Journal of Kerman University of Medical Sciences
2021; 28(6): 589-594
http://jkmu.kmu.ac.ir/
10.22062/JKMU.2021.91831
Original Article

The Relationship of Metabolic Syndrome and its Components with Breast Density

Mohammad Mehrazmay [1], Ensi Khalili Pouya [2], Elham Keshavarz [2*]

1. Radiology resident at Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Radiology, Mahdiye hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ABSTRACT

Background: Breast cancer is a major health problem in Iran with increasing incidence in the recent years. Breast density is one of the most important risk factors for developing breast cancer. Metabolic syndrome that is defined by the presence of multiple clinical and lab data findings has also been shown to be related with breast cancer.

Methods: A sample of 246 cases who referred to Mahdiyeh hospital in Tehran were selected according to the inclusion criteria and a form was prepared including breast density in the screening mammogram done in our center and recent lab tests including FBS, HDL and TG. We also measured the waist circumference, height, weight and blood pressure of all subjects. Data analysis was done through SPSS23 and using fishers exact and ordinal regression tests.

Results: The incidence of metabolic syndrome was 44% among the cases in this study. Mean age ± standard deviation (SD) was 48.08 ± 7.6 years. There was a significant association between lower breast densities and ages greater than 50 years (p = 0.0). There was no significant association between metabolic syndrome or its components and breast density among the patients above 50 years of age but in ages lower than 50 years, there was a significant association between increased breast density and lower abdominal circumference (p=0.017), lower triglyceride levels (p=0.02), higher HDL levels (p=0.018), lower FBS levels and lower frequency of metabolic syndrome.

Conclusion: There was no significant association between metabolic syndrome or its components and mammographic breast density after adjustment for age and BMI.

Keywords: Mammographic Breast Density, Cardiometabolic Syndrome, Breast Cancer

Citation: Mehrazmay M, Khalili Pouya E, Keshavarz E. The relationship of metabolic syndrome and its components with breast density. Journal of Kerman University of Medical Sciences 2021; 28(5): 589-594. doi: 10.22062/JKMU.2021.91831

Received: 19.05. 2021
Accepted: 28.08. 2021
***Correspondence:** Elham Keshavarz; Email: elhamkeshavarz@yahoo.com

Published by Kerman University of Medical Sciences

Introduction

Breast cancer is the most diagnosed cancer among American women that causes nearly 42000 deaths per year in the united states of America and is considered as the second deadliest cancer among the women in USA after lung cancer (1). According to a study conducted in 2017, based on Iranian ministry of health data (2), breast cancer was the most common cancer in Iran with the age adjusted frequency of 33.21 cases in 100,000 people. Since early breast cancer diagnosis has been associated with better prognosis (3) and considering the fact that mammography is an effective screening method in diagnosing breast cancer, it is used for early diagnosis of breast cancer and decreasing its mortality and morbidity (4).

The frequency of this cancer increases with age, especially after 50 years of age (5, 6). There are multiple risk factors for the development of breast cancer including family history, genetic factors (7) like mutation in PTEN, BRCA1,2 and p53 genes, increased breast density (8–11), age of menarche (12) and menopause (6, 13) and nulliparity (14). Breast density is considered as a strong and independent risk factor for breast cancer development. It is also associated with breast cancers with larger masses and positive lymph nodes (15–19). Increased breast density is also important due to decreasing the sensitivity of mammography in the diagnosis of breast masses (20).

Table 1. The association of metabolic syndrome and its components with breast density

Metabolic syndrome and its components			Breast Density (*N*)					(*p* vlue)
			A	B	C	D	Total	
Premenopause	Increased Waist circumference	Yes	9	45	39	1	71	0.017
		No	2	23	43	3	94	
	Raised Blood pressure	Yes	3	12	12	0	27	0.610
		No	8	56	70	4	138	
	Reduced HDL cholesterol	Yes	11	52	52	2	117	0.018
		No	0	12	26	2	40	
	Raised Triglyceride	Yes	7	25	18	1	51	0.020
		No	4	39	60	3	106	
	Raised fasting plasma glucose	Yes	7	27	16	1	51	0.004
		No	4	39	62	3	108	
	Metabolic Syndrome	Yes	8	34	20	1	53	0.000
		No	3	30	58	3	94	
Menopause	Increased Waist circumference	Yes	14	30	11	0	55	0.554
		No	7	12	6	1	26	
	Raised Blood pressure	Yes	5	20	5	0	30	0.190
		No	16	22	12	1	51	
	Reduced HDL cholesterol	Yes	19	38	13	0	70	0.050
		No	1	4	4	1	10	
	Raised Triglyceride	Yes	12	18	5	0	35	0.216
		No	8	24	12	1	45	
	Raised fasting plasma glucose	Yes	13	18	6	0	37	0.164
		No	7	24	11	1	43	
	Metabolic Syndrome	Yes	14	25	8	0	47	0.312
		No	6	17	9	1	33	

Metabolic syndrome is the presence of multiple clinical and lab data findings (21) that has also been investigated for its association with breast cancer risk. A meta-analysis study showed that postmenopausal women with metabolic syndrome are at a higher risk for the development of breast cancer by 52%, exceeding the risk for each of its components (22). Another meta-analysis showed 14% increased risk of breast cancer in women with metabolic syndrome (23). The metabolic syndrome frequency in Iran has been reported to be between 20-35.8% which is higher than the global estimates (24). As with such high frequency of this syndrome and its association with breast cancer risk which is in the same direction with the effect of increased breast density, this study was conducted to shed light on possible link between metabolic syndrome components and breast density in Iranian women mostly among poor socioeconomic people.

Materials and Methods

We collected a sample of 246 patients who referred to Mahdiyeh hospital in Tehran, Iran for screening mammography between July 2018 and

November 2019 and were mostly among poor socieoeconomic people. Two radiology residents and also a few trained health personnel recorded the necessary information in the prepared forms. The patients were asked to bring the last available lab tests (within 6 months ago) including serum triglyceride, fasting blood sugar and HDL with them in the next visit. Digital mammography was done with digital mamographic hologic selenia model. The breast density was categorized by an expert radiologist according to the version 4 of BIRADS in a qualitative manner. All anthropometric measures were taken in light clothing and without shoes. The measured weight, height and waist circumference were written down in the form. History of increased blood pressure and drug history were taken and three consecutive blood pressures were obtained in the sitting position and the average was noted in the form. The patients with history of hormone replacement therapy or other drugs that change breast density, bilateral oophorectomy, history of breast cancer or breast irradiation, history of breast feeding or pregnancy in the past 6 month, mastitis and breast implant were excluded from the study. The data were entered in SPSS23 software and descriptive analysis was done. The data were then analyzed using Fisher's exact test to evaluate the association of breast density with metabolic syndrome and its components. We selected age and BMI as covariates. To remove the effect of covariates, the data were then analyzed using ordinal regression test.

Results

Our study sample volume was 246 cases. Mean age ± standard deviation (SD) was 48.08 ± 7.6 years. The prevalence rates of A, B, C and D density in the sample were 32 (13%), 110 (44.7%), 99 (40.2%) and 5 (2%) respectively. There was a significant association between lower breast densities and ages greater than 50 years (p = 0.0). BMI was normal in 47 cases (19.1%), 103 cases (41.9%) were overweight and 96 ones (39%) were obese.

The prevalence of metabolic syndrome components was as follows: 57 cases (23.2%) had elevated blood pressure, 149 ones (60.6%) had increased waist circumference and 88 ones (36.8%) had FBS more than 100 mg/dl, 187 cases (78.9%) had HDL below 50 mg/dl and 86 ones (36.3%) had triglyceride over 150mg/dl.

Among the 237 cases who had completed the form, 110 ones (44%) had metabolic syndrome. The most common component of metabolic syndrome in the patients was HDL below 50 mg/dl observed in all cases. Ninety seven patients of metabolic syndrome cases had increased waist circumference, 48 patients had elevated blood pressure, 77 patients had FBS more than 100mg/dl and 74 patients had triglyceride equal or more than 150mg/dl.

There was no significant association between metabolic syndrome or its components and breast density among the patients above 50 years of age. In ages lower than 50 years we saw a significant association between increased breast density and lower abdominal circumference (p=0.017), lower triglyceride levels (p=0.02), higher HDL levels (p=0.018), lower FBS levels and lower frequency of metabolic syndrome (Table 1).

Since BMI and age are two covariates, we then analyzed the data with ordinal regression test and figured out that metabolic syndrome and its components had no association with increased breast density.

Discussion

In this population of premenopausal and postmenopausal Iranian women who referred for screening mammography, breast density had no association with serum triglyceride level, waist circumference, fasting blood sugar and metabolic syndrome, while it showed a positive association with HDL in premenopausal women and no association with HDL in postmenopausal women. However, after analyzing the data using ordinal regression test with age and BMI as covariates, we observed no significant association of breast density with metabolic syndrome and its components in pre and postmenopausal women. We also observed a high rate of metabolic syndrome prevalence (44%) compared to the previous studies conducted in Iran.

There are few studies available on the association of breast cancer and metabolic syndrome. In the Study of Women's Health Across the Nation (SWAN) conducted in US, no association between breast density and metabolic syndrome was seen (25). In another study in Mexico in two states, breast density was higher in premenopausal women with metabolic syndrome than those without metabolic syndrome even after adjustment for confounders (26). In a Korean population, a significant positive association was seen between metabolic syndrome and breast density only in

premenopausal women (27). Our study results are similar to the results of the mentioned Korean and Mexican studies that showed positive significant association between breast density and metabolic syndrome only in premenopausal women, but we did not observe this association after adjustment for age and BMI.

In terms of metabolic syndrome components, FBS has not been associated with breast density in other studies (25, 26, 28–30) which is similar to our results. Only the Korean study has reported a relationship between insulin resistance and metabolic syndrome regardless of the menopausal status (27).

Some studies including the SWAN study have showed negative association between breast density and waist circumference similar to our study. Most of studies have shown no association between breast cancer and elevated triglyceride or blood pressure (25, 26, 28).

Low HDL levels have been positively associated with increased breast density in some studies (26, 28, 31, 32), while others have reported the reverse (33) or no association (34-36). Cholesterol as a precursor of steroid hormone is suggested to play a role in breast carcinogenesis. The association between total cholesterol, LDL and HDL levels and breast cancer risk has been investigated in several studies. A higher risk of breast cancer has been associated with lower HDL serum levels in some studies (31, 34). In a cross sectional study conducted on 206 premenopausal Norwegian women, increased blood levels of HDL were associated with higher breast density and at the same time with lower salivary estradiol (33). This might represent a complex association between them.

It should be kept in mind that our study was conducted among a small sized sample of relatively low socioeconomic Iranian women with poor follow up. Therefore, the study results may not be generalized to all Iranian women and a multi-centric study with a large sample may help the evaluation in different Iranian women. As previous studies indicated that quantitative measures of density can predict breast cancer better than qualitative measurements, using a computer thresholding software for the quantitative breast density assessment should be considered in the next studies.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019; 69(1):7-34. doi: 10.3322/caac.21551..
2. Nafissi N, Khayamzadeh M, Zeinali Z, Pazooki D, Hosseini M, Akbari ME. Epidemiology and histopathology of breast cancer in Iran versus other Middle Eastern countries. Middle East J Cancer 2018; 9(3):243-51. doi: 10.30476/mejc.2018.42130.
3. Tabár L, Vitak B, Chen HH, Duffy SW, Yen MF, Chiang CF, et al. The Swedish Two-County Trial twenty years later: updated mortality results and new insights from long-term follow-up. Radiol Clin North Am 2000; 38(4):625-51. doi: 10.1016/s0033-8389(05)70191-3.
4. Humphrey LL, Helfand M, Chan BK, Woolf SH. Breast cancer screening: a summary of the evidence for the US Preventive Services Task Force. Ann Intern Med 2002; 137(5 Part 1):347-60. doi: 10.7326/0003-4819-137-5_part_1-200209030-00012.
5. Moolgavkar SH, Day NE, Stevens RG. Two-stage model for carcinogenesis: epidemiology of breast cancer in females. J Natl Cancer Inst 1980; 65(3):559-69.
6. Colditz GA, Rosner B. Cumulative risk of breast cancer to age 70 years according to risk factor status: data from the Nurses' Health Study. Am J Epidemiol 2000; 152(10):950-64. doi: 10.1093/aje/152.10.950.
7. Rojas K, Stuckey A. Breast cancer epidemiology and risk factors. Clin Obstet Gynecol 2016; 59(4):651-72. doi: 10.1097/GRF.0000000000000239.
8. Carney PA, Miglioretti DL, Yankaskas BC, Kerlikowske K, Rosenberg R, Rutter CM, et al. Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. Ann Intern Med 2003; 138(3):168-75. doi: 10.7326/0003-4819-138-3-200302040-00008.
9. 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. J Natl Cancer Inst 1995; 87(9):670-5. doi: 10.1093/jnci/87.9.670.
10. Boyd N, Martin L, Gunasekara A, Melnichouk O, Maudsley G, Peressotti C, et al. Mammographic density and breast cancer risk: evaluation of a novel method of measuring

breast tissue volumes. Cancer Epidemiol Biomarkers Prev 2009; 18(6):1754-62. doi: 10.1158/1055-9965.EPI-09-0107.

11. McCormack VA, dos Santos Silva I. Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev 2006; 15(6):1159-69. doi: 10.1158/1055-9965.EPI-06-0034.
12. Bernstein L, Ross RK. Endogenous hormones and breast cancer risk. Epidemiol Rev 1993; 15(1):48-65. doi: 10.1093/oxfordjournals.epirev.a036116.
13. Lilienfeld AM. The relationship of cancer of the female breast to artificial menopause and marital status. Cancer 1956; 9(5):927-34. doi: 10.1002/1097-0142(195609/10)9:5<927::aid-cncr2820090510>3.0.co;2-3.
14. Rosner B, Colditz GA, Willett WC. Reproductive risk factors in a prospective study of breast cancer: the Nurses' Health Study. Am J Epidemiol 1994; 139(8):819-35. doi: 10.1093/oxfordjournals.aje.a117079.
15. Aiello EJ, Buist DS, White E, Porter PL. Association between mammographic breast density and breast cancer tumor characteristics. Cancer Epidemiol Biomarkers Prev 2005; 14(3):662-8. doi: 10.1158/1055-9965.EPI-04-0327.
16. Sala E, Solomon L, Warren R, McCann J, Duffy S, Luben R, et al. Size, node status and grade of breast tumours: association with mammographic parenchymal patterns. Eur Radiol 2000; 10(1):157-61. doi: 10.1007/s003300050025.
17. Roubidoux MA, Bailey JE, Wray LA, Helvie MA. Invasive cancers detected after breast cancer screening yielded a negative result: relationship of mammographic density to tumor prognostic factors. Radiology 2004; 230(1):42-8. doi: 10.1148/radiol.2301020589.
18. Kerlikowske K, Zhu W, Hubbard RA, Geller B, Dittus K, Braithwaite D, et al. Outcomes of screening mammography by frequency, breast density, and postmenopausal hormone therapy. JAMA Intern Med 2013; 173(9):807-16. doi: 10.1001/jamainternmed.2013.307.
19. Duffy SW, Tabar L, Smith RA, Krusemo UB, Prevost TC, Chen TH. Risk of breast cancer and risks with breast cancer: the relationship of histologic type with epidemiology, disease progression and survival. Seminars in Breast Disease 1999; 2: 292-300.
20. Leconte I, Feger C, Galant C, Berlière M, Berg B Vande, D'Hoore W, et al. Mammography and subsequent whole-breast sonography of nonpalpable breast cancers: the importance of radiologic breast density. AJR Am J Roentgenol 2003; 180(6):1675-9. doi: 10.2214/ajr.180.6.1801675.
21. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009; 120(16):1640-5. doi: 10.1161/CIRCULATIONAHA.109.192644.
22. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Rafaniello C, et al. Metabolic syndrome and postmenopausal breast cancer: systematic review and meta-analysis. Menopause 2013; 20(12):1301-9. doi: 10.1097/GME.0b013e31828ce95d.
23. Esposito K, Chiodini P, Colao A, Lenzi A, Giugliano D. Metabolic syndrome and risk of cancer: a systematic review and meta-analysis. Diabetes Care 2012; 35(11):2402-11. doi: 10.2337/dc12-0336.
24. Alizade Z, Azadbakht L. Review of epidemiology of metabolic syndrome in iran. Iran J Diabetes Metab 2016; 15(3):143-57. [In Persian].
25. 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. Int J cancer 2011; 129(7):1699-707. doi: 10.1002/ijc.25790.
26. Rice MS, Biessy C, Lajous M, Bertrand KA, Tamimi RM, Torres-Mejía G, et al. Metabolic syndrome and mammographic density in Mexican women. Cancer Prev Res (Phila) 2013; 6(7):701-10. doi: 10.1158/1940-6207.CAPR-12-0475.
27. 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 Res Treat 2015; 153(2):425-34. doi: 10.1007/s10549-015-3544-7.
28. 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 Control 2015; 26(10):1393-403. doi: 10.1007/s10552-015-0630-4.

29. Woolcott CG, Courneya KS, Boyd NF, Yaffe MJ, McTiernan A, Brant R, et al. Association between sex hormones, glucose homeostasis, adipokines, and inflammatory markers and mammographic density among postmenopausal women. Breast Cancer Res Treat 2013; 139(1):255-65. doi: 10.1007/s10549-013-2534-x.

30. Borugian MJ, Spinelli JJ, Gordon PB, Abanto Z, Brooks-Wilson A, Pollak MN, et al. Fasting insulin and endogenous hormones in relation to premenopausal breast density (Canada). Cancer Causes Control 2014; 25(3):385-94. doi: 10.1007/s10552-014-0339-9.

31. Furberg AS, Veierød MB, Wilsgaard T, Bernstein L, Thune I. Serum high-density lipoprotein cholesterol, metabolic profile, and breast cancer risk. J Natl Cancer Inst 2004; 96(15):1152-60. doi: 10.1093/jnci/djh216.

32. Agnoli C, Berrino F, Abagnato CA, Muti P, Panico S, Crosignani P, et al. Metabolic syndrome and postmenopausal breast cancer in the ORDET cohort: a nested case--control study. Nutr Metab Cardiovasc Dis 2010; 20(1):41-8. doi: 10.1016/j.numecd.2009.02.006.

33. Furberg AS, Jasienska G, Bjurstam N, Torjesen PA, Emaus A, Lipson SF, et al. Metabolic and hormonal profiles: HDL cholesterol as a plausible biomarker of breast cancer risk. The Norwegian EBBA Study. Cancer Epidemiol Biomarkers Prev 2005; 14(1):33-40.

34. 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. J Epidemiol 2011; 21(1):52-60. doi: 10.2188/jea.je20100078.

35. 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 Res Treat 2011; 125(1):181-9. doi: 10.1007/s10549-010-0927-7.

36. Aiello EJ, Tworoger SS, Yasui Y, Stanczyk FZ, Potter J, Ulrich CM, et al. Associations among circulating sex hormones, insulin-like growth factor, lipids, and mammographic density in postmenopausal women. Cancer Epidemiol Biomarkers Prev 2005; 14(6):1411-7. doi: 10.1158/1055-9965.EPI-04-0920.