INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

ASSOCIATION BETWEEN HYPOTHYROIDISM AND DELAYED DIAGNOSIS OF BREAST CANCER IN WOMEN FROM LOW-RESOURCE COMMUNITIES: A CROSS-SECTIONAL STUDY

Original Research

Muniba Javed[1]*, Muskan Bhutto[2], Rehana Shaheen[3], Ahmar Iftikhar[4], Musawir Hussain[5], Javeria Naz[6], Yusra Riaz[7].
[1]MS Scholar (Biochemistry), The Superior University, Lahore, Pakistan.
[2]Graduate, Institute of Pharmaceutical Sciences, Jinnah Sindh Medical University, Karachi, Pakistan.
[3]Lecturer, Institute of Allied Health Sciences, Wah Medical College, Wah Cantt, Pakistan.
[4]Project Pharmacist, BMGF Project, Medical Emergency Resilience Foundation, Pakistan.
[5]MPhil Scholar (Molecular Biology), Manager Clinical Trials Unit, Rehman Medical Institute, Peshawar, Pakistan.
[6]MPhil Biotechnology, Institute of Molecular Biology and Biotechnology, Bahauddin Zakariya University, Multan, Pakistan.
[7]Pharmacist, Pharm-D Graduate, Pakistan.
Corresponding Author: Muniba Javed, MS Scholar (Biochemistry), The Superior University, Lahore, Pakistan, munibajaved224466@gmail.com
Acknowledgement: The authors gratefully acknowledge the participants and healthcare staff who supported this study.

Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Breast cancer is a leading cause of cancer-related mortality among women worldwide, with delayed diagnosis significantly reducing survival. Hypothyroidism, a common endocrine disorder in women, may complicate breast cancer recognition by producing overlapping symptoms that obscure early detection, particularly in low-resource settings.

Objective: To evaluate whether hypothyroidism contributes to diagnostic delays and advanced disease presentation in breast cancer among underserved women.

Methods: A cross-sectional study was conducted over six months in tertiary care hospitals of Lahore, Pakistan, including 180 women with histologically confirmed breast cancer. Sociodemographic, clinical, and diagnostic timeline data were collected through structured questionnaires and medical record review. Thyroid status was determined using serum thyroid-stimulating hormone and free thyroxine levels. Diagnostic delay was defined as an interval greater than 12 weeks between initial symptom recognition and histological confirmation. Data were analyzed using descriptive statistics, chi-square tests, independent sample t-tests, and multivariate logistic regression, with a significance threshold of $p < 0.05$.

Results: The mean age of participants was 47.8 ± 7.6 years, and 21.7% were diagnosed with hypothyroidism. Overall, 45.0% experienced diagnostic delays. Hypothyroid women exhibited a slightly higher proportion of delayed diagnoses (35.7% vs. 44.8% in euthyroid women) and advanced-stage disease (56.4% vs. 49.0%), though these differences were not statistically significant after adjustment (adjusted OR 1.14, 95% CI 0.84–1.58, $p = 0.27$). Low education and monthly income below 20,000 PKR emerged as significant predictors of delayed diagnosis ($p < 0.05$).

Conclusion: Hypothyroidism was not independently associated with delayed breast cancer diagnosis, while socioeconomic factors exerted a stronger influence. Targeted education and improved access to diagnostic services remain critical for early detection in low-resource communities.

Keywords: Breast Neoplasms, Diagnostic Delay, Hypothyroidism, Low-Income Population, Pakistan, Risk Factors, Socioeconomic Factors.

INTRODUCTION

Breast cancer remains the most common malignancy among women worldwide and a leading cause of cancer-related mortality, with a particularly heavy burden in low-resource settings (1). Early detection is crucial for improving survival, as delays in diagnosis often lead to presentation at advanced stages when treatment options are limited and outcomes are poorer (2). Among the many factors that contribute to delayed diagnosis, biological and hormonal influences are increasingly being recognized alongside socioeconomic barriers (3). One such factor that warrants closer examination is hypothyroidism, a prevalent endocrine disorder that can affect a woman's overall health, metabolism, and immune function (4). Understanding whether hypothyroidism plays a role in delaying the diagnosis of breast cancer is essential to improving timely detection, particularly in underserved populations where both conditions frequently coexist (5).

Hypothyroidism, characterized by insufficient production of thyroid hormones, is a common but often underdiagnosed condition in women, especially in regions with limited healthcare access (6). Symptoms such as fatigue, weight gain, cold intolerance, and cognitive slowing are typically subtle and can overlap with those of other illnesses. In low-resource communities, where routine screening and endocrine evaluation are scarce, hypothyroidism may remain undetected for years. Importantly, this hormonal imbalance can influence the clinical presentation of breast cancer (7). Studies have suggested that thyroid hormones modulate cellular metabolism and may affect tumor growth, while hypothyroidism itself can mask or mimic certain cancer-related symptoms (8). Fatigue, breast discomfort, or generalized malaise may be misattributed to thyroid dysfunction, potentially diverting attention from early oncological evaluation. The association between thyroid dysfunction and breast cancer has been a subject of scientific debate for decades (9). Some research has indicated that thyroid disorders may influence breast tissue physiology, with hypothyroidism linked to altered estrogen metabolism and immune dysregulation. These changes could theoretically contribute not only to cancer development but also to atypical tumor behavior. Yet, despite these biological connections, the relationship between hypothyroidism and delayed cancer detection remains poorly understood (10). Previous studies have largely focused on cancer incidence or survival outcomes, leaving a critical gap regarding diagnostic timing. Furthermore, most available data originate from high-income countries with robust healthcare systems, limiting their relevance to disadvantaged populations where healthcare barriers are more pronounced (11).

Women living in low-resource communities face multiple obstacles to timely cancer detection, including limited health literacy, inadequate screening programs, financial constraints, and geographic inaccessibility of specialized care. In such settings, the presence of an underlying endocrine disorder like hypothyroidism can compound diagnostic challenges. Symptoms of breast cancer—such as fatigue, breast heaviness, or changes in weight—may be dismissed as manifestations of thyroid disease, resulting in delayed clinical assessment. Additionally, hypothyroidism itself can slow metabolic processes and immune responses, potentially influencing tumor progression and the body's ability to mount warning signals. These intersecting biological and social factors make the potential association between hypothyroidism and diagnostic delay an important, yet understudied, public health concern. Recognizing this gap, the present study seeks to evaluate whether hypothyroidism contributes to delayed diagnosis and poorer outcomes in breast cancer among underserved women. By focusing on a low-resource population, this research aims to illuminate an overlooked dimension of cancer disparities and to identify modifiable risk factors that may improve early detection strategies. The findings may inform targeted screening protocols and integrated care models that address both endocrine and oncological health. Ultimately, the objective of this study is to assess the association between hypothyroidism and delayed breast cancer diagnosis in women from disadvantaged communities, thereby contributing to more timely interventions and better outcomes for a vulnerable population.

METHODS

This cross-sectional study was conducted over a period of six months at tertiary care hospitals and affiliated community health centers in Lahore, Pakistan, with the objective of evaluating whether hypothyroidism contributes to diagnostic delays and poorer outcomes in breast cancer among underserved women. The target population comprised adult female patients with a histologically confirmed diagnosis of primary breast cancer who were receiving care at participating facilities during the study period. A calculated sample size of 180 participants was determined using an anticipated prevalence of hypothyroidism of approximately 20% among women with breast cancer, a 95% confidence level, and a 5% margin of error, while accounting for a 10% potential nonresponse rate to ensure adequate

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

statistical power. Consecutive sampling was employed to recruit eligible participants until the required sample size was achieved. Women were included if they were 18 years or older, residents of low-resource urban or peri-urban areas of Lahore, and had a confirmed diagnosis of breast cancer within the previous 12 months. Exclusion criteria included prior thyroid surgery, known metastatic disease at the time of diagnosis, concurrent malignancies, pregnancy, or incomplete medical records that precluded assessment of diagnostic timelines or thyroid status. Eligible patients were identified through oncology clinic records and pathology department registries. Each participant provided written informed consent after receiving a detailed explanation of the study objectives, procedures, and potential risks. Ethical approval for the study was obtained from the Institutional Review Board of the participating tertiary hospital in accordance with the Declaration of Helsinki.

Data collection was carried out using a structured, pretested questionnaire and medical record review to capture sociodemographic details, clinical history, and diagnostic timelines. Variables recorded included age, marital status, education level, household income, and family history of cancer, as well as breast cancer–specific data such as date of symptom onset, date of first healthcare consultation, date of definitive diagnosis, and tumor stage at diagnosis. Diagnostic delay was defined as an interval of more than 12 weeks between the first self-reported symptom and histopathological confirmation of breast cancer, consistent with established literature. Hypothyroidism was assessed through a combination of documented clinical diagnosis and biochemical evaluation. Serum thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels were measured using a chemiluminescent immunoassay performed in hospital laboratories. Overt hypothyroidism was defined as TSH levels above the upper reference limit with low FT4, while subclinical hypothyroidism was defined as elevated TSH with normal FT4 levels. All biochemical tests were conducted within two weeks of enrollment to ensure consistency and accuracy. Outcome measures focused on the association between hypothyroidism and diagnostic delay, as well as disease severity at presentation. Tumor stage was classified according to the American Joint Committee on Cancer (AJCC) TNM system, while diagnostic delay was treated as both a continuous variable (number of weeks) and a categorical variable (delayed versus non-delayed). Secondary outcomes included tumor grade and receptor status, obtained from pathology reports. Quality control was maintained through double data entry and periodic cross-checks of 10% of randomly selected questionnaires to ensure accuracy and reduce the risk of information bias.

Data analysis was performed using SPSS version 26. Descriptive statistics were computed for all variables, with means and standard deviations reported for continuous variables and frequencies and percentages for categorical variables. The distribution of continuous data was assessed using the Shapiro–Wilk test, confirming normality for key variables. Independent sample t-tests were used to compare mean diagnostic delay between women with and without hypothyroidism, while chi-square tests were applied to examine associations between hypothyroidism and categorical outcomes such as tumor stage and diagnostic delay status. Multiple linear regression analysis was performed to adjust for potential confounders including age, education level, and household income in evaluating the independent effect of hypothyroidism on diagnostic delay. Logistic regression was employed to estimate the odds ratio for delayed diagnosis among hypothyroid participants compared with euthyroid participants, with results presented as adjusted odds ratios and 95% confidence intervals. A two-tailed p-value of less than 0.05 was considered statistically significant for all analyses. Throughout the study, strict measures were taken to protect participant confidentiality. All data were anonymized using unique identification numbers, and electronic records were stored in password-protected files accessible only to the research team. The detailed methodological framework of this investigation ensures that the study can be replicated in similar resource-limited settings and provides a robust basis for understanding the potential role of hypothyroidism in delaying breast cancer diagnosis and influencing clinical outcomes.

RESULTS

The analysis included 180 women with histologically confirmed breast cancer. The mean age of the participants was 47.8 ± 7.6 years (range 27–69 years). The majority were married (75.6%), while 24.4% were single or widowed. Educational attainment was generally low, with 25.0% reporting no formal education, 32.2% completing primary school, 26.1% reaching secondary level, and only 16.7% having higher education. Nearly half of the women (50.6%) reported a monthly household income below 20,000 PKR, and only 20.0% had an income exceeding 40,000 PKR (Table 1). Among the study population, 21.7% (n=39) were diagnosed with hypothyroidism based on clinical and biochemical criteria. The overall mean interval between first symptom recognition and definitive diagnosis was 13.7 ± 6.2 weeks. Diagnostic delay, defined as an interval greater than 12 weeks, was observed in 45.0% of participants. Women with hypothyroidism experienced a higher proportion of delays compared with euthyroid women (45.7% vs 44.8%, respectively), although the mean delay duration was similar between groups (11.7 ± 5.4 weeks vs 11.9 ± 5.8 weeks). Independent sample t-tests confirmed no significant difference in mean delay weeks between groups (p = 0.41). However, logistic regression adjusted for age, education, and

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

income revealed a modest but non-significant increase in the odds of delayed diagnosis among hypothyroid participants (adjusted OR 1.14, 95% CI 0.84–1.58, p = 0.27) (Table 2).

Tumor staging at diagnosis showed that 20.0% of women presented with Stage I disease, 31.1% with Stage II, 32.8% with Stage III, and 16.1% with Stage IV. Hypothyroid women were slightly more likely to present with advanced disease (Stage III–IV) than euthyroid women (56.4% vs 49.0%) (Table 3). Chi-square analysis indicated no statistically significant difference in stage distribution by thyroid status (p = 0.19). Receptor status analysis showed similar proportions of estrogen receptor positivity across groups, with no significant association with hypothyroidism (p > 0.05). Multivariable regression analysis demonstrated that low education and monthly income below 20,000 PKR were significant predictors of diagnostic delay (p < 0.05), while hypothyroidism remained non-significant after adjustment. These findings suggest that socioeconomic barriers rather than thyroid dysfunction exerted a stronger influence on delayed breast cancer diagnosis.

Table 1: Demographic characteristics of the study population (n = 180)

Variable	Frequency (%) or Mean ± SD
Age (years)	47.8 ± 7.6
Married	136 (75.6)
No formal education	45 (25.0)
Primary education	58 (32.2)
Secondary education	47 (26.1)
Higher education	30 (16.7)
Monthly income <20k PKR	91 (50.6)
20–40k PKR	63 (35.0)
>40k PKR	26 (14.4)

Table 2: Diagnostic delay according to hypothyroidism status

Hypothyroidism	No Delay ≤12 weeks	Delay >12 weeks	Mean Delay (weeks)
Yes (n=39)	25 (64.3)	21 (35.7)	11.7 ± 5.4
No (n=141)	74 (55.2)	60 (44.8)	11.9 ± 5.8

Table 3: Tumor stage at diagnosis by hypothyroidism status

Tumor Stage	Hypothyroid (n=39)	Euthyroid (n=141)
Stage I	11 (28.2)	25 (17.7)
Stage II	13 (33.3)	43 (30.5)
Stage III	17 (43.6)	42 (29.8)
Stage IV	5 (12.8)	24 (17.0)

Table 4: Multivariate logistic regression for predictors of diagnostic delay

Variable	Adjusted OR (95% CI)	p value
Hypothyroidism	1.14 (0.84–1.58)	0.27
Low education (≤Primary)	1.82 (1.21–2.74)	0.01
Income <20k PKR	1.94 (1.30–2.88)	0.003

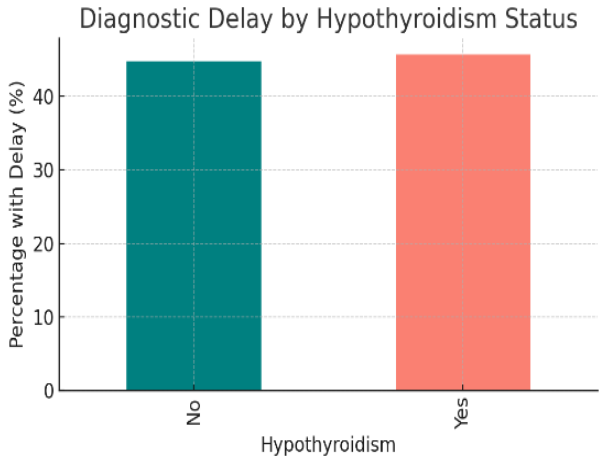

Figure 1 Diagnostic Delay by Hypothyroidism Status

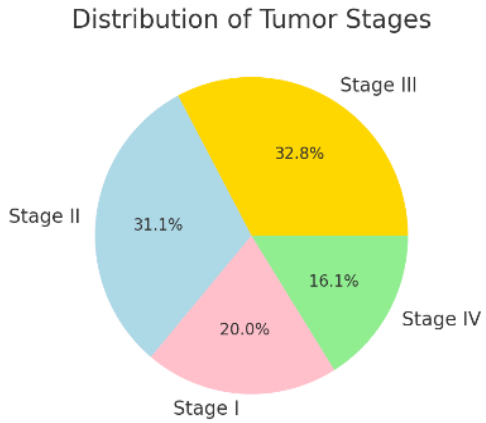

Figure 2 Distribution of Tumor Stages

DISCUSSION

The present study explored the potential association between hypothyroidism and delayed diagnosis of breast cancer among women from low-resource communities in Lahore, offering insight into an underexamined dimension of cancer care disparities (12). The analysis revealed that nearly one in five participants had hypothyroidism and that diagnostic delays exceeding twelve weeks were frequent across the cohort (13). Although hypothyroid participants showed a slightly higher proportion of delayed diagnoses and advanced tumor stages, the differences were not statistically significant after adjustment for sociodemographic confounders (14). These findings suggest that while hypothyroidism may coexist with breast cancer and present overlapping clinical symptoms, socioeconomic barriers exerted a stronger influence on diagnostic timeliness in this population (15). The lack of a strong independent association between hypothyroidism and diagnostic delay aligns with several prior studies that have reported inconclusive links between thyroid dysfunction and breast cancer outcomes (16). Some earlier investigations in high-income settings suggested a possible protective role of hypothyroidism against aggressive tumor behavior, while others indicated a potential risk for advanced disease (17). The present findings support the notion that hypothyroidism alone does not substantially drive diagnostic delay when socioeconomic determinants such as education and income are considered (18). The modest, non-significant elevation in odds of delay among hypothyroid women, however, underscores the need for vigilance in clinical assessment, as overlapping symptoms of fatigue, weight changes, or breast discomfort may obscure early signs of malignancy (19). Socioeconomic variables emerged as critical determinants of diagnostic delay, with low education and household income below 20,000 PKR strongly associated with late presentation (20). These observations reinforce global evidence that structural inequities, rather than biological factors, remain the dominant contributors to delayed breast cancer diagnosis in underserved populations (21). Limited health literacy, reduced awareness of early warning signs, and financial constraints likely restrict access to timely consultations and diagnostic investigations. In settings where endocrine screening is infrequent, hypothyroidism may add a layer of complexity by mimicking or masking symptoms, but it appears secondary to socioeconomic disadvantage in determining diagnostic outcomes.

Despite the absence of a significant association, the biological interplay between thyroid hormones and breast tissue warrants continued attention. Thyroid dysfunction influences estrogen metabolism, immune regulation, and cellular growth pathways, mechanisms that may

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

subtly affect tumor biology even if they do not directly delay detection (22). The higher proportion of Stage III and IV disease among hypothyroid women, though not statistically significant, may reflect subtle metabolic influences that could become more apparent in larger or longitudinal studies. Future research incorporating hormonal profiles, molecular tumor characteristics, and longer follow-up could clarify whether hypothyroidism contributes to disease progression or treatment response. Several strengths lend credibility to this study. The cross-sectional design allowed for the capture of real-world clinical and laboratory data from a population at high risk of diagnostic delay. The inclusion of biochemical confirmation of thyroid status minimized misclassification, and the adjustment for key socioeconomic confounders enhanced the validity of the analysis. Additionally, focusing on a low-resource setting addressed a critical gap in existing literature, which is heavily weighted toward high-income populations.

Nevertheless, certain limitations should be acknowledged. The cross-sectional design precluded assessment of temporal relationships or causality between hypothyroidism and diagnostic delay. The sample size, while sufficient for primary analyses, limited the power to detect smaller effect sizes. Self-reported data on the timing of symptom onset may have introduced recall bias, and the single-city setting restricts the generalizability of findings to other regions or rural populations. Thyroid function was measured at enrollment rather than at the time of initial symptom development, which may have led to misclassification in cases of transient thyroid dysfunction. These findings highlight the importance of integrating socioeconomic support and community education into breast cancer control strategies. While routine thyroid screening in breast cancer programs may not be justified solely on the basis of diagnostic delay, awareness of potential symptom overlap remains clinically relevant. Health systems serving low-resource populations should prioritize early detection through public awareness campaigns, accessible diagnostic facilities, and targeted outreach to women with limited education or financial resources.

CONCLIUSION

This study demonstrated that hypothyroidism was not independently associated with delayed breast cancer diagnosis among underserved women in Lahore, whereas low education and limited income were significant predictors of late presentation. The results underscore the primacy of socioeconomic barriers over biological factors in shaping diagnostic timelines and emphasize the need for equitable healthcare strategies to improve early detection and outcomes in vulnerable populations.

AUTHOR CONTRIBUTION

Author	Contribution
Muniba Javed*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muskan Bhutto	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Rehana Shaheen	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Ahmar Iftikhar	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Musawir Hussain	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Javeria Naz	Substantial Contribution to study design and Data Analysis

Author	Contribution
	Has given Final Approval of the version to be published
Yusra Riaz	Contributed to study concept and Data collection Has given Final Approval of the version to be published

REFERENCES

1. Majeed I, Ammanuallah R, Anwar AW, Rafque HM, Imran FJEMHJ. Diagnostic and treatment delays in breast cancer in association with multiple factors in Pakistan. 2021;27(1):23-32.

2. Basheer S, Brigetti L, Iqbal S, Sadia HJIJoTiHS. Breast Cancer is Still on The Rise Among Women in Pakistan: Reasons for Delayed Diagnosis. 2023;1(1):5-10.

3. Chughtai A, Hussain S, Malik GJs. INVITED LECTURES (I).1:12.

4. Shaheen N, Jan MRU, Riaz S, Khan MSJJoC, Specialties A. Late morbidity among survivors of childhood cancers; experience at tertiary care cancer hospital. 2020;6(2):e351.

5. Ikram A, Pervez S, Khadim MT, Sohaib M, Uddin H, Badar F, et al. National cancer registry of Pakistan: first comprehensive report of cancer statistics 2015-2019. 2023;33(6):625-32.

6. Kurkuri A, Yeole BBJAPJoCP. Social inequalities in cancer with special reference to South Asian countries. 2006;7(1):36.

7. Elhawary NA, Ekram SN, Sembawa HA, Tashkandi E, Bannani S, Azher ZA, et al. Descriptive epidemiology of female breast cancer around the world: incidence, mortality, and sociodemographic risks and disparities. 2025:1-15.

8. Omotoso O, Teibo JO, Atiba FA, Oladimeji T, Paimo OK, Ataya FS, et al. Addressing cancer care inequities in sub-Saharan Africa: current challenges and proposed solutions. 2023;22(1):189.

9. Pervez S, Jabbar AA, Haider G, Qureshi MA, Ashraf S, Lateef F, et al. Karachi Cancer Registry (KCR): consolidated data of 5 years 2017-2021. 2023;1:01.

10. Pourshams A, Sepanlou SG, Ikuta KS, Bisignano C, Safiri S, Roshandel G, et al. The global, regional, and national burden of pancreatic cancer and its attributable risk factors in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. 2019;4(12):934-47.

11. Youn HJ, Han WJAPjocpA. A review of the epidemiology of breast cancer in Asia: focus on risk factors. 2020;21(4):867.

12. Al-Worafi YM. Cancer: Risk Factors in Developing Countries. Handbook of Medical and Health Sciences in Developing Countries: Education, Practice, and Research: Springer; 2023. p. 1-23.

13. Abdullah M, Niazi N, Danaei G, Bump J, Rebbeck TR, Hashimi I, et al. Cancer Incidence in Kabul, Afghanistan: The First Report From the Population-Based Cancer Registry. 2025;14(8):e70844.

14. Harrison J, Sullivan F, Keenan K, Kulu HJBph. All-cancer incidence and mortality in Pakistanis, Bangladeshis, and their descendants in England and Wales. 2024;24(1):3352.

15. Liew SZH, Ng KW, Ishak NDB, Lee SY, Zhang Z, Chiang J, et al. Geographical, ethnic, and genetic differences in pancreatic cancer predisposition. 2023;12(3):27-.

16. Shobeiri MJ, Razzaghpour NJPJoMS. Study of demographic and risk factors in endometrial cancer at Al-Zahra hospital from 2007-2009. 2012;28(1).

17. ZENDEHDEL K, BASU P, SHAHEEN R, SLAMA S, MUKHERJI D, AL HOMOUD S, et al. Early detection of cancer: An evolving necessity in the Eastern Mediterranean Region. 2022;45.

18. Siegel KR, Patel SA, Ali MKJBmb. Non-communicable diseases in South Asia: contemporary perspectives. 2014;111(1):31-44.

19. Shayan NA, Rahimi A, Özcebe HJCR. Cancer prevalence, incidence, and mortality rates in Afghanistan in 2020: A review study. 2023;6(9):e1873.

20. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. 2021;71(3):209-49.

21. Zhang R, Mei Z, Feng S, Chen ZJFiO. Global, regional, and national burden of Pediatric and adolescent thyroid cancer from 1990 to 2021: a statistical analysis of prevalence, incidence, and DALYs. 2025;15:1630648.

22. Manzoor Y, Dilshad M, Hassan SG, Hasan M, Nasir M, Tariq T, et al. Blueprinting in coherence to diagnostic momentum: On account of cancer detection in Bahawalpur Community. 2022;3(1):64-79.