

Review Article

African American Women and Triple Negative Breast Cancer: Widened Disparities Associated with Covid-19 Pandemic

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- Triple Negative Breast Cancer (TNBC), African American Women, disparities, Socioeconomic status, Covid-19 pandemic, disadvantaged neighborhoods

Abstract

Background: Breast cancer accounts for approximately one third of all cancers in women and it is the second most common cancer deaths among women. However, triple negative breast cancer (TNBC) is the aggressive, polymorphic sub-type of breast cancer. It accounts for 10-20% of all breast cancers in the United States, affecting African American (AA) women disproportionately. The lifetime probability of developing breast cancer in African American Women is 1 in 8 versus 1 in 9 for white American Women, yet AA women experience greater mortality rates than their female counterparts (Saini, Ogden, McCullough, Torres, Rida and Aneja, 2019). AA women are diagnosed younger with more advanced tumors. Literature is indecisive to the extent of the impact of disadvantage neighborhood, yet research suggest that segregated disadvantaged poverty neighborhoods are associated with the highest diagnosis TNBC and decreased standard of care during Covid-19 pandemic. This review study focuses on the possible contributing factors associated with the development of TNBC and the effect of delayed treatment during Covid-19 pandemic.

Methods: Forty articles were extracted from PubMed and Google Scholar, but only articles that met the inclusion and exclusion criteria were selected for this review. The inclusions were TNBC, African American women, disparities, Covid-19, socioeconomic and disadvantaged neighborhoods. Exclusions were other subtypes of cancer, ethnic groups and men.

Results: The study indicated a strong link between disadvantaged neighborhoods and lower socioeconomic status and high mortality rate associated with TNBC in AA women population. Additionally, Covid-19 was associated with the widened disparities in treatment delays and high mortality rates among the AA women with TNBC.

INTRODUCTION

Breast cancer accounts for one third of all cancers in women and the second most common cancer deaths among women (1). There has been a decrease in breast cancer mortality in the United States during the past decade, due to improved screening, limited use of hormonal therapy in women and new treatment (2). Yet, despite the advancements in breast cancer detection and treatment, the death rates for cancer continued to be higher for African Americans with higher cancer death rates and lower life expectancy than white men and women (69.8 5 versus 75.7 years and 76.5 versus 80.8 years) respectively. The lifelong possibility of developing breast cancer for white women are 1 in 8 versus 1 in 9 for African American Women African American women. Yet, African American women are more likely to present with breast cancer at an earlier age with larger tumors, more advanced disease and higher rates of triple negative breast cancer likely twice more than white to be diagnosed with TNBC (3).

Specifically, triple negative breast cancer (TNBC) tumors do

not respond to endocrine therapy and other targeted therapies. TNBC do not express estrogen receptor, and progesterone receptors or HER-2 genes. The Human epidermal growth factor receptor -2, (HER-2), is protein found on the surface of breast cells and involved in the normal cell growth that can be over expressed and may contribute to metastasis of cancer cells. TNBC occurs in 20% of diagnosed breast cancer, diverse in character and is disproportionately increased in younger African Americans women 22% compared to 12% White American women (4). It is controversial whether health disparities, socioeconomic factors, genetics and stress contribute to the aggressive behavior and poor diagnosis of African American women. It is worth knowing that there are four hormone receptor strands of hormone receptors. Breast cancer has four primary molecular subtypes, defined in large part by hormone receptors (HR) and other types of proteins involved (or not involved) in each cancer. The main female cancer types are (1) HR+/HER2, (2) HR-/HER2- (Triple Negative), (3) HR+/HER2+ and (4) HR-/HER2+ HER2. HER2 stands for human epidermal growth factor receptor 2. HER2+ means that tumor

cells make high levels of protein called HER2/negative, which has shown to be associated with breast cancer aggression.

Subtle changes in the breast include a finger felt lump, nipple discharge, changes in nipple appearance, persistent pain or swelling to name a few. Yet, it is not uncommon to notice mild changes in the breast pre-menstruation, weight gain/loss and menopause. It is the major changes that linger which gives rise to breast cancer concerns. These cancer cells develop in women breasts, but rarely in men. However, the exact cause of the abnormal cell development is unknown. Hence, it is imperative that providers teach their clients how to be aware of the changes in their body, how it relates to own health and family history. The investigator of this review study has been involved with fundraisers events, participated in the walk-a-thon and talked with survivors and their families. As a Registered Nurse, the investigator has a first-hand information of breast cancer and has noted that these women are courageous, supportive, hopeful, and dedicated to finding a cure. The amount of respect and support that is exhibited amongst these women is exceptional.

The current review is asking the research question on what is the significance of race, genetics, socioeconomic status, the environment and Covid-19 contribution to the outcome of African American women with TNBC? To answer this question, the reader needs to know that breast cancer has touched many of our personal lives or through our loved ones because been diagnosed with breast cancer is a life-changing experience or death sentence to some.

METHOD

Forty articles were assessed for review but only articles met the inclusion and exclusion criteria. The study inclusions were African American women residing in low income neighborhood, socio-economic status, triple negative breast cancer, and Covid-19 while exclusions were other cancer types, ethnic groups, and Asian, Latino, and European American women. PubMed advanced search was utilized to retrieve literature on the chosen research topic by using certain key words.

REVIEW OF LITERATURE AND DISCUSSION

It is estimated that 1.8 million new cases of breast cancer were diagnosed in 2015, worldwide (5). The American Cancer Society reported that 231,840 cases were invasive cancers and 602,290 were non aggressive and that 1 in 8 women will experience breast cancer during their lifetime (5). A study with 177,000 women participants revealed that higher percentages of African American women, American Indians, Hispanics and Alaska natives were diagnosed with stage three cancer, higher than the white participants (6). In their study the investigators reported that the white women in the study were more likely to be enrolled in health insurance, compared with the minority races.

According to (7), the lack of health coverage delays the screening, diagnosis, treatment and access to medical care. Although the incidence of breast cancer is lower in African American women compared to white women, AA women are 42% more likely to die from the disease, frequently diagnosed late, with a stage 3 or a higher aggressive form, called triple

negative breast cancer, accounting for 15-20% of breast cancers in the United States (7). Unfortunately, triple breast cancer are usually detected before menopause and has lower survival rates. It is identified by the absence of estrogen and progesterone receptors and the absence of replication of human epidermal growth factor (HER2). The tumor cells in triple negative breast cancer demonstrate an increased level of invasion, promoting metastasis (7). Gene analysis of various categories display differential gene signatures, but extensive thorough research of its nature, tumor biology, gene expression and pathways needs to be analyzed through clinical trials specifically for the AA women.

The Covid-19 pandemic presents a new set of unique challenges in managing the breast cancer patients, with limiting hospital staff, surgery, treatments and therapies. It is evident that the gap of disparities has widened according to a Chinese study on cancer patients, focusing on the vulnerability, 3 out of 5 patients have an increased chance of being intubated, critically ill or die from the complications (8). It is critical to determine which breast cancer patient needs priority treatment. The prioritization and triage of the breast cancer patients is paramount by a multidisciplinary team is paramount, maximizing care and decreasing mortality (9).

A systematic review of 62 articles by (10) suggest to focus on clinical and non-clinical risk factors. The systematic review on triple negative breast cancer in AA women disparities vs. biology by Dietze, Sistrunk, Miranda-Carboni, O-Reagan & Sewalt concentrated on the tumor suppression gene, whose key role is to repair the DNA double helix's double strand, because 69% of breast cancer with mutation are triple negative breast cancers.

ANALYSIS

Linnenbringer and colleagues in their systematic review study noted possible multilevel pathways for social structural conditions and health disadvantages that contributed to breast cancer in AA women. It is the opinion of many investigators that there are multiple contributing factors involved in the disease development which unfortunately results into poor outcomes and increase in mortality rates of breast cancer in AA women. Hence, the investigators concluded that it is imperative that clinical trials be sponsored by government to personalize treatment needed for triple negative breast cancer, providing standard care, education for the families and healthcare institutions, for effective intervention as it relates to high mortality rate of breast cancer among the African American woman.

It is worth knowing that underserved communities predominantly consist of people of color and low income individuals. These disparities are deeply rooted in the power of politics, economics, racism and discrimination, leading to major health and economic predicaments. According to research studies, the inner cities have the highest rates for late stages of diagnosis of breast cancer. The dependent variables that could contribute to the higher incidence of breast cancer and triple negative breast cancer are (1) environment (2) stress (3) pollution (4) socio-economic status (5) geographic location (6) isolation (7) lack of education (8) obesity (9) diet and (10) genetics. These adverse conditions can contribute to disease and alter DNA (11).

Although there have been advancements in the treatment

of breast cancer through lowering the death rates with early detection and decreased the use of hormonal treatment, not all women have benefited from these advancements. Women of color are often not involved in the trials to cure breast cancer, which may be due largely to the distrust in the system. The majority of genetic trials on breast cancer are done on white females. The inadequate representation of minority women creates a disproportionate gap in genetic studies, treatment and knowledge in the treatment of triple negative breast cancer.

Hence, in an effort to address the history of misrepresentation of the minorities in trial, barriers should be a part of the initial assessments and training of researchers to encourage trial recruitment. According to the Health Belief Model, individuals will take action to prevent illness if they regard themselves as susceptible to the condition and believe that there are potentially serious consequences. The model suggests that specific cues such as one's own environment can impact the final action one may take. The six constructs predicting health behavior are (1) risk of susceptibility, (2) risk of severity (3) benefits to action (4) barriers to action (5) self-efficacy and (6) cues to action as shown in (Figure 1).

The notorious coronavirus (Covid-19) pandemic has affected every facet of life, and has distorted the norm. Immune-suppressed cancer clients have increased risks of infection, compared to the general population. This population have 3 out of 5 more chances of being intubated, critically diagnosed or dying from complications than the average person. Clients who have received chemotherapy 30 days prior to Covid-19 diagnosis, or have a cancer history can present a case with more severe complications (8). The primary risk for the cancer client is having limited access to care with decreased clinical visits. Hence, Covid-19 has added further disparities to women of color diagnosed with breast cancer. Until recently, the focus for Healthcare was on Covid-19 pandemic reduction and prevention, not on other diseases, unless in life threatening cases. At the epic of Covid-19 pandemic, many physicians did not accept new clients; there were delays in diagnosis, screenings, and treatments. Some were afraid to attend appointments, creating feelings of depression and anxiety. The Covid - 19 pandemic prompted other health underlying diseases

such as obesity, hypertension and diabetes. Hospital personnel were limited, making it difficult to contact health care providers. The Covid-19 has intensified the delays in care and treatment of AA women, imposing long term negative effects on prognosis and survival rate. In an effort to improve care during the pandemic, all staff and clients must wear masks, initiate Covid-19 testing prior to treatments and procedures, shortened hospital admissions, limit visitors, use physical distancing and utilize telemedicine for non-urgent visits. The adaptation to the new norms and mass vaccination helped facilitate care and maintain safety for the client and the hospital staff.

RESULTS AND DISCUSSION

The result of this review has shown that disparities in cancer outcomes are as a result of multi-faceted interactions between socioeconomic, biological, educational, nutritional, and environmental and other factors. This systematic review has illuminated the correlation across the continuum, the impact on the disadvantaged neighborhood, environment, health disparities, which lead to an increased risk for breast cancer/triple negative breast cancer in AA women. Based on the articles reviewed, a comprehensive review of level 1 evidence article by Gomez in 2015 showed that 82% of the published articles reviewed published evidence that attributes to social and built environments to breast cancer and increased mortality rates. In addition, a level 3 evidence study published in 2017 by Conway focused on neighborhood environment, with ethnic disparities, genetics variations and key regulatory genes that may underline racial disparities in breast cancer development. Hence, it is imperative to develop networks to assess, design, implement and re-evaluate strategies to educate, provide support via social services, improve health care access, engage the community local /professional and political participation to create safer neighborhoods. Breast cancer patient care pre/post Covid-19 pandemic should not be compromised to enable effective management of care among AA women with TNBC.

Other articles reviewed suggested that Covid-19 pandemic was responsible for treatment delays, delayed surgeries, delayed diagnosis and longer waiting appointment times. Severe

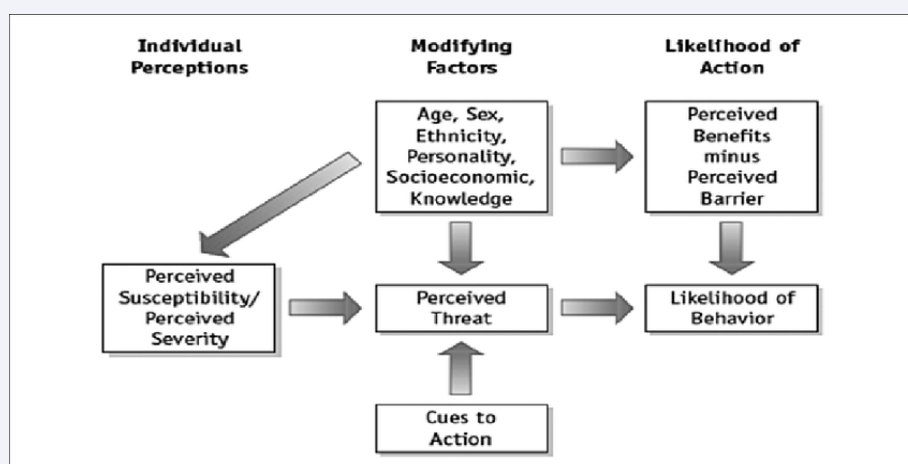


Figure 1 The Health Belief Model.

complications have been reported to occur in 33% of Cancer patients with Covid-19, secondary to the immunosuppression status of some cancer patients (8). These patients have 3.5 fold increased risk of needing the ventilator, ICU or death (8). Therefore, timely diagnosis and treatment of triple negative breast cancer is critical. Delayed diagnosis and treatment can deteriorate status and progression of the cancer. It was projected that a 20% increase in mortality due to delays in treatment and diagnosis (12).

Studies in Wuhan China noted that treatment within 14 days prior to the diagnosed of Covid-19 was a risk factor of developing severe complications. The primary risk for cancer patients is the limited access to health care and the inability to receive the necessary medical services in a timely manner. The Wuhan finding led to the development of Guidelines for Covid-19 prevention and management of cancer patients. It was a guide for health care professionals and cancer treatment facilities on the proper recommendations, Covid-19 contact measures, and maximizing resources to assist in sustaining health services to cancer patients (2). It is therefore, recommended that the risks and benefits of the delay be assessed individually for treatment, to prevent health consequences of TNBC in AA women (8).

SUMMARY

It has been estimated that 1.8 million new cases of breast cancer were diagnosed worldwide in 2015. The American Cancer Society reported that 231,840 cases of invasive cancer and 602,290 non aggressive breast tumors were diagnosed in American women as of 2018. There will be 1 in 8 women who will suffer from breast cancer during their Lifetime (13). Breast cancer estrogen status is a critical prognostic indicator for breast cancer treatment and survival rates. In an event to normalize and strategize treatment for the AA women, health institutions need to be exceedingly aware of the institutional barriers and client-related barriers that prevent quality and timely care and the Covid-19 pandemic new normal inclusive. Controlled historical data on the treatment of triple negative breast cancer is limited secondary to disproportional trials including minorities. There are new treatments for TNBC clients with immune therapies, and antibody drug conjugates under investigation that give hope to those diagnosed. However, awareness and education are the key preventive measures to reduce the mortality of the aggressive cancer in this special population, in addition to increased clinical trial participation for the minority population.

In conclusion, thirty one million Americans have health coverage through the recent placement of the Affordable Care Act (ACA). Research also shows that there have been reductions in un-insurance rates in every state in the country since the law's coverage expansions took effect. People served by the health marketplaces and Medicaid expansion have reached record highs. With the ACA, it would be much more easier for the minorities

and the underserved to find a health insurance plan based on individuals' income and personal health needs. In most states, participants may even qualify for financial subsidies. Minorities may now quickly and easily apply for coverage through the new healthcare marketplace for coverages. Further investigations and resources are needed to bridge the health disparities gap that deprived the minority population of their love ones which ultimately widened the gap despite the Covid-19 vaccine implementation.

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