

Role of metformin in prevention and prognosis of breast cancer

Minahil Binte Saleem, Sarah Fatima, Zoha Ali Khan

Dear Editor, Metformin is a hypoglycaemic drug of the class biguanides used as the first-line treatment for type 2 diabetes mellitus (T2DM). The drug acts by inhibiting hepatic gluconeogenesis, decreasing intestinal absorption of glucose and circulating insulin. It has also been suggested that the drug indirectly increases insulin sensitivity by increasing peripheral glucose utilization. Data from the World Health Organization (WHO) shows that breast cancer (BC) is the most prevalent cancer in women, with an incidence of 1.7 million cases in 2012 (25 % of all female cancers). It is the fifth leading cause of death from cancer overall.¹

A clinical trial conducted in 2019 elaborated that metformin altered host metabolism proving to be a substitute for a fasting-like mechanism that affects cancer cells' metabolism and growth environment of cancer cells including an increase in beta-OH-butyric acid (BHBA).²

It was further corroborated by a research that found an inverse relationship between metformin and BC. This is accomplished by boosting the activity of AMP-dependent protein kinase, which suppresses the mTOR-associated oncogenic signalling pathway. This induces S phase arrest and apoptosis in triple-negative breast cancer cells. Data from 18,527 participants brought about 2,680 participants who used metformin at least three months before the diagnosis of BC. A multivariate study showed that this was negatively associated with BC risk (0.821, 0.726-0.912, $p=0.002$).³

A favourable response on disease-free survival and overall survival in BC patients with T2DM. The number of CD8+ tumour-infiltrating lymphocytes (TILs) has been increased with the use of metformin engendering anti-carcinogenic effects.⁴

3rd MBBS Student, Dow Medical College, Karachi, Pakistan.

Correspondence: Minahil Binte Saleem. e-mail: minahilsaleem602@gmail.com

In the last 15 years, we have seen a drastic change in the demographics of BC, with an estimated increase of 70.7 to 130.6% in 2020 and 2025 relative to 2015 in the 30-34 age group in Pakistan.⁵ There has been a significant increase in T2DM along with increased use of metformin for its treatment which thus raises a question about the efficacy of the drug in a neoadjuvant setting for BC on Pakistani society. Further research, especially clinical trials, needs to be conducted in Pakistan including but not limited to a correlation of metformin use and incidence of BC.

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