https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 1-6
e-ISSN 2830-506X
p-ISSN 2830-6007

The Relationship between Lipid Profile and Breast Parenchymal Density From Mammography Examination

Dewangga Yudisthira[1]*, Agung Setyawan [2], Yuyun Yueniwati P.W[3]
1. Bachelor Student of Medical Faculty Universitas Brawijaya Malang
2. Radiologist of Radiology Department of Universitas Brawijaya Malang
3. Radiologist of Radiology Department of Universitas Brawijaya Malang
*Corresponding Author Email Address: dewanggay369@student.ub.ac.id

Abstract

Breast cancer is a type of cancer that has the highest incidence and mortality rate in the world and in Indonesia among other cancers. One of the causes of death due to breast cancer is influenced by poor prognosis due to cancer's late detection. One method of early detection is mammography. Mammography is an examination method to detect cancer cells and assess breast density, which is a risk factor for breast cancer. Reporting the results of breast density types uses the BI-RADS grading, which is divided into 4 categories. Breast density is influenced by various factors, one of which is the lipid profile (triglycerides, total cholesterol, LDL, and HDL). This study used an analytic observational method with a cross-sectional study design. The samples were members of Dharma Wanita group of Universitas Brawijaya and female members of the Indonesian Radiographers Association in Malang from October 2021 to January 2022. The data was analyzed using the non-parametric chi-square test. The results of each component of the lipid profile showed p-values ($p < 0.05$) = 0.172, 0.619, 0.226, 0.829, for triglycerides, total cholesterol, LDL, and HDL, respectively. This means all lipid profile components do not have a significant relationship with the density of the breast parenchyma.

Keywords: *Lipid profile, Breast Density, Mammography*

INTRODUCTION

Breast cancer is the most common type of cancer and a deadly disease in women. Breast cancer is known to have the highest incidence rate when compared to other cancers, both in the world and in Indonesia.[1,2] The incidence ratio of breast cancer in Indonesia for women is 42.1/100,000 population with an average mortality of 17/100,000 population.[2] Death due to breast cancer is influenced by various factors, one of which is related to the detection of breast cancer[3,4]

One of the methods of early detection of breast cancer that is both sensitive and valid is mammography.[5] Mammography is an examination method using X-ray modalities to find cancer cells before the appearance of lumps in breast tissues and assess breast density, which is a risk factor for breast cancer.[6] Breast density is the ratio between the fatty tissue and the stromal and epithelial breast tissue, which can be analyzed by mammography. Reporting the results of breast density type uses the BI-RADS grading, which is divided into 4 categories[6].

The categories of breast density are divided into; 1) The breast is composed of almost entirely fatty tissue, 2) there are scattered areas of dense glandular and fibrous tissue, 3) most of the breast is made of dense glandular and fibrous tissue (described as a heterogeneous solid), 4) the breasts are very dense, consisting of glandular and dense fibrous tissue (extremely dense).[7]

Breast density is influenced by several factors, such as genetics, age, BMI, premenopausal status, menarche, and lipid levels.[8] The components of lipid levels are total cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL).[9] Triglyceride is an independent source for fatty acid oxidation, an important process that promotes cell

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 1-6
e-ISSN 2830-506X
p-ISSN 2830-6007

proliferation and tumor growth.[10] In addition, excessive levels of circulating lipids can affect cholesterol transport processes. Cholesterol, through its metabolite, 27-OHC (27-Hydroxycholesterol), has a role to increase the rate of cancer cell division and decrease the inhibitory action of abnormal cell growth.[11] LDL-C promotes the proliferation and migration of cancer cells. In addition, the accumulation of cholesterol esters due to increased internalization and esterification of LDL-C has been associated with breast cancer proliferation.[12] Another component of lipid levels, HDL-C levels, is compared inversely with insulin growth factor 1 (IGF-1), which acts as a marker associated with increased breast density.[13] However, research that discusses the relationship between breast density and lipid profile is still very limited.

According to the description above, the authors are interested in learning more about the relationship between lipid profile and breast parenchymal density from mammography examination.

METHODS

This study used an analytic observational design with a cross-sectional study design. The samples used are in the form of primary data involving the results of the type of breast parenchymal density through mammography examination and lipid profile through laboratory examination. This study was conducted at the Radiology Installation of Saiful Anwar Hospital, Malang from October 2021 to January 2022.

In this study, the population was all members of the Dharma Wanita group of Universitas Brawijaya and female members of the Indonesian Radiographers Association in Malang. This study has inclusion and exclusion criteria as follows.

1. Inclusion Criteria:
    a. Participants who are willing to take part in the study.
    b. Female participants aged > 40 years.
    c. There is a report on the results of the lipid profile examination.
2. Exclusion Criteria:
    a. Research participants who cannot have mammography examinations.
    b. Invalid mammography results which cannot be interpreted.
    c. Invalid lipid profile test results which cannot be interpreted

Data collected from this study was processed using the Statistical Product and Service Solution (SPSS) 26 program and analyzed for different tests using the non-parametric chi-square test.

RESULTS AND DISCUSSION

The research data was obtained from 33 research subjects who performed mammography examinations at the Radiology Installation, Saiful Anwar Hospital, Malang City, and laboratory examinations of lipid profiles.

Based on the characteristics of the samples obtained, there were 33 samples of whom were all women (100%) of various ages, with the majority being in the range of 51–60 years, which can be seen in Table 1.

Table 1. Characteristics of Research Subjects (N = 33)

Characteristics		n (%)
Sex	Female	33 (100%)
Age (years)	41–50	11 (33.33%)
	51–60	20 (60.60%)
	> 60	2 (6.06%)

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 1-6
e-ISSN 2830-506X
p-ISSN 2830-6007

Lipid Profile (mg/dL)		Median (*Range*)
Triglycerides		127 (353–53)
Total Cholesterol		213 (287–165)
LDL		144 (217–90)
HDL		56 (81–41)
Breast Density	Type A	2 (6.06%)
	Type B	11 (33.33 %)
	Type C	17 (51.51 %)
	Type D	3 (9.1 %)

Table 1 shows the results of the study in the form of lipid profiles, consisting of triglycerides, total cholesterol, LDL, and HDL, with the addition of parenchymal density, which is divided into 4 types: A, B, C, and D.

Based on Table 1 in the age characteristics, most of the research subjects are 51–60 years, accounting for 20 samples (60.6%), followed by those aged 41–50 years with 11 samples (33.3%), and those > 60 years old as many as 2 samples (6.06%). Based on the table, it was found that data on triglyceride levels has a median of 127 (353–53), total cholesterol of 213 (287–165), LDL of 144 (217–90), and HDL of 56 (81–41). The results of the breast density examination show that most of the samples (17) have a type C breast density (51.51%).

The results of the data in this study were analyzed using the SPSS Statistics 26 program. The method used in data analysis was chi-square. This method was used for each component of the lipid profile of the density type of breast parenchyma. Each lipid profile variable was divided into 2 groups, namely: 1) Lowest Level - Median Level and 2) Above Median Level - Highest Level. In addition, the breast parenchymal density variable was also divided into 2 groups according to the parenchymal density level, namely: 1) Type A and Type B; 2) Type C and Type D.

The following are the results of the analysis obtained through the SPSS program:

Table 2. Analysis of the Relationship between Lipid Profile and Breast Density

Lipid Profile		**Breast Density**		***p****
		Type A - B	Type C - D	
Triglycerides	≤ 127 mg/dL	9	9	0.172
	> 127 mg/dL	4	11	
Total Cholesterol	≤ 213 mg/dL	6	11	0.619
	> 213 mg/dL	7	9	
LDL	≤ 144 mg/dL	5	12	0.226
	> 144 mg/dL	8	8	
HDL	≤ 56 mg/dL	7	10	0.829
	> 56 mg/dL	6	10	

*Significant if $p < 0.05$

Based on Table 2, it was found that the result of the chi-square statistical test between triglycerides and breast parenchymal density is not significantly different, with a p-value = 0.172. This shows that there is no significant relationship between triglycerides and breast parenchymal density.

https://ijri.ub.ac.id/
International Journal of Radiology and Imaging. 01 (02). 30 Desember 2022: 1-6
e-ISSN 2830-506X
p-ISSN 2830-6007

Chi-square analysis of the total cholesterol component with breast parenchymal density obtains a p-value of 0.619. The results of the analysis show that there is no significant relationship between total cholesterol and breast parenchymal density. In Table 2, the results of the chi-square statistical test between LDL and breast parenchyma density also show no significant difference, with a p-value = 0.226. Similar results are also obtained in the analysis between HDL and the density of breast parenchyma with a p-value of 0.829 according to Table 2.

According to the analysis of the research data carried out, it was found that there is no significant relationship between triglycerides and breast parenchymal density (p-value = 0.172; significant if $p < 0.05$). This is in accordance with two previous studies.[6,14] Research conducted by Lucht (2019) stated that there is no significant relationship between triglyceride levels and breast parenchymal density because triglycerides—which have a role in the transport and regulation of adipose fat and glucose—are only associated with BMI.[6] This is also in line with research conducted by Sung (2011), which found similar results in Korean women.[14] However, different results were found in a study conducted by Tamburrini (2010), which noted that there was a negative correlation between triglyceride levels and breast parenchymal density in women who drank more than one bottle of alcohol per day; meanwhile, in women who did not drink alcohol, there was no relationship.[15]

In the analysis of total cholesterol, it was found that there is no significant relationship between total cholesterol and breast parenchymal density (p-value = 0.619; significant if $p < 0.05$). The results of this study are similar to the results of research conducted by Sung (2011).[14] Research conducted by Tamburrini also mentioned the same results. This is because cholesterol is a poor predictor in studies conducted to measure breast parenchymal density due to genetic involvement and the results are speculative and vary from one patient to another.[15] This genetic variation also causes differences in the results of a study conducted by Kim (2015), in addition to ethnic variations, which show a positive correlation between total cholesterol levels and breast parenchymal density.[16]

In this study, the results reveal that LDL does not have a significant relationship with breast parenchymal density (p-value = 0.226; significant if $p < 0.05$). These results are in accordance with research conducted by Sung (2011), which pointed out that there was no correlation between LDL and breast parenchymal density.[14] Research conducted by Tamburrini (2011) also provided the same results, especially in the postmenopausal female population.[15] However, another study conducted by Boyd (1995) showed that LDL was inversely related to breast parenchymal density because patients who had not undergone menopause had higher parenchymal density and estrogen levels.[17]

The results of the analysis of the relationship between HDL and breast parenchymal density show that there is no significant relationship between the two (p-value = 0.829; significant if $p < 0.05$). These results are in accordance with those found in research conducted by Lucht (2019) and Kim (2015).[6,16] This is because HDL has no significant effect on body mass index (BMI).[6]

Different results were found in a study conducted by Flote (2015), which suggested an inverse relationship between HDL levels and breast parenchymal density in women with low HDL levels and low sex hormones.[18] This situation will stimulate the growth of epithelial and stromal tissues. The same results were also shown in a study conducted by Tehranifar (2015) where HDL was associated with breast density in pre-menopausal women and influenced the incidence of breast cancer.[19]

The difference in results related to the relationship between HDL levels and breast

parenchymal density can be answered by a study conducted by Conroy (2011), which found no significant correlation between the two. This difference is caused by the lack of adequate adjustment for confounding variables, such as BMI and abdominal adipocytes.[20]

CONCLUSION

According to the results of the study that has been carried out, it can be concluded that there is no significant relationship between lipid profiles (triglycerides, total cholesterol, LDL, and HDL) and breast parenchymal density from mammography examinations performed on members of Dharma Wanita group of Universitas Brawijaya and members of the community of Indonesian Radiographers Association in Malang.

This study has potential limitations, which are the limited number of samples and uncontrolled confounding factors, which can affect the research results.

REFERENCE

1. Waks AG, Winer EP. Breast Cancer Treatment: A Review. *JAMA - Journal of the American Medical Association* 2019;321:288–300. https://doi.org/10.1001/jama.2018.19323.
2. Komite Penanggulangan Kanker Nasional. *PANDUAN PENATALAKSANAAN KANKER PAYUDARA*. 2018.
3. Caplan L. Delay in breast cancer: Implications for stage at diagnosis and survival. *Frontiers in Public Health* 2014;2. https://doi.org/10.3389/fpubh.2014.00087.
4. Dewi TK, Massar K, Ardi R, Ruiter RAC. Determinants of early breast cancer presentation: a qualitative exploration among female survivors in Indonesia. *Psychology and Health* 2020. https://doi.org/10.1080/08870446.2020.1841765.
5. Winters S, Martin C, Murphy D, Shokar NK. Breast Cancer Epidemiology, Prevention, and Screening. *Progress in Molecular Biology and Translational Science*, vol. 151, Elsevier B.V.; 2017, p. 1–32. https://doi.org/10.1016/bs.pmbts.2017.07.002.
6. Lucht SA, Eliassen AH, Bertrand KA, Ahern TP, Borgquist S, Rosner B, et al. Circulating lipids, mammographic density, and risk of breast cancer in the Nurses' Health Study and Nurses' Health Study II. *Cancer Causes and Control* 2019;30:943–53. https://doi.org/10.1007/s10552-019-01201-2.
7. Balleyguier C, Ayadi S, van Nguyen K, Vanel D, Dromain C, Sigal R. BIRADSTM classification in mammography. *European Journal of Radiology* 2007;61:192–4. https://doi.org/10.1016/j.ejrad.2006.08.033.
8. Norman F. Boyd. Mammographic Density: A Heritable Risk Factor for Breast Cancer 2009;472. https://doi.org/10.1007/978-1-60327-492-0.
9. Restiviona R, Yoel C, Sianturi P. Hubungan Profil Lipid dan Derajat Keparahan Penyakit berdasarkan Skor Pediatric Logistic Organ Dysfunction-2 pada Anak dengan Sepsis. vol. 20. 2019.
10. Lofterød T, Mortensen ES, Nalwoga H, Wilsgaard T, Frydenberg H, Risberg T, et al. Impact of pre-diagnostic triglycerides and HDL-cholesterol on breast cancer recurrence and survival by breast cancer subtypes. *BMC Cancer* 2018;18. https://doi.org/10.1186/s12885-018-4568-2.

11. Garcia-Estevez L, Moreno-Bueno G. Updating the role of obesity and cholesterol in breast cancer. *Breast Cancer Research* 2019;21. https://doi.org/10.1186/s13058-019-1124-1.
12. Cedó L, Reddy ST, Mato E, Blanco-Vaca F, Escolà-Gil JC. HDL and LDL: Potential New Players in Breast Cancer Development. *Journal of Clinical Medicine* 2019;8:853. https://doi.org/10.3390/jcm8060853.
13. SUN W-Y, YUN H-Y, SONG Y-J, KIM H, LEE O-J, NAM S-J, et al. Insulin-like growth factor 1 receptor expression in breast cancer tissue and mammographic density. *Molecular and Clinical Oncology* 2015;3:572–80. https://doi.org/10.3892/mco.2015.497.
14. Sung J, Song YM, Stone J, Lee K, Kim SY. High-density lipoprotein cholesterol, obesity, and mammographic density in korean women: The healthy twin study. *Journal of Epidemiology* 2011;21:52–60. https://doi.org/10.2188/jea.JE20100078.
15. Tamburrini AL, Woolcott CG, Boyd NF, Yaffe MJ, Terry T, Yasui Y, et al. Associations between mammographic density and serum and dietary cholesterol. *Breast Cancer Research and Treatment* 2011;125:181–9. https://doi.org/10.1007/s10549-010-0927-7.
16. Kim BK, Chang Y, Ahn J, Jung HS, Kim CW, Yun KE, et al. Metabolic syndrome, insulin resistance, and mammographic density in pre- and postmenopausal women. *Breast Cancer Research and Treatment* 2015;153:425–34. https://doi.org/10.1007/s10549-015-3544-7.
17. Boyd NF, Byng JW, Jong RA, Fishell EK, Little LE, Miller AB, et al. Quantitative Classification of Mammographic Densities and Breast Cancer Risk: Results From the *Canadian National Breast Screening Study*. 1995.
18. Flote VG, Frydenberg H, Ursin G, Iversen A, Fagerland MW, Ellison PT, et al. High-density lipoprotein-cholesterol, daily estradiol and progesterone, and mammographic density phenotypes in premenopausal women. *Cancer Prevention Research* 2015;8:535–44. https://doi.org/10.1158/1940-6207.CAPR-14-0267.
19. Tehranifar P, Protacio A, Schmitt KM, Desperito E, Oskar S, Potter AJ, et al. The metabolic syndrome and mammographic breast density in a racially diverse and predominantly immigrant sample of women. *Cancer Causes and Control* 2015;26:1393–403. https://doi.org/10.1007/s10552-015-0630-4.
20. Conroy SM, Butler LM, Harvey D, Gold EB, Sternfeld B, Greendale GA, et al. Metabolic syndrome and mammographic density: The Study of Women's Health Across the Nation. *International Journal of Cancer* 2011;129:1699–707. https://doi.org/10.1002/ijc.25790