associated with emotional and behavior problems (OR=2.28; 95%CI 1.42;3.49), but on multivariate analysis the association was not statistically significant. Stradmeijer et al²⁶ who examined children aged 10-16 years old also found that the prevalences among age groups were not statistically different. The limitation of this study was the age of the subjects was not distributed evenly.

All the respondents of this study had moderate to high educational level so they could fill the questionnaire appropriately. According to Achenbach, CBCL is best applied for parents who are at least senior high-school graduated. In this study, moderate educational level (senior high school graduated) in either father or mother seemed to be a risk factor for emotional and behaviour problems in obese children compared to high educational level (OR=24.2; 95%CI 4.8 to 120.8) and OR=33; 95%CI 6.6 to 164.0 for fathers' and mothers' education, respectively). It might due to that parents with lower educational level had less knowledge about good parenting practice including how to deal appropriately with emotional and behaviour problems of their children. The result was similar to that was found by Garnezy et al²⁴⁻²⁵ on normal child population, but it was different from a study in Solo¹¹ which revealed that low educational level was not a risk factor of emotional and behavior problems in obese children. The different result was probably caused by different diagnostic instrument (they used the PSC-35 questionnaire) and classification of parental education. In that study, high-school graduated parents were considered to have high educational levels while in our study, they were classified as low to moderate educational level.

In studies on normal child population, socio-economic level as reflected by family income is associated with the occurrence of emotional and behavior problems. This was also shown by this study which found that obese children with low family income had higher risk of having emotional and behavior problems compared to those with moderate to high family income (OR 14.1; 95%CI 4.8 to 41.4). Parents with low income often feel anxious and depressed and these would cause them to be less responsive and attentive to their children. The children intern could have depression, low self-esteem, and academic as well as behavior problems.

The finding of this study was similar to previous studies which found that poverty was a risk factor for emotional and behavior problems in children.^{22,25}

Another risk factor for emotional and behavior problems found in this study was the family size, in which children with four or more family members were more often to have emotional and behavior problems (OR 18.7; 95%CI 5.2 to 66.5). It might be caused by less time and attention given by parents who have to divide their time and attention to many things and people. The result was similar to a study by Seifer et al.²³ However, a study in Solo¹¹ found different results which might be due to the uneven distribution of family size among subjects, only four of 146 subjects who had family members of more than three.

In this study, no subjects had history of parental divorce. School-age children will be very anxious if their parents have divorce because of the fear or being neglected and rejected. However a complete but inharmonious or conflicting family also would cause problems in the children.¹⁵ A previous study²⁴ found a correlation between parental divorce and emotional and behaviour problems in children, while the Solo¹¹ study reported that obese children who were not grown by their mothers had more risk to experience emotional and behaviour problems (OR 8.81; 95% CI 1.1 to 70.6).

History of parental mental illness is correlated by emotional and behaviour problems in their children.^{12,24} In this study, no children had history of parental mental illness although it was not evaluated by standard instrument, such as *Symptoms Checklist-90* (SCL-90) which was the limitation of our study. Some researchers reported that mothers with psychological problems tend to report that the children have problems too.²⁴⁻²⁵ On multivariate analysis, we found that family size of more than four and parents' educational level was significantly associated with emotional and behaviour problems in obese children.

The CBCL questionnaire is a standard tool for evaluating emotional and behaviour problems in children including those with obesity, so we used it as the gold standard to find out the diagnostic value of PSC-17 questionnaire. In this study we found that the sensitivity of PSC-17 was 69.2% (95%CI 48.2 to 85.7%). It meant that the PSC-17 could detect 69.2% obese children who had emotional and behaviour problems. The specificity of PSC-17 found in this study was 95.6% (95%CI 87.6 to 99.1%), which meant that it

would give negative results in 95.6% of children who did not have emotional and behaviour problems.⁷¹ These results were similar to those of previous studies²⁷⁻²⁸ who found the sensitivity and specificity of PSC-35 around 71.7-74% and 93-94%, respectively. The PSC-17 is a simplification of PSC-35 with reduced number of questions from 35 to 17, however the sensitivity and specificity is almost the same.

The positive predictive value of PSC-17 found in this study was 85.7% (95%CI 63.7 to 97%) which meant that if a child had positive test then the probability of him/her to have emotional and behavior problems would be 85.7%. The negative predictive value of PSC-17 was 89%. The predictive values are fluctuative and depend on disease prevalence. Since it was found after the result of a diagnostic test is known, it is called the posterior probability.

The positive likelihood ratio of PSC-17 found in this study was 15.7 (95%CI 5.04-48.9), meaning that it would reveal positive results in children with emotional and behavior problems 15.7 times more than in those without emotional and behaviour problems. With this high likelihood ratio, the PSC-17 was a good test for differentiating children who had emotional and behaviour problems from those who had not.²⁹

Other limitation of this study was the cross-sectional design that could not always show clear temporal relationship between risk factors and the effects. Because of that, we can not make a clear-cut conclusion whether obesity was really the cause of emotional and behaviour problems in our subjects.

In conclusion, the prevalence of emotional and behavior problems detected using CBCL and PSC-17 in obese children is 28% and 22%, respectively. The PSC-17 has moderate sensitivity for screening emotional and behavior problems in obese children and a good likelihood ratio to differentiate children who have problems from those who do not. Somatic problem is the most common emotional and behaviour problems found in obese children. Risk factors for emotional and behaviour problems in obese children are low to moderate educational level of the fathers or mothers and family size of more than four. To obtain better results regarding risk factors of emotional and behaviour problems in obese children, we recommend further studies with cohort design and more accurate measurement of parents' mental illness as one of possible risk factor.

References

1. Kimm SYS, Obarzanek E. Childhood obesity: a new pandemic of the new millenium. *Pediatrics*. 2002;110:1003-7.
2. Thibault H, Rolland-Cachera MF. Prevention strategies of childhood obesity. *Arch Pediatr*. 2003;10:1100-8.
3. Sjarif DR. Obesitas pada anak dan permasalahannya. *Hot topics in pediatrics II*. Prosiding Pendidikan Kelanjutan Berkala Ilmu Kesehatan Anak XV; 2002 Feb 18-19; Jakarta, Indonesia. Jakarta: Balai Penerbit Universitas Indonesia, 2002; p. 219-34.
4. Susanti TE. Prevalensi dan faktor risiko obesitas pada anak sekolah dasar usia 10-12 tahun di lima wilayah DKI Jakarta [tesis]. Jakarta: Universitas Indonesia; 2007.
5. Janssen I, Craig WM, Boyce WF, Pickett W. Association between overweight and obesity with bullying behaviors in school-age children. *Pediatrics*. 2004;113:1187-94.
6. Puhl RM, Brownell KD. Psychosocial origins of obesity stigma: toward changing a powerful and pervasive bias. *Obes Rev*. 2003;4:213-27.
7. Schwimmer JB, Burwinkle T.M, Varni, JW. Health-related quality of life of severely obese children and adolescents. *JAMA*. 2003;289:1813-9.
8. Mellin AE, Neumark-Sztainer D, Story M, Ireland M, Resnick MD. Unhealthy behaviors and psychosocial difficulties among overweight adolescents: The potential Impact of familial factors. *J Adolesc Health*. 2002;31:145-53.
9. Achenbach TM. Manual for child behavior checklist/ 4-18 and 1991 profile. Burlington: University of Vermont, Department of Psychiatry; 1991.
10. Jellinek MS, Murphy JM, Robinson J, Feins A, Lamb S, Fenton T. Pediatric Symptom Checklist: screening school-age children for psychosocial dysfunction. *J Pediatr*. 1988;112:201-9.
11. Muhammad R, Endang DL, Suci M, Dwi H, Sri M. Prevalensi dan beberapa faktor yang memengaruhi gangguan psikososial pada anak obes usia sekolah dasar di Kotamadya Surakarta. *Cermin Dunia Kedokteran*. 2007;34:304-6.
12. Myers MD, Raynor HA, Epstein LH. Predictors of child psychological changes during family-based treatment for obesity. *Arch Pediatr Adolesc Med*. 1998;152:855-61.
13. Reck UK, Korsten K, Haeberle K, Hauschild KK, Dickhuth HH, Schulz E. The psychosocial situation of obese children: psychological factors and quality of life. *Psych Res Behav Manage*. 2009;2:23-9.
14. Vila G, Zipper E, Dabbas M, Bertrand C, Robert JJ, Ricour C, Mouren-Simeoni MC. Mental disorders in obese children and adolescents. *Psychosom Med*. 2004;66:387-94.
15. Psychosocial development in middle childhood. In: Papalia DE, Olds SW, Feldman RD, editors. *Human development*. 10th ed. New York: Mc-Graw-Hill, 2007; p. 354-90.
16. Bradley RH, Hours R, Nader PR, O'Brien M, Belsky J, Crosnoe R. The relationship between body mass index and behavior in children. *J Pediatr*. 2008;153:629-34.
17. Flodmark CE. The happy obese child. *Int J Obes*. 2005;29:531-3.
18. Epstein LH, Klein KR, Wisniewski L. Child and parent factors that influence psychological problems in obese children. *Int J Eat Disord*. 1994;15:151-8.
19. Hastings PD, Zahn-Waxler C, Robinson J, Usher B, Bridges D. The development of concern for others in children with behavior problems. *Dev Psychol*. 2000;36: 531-46.
20. Wardle J, Cooke L. The impact of obesity on psychological well-being. *Best Pract Res Clin Endocrinol Metab*. 2005;19:421-40.
21. Stunkard AJ, Sorensen TIA. Obesity and socioeconomic status—a complex relation. *N Engl J Med*. 1993;329: 1036–7.
22. Costello EJ, Keeler GP, Angold A. Poverty, race/ethnicity and psychiatric disorder: a study of rural children. *Am J Public Health*. 2001;91:1494–8.
23. Seifer R, Sameroff AJ, Baldwin CP, Baldwin A. Child and family factors that ameliorate risk between 4 and 13 years of age. *J Am Acad Child Adolesc Psychiatry*. 1990;31:893-903.
24. Rae-Grant N, Thomas H, Offord RD, Boyle MH. Risk, protective factors, and prevalence of behavioral and emotional disorders in children and adolescents. *J Am Acad Child Adolesc Psychiatry*. 1989;28:262-8.
25. Jensen PS, Bloedau L, Degroot J, Ussery T, Davis H. Children at risk: I. Risk factors and child symptomatology. *J Am Acad Child Adolesc Psychiatry*. 1990;29:51-9.
26. Stradmeijer M, Bosch J, Koops W, Seidell J. Family functioning and psychosocial adjustment in overweight youngsters. *Int J Eat Disord*. 2000;27:110–4.
27. Reijneveld SA, Vogels AG, Hoekstra F, Crone MR. Use of the Pediatric Symptom Checklist for the detection of psychosocial problems in preventive child healthcare. *BMC Public Health*. 2006;6:197.
28. Jutte DP, Burgos A, Mendoza F, Ford CB, Huffman LC. Use of the Pediatric Symptom Checklist in a low-income, mexican american population. *Arch Pediatr Adolesc Med*. 2003;157:1169-76.
29. Madiyono B, Moeslichan S, Sastroasmoro S, Budiman I, Purwanto H. Perkiraan besar sample. In: Sastroasmoro S, Ismael S, editors. *Dasar-dasar metode penelitian klinis*. 2nd ed. Jakarta: CV Sagung Seto, 2002; p. 259-87.