RESEARCH ARTICLE

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Determinants of Diagnosis Delay in a Sample of Breast Cancer Patients from the Mohammed VI Centre for Cancer Treatment

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Abstract

Background: Breast cancer (BC) is the most common type of cancer in women; a delayed diagnosis of BC is associated with advanced stages at diagnosis and reduced survival rates. This study aims to identify the barriers and factors contributing to delayed BC diagnosis among Moroccan women admitted to the Mohammed VI Oncology Center in Casablanca. Methods: We conducted a cross-sectional study from January 2023 to July 2024 at the Mohammed VI Oncology Center in Casablanca. A questionnaire was administered to collect sociodemographic, clinical, behavioral, and healthcare system data. Stages I and IIa were classified as "early diagnosis," while stages IIb and above were classified as "delayed diagnosis." We used the Chi-square test to examine the association between independent variables and outcomes. All variables were included in a multiple logistic regression model using the stepwise backward method, and those with a p < 0.05 were retained in the final model. **Result:** A total of 436 patients were interviewed, and the majority had been diagnosed at a late stage (65.1%). The main factors and barriers included individuals residing in rural or semi-urban areas (OR=2.24, 95% CI [1.22-4.11]), opting for traditional treatments (OR=3.41, 95% CI [1.44-8.04]); individuals expressed a willingness to consult a doctor but faced barriers such as lack of time, financial constraints, or fear (OR=2.23, 95% CI [0.98-5.07]), and poor communication quality among administrative staff (OR = 7.48, 95% CI [1.06-52.68]). Conversely, having a family history of BC (OR=0.52, 95% CI [0.28-0.97]), knowledge about free-ofcharge diagnostic services (OR=0.53, 95% CI [0.29-0.97]), and a positive behavior of the practitioner during the initial consultation (OR = 0.21, 95% CI [0.05-0.9]) emerged as protective factors against delayed presentation and diagnosis. Conclusion: Efforts should concentrate on improving access to affordable, high-quality healthcare and increasing cancer awareness among the population and health professionals.

Keywords: Delayed diagnosis- Breast Cancer- Morocco- Determinant

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Introduction

Breast Cancer (BC) is a significant public health concern and was projected to be the most commonly diagnosed cancer in women worldwide in 2022, according to the International Agency for Research on Cancer (IARC). It accounts for 23.8% of all cancer cases [1]. In Morocco, BC is the most prevalent type of cancer among women, representing 38.8% of cases as reported by the IARC [2]. Casablanca, one of Morocco's largest cities, has a standardized incidence of BC of 49.3 per 100000 women, based on data from the Grand Casablanca Cancer Registry covering the years 2018 to 2021. Delays in diagnosis and the initiation of treatment can lead to more advanced stages of the disease at diagnosis and result in lower survival rat [3-5].

Numerous studies conducted in both developed and developing countries have shown that 14% to 53% of participants experienced a delay in presentation and diagnosis of more than three months [6-12]. A similar statement has been observed among Moroccan women diagnosed with BC [13-16].

The Moroccan Ministry of Health is actively working to improve access to both general and specialized healthcare services. These efforts are further supported by the Lalla Salma Foundation, a non-profit organization established in 2005, which aims to make the fight against cancer a public health priority in Morocco and the surrounding region. The purpose of the Foundation is to develop a national plan for cancer control. Despite these initiatives, many patients are still diagnosed at advanced stages of the disease.

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To address these concerns, numerous studies have been conducted over time in various locations to identify the main factors and barriers influencing BC diagnosis. Key contributing factors identified in these studies include sociodemographic disparities [17, 18], geographic barriers [19], financial constraints [17, 20], insufficient public awareness [17, 19, 20], fear of mortality linked to a BC diagnosis [18], and issues within the healthcare system [21]. In the context of Morocco, empirical research that simultaneously examines sociodemographic and clinical factors, behavioral factors, medical history, accessibility barriers, and healthcare system issues remains notably lacking. Given this research gap and the urgent need for a comprehensive understanding of the factors influencing BC presentation and diagnosis intervals, this study aims to identify the various barriers and factors associated with delayed BC diagnosis. This cross-sectional study was conducted among BC patients receiving care at the Mohamed VI Oncology Center, which is part of Ibn Rochd University Hospital in Casablanca. This institution plays a crucial role in providing oncological care in Morocco. Understanding the factors associated with delayed diagnosis is essential for identifying critical elements impacting BC presentation and diagnosis intervals. The objective is to develop effective interventions aimed at promoting timely diagnosis, identifying women at higher risk, and improving their quality of life.

Materials and Methods

Study design and setting

A cross-sectional study was conducted to explore the determinants contributing to delays in the diagnosis of BC patients at the Mohamed VI Oncology Center, within the Ibn Rochd University hospital center of Casablanca.

Participant's

The study included Moroccan patients aged 18 years and older who newly diagnosed (incident cases) and admitted to, as well as followed up at, the Mohammed VI Oncology Center of the Ibn Rochd University Hospital in Casablanca during the study period. All participants had given their consent to be part of the study. Women who declined to participate or had completed their treatment were excluded from the study.

Data collection

Population recruitment was conducted by using a convenience sampling strategy, the process started in the first of January 2023 until July 2024. Data were collected using a questionnaire administered by the authors through of face-to-face interviews, supplemented by clinical data from medical records. A total of 436 women from the target population admitted in the study.

To develop the questionnaire, we conducted a narrative review of relevant studies in the literature [13, 22-27], and was validated for content by clinical experts. It also underwent pilot testing with 25 participants. This process led to a structure divided into two modules, each containing five sections. Module 1 focuses on patient-related factors, including sociodemographic and

clinical characteristics, behavioral factors, and medical history. Module 2 consists of two sections that address accessibility issues and barriers related to the healthcare system.

The following variables were collected Sociodemographic and clinical Variables

Age, educational level, monthly household income, matrimonial status, health insurance, type of health insurance (CNOPS: The National Fund for Social Security Organizations, is a Moroccan institution. It is responsible for managing health insurance for the public sector and students. CNSS: The National Social Security Fund, is a public institution in Morocco that constitutes a social security system mandatory for employees in industry, services, and liberal professions), profession, residence area, Clinical staging (TNM) according to the American Joint Committee on Cancer (AMJCC).

Behavioral Factors

Circumstances of discovery, attitude regarding the onset of initial symptoms, the use and duration of traditional medicine, embarrassment issues related to the party examined.

Medical history

Family history of BC, follow-up history of benign breast disease, follow-up history of other type of cancer, menopausal status, the use of hormonal therapy as an oral contraceptive and it's duration.

Accessibility

Distance from home to nearest primary care center, distance from home to the specialized care center (the Oncology Center Mohamed VI), duration of Travel, administrative procedure and service (including complexity, process time, and quality of communication throughout staff), and free-of-charge and its source of information.

Healthcare system factors

Diagnostic interval, delayed communication of histological examination results (The interval was qualified as delayed if the process took more than two weeks), number of consultations before confirmation of diagnosis, receiving a consultation from a screening campaign, benefited from BC awareness at an awareness campaign, benefited from training on Breast Self-Examination (BSE) techniques, The behavior of practitioners during the initial consultation is evaluated to determine whether there are signs of negligence regarding the symptoms presented by patients. This is assessed through three key aspects: providing misleading reassurance without referring the patient to a specialist, failing to recommend regular follow-ups, or fully understanding the nature of the patient's concerns.

Data analysis

A descriptive analysis was conducted by determining the central tendency and dispersion for quantitative variables, and the frequencies for qualitative variables.

The bivariate analysis was conducted using the Chi Square Test. All the variables were included in the multivariate analysis model by stepwise backward method. Variables with P < 0.5 were retained in the final model. The Hosmer and Lemeshow test were performed to assess the model fit. The collected data were analyzed using the Jamovi (Version 2.3.28).

Diagnosis delay definition

In this study, the outcome delay in diagnosis was defined using two modalities to evaluate the variables associated with each definition: time interval and stage at diagnosis. These definitions are commonly adopted in prior studies within the literature [11, 23, 26, 28-31].

Related to the stage of diagnosis, we categorized the diagnosis as follows

- Late, when the cancer stage is classified as Stage IIb or higher according to the AJCC.
 - Early, when the stage is classified as Stage I or IIa.

Related to the total diagnostic interval time, we categorized the diagnosis as follows

-The outcome delay in diagnosis was defined as a time interval greater than 90 days between the onset of the first symptoms and the confirmation of BC diagnosis.

Ethical consideration

Ethical approval for this study was obtained from the Ethics Committee for Biomedical Research of Rabat (CERB), under ethical clearance number 157/22. Participation in this study was voluntary, and formal consent was obtained from all individuals who agreed to participate. Participants received an information sheet and a full explanation of the purpose of the study. They were assured that their participation would be anonymous and identifying information would not be collected. All data collected were kept confidential and only used for research purposes.

Results

Descriptive analysis

Participant's characteristics

The study included 436 participants, the mean age of the participants was 54.0 ± 12.0 years and the mean total diagnosis interval time was 113.9 day (S.d. =256.3, Median =30.0) (see Table 1).

In our results, more than half of the participants (65.1%)

were diagnosed at a late stage. The sample primarily consists of middle-aged and older adults, with the largest group being those aged 40 to 59 years (57.8%), followed by individuals over 60 years old (31.8%). Additionally, 59.8% of the participants are married. Occupational data reveals that a significant majority of participants are unemployed (91.9%). Regarding educational attainment, our population predominantly has a low level of education, with 77.2% having none or only primary education, and most participants reside in urban areas (73.2%). Economic data highlights that a substantial majority of participants (97.5%) have a low monthly income of less than 4000 DH. Furthermore, 94.5% of the sample has health insurance, with the majority holding universal coverage (76.3%), followed by CNSS (18.7%), CNOPS (3.3%), and private insurance (1.7%) (see Supplementary Table 1).

Behavioral factors

In our population study, we found that 12.2% of cases were diagnosed incidentally, while 87.6% were identified through the appearance of symptoms. Additionally, 92.6% of participants had a positive attitude toward consulting a health professional. However, a minority held a negative attitude, believing that their symptoms would resolve independently. This reluctance to seek medical assistance was primarily attributed to time constraints (4.5%), and financial concerns (2.9%).

Furthermore, 8.0% of participants reported using traditional medicine as their initial action, with a mean duration of 2.9 months (S.d.=5.2) (see Table 1). Lastly, about 9.6% of participants expressed those issues related to the examined party were the barriers to seeking care (see Supplementary Table 1).

Medical History related to BC

In our study, 12.4% of participants had a previous follow-up related to another type of cancer, while 12.7% had follow-ups for benign breast disease. Additionally, 28.7% of participants reported a family history of BC, with 48.4% noting it among their first- and second-degree relatives and 52.6% among their third- and fourth-degree relatives. Concerning menopause status, 43.6% of participants were classified as menopausal and 56.4% as premenopausal. Among the premenopausal individuals, approximately 47.6% reported using hormonal therapy as oral contraceptives, with a median duration of 55 months. (see Table 1 and Supplementary Table 1).

Table 1. Descriptive Analysis of Quantitative Variables

	N	Mean	Median	S.D.
Age	436	54.0	53.0	12.0
Patient Interval (day)	259	113.9	30.0	265.3
Duration of use of traditional medicine (month)	20	2.9	1.0	5.2
Number of consultations before confirmation of diagnosis	420	2.1	2.0	0.8
Duration of use of oral contraceptive (Months)	151	89.0	55.0	90.7
Duration of Travel (Hour)	432	1.6	1.0	1.9

[†] S.D. Standard Deviation

Healthcare system factors

The majority of our participants (80.9%) experienced an interval of less than three months between the onset of their first symptoms and the diagnosis of BC. Additionally, 37.1% of individuals faced delays in receiving the results of their histological examinations. About 43.5% of participants reported experiencing some communication issues with administrative staff. However, most participants (93.8%) rated the quality of communication from medical staff as good and appropriate.

Less than half of the participants indicated experiencing moderate difficulties in accessing care, particularly regarding the complexity and duration of the process (44.1% and 40.2%, respectively). When evaluating responses of practitioners at the initial consultation, 54.4% of participants perceived their interactions as positive, indicating an understanding of their concerns. In contrast, about 45.6% reported feeling misinformed or received inadequately reassured. Specifically, 16.2% stated that no referral to a specialist was made, while 29.4% felt that a regular follow-up was not recommended. Furthermore, in 95.7% of cases, the number of consultations prior to diagnostic confirmation was less than three.

The benefits of consultations within screening campaigns, educational initiatives related to BC, or training related to BSE techniques were assessed as very low in our population, exceeding 90%. Additionally, awareness of the availability of free care was limited, with 73.6% of individuals remaining uniformed.

Geographic accessibility to primary health care services is considered adequate, with only 11.6% of individuals living more than 10 kilometers from a primary care center. Conversely, accessibility to specialized care centers was rated as unsatisfactory, with 39.6% of participants living more than 60 kilometers from their homes. The median of duration of travel was about one hours (see Table 1 and Supplementary Table 1).

Bivariate analysis

Bivariate analyses concerning the stage of diagnosis and the total diagnostic interval are presented in Supplementary Table 1.

A chi-square test for independence was conducted to examine the association between the stage of diagnosis and the study variables. The results revealed a significant association between educational level and the stage of diagnosis (p-value =0.05). Furthermore, several healthcare system-related factors specifically, the quality of communication from administrative staff, awareness of

free healthcare services, and the distance from home to the nearest primary care center demonstrated significant associations with the stage of diagnosis, with p-values of less than 0.05.

The results of the Chi-Square Test revealed significant associations related to the total diagnostic interval, complementing the earlier findings regarding the stage of diagnosis. Notably, sociodemographic factors such as residence area and type of health insurance were significantly linked to the duration of the diagnostic process. Additionally, behavioral factors, including attitudes towards the onset of initial symptoms and the tendency to use traditional medicine as the first response, were associated with the length of the total diagnostic interval. Furthermore, a history of previous follow-up for benign breast disease demonstrated a significant relationship with both the overall presentation and diagnosis timeframe.

The administrative procedure for accessing care, including its complexity and duration, the distance from home to the specialized care center (in kilometers), and awareness of the availability of free-of-charge services are significant factors associated with the total time interval for receiving a diagnosis within the healthcare system.

Multivariate analysis

A binary logistic regression analysis was conducted to examine the effect of the factors included in the study on:

The interval of time (<3months or >3 months)

The independent variables linked to a delayed presentation and diagnosis of over three months included participants living in rural or semi-urban areas (OR=2.24, 95% CI [1.22-4.11]). This was identified as a significant sociodemographic factor. Additionally, behavioral factors such as the use of traditional medicine as the first course of action (OR=3.41, 95% CI [1.44-8.04]) contributed to delays.

Other factors included an attitude towards the onset of initial symptoms, where individuals expressed a willingness to consult a doctor but faced barriers such as lack of time, financial constraints, or fear (OR=2.23, 95% CI [0.98-5.07]).

Conversely, having a family history of breast cancer (BC) (OR=0.52, 95% CI [0.28-0.97]) and knowledge about free-of-charge diagnostic services (OR=0.53, 95% CI [0.29-0.97]) emerged as protective factors against delayed presentation and diagnosis (Table 2).

Table 2.Independent Factors associated with Delay in the Total Diagnosis Interval

	OR	95% IC	P.value
Residence area "Rural or urban area"	2.24	1.22 - 4.11	< 0.00
Attitude regarding the onset of initial symptoms "willingness to consult a doctor but faced barriers such as lack of time, financial constraints, or fear"	2.23	0.98 - 5.07	< 0.00
The use of traditional medicine	3.41	1.44 - 8.04	< 0.00
The knowledge of the free-of-charge	0.53	0.29 - 0.97	0.04
Family history of BC	0.52	0.28 - 0.97	0.04

Abbreviations: CI, Confidence Interval; OR, odds ratio; P.Value: <0.05

Table 3. Independent Factors associated with Delayed Stage at Diagnosis

	OR	95% IC	P.value
The quality of communication of the administrative staff "Insufficient and need more works"	7.48	1.06 - 52.68	0.04
Practitioner behavior at the first presentation "Understanding the Scope of Concern"	0.21	0.05 - 0.90	0.03

Abbreviations: CI, Confidence Interval; OR, odds ratio; P.Value: <0.05

The Stage at diagnosis (Late/Early)

The independent variables linked to a late-stage diagnosis include poor communication quality among administrative staff (OR = 7.48, 95% CI [1.06-52.68]). Additionally, a positive behavior of the practitioner during the initial consultation serves as a protective factor against a delayed diagnosis (OR = 0.21, 95% CI [0.05-0.9]) (Table 3).

Discussion

In our study, 65.1% of participants were diagnosed at advanced stages, specifically stage IIb or higher, with a median total diagnosis interval of 30 days. Several factors contribute to this delayed diagnosis, including living in rural or semi-urban areas, reliance on traditional treatments, individual barriers such as lack of time and financial constraints, and poor communication quality among administrative staff. On the other hand, having a family history of breast cancer, awareness of free diagnostic services, and a positive attitude from the practitioner during the initial consultation were identified as protective factors that help reduce delays in presentation and diagnosis.

The median total diagnosis interval time is comparatively lower than what was reported in a study of Moroccan women in Casablanca, which took place in both public and private institutions. In that study, the median patient interval was approximately 35 days, and 51.7% of the cases were diagnosed at a late stage [32]. It is also lower than the study of S. Aloulou et al. [22], which included Moroccan women in Marrakech; their study found a median total diagnostic interval of 8.47 months, and lower than reported in the research conducted by M. Hannaoui et al. (2022) (90 days) [33] and by Maghous et al. (2016) (6 months), with many diagnoses occurring at a late stage [14]. Conversely, a shorter patient interval was observed in the findings of a study conducted at the National Institute of Oncology in Rabat, which reported a median patient interval of 20 days, with 46% classified as having a late diagnosis (stages III and IV) [13].

Living in rural or semi-urban areas significantly contributes to delays in the total diagnostic interval for patients. Women in these locations often need to travel long distances for diagnosis and to complete their care, which can result in high transportation costs. This finding is consistent with the work of B. Benbakhta et al. [13], who studied Moroccan women in Rabat, as well as research involving patients from four major oncology centers located in Marrakech, Casablanca, Rabat, and Fez [34] These results are similar to those reported in the literature [35-38].

In our population study, the median duration of travel

was about 1.0 hours. This result may be due to the fact that most patients relocated from their homes to Casablanca city to be closer to the care center. This relocation can increase the effective cost of care and may lead to delays in seeking treatment if support is lacking. An important aspect of Moroccan culture is its emphasis on solidarity, primarily within the immediate family. Aid may also come from community members as donations or from neighbors.

Since the launch of the National Cancer Control Plan in 2010, access to specialized cancer care has significantly improved, aided by the implementation of a medical assistance program for individuals with low or no income. By the end of 2022, universal health coverage had also been established. Our study showed that a majority of the population (76.3%) had universal coverage as their type of health insurance, which provides free healthcare services in the public sector. Our findings indicate that unawareness of these free services can be a barrier to seeking medical assistance. It is important to note that additional charges apply when diagnostic procedures are not available at oncology centers. This situation highlights the high costs of treatment and the financial challenges faced by our population in accessing care, which negatively affects the timeliness of medical consultations. Numerous studies conducted among Moroccan women [13, 16, 22, 33], as well as in Libya [39], Pakistan [40], France [41], have found similar results indicating that financial constraints are predictors of delayed diagnosis.

Traditional medicine is an integral part of Moroccan culture. In our study, 8% of women reported using traditional medicine before seeking any medical advice, with a median duration of one month for its use. This practice is considered a predictor of delayed diagnosis. Similar findings were reported by C. Sauvaget et al. [34] in their research on Moroccan women, as well as in studies on Tunisian women [10], and Libyan women [11]. Additionally, Marc-Éric Gruénais and Élise Guillermet confirmed the low prevalence of traditional medicine usage among the Moroccan population in their work [42].

Interestingly, our studied population had a positive attitude towards addressing initial symptoms, which is reflected in their tendency to seek medical services, underscores the importance of addressing the barriers related to diagnostic intervals. Many studies conducted in Tunisia [10], in Libya [11], in Nigeria [12] and elsewhere [33, 43], have reported that individuals tend to seek medical attention only when their symptoms become more debilitating or start to interfere with daily activities.

To assess factors such as hormonal therapy use and history of other types of cancer, we evaluated women's awareness, healthy behaviors, and practices, as well as their readiness to detect bodily changes. These behavioral and awareness factors are highly correlated with early

presentation for diagnosis. Our findings align with numerous studies in the literature [44] that emphasize the importance of these aspects in determining the time interval between symptom onset and seeking medical care.

Our studied population reported experiencing communication issues, and the quality of communication stated as a factor impacting the overall diagnosis interval. Effective communication is crucial for every health care interaction, from making appointments and registering for visits to describing symptoms, discussing the risks and benefits of treatments, and understanding care instructions. Good communication is associated with improved patient satisfaction, adherence to medical recommendations, and enhanced health outcomes. Wynia et al. [45] aimed to assess the quality of communication in health organizations and found that the communication scored lower on their scale when patients indicated that staff did not communicate clearly or ensure patient understanding. These findings suggest that improving communication quality in health care organizations could help address the challenges faced by patients with limited health literacy. Additionally, Sharkiya [46] reported that various verbal and non-verbal communication strategies positively impacted all patient-centered outcomes.

Implications for practice and / or health policies

The delayed diagnosis and presentation of BC is common in developing countries. Identifying at-risk populations is essential and will guide the development of specific public policies and support strategies aimed at improving health care management for breast cancer patients

Our findings, along with results from other studies involving Moroccan women in various cities, indicate that several factors indirectly impact cancer awareness. This highlights the need to invest more in promoting healthier lifestyles specifically by reducing exposure to risk factors—and encouraging behaviors such as BSE among the general population, rather than focusing solely on targeted groups. A thoughtful and evidence-based approach is recommended to identify effective educational strategies, considering the high rate of illiteracy and varying educational levels. An integrative approach should mobilize social, psychological, and behavioral theories while also incorporating technology. Engaging NGOs, government services, and social media influencers is vital for promoting this content. Strategies to reduce diagnosis delays should focus on the coordination of health resources, allocation of services, and distribution of diagnostic and treatment options. Additionally, establishing target timelines for urgent referrals after a suspected cancer diagnosis or following an abnormal screening test is essential to improve the quality of patient navigation systems.

Study strength and limitation

This study is the first to examine various factors influencing time intervals among Moroccan women, incorporating a total of 32 variables. It addresses a wide range of barriers and facilitators, including clinical, sociodemographic, personal, health care system factors,

and medical history data. The study primarily relies on qualitative data, acknowledging the challenges of collecting such information directly from participants.

However, there are some limitations that should be considered. Since it was conducted at the Mohammed VI Center in the Casablanca region, the results may not be applicable to all Moroccan women. This is due to potential variations in healthcare services, demographic characteristics, and socioeconomic conditions across different regions of Morocco. Future multi-center studies involving more geographically diverse populations should utilize geospatial analysis methods to gain a better understanding of how geographic factors affect healthcare access. Memory and information bias may be present, despite implementing several strategies to mitigate this issue. Data was collected through in-person interviews during patient consultations at the center, and we included the recency of breast cancer diagnosis as part of our inclusion criteria. We also used religious and national events to help patients remember specific details. Furthermore, the predictive potential of our model may be limited due to the insufficient sample size.

In conclusion, in this study, 65.1% of participants experienced delays in breast cancer (BC) diagnosis. Factors associated with a higher risk of delayed diagnosis included individuals who reside in rural or semi-urban areas, opt for traditional treatments, are unaware of the availability of free care, do not engage in follow-up for other cancer types. Furthermore, inadequate communication with administrative staff was identified as a barrier to early presentation and diagnosis. Thus, it is essential to focus efforts and interventions toward enhancing access to affordable, high-quality healthcare and increasing cancer awareness among both the public and health professionals. This will help accelerate and optimize the referral process.

Author Contribution Statement

Sbabou Mohammed: Writing – original draft, Writing – review & editing, Methodology, Investigation, Formal analysis, Conceptualization. Bendahhou Karima: Writing – review & editing, Methodology, Conceptualization, Validation, Investigation (Co-investigator), Formal analysis. Errahmani Mohamed-Yasir: Writing – review & editing, Formal analysis, Resources. Mouafik Abdelilah: Formal analysis, Resources. Tabiti Hajar: Formal analysis, Resources. Tahiri Jouti Nadia: Writing – review & editing, Visualization, Validation, Supervision, Methodology, Conceptualization.

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Approval

This study originated from an approved student thesis

project.

Ethical Declaration

Ethics Committee for Biomedical Research. University Mohammed V – Rabat (ECBR) approved the study (N 157/22).

Data Availability

The data supporting this study's findings are available from the corresponding author upon reasonable request.

Conflict of Interest

All authors declare no financial, professional, or personal conflicts of interest that could influence the design, execution, or interpretation of this research.

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