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The Impact of Age on Breast Cancer Incidence Among Libyan Women: A Meta-Analysis.

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ABSTRACT

This meta-analysis, which draws on eight original studies, looks at the average age of Libyan women diagnosed with breast cancer. A full review of the original articles published in English between October 2016 and August 2024. A systematic review of five main databases was conducted to identify studies including Embase, Scopus, PubMed, Google Scholar and Web of Science. Only studies with unambiguous age data were included, as determined by the Population, Exposure, Comparator, Outcome, and Study Design (PECOS) criteria. The effect sizes were pooled using a random-effects model, and heterogeneity was measured with Cochran's Q and I^2 statistics. The pooled mean age across studies was 47.81 years (95% CI: 46.87–48.74), indicating high variability (I^2 = 98.1%). Influence diagnostics identified one outlier study that contributed to the high heterogeneity. These findings highlight age distribution patterns in breast cancer cases in Libya, suggesting avenues for targeted early intervention strategies. Overall, these findings emphasize the demand for age-specific screening programs in Libya.

Keywords: Breast Cancer; Meta-Analysis; Age Factor; Heterogeneity; Random-Effects Model; Incidence Rate; Libyan Women

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1.INTRODUSTION

Breast cancer is still the most frequent cancer among women worldwide, and it is the leading cause of cancer-related deaths among women in many nations [1]. Despite substantial breakthroughs in early detection and treatment, differences in breast cancer incidence and mortality remain global, affected by different demographics, lifestyles, and genetic factors [2]. The Middle East and North Africa (MENA) area, including Libya, has seen an increase in breast cancer cases over the last two decades, which can be ascribed to demographic shifts and rising life expectancy[3].

Breast cancer is the most frequent cancer among women in Libya, and the incidence rate has been gradually rising, posing a huge public health challenge. While there are several studies on breast cancer in Western populations, regional studies concentrating on Libyan women are limited, leaving gaps in our understanding of the population's distinctive epidemiological characteristics [4]. Addressing these gaps is critical for designing targeted prevention and intervention methods, as risk factors like age, reproductive history, and genetic susceptibility can differ greatly among populations [5].

Age is one of the common factors that is considered by many Libyan studies on breast cancer. Because of cultural, genetic, or healthcare-access nuances, age is considered a critical factor. The occurrence of breast cancer among Libyan women normally rises as women age. However, late diagnosis and aggressive tumors are considered more concerning factors that are associated with young females who have breast cancer, especially in developing nations [6] . Libya is one of these developing nations that face many challenges, including community awareness that breast cancer is a treatable disease_ an important factor for encouraging early diagnosis. In addition, the country has few advanced pathology services and limited treatment options, including radiotherapy and the full range of systemic treatments available in high-resource settings. Moreover, due to the small sample sizes and conflicting methodologies, research in Libya has shown variations in the age distribution of breast cancer patients[7]. A meta-analysis approach is a good statistical tool that gives a more accurate estimate of age as a risk factor, which facilitates comparing different areas and insights into targeted age-specific interventions [8].

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The meta-analysis technique is based on collecting data from different studies, which helps researchers draw useful conclusions, particularly when individual studies report different effect sizes. This technique can estimate heterogeneity and precision, which are critical for understanding policy and practice in health treatments [9]. Due to the lack of meta-analysis studies on breast cancer and conflicting age estimates due to small samples in Libya, this work attempts to show the link between age and breast cancer incidence among Libyan women and make recommendations for healthcare policies in Libya that focus on breast cancer prevention and early identification.

2.MATERIALS AND METHODS

2.1.Search Strategy

Eight original studies published in English from October 2016 to August 2024 were considered and conducted using Embase, Scopus, PubMed, Google Scholar, and Web of Science databases. The research utilized keywords such as “Breast Cancer,” “Risk Factors,” “Awareness and Knowledge of Breast Cancer,” and “Libyan Women” to capture relevant studies focusing on breast cancer demographics within Libya.

2.2.Study Design

Studies were screened at the title and abstract level to assess their relevance and eligibility. Each included article met the following criteria: 1) full text available in English, 2) original research, and 3) compliance with the Population, Exposure, Comparator, Outcome, and Study Design (PECOS) criteria. Table 1 outlines the specific PECOS criteria applied to guide the inclusion and exclusion of studies.

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Table .(1): Research question based on PECOS criteria.

(**P** (Population	Libyan women diagnosed with breast cancer
(**E** (Exposure	Age as a risk factor
(**C** (Comparator	Comparison of age's effect on breast cancer risk
(**O** (Outcome	Incidence of breast cancer
(**S** (Study Design	Cross-Sectional Study
Exclusion criteria	.Studies without age-specific data have been excluded

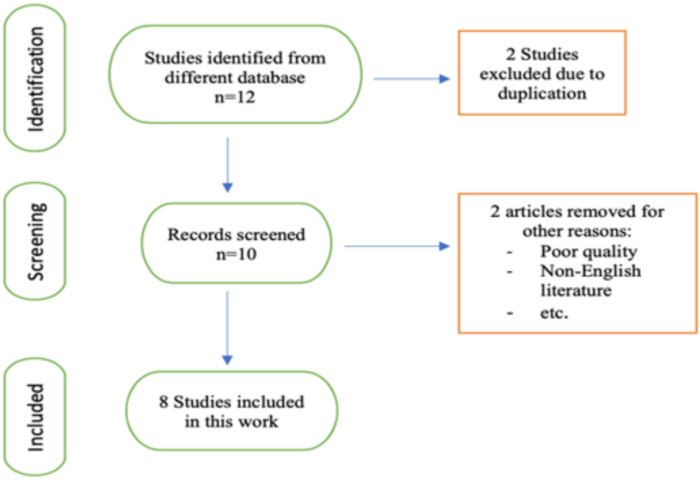

Figure .(1): PRISMA flow diagram of the included studies.

3.STATISYICAL ANALYSIS

The analysis was implemented by using random-effect and common-effect models. In this work, studies were merged according to the sample size, mean, and standard deviation. The analysis was focused on the mean age of Libyan women who have breast cancer. Since the main aim of meta-analysis is minimizing the variance and assessing the dispersion of the effect sizes from study to study, the heterogeneity of the included studies was evaluated. In the random effect model analysis, each study was weighted by the inverse of its variance. Moreover, sensitivity analysis and forest plots were two criteria used to identify any outlier studies in this meta-analysis.

3.1.Computing Q

It is the first step to estimate the heterogeneity, where Q is defined as a mea-

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sure of weighted squared deviations, and expressed as follows:

$$\boldsymbol{Q} = \sum_{i=1}^{k} W_i Y_i^2 - \frac{\left(\sum_{i=1}^{k} W_i Y_i\right)^2}{\sum_{i=1}^{k} W_i}$$

Where W_i is the study weight ($\frac{1}{V_i}$),V_i is the within-study variance, and is the study effect size.

3.2.Estimating τ^2

Next, the parameter **τ^2** is between-studies variance (the variance of the effect size parameters across the population of studies), which is defined as follows: **τ^2=(Q-df)/C**

where df=k-1 is the degree of freedom , K is the number of studies, and

$$c = \sum_{i=1}^{k} W_i - \frac{\sum_{i=1}^{k} {W_i}^2}{\sum_{i=1}^{k} W_i}$$

The amount Q-df is the excess variation, which represents the dispersion in true effects, i.e., the differences in the true effects from study to study.

3.3.The I² Statistic

The statistics **τ^2** (and **τ**) reflect the amount of true heterogeneity (the variance or the standard deviation), while the **I²** Statistic is the proportion of the observed variance that reflects real differences in the effect size, and can be written as follows:

I^2=((Q-df)/Q)×100%

From the above equation, it can be seen that is a ratio scale from 0% to 100% and is affected by the amount of excess variation [8].

3.4.Testing the Heterogeneity

To test the heterogeneity, the null hypothesis states that all studies have a common effect size. The follows a central chi-squared distribution with df equals k-1. The p-value will be calculated.

A significant p-value indicates that the null hypothesis is rejected, and the true effect sizes vary.

The computational part of this study was conducted using the Comprehensive Meta-Analysis and R software.

4.RESULTS

This section provides a detailed summary of the age at breast cancer diagnosis among Libyan women based on eight studies. The estimates of heterogeneity, tests of publication bias, and meta-analysis summaries for each of the studies were considered in this analysis.

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1. Individual Study Summaries

The mean age, standard deviation, sample size, and 95% confidence Interval (CI) of the eight articles were summarized and displayed in the table below.

Table .(2): The meta-analysis summaries of the age at breast cancer diagnosis among Libyan women based on eight studies.

Study	Study Population	Year	Mean Age	Standard Deviation	Sample Size (n)	95% CI for Mean Age
Mouna[10]	Different cities in Libya*	2020	46.90	8.70	918	[46.3, 47.5]
Mufida[11]	Zawia city	2022	48.00	12.10	200	[46.3, 49.7]
Taher[12]	Tripoli city	2016	48.00	5.00	292	[47.4, 48.6]
Aisha[13]	Tripoli city	2024	47.35	1.00	501	[47.3, 47.4]
Mamduh[14]	National Cancer Institute (NCI Misurata and Sabratha)	2023	48.60	1.09	400	[48.5, 48.7]
Samira[15]	Tripoli city	2020	46.70	15.60	38	[41.7, 51.7]
Huda[16]	Benghazi city	2021	50.50	13.30	336	[49.1, 51.9]
Houssein[17]	Different cities in Libya*	2024	46.10	11.70	984	[45.4, 46.8]

(*) The different cities in Libya include Tripoli, Benghazi, Tobruk, Sabha, Gharyan, Ghadames, Al Jufra, and Murzug.

Studies with small sample sizes have shown that the mean age at diagnosis is steady in the late 40s with large variance, for example, the study of Samira [15].

In general, studies with larger sample sizes have shown more stable mean age; moreover, within study populations, standard deviations have denoted different levels of age diversity.

2.Meta-Analysis Summary

The results from the common effect model and random-effects model were summarized below:

Common Effect Model: The pooled mean age is 47.83 years with a 95% confidence interval [47.77, 47.90].

Random Effects Model: The pooled mean age under the random effects model is 47.81 years, with a 95% confidence interval [46.87, 48.74].

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To visualize these results, a forest plot (see Figure 2) provides a comparative display of mean ages from each study, including their confidence intervals. This helps illustrate the overlap and variation among studies.

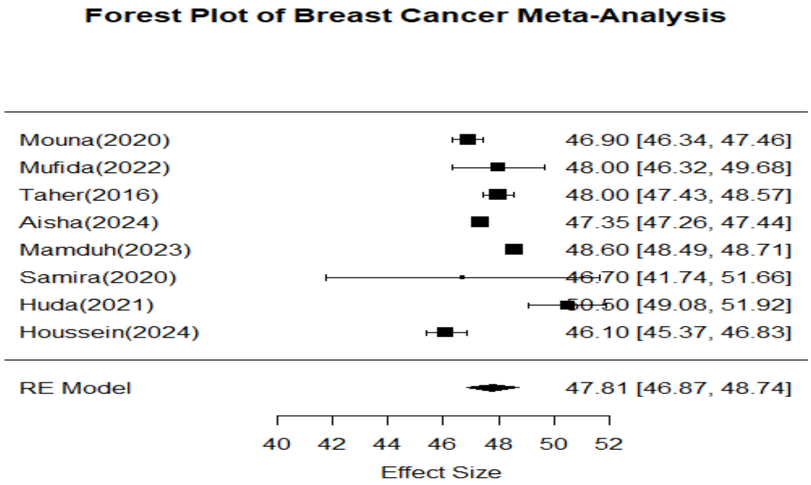

Figure .(2): Forest plot displaying mean age and 95% confidence intervals for each study. Studies with wider confidence intervals indicate more variability and/or smaller sample sizes, while those with narrower intervals are based on larger or more uniform samples.

The random effects model, which accounts for variability between studies, provides a mean age slightly lower than the common effect model. This finding suggests that, despite some variation, the mean age at diagnosis for Libyan women is relatively stable around the 46–48 year range.

3.Heterogeneity Analysis

To examine differences across studies, heterogeneity tests were conducted:

1.**I^2 Statistic**: The I^2 value is 98.1%, indicating high heterogeneity. This means that a large portion of the variability in age at diagnosis is due to differences between studies, differences in study target populations or targeted effects, survey recruitment and administration methods, measurement instruments, doses of interventions, and timing of outcome measurements.

2.Q Statistic: The Q-test was statistically significant ($p < 0.0001$), confirming the pres-

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ence of substantial heterogeneity.

These findings are further illustrated in the funnel plot below (Figure 3), which shows the distribution of studies around the pooled mean. Studies dispersed widely from the mean suggest heterogeneity.

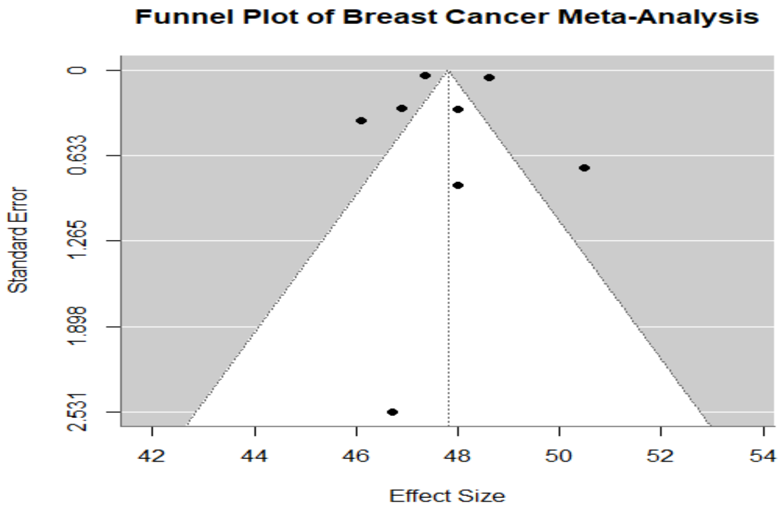

Figure .(3): Funnel plot displays individual study mean ages and sample sizes. While Studies clustering symmetrically around the mean would indicate lower heterogeneity, the observed dispersion highlights significant variability.

The abnormal heterogeneity across studies suggests that factors, such as geographic, genetic, or methodological differences, might influence the age of diagnosis, necessitating a random-effects model to provide more reliable conclusions.

5. PUBLICATION BIAS

A regression test for funnel plot asymmetry (p = 0.8602) suggests no significant publication bias.

The lack of significant publication bias indicates that the pooled mean age estimate is likely robust and unaffected by the selective publication of studies.

6.DISCUSSION

According to this study, the average age of breast cancer diagnosis in Libya is (47.81 years, 95% CI: 46.87–48.74), which appears to be lower than that of other African and Asian countries. In 2004, Schlichting et al[18]. reported a mean age of 51.0 years for 3819 Egyptian women, while Missaoui et al[19]. found a mean age of 50.2 years for 7736 Tunisian women in 2012. In Asian countries, Mehdi I et al[20]. reported a mean age of 49.05 for 1248 women in Oman and a mean age of 49.42 for 536 Iraqi Kurdish women, as reported by Karim et al[21]. When comparing these results to developed countries, such as Canada[22] with a mean age of 60.1 for 36455 women and the United States with a mean age of 58.4 for 110,153 women, it is evident that the age at diagnosis of breast cancer in Libya is significantly lower.

The age factor of breast cancer was considered by a number of studies using a meta-analysis approach. Kumar et al.[23] and Solbana1 and Chaka[24] have addressed that the age at menarche of those <12 years old has a high risk of developing breast cancer three times more than older age. Moreover, the age at first birth has been studied by Argenal et al. [25], where they found that the risk of having breast cancer was three times higher in women aged 30 years and older than in younger women. Again, the study by Ewartz et al.[26] indicated that women who give a first birth at an age older than 35 years have a higher risk (40%) than those women with an age of less than 35. The late 40s are also considered a significant factor affecting the development of breast cancer. In this study, the development of breast cancer in Libyan women was estimated at an age of 48 years. Also, the study, which was conducted by Liu, et al.[27] found that women aged over 50 years

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have a high risk of having breast cancer.

The results of this meta-analysis indicate that the pooled mean age of breast cancer patients in Libya is 47.81 years, with significant heterogeneity among the studies (I^2 = 98.1%). This variability may be influenced by factors such as sample size differences, methodological variations, and potential demographic diversity within the studied populations. For example, the study of Mamduh[14] had pointed out that a high influence on the pooled estimate, which may imply different diagnostic practices and rare population characteristics.

The estimated excessive heterogeneity of our findings implies that age alone may not account for the variance in incidence of breast cancer, which recommends further research about other risk factors that could be related to age, such as genetic predispositions, lifestyle factors, and access to healthcare services. The absence of significant publication bias, as assessed by funnel plot asymmetry, supports the reliability of the included studies despite the heterogeneity.

The awareness and screening programs for women who are aged 40 years and older were one of the needs for public health in Libya, and genetic predisposition, cultural delays in seeking care, may explain why Libyan women may be diagnosed younger.

Future research should consider larger, multi-center studies within Libya to better account for regional and socioeconomic variations, further clarifying age-related breast cancer risks and contributing to comprehensive cancer prevention efforts in the region.

The strengths of this study include its status as the most recent systematic review and meta-analysis, with a sample size of 3669 female breast cancer patients between 2016-2024 in Libya. This allows for an overview of the estimated age of diagnosis for breast cancer in women and the pooled prevalence of breast cancer in Libya. However, our study was not free of some limitations. The first limitation was the geographic distribution of the included studies, as most were conducted in the Western regions of Libya. This could cause bias in generalizing the findings to the whole country of Libya. Also, acknowledging small sample sizes in some studies was one of these limitations. Finally, another limitation could be the narrow scope of the review, which focused only on Libya.

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7.CONCLUSION

The results suggest that breast cancer is typically diagnosed among Libyan women at an age of approximately 46–48 years, notably younger than the average diagnosis age in Western populations, which often exceeds 50 years. High heterogeneity between studies implies that various factors may influence these estimates, indicating a need for additional research to explore such influences, including potential regional, environmental, or genetic factors.

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