

Risk Factors Affecting the Prevalence of Breast Cancer among Female aged 40-69 years in Australia.

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Abstract

In Western World, the prevalence of breast cancer has become a public health issue and increasing with high mortality rate. Currently, such increasing trend has been recorded in Australia with approximately 1.38 million female population diagnosed of breast cancer. Advances in cancer screening, detection and treatment have improved the survival rate of those diagnosed with breast cancer. Studies conducted using randomized control trial, Cohort studies and Case- control studies have identified life style factors, medical and socio-economic factors as risk factors predisposing individual to the risk of developing breast cancer. In this systematic review, high quality assessment was graded on some of the studies. There were strong evidence with high consistent finding on the association between the physical inactivity, post-menopausal obesity and alcoholic consumption on the risk of developing breast cancer. There was moderate evidence on the association of hormonal contraceptive and family history in causing breast cancer; and limited evidence on the association of body mass obesity, fat consumption and age in breast cancer formation. To reduce the risk factors affecting the prevalence of breast cancer among the targeted age group in Australia, gymnastic facilities for physical activities should be provided

to the population. Life style factors such as adequate dietary intake, cessation of cigarette smoking and reduction in pre-and post- menopausal exposures to hormones should be promoted among the population residing in rural and urban regions. The use of X-ray mammography, chemo preventive, prophylactic surgery or prophylactic prevention mastectomy should be encouraged. Financial and emotional support should be provided to those residing in rural areas that are unmarried and jobless, and finds it difficult to cope with living conditions.

Keywords: Breast Cancer; Risk factors for breast cancer; Prevalence; Aboriginal or Indigenous Australian; Death rate; Randomized control trial; Cohort study; Case control study; Cancer screening; Pre-and Post-menopausal hormones, etc.

1. Introduction

Globally, the prevalence and occurrence of female breast cancer has become a public health issues. Breast cancer is defined as invasive malignant cells in the breast tissues that undergoes cell proliferation and extends to other part of the body through the lymphatic system (Abu-Reza A. N. 2004).

In Western populations, breast cancer has remained the most common cancer among women and the main cause of death. In spite of several epidemiological studies conducted to identify the risk factors that predispose an individual to breast cancer, it has become difficult to lower the incidence and prevalence of the disease. According to Ferlay J. et al. (2010), it has been documented that approximately 1.38 million people were diagnosed of breast cancer at the age of 40 years and above, and roughly 60% of death rate has been recorded in developing countries with poor income status.

Advances in cancer screening, detection and treatment have improved the survival rate of breast cancer in high income countries. According to Coleman et al. (2008), the survival rate of breast cancer in high income country over the 5 years survival rate was 80% when compared with 40% in some countries with low income status. The significant decrease in the mortality rate and increase in the rate of survival are due to success in mammography screening and treatments in countries with high income status (Berry DA. Et al. 2005).

The incidence and prevalence of breast cancer in Australia is escalating and it is regarded as the second most common type of cancer among women above 40 years of age (Australian Institute of Health and Welfare and National Breast and Ovarian Cancer Centre, 2009). Data from the Australian Institute of Health and Welfare cancer data base (2008) have reported the prevalence of breast cancer with increase in age, which varies in different states and territory. In 2008, the number of Australian women diagnosed of breast cancer at the age of 40 years and above was 13,567; of these numbers, the percentage of women diagnoses between 40-69 years was 69% and above 70 years was 25% (AIHW Cancer database, 2008). With a 5 years prevalence rate in different states and territory, the

number of women diagnosed with breast cancer in 2004 was 4,027 in New South wale, 2,940 cases in Victoria, 2177 cases in Queensland, 1112 in Western Australia, 1010 in Southern Australia, 300 cases in Tansmania, 200 in Australian capital and 60 cases in Northern Australia (AIHW, 2005). In 2008, the prevalent rate increases, accounting to 14,223 new cases in Victoria, 11,251 in Queensland, 5,537 in Western Australia, 4,787 cases in Southern Australia, 1,376 in Tansmania, 943 cases in Australian Capital and 278 in Northern Territory (AIHW Cancer database, 2008). As a result of these significant increase and lack of screening programs in different states and territories, it is predicted that in the future, the number of women diagnose with breast cancer will rise. In spite of these predictions, there are insufficient data about the risks factors of breast cancer among the female population in Australia, which has reduced the provision of health care services to the population. Therefore, conducting a systematic review on this risk factors will help to lower the prevalent rate, facilitate the early diagnosis and screening among the Australian female population.

Aims and Objectives of the study

With the availability of documented evidence, the aim of this study is to investigate the risk factors affecting the prevalence of breast cancer among the female population aged 40-69 years in Australia. As requested by the National breast and ovarian cancer centre, the objective of this systemic review was to identify the risk factors associated with increase in female breast cancer. These risk factors were age, family and genetic history, increase in breast density, inadequate physical activity, obesity, smoking, alcohol, fats consumption, pregnancy termination, postmenopausal and endogenous hormones, oral contraceptive, and hormonal replacement therapy.

The objectives were accomplished by looking into the different studies conducted in Australia and putting them together. Reference was also made in other studies conducted outside Australia to see that their findings on the risk factors of breast cancer were consistent with the findings of studies conducted in Australia. The following research questions were address:

- (a) What is the risk factor that increases female breast cancer in Australia?
- (b) What are the socioeconomic factors and individual characteristic that increases the risk of breast cancer among this targeted age group population?
- (c) What are the current intervention strategies to reduce the risk factors associated with high prevalence of female breast cancer in Australia?

Literature Review

Increase in age of the population increases the risk of developing breast cancer. According to a surveillance and epidemiological study conducted in USA, it was documented that 1 in 202 females were diagnosed with breast cancer below 39 years, 1 in 26 females diagnosed between 40-59 years, and 1 in 28 diagnosed between 60-69 years (Siegel R. et al. 2013). Based on the literature evidence documented by the Australian Institute of Health and Welfare (2015a), the percentage of women

diagnosed with breast cancer above 50 years of age was 77%. Further documented information by the Australian cancer database (2008) have reported that 'approximately 9,128 women in Australia have been diagnosed with breast cancer at the age 40-49; 15,037 women diagnosed at the age of 50-59; 15,449 women at the age of 60-69 and 9,327 women diagnosed at the age of 70 years and above'.

Genetic factors have been recognized as a factor that predispose women to the risk of developing breast cancer. Literature evidence have suggested that the percentage of women diagnosed with breast cancer and are associated with family history was 20-25%, of which approximately 5-10% of this population were associated with autosomal genetic inheritance (Lynch HT. & Lynch J. 1986; Margolin S. et al. 2006). According to Sharif S. et al (2007), some genes mutation have been identified as risk factor for breast cancer, and these includes 'BRCA1 and BRCA2 genes, TP53 genes, PTEN genes, STK genes, NF1 genes and CDH-1 genes'.

According to the information documented by the Collaborative Group on Hormonal Factors in Breast Cancer (2012), it has been reported that women experiencing delay in their menopause stage increases their risk of having breast cancer by 3%, which can be increased to 17% in every 5 years. Women experiencing their menopause at 55 years and above increases their risk by 12% (Collaborative Group on Hormonal Factors in Breast Cancer, 2012), this occurs as a result of continuous use of reproductive hormones (Anderson KN. Et al. 2014), and a strong evidence have suggested an association between hormonal receptor therapy and risk of developing breast cancer (Anderson KN. et al. 2014; Reeves et al., 2006). Based on the available evidence, it was documented that the risk increases among the pre- menopausal women when compared to the risk experienced by post- menopausal women (Chlebowski RT. Et al. 2013; Manson JE. Et al. 2013).

Excessive consumption of alcohol among women has been established as a risk factor for breast cancer (Ferrini et al., 2015; Mourouti et al., 2015). According to recent epidemiological studies that was carried out, it has been documented that women consuming 10g of alcohol daily increases the risk by 7.1% (Hamajima et al., 2002 & Jung S. et al. (2016); and the risk increases by 20% among those that consume more than 30g of alcohol daily (Key et al., 2003).

It has been established that physical activities are inversely related with risk of breast cancer (Ballard-Barbash R. et al. 2012; Ellsworth RE. et al. 2012). Adequate physical activities helps to keep fit, maintain the normal body physiological activities and reduces the risk of obesity and breast cancer among the adolescent (World Health Organization, 2010; Loprinzi et al. 2012). According to a documented report from the Australian Bureau of Statistics (2013), it was established that women from Aboriginal and Torres Strait Islander were engaged in less physical activity per week, and this have predispose them to a high risk of breast cancer when compared with non-aboriginal Australian population.

The American Cancer Society Journal have reported a strong evidence that increase in smoking increases the risk of breast cancer, and women that participate actively in smoking have about 24% increase in the risk when compared with 13% of risks among the inactive smokers (Guadet et al., 2013). A study conducted in the laboratory settings have also reported a strong evidence that active female smokers are at high risk of developing metastatic breast cancer (Di Cello et al., 2013). According to Irwin et al. (2013), inability to sleep and restlessness have been known to contribute to

the risk of breast cancer among women. A recent study on breast cancer research conducted in Australia have documented that poor quality sleep, insomnia and restlessness stimulates for the release of cytokines, adokines and other inflammatory proteins which are known to increase the risk of developing the disease (Bower JE.et., 2005; Mullington JM.et al., 2010; Besedovsky L. et. Al., 2012).

Materials and Methods

Eligibility criteria and study selection

Studies were included in the systematic review if they met the following criteria:

- (a) The population included women at the age of 40-69 years
- (b) Cohort studies, Case-Control studies and Random control studies were included
- (c) Studies selected includes authors name, year of publication and the study design
- (d) Population with risk factors such as family history and genetics, life style factors, reproductive and menstrual history, socio-economic factors (type of residence, marital status, education and occupation), exogenous and endogenous hormones, breast conditions and body size) were included.
- (e) The quality score was 73% and above.

Principle source of information and the search strategy

A computerized search strategy was conducted using the following database:

- (a) Australian Cancer database which contains information of the entire participant diagnosed with breast cancer in Australia.
- (b) GLOBOCAN database and breast screen Australia data which provides the information on the prevalent rate of breast cancer and its associated risk factors.
- (c) Data from the New South Wales cancer registry, Queensland cancer registry and the Cancer Council Victoria was collected, and these data reported the prevalence and diagnosis of breast cancer in Australia.
- (d) Data from the Australian Institute of Health and Welfare which contain information on the prevalence of breast cancer in Australia from 2001-2019.
- (e) Data from the Australian Longitudinal Study on Women's Health database which reported the socioeconomic and life style factors affecting the health and well being of the targeted aged group.

Quality Assessment

The quality of this review was assessed competently and reviewed by (Ugochukwu O. Maluze and Prof.

Fahad Hanna). The quality of this review was based on the studies observed from various articles that investigated the risk factors affecting the prevalence of breast cancer in Australia. High risk (+++), medium risk (++) and low risk (+) was used to quantify the risk factors. The criterion used to assess the study includes:

- (a) Aboriginal and non-aboriginal Australian population that falls within the targeted age group was included.
- (b) Assessment of risk factors and its outcome
- (c) Good techniques used to analyze the study
- (d) Appropriate data presentation.

Random control study was the preferred study design, followed by the Cohort and then the Case Control study.

Type of Participants

Participants that falls within the age group 40-69 years were included in this review. The Participants were selected from the random control trial, cohort studies and case-control studies. For references and consistency purposes, studies conducted outside Australia were also included to ensure that their findings are in consistent with the findings of studies conducted in Australia. Studies will indicate a wider generalization if the results of their investigation are consistent using the same targeted age group on the participants.

Levels of evidence for the selected studies

Strong evidence: 1 randomized control study, > 2 Cohort Studies with high quality consistent finding

Moderate evidence: Single high quality cohort, >2 high quality cohort Studies

Limited evidence: Single cohort, 2 case control studies, > 2 Cross-sectional studies

No evidence: there were no findings.

Ethical Consideration

This systematic review was conducted without the ethical approval as it was not required. This is because the clinical details of the participants were de-identified.

Searched Keywords

The following searched keywords was used in this review: "Prevalence, Breast Cancer, Australian, Aboriginal or indigenous, risk factors for breast cancer, death rate, genetic, hormones, pre-menopausal, post-menopausal, endogenous hormone, exogenous hormone", etc.

Results/Findings

Study Selection

The computerized search yielded 742 articles; of these articles, only 24 studies met the inclusion or eligibility criteria for this systematic review. 23 Studies investigated the life style factors, genetic and medical factors contributing to the risk of breast cancer among the targeted population. One study investigated the socio-economic factors predisposing the population to the risk of invasive breast cancer. Reasons for choosing the studies that met the eligibility criteria were considerations on the physical activity, nutritional intake, smoking, genetic and family history, hormonal replacement therapy, menstruation stage, rural and urban residence, education and income status.

Description of studies

The studies conducted in this systematic review are summarizing on the table 1 and 2. One study was randomized control study, 16 studies were Cohort studies and 7 studies were case control studies. The sample size for cohort ranges from 204 to 200,000, and for the case control, the sample size ranges from 98 cases to 98,067 controls. All the studies involved a population based study. Majority of the studies were conducted in Australia. For the purpose of references, generalization and consistency of studies, only few studies were done in New Zealand, France, Norway and USA to ensure that their findings on the risk factors of breast cancer were consistent with the findings of the studies conducted in Australia.

Methodological quality of included studies: evidence synthesis

Following the criteria's and guidelines for the methodological qualities, the scores for the quality assessment were expressed in percentage and were graded from 72-85%. By referring to table 1 that contains the quality assessment scores, the media quality score was calculated as 81% and the mean cut off as 79%. Using 79% as the cut off score, it can be seen from the table that only 12 out of 23 studies were considered to be on a high quality standard. By considering table 1, studies on physical inactivity shows a strong evidence as these involves one randomized control study and 2 Cohort studies that has a generalized consistent finding. Studies on the exposure to post-menopausal hormones and oral contraceptive demonstrate moderate evidence which involves two cohorts study and four case control studies. Studies on Alcohol consumption shows a strong supportive evidence as daily alcoholic consumption contributes significantly to the risk of having breast cancer, these studies involves three cohort studies and 2 case control studies. Studies on cigarette smoking, age, fat consumption and obesity have been supported by only one study, indicating limited evidence.

Table 1: Shows the studies on the risk factors of breast cancer among the targeted aged group 40-69 years.

Arthur (ref), Country, Year.	Age	Risk factors / Risk level	Marital Status	Study Subject	Follow up	Score (%)	Evidence Synthesis / Interpretation
RCT Courneya 2014), Australia	>40	Physical inactivity Low risk (+)	Not Stated	Cases-242	8 yrs	73	Strong evidence
Cohort Van den Brandt, 2000, Australia	>40	Physical inactivity Low risk (+)	Not Stated	Cases-4385	4.5 Yrs	81	Strong evidence
Cohort Stewart et al 2003, Australia.	>40	Physical inactivity. Low risk (+)	Not Stated	Cases-385	-	75	Strong evidence
Cohort McKenna 2001, Australia .	>40	Post-menopausal exposure to Hormonal Replacement Therapy.	Not stated	313		81	Moderate evidence
		Moderate risk (++)					
Case-Control McCredie et al. 1998b, Australia	>40	Hormonal Contraceptive. Moderate risk (++)	Not Stated	Cases-467 Control-406		85	Moderate evidence
Case-Control Key 2002, Australia .	>40	Post-menopausal exposure to hormones (Oestrogen) Moderate risk (++)	Not stated	663 cases 1765 control	2 yrs	80	Moderate evidence

Cohort Heinemann et al. 2002, New Zealand .	>40	Oral Contraceptive Moderate risk(++)	Not stated	610,328	-	76	Moderate Evidence
Case- Control March banks et al. 2002, New Zealand.	>40	Oral Contraceptive Moderate risk (++)	Not stated	Cases - 4576. Control- 4682		84	Moderate evidence
Case Contr Price et al. 1999, Australia	>40	Hormonal Contraceptive Moderate risk (++)	Not Stated	Cases- 298. Control- 1926		78	Moderate evidence
Cohort Maclinnis et al. 2004, Australia	>40	Post- menopausal obesity Moderate risk (++)	Not stated	Cases- 13,598	-	84	Strong evidence
Cohort Tehard & Clavel- Chapelon 2006, France	>40	Pre- & Post- menopausal obesity Moderate risk (++)	Not Stated	Cases for pre- menopa usal obesity – 275. Cases for post menopa usal obesity- 860.	-	75	Strong evidence
Cohort Dumeaux et al. al 2004, Norway	>40	Post- menopausal obesity High risk (+++)	Not Stated	Cases- 87,084	-	81	Strong evidence

Cohort Smith- Warner 1998, Australia	>40	Alcohol Low risk (+)	Not stated	Cases- 4335/32 2647	-	76	Strong evidence
Cohort Baglietta et al. 2005, Australia	>40	Alcohol Low risk (+)	Not stated	Cases- 41,528	-	84	Strong evidence
Cohort Horn-Ross et al. 2004, Australia	>40	Alcohol Low risk (+)	Not stated	Cases - 103,460	-	84	Strong evidence
Case- control McDonal d et al. 2004 USA	>40	Alcohol Low risk (+)	Not stated	Cases - 4,575 Control- 4,682	-	80	Strong evidence
Case- control Hamajima 2002, Australia.	>40	Alcohol Low risk (+)	Not stated	Cases- 58,515 Control- 98,067	-	72	Strong evidence
Cohort Cui 2006, Australia	>40	Cigarette Low risk (+)	Not stated	Cases- 189,000	-	78	Limited evidence
Cohort Stewart 2012, Australia	>40	Body Mass and Obesity Moderate risk (++)	Not Stated	Cases- 204	-	75	Limited evidence
Cohort Bernardis 2004, Australia	>40	Family History High risk (+++)	Not Stated	Cases- 252	-	80	Moderate evidence
Cohort Liet al al. 2003, USA	>40	Family History High risk (+++)	Not Stated	Cases- 1,488	-	82	Moderate evidence

Cohort Missmer, 2002,	>40	Fat consumption Low risk (+)	Not Stated	Cases- 7379	-	78	Limited evidence
Europe							
Cohort Gnerlich, 2009, Australia .	>40	Age High risk (+++)	Not Stated	Cases- 200,000	-	74	Limited evidence

Table 2 Multivariate logistic regression results on socio-economic factors showing adjusted odds ratios (95% confidence intervals) of late stage of breast cancer at diagnosis by explanatory variables with early stage as the reference category (n = 195).

Individual level Characteristics	O R	95%cl	Advance d Stage (%)
<i>Area of residence:</i>			
Rural	1.08	0.53–2.23	39.8
Urban	1.00		36.1
<i>Country of Birth:</i>			
Australia.	1.00	-	37.3
-	-		
English Speaking.	1.05	0.42-2.67	41.4
Non-English Speaking.	1.42	0.51-3.97	41.7
<i>Education:</i>			
School Certificate.	1.00	-	33.8
Higher School.	1.71	0.83–3.53	39.3

University.	2.20	0.80–6.03	48.3
Marital Status:			
Not partnered	1.00	- 0.54–	37.8
Partnered	1.20	2.67	38.8
Financia l status:			
Poor	0.72	(0.58-0.9)	
Good	1.00	-	

*p < 0.05 chi-squared test.

Sources: (WHO,2006; Berecki J. & Brgum N. 2008; Leung J. et al. 2014)

Available online: <https://www.cancer.nsw.gov.au/how-we-help/reports-and-publications/rural-urban-disparities-in-stage-of-breast-cancer>.

Discussions

Physical inactivity

Physical activity is a risk that affects the prevalence of breast cancer and it has been identify to be inversely associated to the development of breast cancer. In table 1.0 above, 3 studies (one randomized and two cohort studies) examines the relation between physical inactivity and breast cancer. The study on cohort indicates a high quality score that is above the mean cut off for quality assessment. With strong evidence, the studies found a strong association between physical inactivity and the risk of breast cancer, and this was found consistent with the previous findings documented by the World Cancer Research Fund and American Institute for Cancer Research (2018).

Post menopausal exposure to hormones and oral contraceptives

Two prospective cohorts and four case controls studies were used to establish the association and impact of post-menopausal exposures and oral contraceptives to the risk of breast cancer. Three case controls and two cohorts study were identified with high quality standard. There were sufficient strong evidence to establish that pre-and post-menopausal exposures to hormonal replacement therapy increase the risk of breast cancer.

Alcohol

Three cohorts and two case controls study were used to investigate the link between alcoholic consumption and predisposition to the risk of breast cancer. Of these studies, only two cohorts and one case controls study were of high quality, with a quality score above the mean quality assessment score. With strong supportive evidence, the findings of the study demonstrate that daily consumption of

alcohol increases the risk of late stage of breast cancer, and this has been found to be consistent with the report documented by the World Cancer Research Fund and America Institute for Cancer Research (2018).

Family History

The association of family history with breast cancer was investigated in this study using two cohorts study that of high quality consistent findings. With moderate sufficient evidence, the studies identified that family and genetic history increases the risk of breast cancer among the targeted participants, and this has found to be consistent with the findings of previous study (Bethea TN. Et al. 2016).

Age, Cigarette smoking and Obesity

The influence of age, cigarette smoking and obesity in breast cancer was established using three cohort studies with low quality score. With limited evidence and consistent findings, the study found that these risk factors increase the risk of developing female breast.

Area of Residence

Table 2 above shows the impact of socio-economic factors on the risk of developing breast cancer. In this study, the author reported that women residing in the rural remote areas have a late stage of breast cancer when compared with those residing in urban metropolitan areas. This is because they experience difficulties in accessing the breast cancer health services such as mammogram and self examination screening which put them at risk of developing the disease (Mitchel et al. 2006; Wilkinson D. & Cameron K. 2004; Krzyzak et al. 2010; Halls et al. 2004). These findings have showed to be consistent with the previous findings of various authors, showing the differences in the prevalence of breast cancer in urban- rural regions (Bettencourt BA et al. 2007). The odds and 95% confidence interval of women developing late stage of cancer in rural area were shown in table 2, as compared with the odds of women in the urban areas.

Marital Status

Another socio-economic factor that affects the prevalent of breast cancer is marital status. According to (Williams K. 2003), it was reported that married women experienced a high advantage socio-economic status when compared with unmarried women which enable them to have access to a better health care services, promoting and influencing their normal healthy lifestyle and reduces the risk of breast cancer (Lee S. et al. 2005). Unmarried women are more disadvantageous and at a high risk of being exposed to the risk of late stage of breast cancer (Lee S. et al. 2005). Considering the table 2 above, the odds and the percentage of married women with late stage of breast cancer is insignificantly higher than that of unmarried women. This finding is inconsistent with the findings of Williams K. 2003).

Country of birth

Woman's country of birth has been reported in New South Wales as a risk factor for breast cancer (Feletto E and Sitas F. 2015). The high increase in breast cancer have been documented on women born in Australia and other English Speaking country (Feletto E. & Sitas F. 2015) when compared with women born in non-English speaking (Tamimi RM. 2017). This has been consistent with the findings of this study. By referring to table 2 above, Women born in Australian and speaks English have odds of a late stage of breast cancer, when compared with women that does not speak English (WHO, 2006; Berecki J.

& Brgum N. 2008; Leung J. et al. 2014).

Available online: <https://www.cancer.nsw.gov.au/how-we-help/reports-and-publications/rural-urban-disparities-in-stage-of-breast-cancer> .

5.0 Strength of the studies

The design of this systematic review in a prospective cohort setting is the Strength of the study. The study establishes the relationship between the risk factors and breast cancer outcomes, and also compares the rural-urban disparities in the stage of breast cancer, which has been reported as the first Australian study to compare the differences in rural and urban stage of breast cancer diagnosis.

6.0 Conclusion and future recommendation

In conclusion, the prevalence of breast cancer in Australia is high. In spite of several epidemiological studies conducted to identify the risk factors that predispose an individual to breast cancer, it has become difficult to lower the incidence and prevalence of the disease. Detecting breast cancer at the early stage of development will facilitate for a quick response in treatment and improvement in the survival rate. For preventive measures, the use of X-ray mammography, chemoprevention, prophylactic surgery or prophylactic preventive mastectomy can be use to lower the risk of the disease.

However, it has been identified in the study that women residing in rural areas have low socioeconomic status which prevents them from getting access to the health care services. For public health concern, this factor should not be ignored. It is recommended that mobile mammography screening should be supplied efficiently to the indigenous rural population. Women without partners, jobless and living in rural areas may lack financial support, social and emotional support, which in turn predispose them to the risk of breast cancer. Adequate support should be provided to them; which will improve their normal healthier lifestyle and reduce the risk of breast cancer and obesity related disease.

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