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Impact of Metformin on BRCA1 Expression and Breast Cancer Risk in T2DM Patients

Hanan Hamed Hassan
Department of Chemistry, College of Sciences for Women, University of Baghdad, Baghdad, Iraq,
hnanhamd739@gmail.com

Perry Habeb Saif ullah
Department of Chemistry, College of Sciences for Women, University of Baghdad, Baghdad, Iraq,
perryhs_chem@csw.uobaghdad.edu.iq

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RESEARCH ARTICLE

Impact of Metformin on BRCA1 Expression and Breast Cancer Risk in T2DM Patients

Hanan Hamed Hassan *, **Perry Habeb Saif ullah**

Department of Chemistry, College of Sciences for Women, University of Baghdad, Baghdad, Iraq

ABSTRACT

This study aims at detecting the level of BRCA1 protein as a marker of breast cancer in Iraqi women previously suffering from type 2 diabetes mellitus. The study includes: 80 participants they were divided into three subgroups based on drugs strategy and duration of disease, with ages (40–70) years. Blood samples were collected from Ibn AL-Bitar Hospital in Baghdad/Iraq between the period from November 2022 to February 2023. Some biochemical parameters were measured for all study groups, which include: -Fasting blood sugar (FBS) and Lipid profile, which were measured by enzymatic oxidation method. Using an enzymatic process, Insulin levels and Insulin-like Growth Factors (IGF-1) and Estrogen-receptor-alpha (ERα) levels, and Breast Cancer Susceptibility Protein1(BRCA-1) were measured via an ELISA. Glycated Hemoglobin (HbA1c) level was measured with a sandwich-immunodetection method. Finally, Homeostasis model assessment-insulin resistance (HOMA-IR) was calculated according to the specific formula. The result showed that the P-value for the comparison of groups were not significant for FBS, HbA1c, and lipid profile, while BRCA1, ERα, Insulin, IGF-1, and HOMA IR showed significance with P-value of 0.0001. The main finding is that patients taking metformin only less than one year which contributed to increase the level of BRCA1. There is a positive association between BRAC1 level with ERα, insulin, and IGF-1 levels. According to ROC-analysis, BRCA1 showed high sensitivity and specificity. We conclude that BRCA1protin is a good parameter to predict the incidence of breast cancer in women with type 2 diabetes and metformin increases the concentration of BRCA1-portien.

Keywords: BRCA1 protein, Breast cancer, ERα, Metformin, Type 2 diabetes mellitus

Introduction

Diabetes and breast cancer are within the category of most difficult disorders. Numerous epidemiological studies indicated that individuals with diabetes have a notably increased chance of developing cancer due to its complicated and varied nature.[1] The combination of these disorders presents the greatest diagnostic challenge. It can also be stated that genetic lesions, metabolic problems, post-translational modifications (PTMs), and aberrant signaling are the causes of failure at numerous levels in multicellular organisms, which result in cancer and/or diabetes. Affected cell-fate decisions (proliferation, apoptosis, growth and differentiation) may result from these modifications. Following such modifications, the cell seems to exhibit distinct physiological behavior and morphology in contrast to the corresponding normal cells.[2] Type 2 diabetes mellitus (T2DM), is a chronic metabolic disorder that is characterized by elevated blood glucose levels,[3] this disease is caused by either inadequate insulin synthesis, poor insulin utilization, or both. If left untreated, this disorder impairs the body's capacity to efficiently control glucose, which can result in a number of health issues.[4]

The oral anti-hyperglycemic medication metformin is frequently used to treat type 2 diabetes. By blocking basal hepatic glucose synthesis, it raises both hepatic and peripheral insulin sensitivity in the liver. It also enhances glucose uptake in skeletal muscles

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* Corresponding author.
E-mail addresses: hnanhamd739@gmail.com (H. H. Hassan), perryhs_chem@csw.uobaghdad.edu.iq (P. H. S. ullah).

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and adipocytes.[5,6] The most frequent cancer in the world and the primary cause of cancer-related fatalities is breast cancer. Since breast cancer is a complex disease, the exact method by which it starts is unknown. Nonetheless, the pathogenesis of breast cancer involves a complex interaction between hereditary, environmental, and lifestyle variables.[7] BRCA1 protein is a tumor suppressor protein that aids in keeping the DNA of the cell stable. BRCA1 plays a role in mending double-strand breaks and other DNA damage in order to stop mutations that can cause cancer. It is involved in cell cycle checkpoints, which stop genetically unstable or damaged cells from proliferating.[8,9] Up to 10% to 20% of individuals with breast cancer also have type 2 diabetes, which is thought to be a risk factor for the disease. Three possible mechanisms have been proposed to link diabetes to breast cancer: the modulation of endogenous sex hormones, the activation of the insulin-like growth factor pathway, and the activation of the insulin pathway. The Warburg effect, a prolonged state of hyperglycemia that may raise the risk of breast cancer, is another mechanism that has been proposed. Elevated levels of inflammatory cytokines and insulin-like growth factor 1 (IGF-1) are linked to hyperglycemia, which can have a direct or indirect impact on the growth, death, and metastasis of cancer cells.[10] The objective of this study was to detect the relation between metformin intake in patients with type 2 diabetes mellitus and the expression of BRCA1 protein and if metformin intake will reduce the incidence of breast cancer in women with type 2 diabetes.

Materials and methods

Analysis of the samples

This study was conducted at the College of Science for Women, University of Baghdad. The samples were collected from Ibn AL-Bitar Center for Cardiac Surgery Hospital in Baghdad/Iraq. This cross-sectional study included (80) subjects, ages ranging from 40–70 years. The participants were divided into three groups according to the drugs strategy and duration of disease as follows: first group included (n = 20) patients taking metformin only more than ten years. Second group included (n = 20) patients taking metformin with sulphonylurea for more than ten years. Third group included (40) patients taking metformin only during less than one year. In this study, samples were collected from women with type 2 diabetes who did not have breast cancer and within the required age group. While patients infected with Coved -19, pregnant women, patients with breast cancer, smokers were excluded. Blood serum was used for checking for glucose levels, and lipid profile that was measured manually by using Biosystem Spine kit, and Brca1, Insulin, insulin growth factor, estrogen receptor alpha by ELISA (My Sunlong, China). Blood was used for checking for HbA1c by (Boditech I-chroma, Korea).

Serum sample preparation

Seven milliliters of blood sample were collected and divided into two tubes; the first used an EDTA tube for HbA1c, whereas the second used a gel tube for BRCA1, Estrogen receptor alpha, Insulin, Insulin growth factor, FBS and lipid profile from diabetic type 2 individuals. The blood tubes were left for 20–25 minutes at room temperature 25 ˚C, blood tubes then were centrifuged at 2000–3000 rpm for 10 minutes, the separated serum was kept in deep freeze at –20 ˚C.

Statistical analysis

The statistical analysis was done using by version 26 of the SPSS program. The data was shown as a median mean ± SE. ANOVA test was used to find the difference between the factors. In the statistics test, an estimation was made by looking at the linear regression. The probability value was used to figure out the statistical significance, when the probability value was ($p \leq 0.05$), it was considered significant, and when it was ($p \geq 0.05$), it was not.

Results

Demographic data depicted in Table 1 showed age and duration of disease (years) for all study participants and for subgroups.

The P value for the comparison of groups was not significant for FBS (mg/dL), Hba1c%, Cholesterol (mg/dL), TG (mg/dL), HDL-C (mg/dL), LDL-C (mg/dL) and VLDL-C (mg/dL). The FBS gave the lowest level of 187.07 mg/dL for patients taking metformin less than one year, while the value was 191.20 mg/dL for patients taking metformin + sulphonylurea more than ten years. Hba1c showed a closer value with 8.26 for patients on metformin + sulphonylurea, and 7.80 for patients on metformin that they had DM for less than one year. Cholesterol marked its highest level in patients on metformin with a value of 180.42, as shown in Table 2.

The triglyceride was on its highest value in patients who took metformin only during more than ten years (181.75) while it was only) 165.47 (in the group of patients taking metformin only during less than one year of patients. The value HDL was elevated in the

Table 1. The age and duration of disease of the study participants.

Groups	Patient take metformin only Group (1) No. (20)	Patient take metformin with sulphonylurea Group (2) No. (20)	Patient take metformin only during less than one year's Group (3) No. (40)
Age (year)	64.35 ± 1.19 (66)	60.20 ± 1.90 (61)	52.27 ± 1.00 (53)
Duration of disease (years)	10.00 ± 0.001 (10)	10.00 ± 0.001 (10)	1.55 ± 0.079 (2)

Table 2. Comparison of biochemical parameters FBS, HbA1c and lipid profile in study groups.

Groups Parameters	Patient take metformin only Group (1) No. (20)	Patient take metformin with sulphonylurea Group (2) No. (20)	Patient take metformin only during less than one year's Group (3) No. (40)	P-value
FBS -(mg/dL)	187.60 ± 21.58 [a] (171)	191.20 ± 20.16 [a] (173)	187.07 ± 14.49 [a] (159)	0.302
Hba1c%	7.97 ± 0.55 [a] (6.80)	8.26 ± 0.521 [a] (7.39)	7.80 ± 0.211 [a] (7.35)	0.153
Cholesterol (mg/dL)	156.15 ± 12.52 [a] (136)	169.05 ± 9.09 [a] (173)	180.42 ± 9.43 [a] (180)	0.223
TG (mg/dL)	181.75 ± 48.94 [a] (133)	168.65 ± 13.04 [a] (153.5)	165.47 ± 14.84 [a] (146)	0.984
HDL-C (mg/dL)	37.68 ± 1.93 [a] (36.5)	35.80 ± 1.54 [a] (36.5)	40.72 ± 1.26 [a] (40)	0.129
LDL-C (mg/dL)	81.17 ± 10.64 [a] (63.5)	99.60 ± 8.01 [a] (97)	106.6 ± 9.072 [a] (106)	0.134
VLDL-C (mg/dL)	36.45 ± 9.78 [a] (26.5)	33.65 ± 2.61 [a] (30.5)	33.10 ± 2.97 [a] (29)	0.982

group of patients taking metformin only for less than one year (40.72 mg/dL) more than the others, while LDL marked the highest with the group of patients taking metformin less than one year (106.6 mg/dL). VLDL also showed its highest levels in patients taking metformin only group 36.45 mg/dL. The lowest levels were with the group of patients on metformin only 33.10 mg/dL during less than one year, Table 2.

According to Table 3, all comparisons showed significance with P- value of 0.0001, BRCA-1 (ng/ml) gave lowest level of 2.28 for the group of patients taking metformin only and the highest level 3.51 for the group of patients taking metformin only during less than one year. Estrogen Receptor Alpha (ERα) (pg/ml) values also gave the lowest level of 318 for the patients taking metformin only group and highest level 409.32 for the group of patients taking metformin + sulphonylurea. While the mean Insulin like growth factor IGF-1 (ng/ml) elevated its most among patients taking metformin, it was only 6.56 ng/ml in one year's group. Insulin (mU/L) gave the highest level for the patients taking metformin + sulphonyl

Table 3. Comparison between study groups by: BRCA-1, Estrogen Receptor Alpha (ERα), IGF-1, Insulin, HOMA IR.

Groups Parameters	Patient take metformin only Group (1) No. (20)	Patient take metformin with sulphonylurea Group (2) No. (20)	Patient take metformin only during less than one year's Group (3) No. (40)	P-value
BRCA-1 (ng/ml)	2.28 ± 0.117 [a] (2.45)	2.46 ± 0.129 [ab] (2.63)	3.51 ± 0.185 [c] (3.96)	0.0001*
Estrogen Receptor Alpha (ERα) (pg/ml)	318.15 ± 24.25 [a] (293.30)	409.32 ± 25.04 [b] (445.64)	404.70 ± 15.15 [ab] (442.90)	0.0001*
IGF-1 (ng/ml)	4.56 ± 0.263 [a] (4.79)	5.62 ± 0.395 [ab] (5.85)	6.56 ± 0.448 [bc] (7.13)	0.0001*
Insulin (mU/L)	1.46 ± 0.112 [a] (1.53)	1.96 ± 0.135 [bc] (2.10)	1.75 ± 0.07 [ab] (1.90)	0.0001*
HOMA IR	0.70 ± 0.110 [a] (0.64)	0.93 ± 0.132 [ab] (0.82)	0.80 ± 0.074 [ab] (0.69)	0.0001*

Table 4. Correlation of BRCA1 with other parameters.

	BRCA-1 (ng/ml)		
	Patient take metformin only Group (1) No. (20)	Patient take metformin with sulphonylurea Group (2) No. (20)	Patient take metformin only during less than one year's Group (3) No. (40)
Age (years)			
R	0.046	0.296	–0.152
P	0.848	0.206	0.349
Duration of disease (years)			
R	—	—	–0.319*
P	—	—	0.045
FBS (mg/dL)			
R	0.173	–0.030	–0.070
P	0.465	0.899	0.669
HbA1C %			
R	–0.454*	–0.014	0.103
P	0.045	0.954	0.527
Cholesterol (mg/dL)			
R	0.163	–0.233	–0.227
P	0.494	0.322	0.159
TG (mg/dL)			
R	0.070	–0.449*	0.006
P	0.770	0.047	0.971
HDL-C (mg/dL)			
R	–0.083	0.304	0.266
P	0.727	0.192	0.097
LDL-C (mg/dL)			
R	0.127	–0.173	–0.275
P	0.592	0.467	0.086
VLDL-C (mg/dL)			
R	0.071	–0.463*	0.006
P	0.767	0.040	0.968
Estrogen Receptor Alpha (ERα) (pg/ml)			
R	0.689**	0.856**	0.571**
P	0.001	0.0001	0.0001
IGF-1 (ng/ml)			
R	0.602**	0.769**	0.620**
P	0.005	0.0001	0.0001
Insulin (mU/L)			
R	0.822**	0.931**	0.668**
P	0.0001	0.0001	0.0001
HOMA IR			
R	0.468*	0.452*	0.278
P	0.037	0.045	0.083

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level.
Receiver operator characteristics (ROC)

urea 1.96 mU/L, while it showed less mean among the group of patients taking metformin only more than ten years 1.46mU/L. Least means of HOMA IR appeared in patients taking metformin only and patients taking metformin only during less than one year's group with values of 0.7 and 0.8 respectively.

The result of the correlation of BRCA1 with other parameters showed no significance. The duration of disease differed in patients taking metformin only during less than one year's group from other groups with (–0.319). FBS, cholesterol, HDL, LDL showed no significant differences when compared to other groups, as shown in Table 4.

HbA1C% had some significance among the group of patients taking metformin only with (–0.454) while in other groups comparison, it was of non-significance. TG and VLDL was significant among the second group with (–0.449 and –0.463) respectively. Estrogen Receptor Alpha showed significance among all age groups with values of (0.689, 0.856, 0.571) from the first to the third group respectively. The significance appeared in IGF-1 and insulin among all groups

Table 5. Receiver operator characteristics of principle parameters of overall participants.

Test Result Variable(s)	Area	Cut-Off Point	Sensitivity	1-Specificity	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
							Lower Bound	Upper Bound
BRCA1	.898	2.77	0.8	0.1	.048	.000	.803	.992
IGF1	.933	5.85	.800	.100	.037	.000	.860	1.000
ERα	.818	333.44	.900	.400	.068	.001	.685	.950
HbA1C %	.699	7.60	.800	.350	.091	.032	.520	.878

with values of 0.602**,0.769*,0.620** for IGF-1 and 0.822**, 0.931**, 0.668** for insulin. While, only first and second groups was significant regarding HOMA IR with 0.468*, 0.452* respectively as illustrated in Table 4.

Receiver operator characteristics (ROC) curve used to assess the optimal diagnosis (BRCA-1, IGF1, ERα and HbA1C) for the onset of breast cancer in participants of study, as shown in the Table 5.

According to the results of association analysis, the ROC curve analysis was used to examine whether BRCA1 has the potential to predict future breast cancer, as shown in the Table 5. The area under curve (AUC) for brca1 was (0.898) with (sensitivity 0.82; specificity 0.1).

The area under curve for BRCA1 showed higher values as shown in Fig. 2. Therefore, BRCA1 could be a major factor that predicts the susceptibility to breast cancer in women with type 2 diabetes, as shown in Figs. 1 and 2. A high level of BRCA1 protein expression in breast tissue is associated with a reduced risk of breast cancer. A low level of BRCA1 protein expression in breast tissue is associated with an increased risk of breast cancer, especially in women with a genetic mutation in the BRCA1 gene.[11]

Discussion

Type 2 diabetes mellitus is a metabolic disorder marked by persistently elevated blood sugar levels. Gender and age have an impact on diabetes management. Due to their many medical disorders involving the heart and kidneys, women and elderly people older than 60 years of age are more affected, this restricts and hinders medical treatment.[12,13] A potent hormone insulin stimulates many signaling pathways, some of which are essential to the biology of cancer. Insulin can either directly or indirectly increase the risk of cancer by influencing the levels of other modulators, including hormones, adipokines, and the insulin-like growth factor 1 (IGF1).[14] Metformin is a widely prescribed oral antidiabetic medication. This biguanide is considered a first-line drug for the management of T2D.[15] Due to its efficacy and good safety profile, metformin has been on the World Health Organization's list of essential medicines since the 1960s.[16] Metformin lowers blood glucose levels by reducing hepatic gluconeogenesis, improving peripheral insulin sensibility, and enhancing glucose uptake and blocks the release of free fatty acids from adipose tissue.[17] Metformin is a difficult anticancer drug.

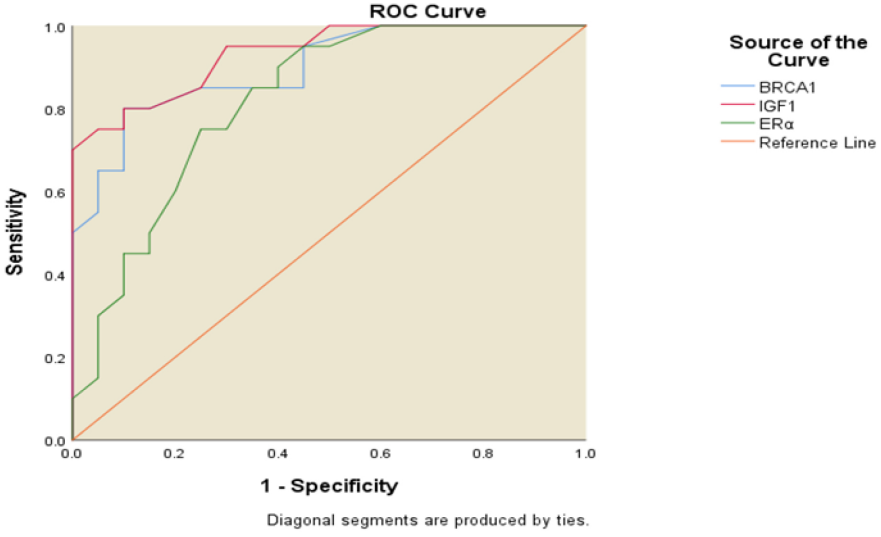

Fig. 1. ROC curves between study markers and reference line.

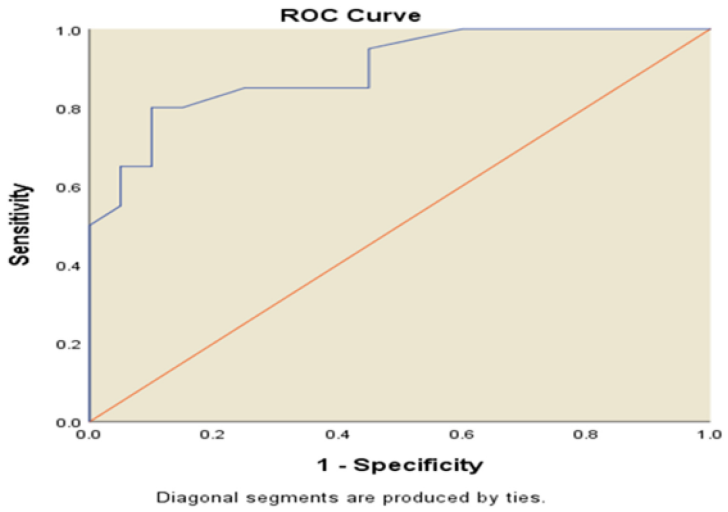

Fig. 2. ROC curves between BRCA-1 and reference line.

Additionally, people with diabetes who took the medication had greater survival rates than those who did not.[18] Metformin also exhibits anti-proliferative effects in breast cancer patients with a high body mass index and significant insulin resistance. Furthermore, metformin has been demonstrated to raise the levels of insulin- and metabolic-related indicators linked to carcinogenesis and reduce metastatic occurrences.[19] The results demonstrated that there was a higher level of BRCA-1 in the third group than in other groups Table 3, which is in agreement with Samuel, Samson Mathews, et al,[20] who found that BRCA1 protein levels increase in patients taking metformin for less than one year because metformin can activate the AMPK pathway, which is a signaling pathway that regulates cell growth and metabolism. The AMPK pathway has been shown to increase BRCA1 gene expression also metformin may reduce BRCA1 protein degradation. Metformin can inhibit the activity of the proteasome, which is a complex that degrades proteins. This could lead to an increase in BRCA1 protein levels. The result agrees with Boucher et al., who noticed a slight increase in the concentration of BRCA 1 protein in the third group.[21,22] Patients who have been using metformin for more than 10 years had lower levels of BRCA1 protein as shown in Table 3, because metformin's effectiveness may decline with prolonged disease duration.[23] We observed a decrease in the level of BRCA1 protein in patients who take sulfonylurea in addition to metformin Table 3. This could be because both sulfonylurea and metformin can raise the production of reactive oxygen species (ROS), which can damage DNA and cause a decrease in BRCA1 protein levels.[20] Metformin has been demonstrated to have some anticancer effects when used by patients taking metformin for more than ten years, as seen by a remarkable drop in estrogen receptor alpha (ERα) levels, which is present in breast cancer cells. Estrogen has the ability to boost the development and division of cancer cells when it attaches to ERα.[24] Metformin inhibits the insulin/IGF signaling pathway, lowers insulin levels, and modifies cellular metabolism, among other advantageous effects in both healthy and malignant cells.[25] Insulin/IGF-1 plays multiple roles in controlling glucose absorption and regulating the development of cancer by upregulating signaling pathways linked to the insulin/IGF receptor.[26] The rationale in comparison to a gold standard for rating and continuous diagnostic test results ROC analysis. Derived accuracy indices have a meaningful interpretation from a healthy subject for disease classifications in a specific area under the curve (AUC). The present study showed that BRCA1protin was a good parameter to predict the incidence of breast cancer in women with type 2 diabetes.

Conclusion

We conclude from this study that patients taking metformin for less than one year contributed to an increase in the level of BRCA1. It is also demonstrated that there was a positive association between Brca1 level with ERα, insulin, and IGF-1 levels. Metformin enhances insulin sensitivity and lowers elevated insulin levels, which may trigger cancer-related cell signaling. Metformin has the potential to inhibit the progression of breast cancer by triggering adenosine monophosphate-activated protein kinase, which obstructs a pathway implicated in the dissemination of cancer cells.

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Authors' declaration

- Conflicts of Interest: None.
- We hereby confirm that all the figures and tables in the manuscript are ours. Besides, the figures and images that are not ours have been given permission for re-publication attached to the manuscript.
- Authors signed ethical consideration approval.
- No animal studies are presented in manuscript.
- Ethical Clearance: The project was approved by the local ethical committee at University of Baghdad.

Authors' contribution statement

H. H. H. collected research data and wrote the primary manuscript. P. H. S. supervised the study, contributed to the design, and helped with the completion of the manuscript.

References

1. Abu dawood M. Diabetes and cancer: a comprehensive review. Res J Med Sci. Jan 1 2019;24(1):94. https://doi.org/10.4103/jrms.JRMS_242_19.
2. Rahman I, Athar MT, Islam M. Type 2 diabetes, obesity, and cancer share some common and critical pathways. Front. oncol. Jan 20 2021;10:600824. https://doi.org/10.3389/fonc.2020.600824.
3. Ali SE, Khaleel FM, Ali FE. A study of apelin-36 and GST levels with their relationship to lipid and other biochemical parameters in the prediction of heart diseases in PCOS women patients. Baghdad Sci J. Sep 8 2020;17(3(Suppl.)):0924. http://dx.doi.org/10.21123/bsj.2020.17.3(Suppl.).0924.
4. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. Avicenna J Med. Oct 2020;10(04):174–188. https://doi.org/10.4103/ajm.ajm_53_20.
5. Ali SE, Khaleel FM. Effect of COVID-19 on the Role of Renin Enzyme and ACE2 and Hormones in PCOS Females. Baghdad Sci J. Dec 1 2023;20(6). https://dx.doi.org/10.21123/bsj.2023.7746.
6. Aroda VR, Ratner RE. Metformin and type 2 diabetes prevention. Diabetes Spectr. Nov 1 2018;31(4):336–42. https://doi.org/10.2337/ds18-0020.
7. Dongsar TT, Dongsar TS, Abourehab MA, Gupta N, Kesharwani P. Emerging application of magnetic nanoparticles for breast cancer therapy. Eur olym J. Apr 3 2023;187:111898. https://doi.org/10.1016/j.eurpolymj.2023.111898.
8. Premnath N, O'Reilly EM. BReast CAncer (BRCA) gene mutations as an emerging biomarker for the treatment of gastrointestinal malignancies. Chin Clin Oncol. Oct 2020;9(5):64. https://doi.org/10.21037/cco-2019-ddp-05.
9. Zhong AX, Chen Y, Chen PL. BRCA1 the versatile defender: molecular to environmental perspectives. International Int. J Mol. Sci. Sep 19 2023;24(18):14276. https://doi.org/10.3390/ijms241814276.
10. Eketunde AO. Diabetes as a risk factor for breast cancer. Cureus. May 2020;12(5):e8010 https://doi.org/10.7759/cureus.8010.
11. Paul A, Paul S. The breast cancer susceptibility genes (BRCA) in breast and ovarian cancers. Front. Biosci. (Landmark edition). 2014;19:605. https://doi.org/10.2741/4230.
12. Scordamaglia D, Cirillo F, Talia M, Santolla MF, Rigiracciolo DC, Muglia L, *et al.* Metformin counteracts stimulatory effects induced by insulin in primary breast cancer cells. J Transl Med. Jun 7 2022;20(1):263. https://doi.org/10.1186/s12967-022-03463-y.
13. Thomas DD, Corkey BE, Istfan NW, Apovian CM. Hyperinsulinemia: an early indicator of metabolic dysfunction. J Endocr Soc. Sep 2019;3(9):1727–47. https://doi.org/10.1210/js.2019-00065.
14. Senapati P, Kato H, Lee M, Leung A, Thai C, Sanchez A, *et al.* Hyperinsulinemia promotes aberrant histone acetylation in triple-negative breast cancer. Epigenet Chromatin. 2019;12:44.https://doi.org/10.1186/s13072-019-0290-9.
15. Baker C, Retzik-Stahr C, Singh V, Plomondon R, Anderson V, Rasouli N. Should metformin remain the first-line therapy for treatment of type 2 diabetes. Ther Adv Endocrinol Metab. Jan 12 2021;20(42):1882–9825. https://doi.org/10.1177/2042018820980225.
16. De A, Kuppusamy G. Metformin in breast cancer: Preclinical and clinical evidence. Curr Probl Cancer 2020;44:100488. https://doi.org/10.1016/j.currproblcancer.2019.06.003.
17. Bailey CJ. Metformin: Historical overview. Diabetologia. 2017;60:1566–1576. https://doi.org/10.1007/s00125-017-4318-z.
18. Cejuela M, Martin-Castillo B, Menendez JA, Pernas S. Metformin and breast cancer: where are we now. Int J Mol Sci. Feb 28 2022;23(5):2705.https://doi.org/10.3390/ijms23052705.
19. Barakat HE, Hussein RR, Elberry AA, Zaki MA, Elsherbiny Ramadan M. Factors influencing the anticancer effects of metformin on breast cancer outcomes: A systematic review and meta-analysis. Expert Rev Anticancer Ther. Apr 3 2022;22(4):415–436. https://doi.org/10.1080/14737140.2022.2051482.
20. Samuel SM, Varghese E, Kubatka P, Triggle CR, Büsselberg D. Metformin: the answer to cancer in a flower? Current knowledge and future prospects of metformin as an anticancer agent in breast cancer. Biomol. Dec 9 2019;9(12):846. https://doi.org/10.3390/biom9120846.
21. Gholami M, Klashami ZN, Ebrahimi P, Mahboobipour AA, Farid AS, Vahidi A, *et al.* Metformin and long non-coding RNAs in breast cancer. J Transl Med. Feb 27 2023;21(1):155. https://doi.org/10.1186/s12967-023-03909-x.
22. Finley J. Cellular stress and AMPK activation as a common mechanism of action linking the effects of metformin and diverse compounds that alleviate accelerated aging defects in Hutchinson-Gilford progeria syndrome. Med Hypotheses. Sep 1 2018;118:151-62. https://doi.org/10.1016/j.mehy.2018.06.029.
23. Teng Z, Feng J, Qi Q, Dong Y, Xiao Y, Xie X, *et al.* Long-term use of metformin is associated with reduced risk of cognitive impairment with alleviation of cerebral small vessel

disease burden in patients with type 2 diabetes. Front Aging Neurosci. Oct 29 2021;13:773797. https://doi.org/10.3389/fnagi.2021.773797.

24. Kim J, Lee J, Jang SY, Kim C, Choi Y, Kim A. Anti-cancer effect of metformin on estrogen receptor-positive and tamoxifen-resistant breast cancer cell lines. Oncol Rep. May 1 2016;35(5):2553–60. https://doi.org/10.3892/or.2016.4675.
25. Kasznicki J, Sliwinska A, Drzewoski J. Metformin in cancer prevention and therapy. Ann Transl Med. 2014 Jun;2(6):57. https://doi.org/10.3978/j.issn.2305-5839.2014.06.01.
26. Drzewoski J, Drozdowska A, Sliwińska A. Do we have enough data to confirm the link between antidiabetic drug use and cancer development? Pol Arch Med Wewn. Mar 1 2011;121(3):81–7. https://doi.org/10.3389/fnagi.2021.773797.

وخطر الإصابة بسرطان الثدي لدى النساء المصابات BRCA1تأثير الميتفورمين على تعبير بمرض السكري من النوع الثاني

حنان حامد حسن ، بري حبيب سيف الله

قسم الكيمياء، كلية العلوم للبنات، جامعة بغداد، بغداد، العراق.

المستخلص

تهدف هذه الدراسة إلى الكشف عن مستوى بروتين BRCA1 كعلامة لسرطان الثدي لدى النساء العراقيات اللاتي يعانين سابقاً من داء السكري من النوع الثاني. شملت الدراسة: 80 مشاركاً تم تقسيمهم إلى ثلاث مجموعات فرعية بناءً على استراتيجية الأدوية ومدة المرض، بأعمار (40-70) سنة. تم جمع عينات الدم من مستشفى ابن البيطار في بغداد / العراق بين الفترة من تشرين الثاني 2022 الى شباط 2023. وتم قياس بعض المعايير الكيموحيوية لجميع مجموعات الدراسة والتي تشمل: - نسبة السكر في الدم الصائم (FBS) والدهون الشخصية والتي تم قياسها بطريقة الأكسدة الأنزيمية. باستخدام عملية إنزيمية، تم قياس مستويات الأنسولين وعوامل النمو الشبيهة بالأنسولين (IGF-1) ومستويات مستقبلات هرمون الاستروجين ألفا (ERα)، وبروتين القابلية للإصابة بسرطان الثدي 1 (BRCA-1) عبر ELISA. تم قياس مستوى الهيموجلوبين السكري (HbA1c) باستخدام طريقة الكشف المناعي للساندويتش. أخيرًا، تم حساب نموذج الاستتباب لتقييم مقاومة الأنسولين (HOMA-IR) وفقًا للصيغة المحددة. أظهرت النتيجة أن القيمة P لمقارنة المجموعات لم تكن مهمة بالنسبة لـ FBS وHbA1c وملف الدهون، بينما كانت BRCA1 وERα وInsulin وIGF-1 وHOMA أظهر IR أهمية بقيمة P-0.0001النتيجة الرئيسية هي أن المرضى الذين يتناولون الميتفورمين لمدة أقل من عام واحد فقط مما ساهم في زيادة مستوى BRCA1. هناك ارتباط إيجابيًا بين مستوى BRAC1 ومستويات ERα والأنسولين وIGF-1. وفقًا لتحليل ROC، أظهر BRCA1 حساسية وخصوصية عالية. نستنتج أن بروتين BRCA1 يعد معلما جيدا للتنبؤ بحدوث سرطان الثدي لدى النساء المصابات بداء السكري من النوع الثاني وأن الميتفورمين يزيد من تركيز BRCA1-portien.

الكلمات المفتاحية: بروتين BRCA1، سرطان الثدي، ERα، الميتفورمين، داء السكري من النوع 2.