Obesity and the Risk of Breast Tumors in Indonesian Women Based on Clinical Breast Examination

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ABSTRACT

Obesity in women is often associated with breast cancer. Obese women are at greater risk of breast cancer even though many other factors also influence the degree of risk. This analysis aimed to determine the role of obesity and overweight in breast tumor risk among Indonesian women who participated in the 2016 Non-Communicable Diseases Research Project in Indonesia. This research used a cross-sectional survey design, with national urban representation. We selected households by multi-stage sampling. Each selected household was assigned one woman who met the criteria using the Kish table. The number of subjects analyzed were 37,984 people, aged 25-64 years. Breast tumor was examined by clinical breast examination by trained health personnel. Data were analyzed using chi square and logistic regression. After controlling for several sociodemographic and reproductive variables and history of individual and family cancers, abdominal obesity was a breast tumor protection factor (OR = 0.803; 95% CI 0.698-0.922, p = 0.002). Abdominal obesity is a protective factor that plays a role in breast tumors in women aged 25-64 years in Indonesia. Women, especially those who have not entered menopause, are still encouraged to do regular physical activity to maintain an ideal body weight for optimal general health.

Keywords: Obesity, Breast tumor, Non-communicable disease

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Introduction

Obesity is often associated with the incidence and prognosis of breast cancer in women. Obesity is not always associated with breast cancer, but studies on breast cancer often include an obese variable as one of the factors assessed in terms of both genetics and fat tissue stores in obesity[1,2]. The relationship between obesity and breast cancer is explained in several ways. One opinion, based on a literature review, states that obesity only plays a role as a cause of breast cancer in menopausal women, whereas in women who have not yet been through the menopause, obesity is a protective factor[3]. Another opinion states that adipose fat stores are associated with non-density lesions, but these non-density lesions are not associated with breast cancer[4]. Fat deposits promote inflammation that can trigger tumors and cancer, especially in menopausal women[2,5]. In addition, an argument sometimes mentioned is that insulin-like growth factor (IGF) plays a role in the relationship between obesity and breast cancer[6].

Other factors contributing to breast cancer include individual characteristics, race, reproductive factors, a history of cancer in individuals and families, long-term consumption of hormonal drugs and various other factors[7]. Another previous study also assessed the relationship of variables that are almost the same as breast cancer in women in Saudi Arabia[8]. The factors mentioned above can be determined through interviews and measurements, but there are still factors that are obtained only through endocrinology and hematology laboratory tests such as IGF, human epidermal growth factor receptor 2 (HER2) and other markers. The purpose of this study was to determine the role of obesity and overweight on breast tumors assessed through clinical breast examination in Indonesian women who participated in the 2016 Non-Communicable Disease (NCD) Research Project.

Materials and Methods

The NCD research was conducted by the National Institute of Health Research and Development (NIHRD) of the Indonesian Ministry of Health in 2016. This analysis is a part of the NCD research. The NCD research results have been reported descriptively in the project report[9]. The research was carried out in 34 provinces. Two to four districts or cities which met the urban criteria were selected in each province; 76 districts/cities were designated as implementation locations. This research used a cross-sectional survey design, with national urban representation. Households were selected by multistage sampling. The first step was to choose districts by probability proportional to size (PPS) of

the urban household. The second step was to choose census blocks by PPS of common households. The third step was to choose 50 census buildings by systematic sampling. The fourth step was to choose the selected household by random sampling within the census building. In each selected household, one eligible woman was selected using the Kish table and included in this survey[9].

Originally, NCD research assessed breast tumor and pre-cervical cancer lesions, therefore we used the smallest proportion for calculating the minimum sample size. Based on that calculation, 70,000 subjects were needed. The inclusion criteria were women aged 25-64 years, not pregnant and not breastfeeding in the 0-4-month period after the infant was born. The exclusion criteria were women who suffered from very severe physical illnesses, and who were therefore not expected to be able to attend the examination site[9].

The enumerator team visited selected households then verified and selected the eligible subjects. Interviews and measurements of height and weight were carried out at home. After that, subjects were invited to visit the examination site in the Community Health Care Center (CHC) (Puskesmas) or the Sub-Community Health Care Center (SCHC) (Pustu) for clinical breast examination (CBE). The examination was carried out in a special and closed room. CBE examiners were female general practitioners, midwives or female nurses who had received special training from the Ministry of Health. The subjects were classified as having a breast tumor if the results of CBE were positive. A positive result was the detection of potentially cancerous lumps in the breast and its surrounding tissues (including the lymph nodes in the armpit)[9].

Subjects gave their written informed consent to participate in the study before the interview and examination. This study obtained ethical clearance from the Ethics Committee of NIHRD (number LB.02.01 / 5.2 / KE.154 / 2016). The data were obtained through interviews and examinations then written on a questionnaire sheet. The leader of the enumerator team then checked the data. After that, the data were entered into a computer using the CS Pro program. Data entry was carried out at the survey location. After the data entry processing was finished, data were sent to the central data management of the National Institute of Research and Development (NIHRD) in Jakarta using electronic mail. The data management team proceeded with cleaning and coding procedures. The author team proposed the objective of the work published here to the Director General (DG) of NIHRD, and then the central data management team provided the dataset.

For the purposes of analysis, we grouped several variables. Age was grouped by 10-year intervals. There are two types of obesity, namely obesity which is assessed by measuring abdominal circumference and obesity measured by body mass index (BMI). Abdominal obesity is defined as an abdominal circumference >80 cm[10]. Obesity according to BMI was based on the criteria of the International Obesity Task Force (IOTF), WHO 2000 for adults in Asia, as follows: BMI <18.5 kg/m^2 is underweight, BMI 18.5-22.9 kg/m^2 is normal weight, BMI 23.0-24.9 kg/m^2 is overweight, and BMI ≥25.0 kg/m^2 is obese[11]. Peri-menopause was defined as the stage of a woman's life where menstruation had begun to be irregular, while menopause was defined as the stage where menstruation had not occurred for 12 months or more and was not caused by the use of contraception. Subjects who had experienced hysterectomy were grouped into menopausal groups. Having been pregnant was defined as a pregnancy that ended in childbirth or miscarriage. Using contraception was defined as the use of ingredients or methods continuously for some time which aimed to prevent conception and pregnancy. Household Ownership Index was defined as a prediction of economic status obtained from composite questions, and some ownership of durable goods in a family. The number of children was the number of children born either alive or stillborn. Family history of cancer was defined as having a 1st to 3rd degree relative who had been diagnosed with cancer[12]. The dependent variable in this analysis was breast tumors examined by CBE. In this analysis, inflammation was categorized as CBE negative.

Chi square was carried out to assess the association of breast tumor with obesity and several other variables. Variables that had Chi square *p*-value of less than 0.25 were included into the multiple binary logistic regression analysis. Statistical analyses were carried out using SPSS version 21, with the complex sample method.

Results

From 43,035 subjects, 5,051 were not examined. These were respondents who had not attended CHC or SCHC (Puskesmas or Pustu) for reasons such as not being in the place, working, having other needs on that day, refusing to be examined, etc. The final analyzed dataset included the data of 37,984 subjects, from whom complete data for all variables had been collected. There were no differences between those examined and not examined in certain variables (p>0.05), as disseminated in the study report[9]. Of the 37,984 examined, 2,983 (7.8%) subjects had breast tumors. The sociodemographic characteristics of the subjects are illustrated in Table 1.

Table 1 Relationship between general characteristics of women and breast tumors

Characteristics	Total		CBE Positive		p^a
	n	%	n	%	
Total	**37,984**	**100.0**	**2983**	**7.9**	
Age (years)					0.002
25-34	8,411	22.1	650	7.7	
35-44	13,397	35.3	1,101	8.2	
45-54	11,099	29.2	910	8.2	
55-64	5,077	13.4	322	6.3	
Education					0.006
Low	12,839	33.8	965	7.5	
Moderate	20,938	55.1	1,624	7.8	
High	4,207	11.1	394	9.4	
Occupation					0.001
Unemployed/student	24,025	63.3	1,822	7.6	
Employee	4,557	12.0	403	8.8	
Entrepreneur	4,655	12.3	395	8.5	
FFL	3,279	8.6	234	7.1	
Other	1,468	3.9	129	8.8	
Marital status					0.001
Never married	450	1.2	58	12.9	
Married	34,529	90.9	2,702	7.8	
Divorced	3,005	7.9	223	7.4	
Economic status					0.597
Low	7,142	18.8	599	8.4	
Low moderate	9,152	24.1	716	7.8	
Moderate	6,179	16.3	490	7.9	
Moderate high	7,640	20.1	606	7.9	
High	7,871	20.7	572	7.3	
Health insurance					0.309
National health insurance	22,002	57.9	1,736	7.9	
Private insurance	1,546	4.1	127	8.2	
None	14,436	38.0	1,120	7.8	

CBE: Clinical breast examination; FFL: Farmer, Fisherwoman, Laborer; [a] Chi-square test

Table 1 shows the subjects who took part in the study were mostly aged 35-44 years, had attained secondary education, namely graduating junior high school to senior high school, and were not working (i.e. they were housewives and students). In general, the subjects were married and almost 60% had national health insurance. Economic status did not seem to differ much in each group. Factors of age, education, work and marital status had a strong relationship with breast tumors.

In this study, drinking alcohol, smoking, history of having a uterine myoma, removal of an ovary and age of menarche did not have a significant relationship with breast tumors (Table 2). Around 70% and 50% of subjects were obese based on their abdominal circumference and BMI, respectively. A large proportion, around 50%, of subjects had never done breast self-examination.

Table 2 Biological and personal characteristics associated with breast tumors

Characteristics	Total		CBE Positive		p^a
	n	%	n	%	
Total	**37,984**	**100.0**	**2,983**	**7.9**	
Menopausal (included peri and post)					0.001
Yes	9,296	24.5	623	6.7	
No	28,688	75.5	2,360	8.2	
Abdominal obesity					0.001
Yes	26,877	70.8	1,995	7.4	
No	11,107	29.2	988	8.9	
BMI					0.017
Thin	1,534	4.0	131	8.5	
Normal	16,259	42.8	1,394	8.6	
Overweight	6,347	16.7	481	7.6	
Obese	13,844	36.4	977	7.1	
Ever had breast surgery					0.001
Yes	242	0.6	55	22.7	
No	37,742	99.4	2,928	7.8	

[a] Chi-square test

Table 2 Biological and personal characteristics associated with breast tumors (cont.)

Characteristics	Total		CBE Positive		p^a
	n	%	n	%	
Had family member with cancer					0.001
Yes	3,133	8.2	338	10.8	
No	34,459	90.7	2,596	7.5	
Drank alcohol					0.222
No	37,965	99.9	2,980	7.8	
Yes	19	0.1	3	15.8	
Was a smoker					0.593
Everyday	750	2.0	59	7.9	
Often	626	1.6	45	7.2	
Past smoker everyday	214	0.6	17	7.9	
Past smoker often	766	2.0	59	7.7	
Never	35,628	93.8	2,803	7.9	
Was a passive smoker					0.099
Everyday	12,866	33.9	941	7.3	
Often	13,603	35.8	1,116	8.2	
Never	10,139	26.7	822	8.1	
Ever had myoma uteri					0.435
Yes	835	2.2	83	9.9	
No	37,149	97.8	2,900	7.8	
Had ovariectomy					0.298
Yes	528	1.4	54	10.2	
No	36,446	96.0	1,919	5.3	
Used birth control					0.001
Never	11,672	30.7	1,040	8.9	
Non hormonal	6,501	17.1	517	8.0	
Hormonal	19,811	52.2	1,426	7.2	

[a] Chi-square test

Table 2 Biological and personal characteristics associated with breast tumors (cont.)

Characteristics	Total		CBE Positive		p^a
	n	%	n	%	
Breast self-examination history					0.001
Never	21,770	57.3	1,590	7.3	
Normal	15,345	40.4	1,103	7.2	
Wound	112	0.3	15	13.4	
Infection	777	2.0	275	35.4	
History of individual cancer					0.001
Never	37,531	98.8	34,643	92.3	
Endometrial/cervical cancer	57	0.2	54	94.7	
Breast and/ovarian cancer	305	0.8	220	72.1	
Other	92	0.2	85	92.4	
Number of children					0.001
None	3,028	8.0	347	11.5	
1-2	16,728	44.0	1,332	8.0	
3-4	13,783	36.3	1,028	7.5	
>4	4,445	11.7	276	6.2	
Age of menarche (years)					0.575
<9	21	0.1	1	4.8	
≥9	37,963	99.9	2,982	7.9	
Pregnancy					0.001
Ever	36,341	95.7	2,786	7.7	
Never	1,532	4.0	196	12.8	
Breastfeeding					0.001
Ever	31,770	83.6	2,329	7.3	
Never	6,214	16.4	654	10.5	

[a] Chi-square test

Based on bivariate analysis, from 17 variables that met the criteria, eight variables had $p>0.05$. These variables were occupational status, marital status, drinking alcohol, passive smoking, having been pregnant, obesity based on BMI, perimenopause/menopause, and having breast surgery.

In multivariate analysis there were nine variables; the results are shown in Table 3. No confounding variables were found. In the final stage, modeling was done by including interaction variables, namely abdominal obesity with obesity based on BMI. The results showed that there were no interactions between the two variables (p = 0.776). R-square values ranged from 22-52%. Abdominal obesity was a breast tumor protection factor, after controlling for several variables such as sociodemographic factors, reproductive factors, history of individual cancer and family cancers (AOR = 0.803, 95% CI 0.698-0.922; p = 0.002). Other factors that were found to have a significant relationship with breast tumors include age, education, history of cancer in individuals and families, number of children, breastfeeding, self-examination, and the use of hormonal contraception.

Table 3 Multiple binary logistic regression analysis of variables associated with breast tumors

Variable	Estimated	95% CI		p^a
	AOR	LL	UL	
Age (years) (25-34 [ref])				
35-44	1.28	1.09	1.49	0.020
45-54	1.31	1.10	1.58	0.017
55-64	1.05	0.84	1.37	0.112
Education (High [ref])				
Moderate	0.98	0.81	1.18	0.555
Low	1.16	0.93	1.43	0.068
Abdominal obesity (No [ref])	0.80	0.70	0.92	0.002
Have family member with cancer (No [ref])	1.63	1.35	1.95	0.000
History of individual cancer (No [ref])				
Endometrial/cervical cancer	0.32	0.10	1.09	0.043
Breast and/or ovarium cancer	2.88	1.58	5.23	0.000
Other	1.85	0.71	0.83	0.061

ref. = reference; AOR, Adjusted Odds Ratio; CI, Confidence Interval; LL, Lower Limit; UL, Upper Limit, [a] Likelihood Ratio Test

Table 3 Multiple binary logistic regression analysis of variables associated with breast tumors (cont.)

Variable	Estimated	95% CI		p^a
	AOR	LL	UL	
Number of children (5+ [ref])				
3-4	1.34	1.08	1.67	0.06
1-2	1.19	0.96	1.47	0.03
None	1.22	0.84	1.76	0.19
Breast self-examination (Normal [ref])				
Wound	1.29	0.54	3.06	0.021
Tumor	5.52	4.26	7.15	0.000
Never	1.01	0.89	1.15	0.217
Breastfeeding (Ever [ref])	1.30	1.07	1.57	0.009
Birth control practice (Never [ref])				
Non hormonal	0.96	0.81	1.14	0.287
Hormonal	0.83	0.72	0.95	0.002

ref. = reference; AOR, Adjusted Odds Ratio; CI, Confidence Interval; LL, Lower Limit; UL, Upper Limit. [a] Likelihood Ratio Test

Discussion

Based on these study results, obesity based on BMI was not associated with breast tumors, while abdominal obesity was a breast tumor protection factor even though the association was not large (AOR = 0.803). Obesity is mainly associated with breast cancer, especially in women in all stages of menopause (including peri- and post-menopause). This association was explained by an animal study; when the ovaries of the rats were removed (oovorectomy), the weight of the rats increased. In that case, the type of tumor in the obese rats was positive for estrogen receptor (ER positive). In menopausal women, the ovaries are almost non-functional and will interfere with the body's metabolic processes which ultimately lead to weight gain[13].

In this analysis, abdominal obesity was a protective factor in relation to breast tumors. The differing result, in contrast with the literature, may be explained by the method used to measure the dependent variable. In this research, the dependent variable was

a tumor or lump in the breast which was assessed based on CBE, while the literature generally links the risk factors for obesity with breast cancer, namely tumors that have been analyzed and confirmed by examination of anatomical pathology containing malignant cells. Results of this study are also slightly different from the results of previous studies. One study stated that obesity, measured by BMI, smoking, and menarche were risk factors for the development of breast cancer[8]. Obesity is associated with breast cancer, especially in women who are in the phases of menopause[3]. The analysis in this paper does not distinguish the condition of obesity in menopausal or non-menopausal women, but our data showed that 75% of subjects were not in the stages of menopause. The interpretation of these results must also consider the limitations of a cross-sectional research design.

More than 50 percent of subjects had abdominal obesity. It can be explained by food consumption and physical activity. Obesity is often associated with poor consumption of carbohydrates and excessive fat and eating less than the recommended amounts of vegetables and fruit, but this is not easy to prove. During interviews about food consumption, people will tend to mention healthy foods and hide high-calorie foods[14]. Based on national basic health research from 2018, 33.5% of Indonesia's adult population had low physical activity[15].

Abdominal obesity is more of a risk factor for NCD, especially cardiovascular diseases and type 2 diabetes versus general obesity assessed by BMI[11, 16]. IGF associated with obesity, especially abdominal obesity, is related to insulin-like growth factor binding-protein 1 (IGFBP). IGF inhibitors work so that low IGFBP levels are predictors of type 2 diabetes mellitus, especially in people with abdominal obesity[16]. One opinion also indicates that the relationship between obesity and cancer depends on region, as only weak relationships between obesity and cancer have been found in the Asia-Pacific Region[11]. The risk of breast cancer from obesity because of race or poor diet has the same potential risk[17].

The most dominant factor contributing to breast tumors, based on this analysis was self-examination that detected lumps (AOR = 5.52). It can be understood that if a woman finds a lump in her breast, a health worker will find the same thing. Early examination is highly recommended in the prevention of cancer in women[18]. The self-breast examination is the simplest screening tool but should be complemented by more sophisticated screening, for example by ultrasonography and mammography. Women's compliance with more sophisticated screening is largely determined

by the ownership of health insurance and race. Racial factors are associated with socio-economic abilities besides health insurance[19,20]. Other factors that cause women not to do screening include shame, fear, forgiveness, etc[21].

Factors of age, education, number of children, breastfeeding children, use of hormonal drugs to prevent pregnancy, and individual and family history of cancer showed almost the same results as previous studies[22,23]. After the age of 50 years, the risk of developing cancer increases. In the USA, mammography is required for women aged 40 years and above because from this age, risk is assumed to increase[24]. Low education is associated with greater risk than higher education. Having more than one child and breastfeeding are protective factors. The use of hormonal drugs, especially for contraceptive purposes is linked to greater risk[22]. Previous history of having breast and/or ovarian cancer and/or a blood relative that has had cancer increases the risk of having a positive outcome[23]. Individual history of having ovarian and breast cancer resulted in an AOR of 2.8. This is in line with other literature which states that ovarian and colorectal cancers are associated with breast cancer. Hereditary factors also play a role in this study, namely people who had a family member with cancer were at greater risk of developing breast tumors[23]. A history of having had breast cancer surgery did not show a significant association with breast tumors. It might be because any affected person had already recovered.

This research was conducted nationally with a large sample size. The limitation of the study was that it was only carried out in urban areas and outputs assessed such as breast tumors still require confirmation with a higher examination such as mammography, ultrasonography and biopsy.

Conclusion

Abdominal obesity was found to be a protective factor that played a role in breast tumors in women aged 25-64 years in Indonesia. This result should be interpreted whilst considering other factors such as the characteristics of respondents and methodology of the study. Abdominal obesity is a condition that can be modified. By doing enough physical activity, obesity will be prevented and reduced[25,26]. Due to the role of obesity in relation to breast cancer in menopausal women, more physical activity is recommended for women to maintain their body weight from a young age. Besides that, both active and passive smoking should be avoided. BMI should also be maintained within the ideal range by consuming a healthy and balanced diet.

Author Contributions

SI and TAJ proposed the data. SI drafted the manuscript and analyzed the data. DFM and WP completed and translated the manuscript. All authors read and approved the manuscript prior to submission for publication.

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Conflicts of Interest

The authors declare they have no conflict of interests regarding the publication of this article.

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