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RESEARCH ARTICLE

BREAST CANCER IN YOUNG WOMEN UNDER 40 YEARS: CLINICAL CHARACTERISTICS, TREATMENT PATTERNS, AND OUTCOMES

F. Babaouyoub, S.El Jay, S. Balla, G. Hatime, M. Belhouari, T. Chekrine, M. Bourhafour, Z. Bouchbika, N. Benchakroun, H. Jouhadi, N. Tawfiq and S. Sahraoui

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Abstract

Background: Breast cancer in young women (≤40 years) presents unique clinical challenges with distinct biological characteristics and poorer prognosis. Limited data exists from North African populations regarding the epidemiology and outcomes of breast cancer in this demographic.

Methods: We conducted a retrospective analysis of 153 women aged ≤40 years diagnosed with breast cancer at Mohamed VI Oncology Center, Casablanca, Morocco, between January 2023 and December 2024. Clinical, pathological, therapeutic, and survival data were analyzed. Molecular subtypes were classified based on hormone receptors and HER2 status.

Results: Young women comprised 9.2% (153/1663) of all breast cancer cases. Mean age was 35.07 years (range 21-39). Self-detection was the primary mode of discovery (82.35%). Invasive ductal carcinoma predominated (91.5%), with 58.96% grade II and 39.55% grade III tumors. Hormone receptors were positive in 85.71% of cases, HER2 overexpression in 25%. Luminal B subtype was most common (66.91%). Notably, 30% presented with metastatic disease at diagnosis. Among 86 patients who underwent surgery, 52.32% had breast-conserving therapy and 47.67% had mastectomy. Two-year overall survival was 90.6% in the followed cohort (n=53).

Conclusions: Breast cancer in young Moroccan women demonstrates aggressive features with high rates of advanced disease at presentation. The predominance of Luminal B subtype and high metastatic rates at diagnosis underscore the need for enhanced screening strategies and age-specific treatment protocols in this population.

Introduction:-

Breast cancer represents the most common malignancy in women worldwide, with over 2.3 million new cases diagnosed annually [1]. While the incidence increases with age, approximately 5-10% of cases occur in women under 40 years, presenting unique clinical, biological, and psychosocial challenges [2]. Young women with breast cancer typically experience more aggressive tumor biology, advanced disease at presentation, and poorer long-term outcomes compared to their older counterparts [3,4].

Corresponding Author:- F. Babaouyoub

The definition of "young" in breast cancer varies across studies, generally encompassing women under 35, 40, or 50 years, or simply premenopausal status. The recent ESMO consensus recommends differentiating three categories: young women (<40 years), premenopausal women (40-50 years), and postmenopausal women (>50 years) **[2]**. This stratification acknowledges the distinct biological behavior and clinical implications specific to each age group.

Epidemiological studies demonstrate significant geographic and ethnic variations in breast cancer incidence among young women. While Western countries report rates of 2-8%, developing nations show higher proportions, with some studies from Asia and Africa reporting up to 20% of breast cancer cases occurring in women under 40 [5,6,7]. These disparities reflect differences in population demographics, genetic susceptibility, environmental factors, and healthcare access.

The biological characteristics of breast cancer in young women are notably distinct. These tumors tend to be larger at diagnosis, exhibit higher histological grades, demonstrate increased proliferation indices, and more frequently express adverse prognostic markers [4,8]. Molecular profiling reveals a predominance of triple-negative and HER2-positive subtypes, which are associated with more aggressive clinical behavior and resistance to conventional therapies [9,10].

Furthermore, young women face unique challenges including delayed diagnosis due to perceived low risk, dense breast tissue limiting mammographic sensitivity, and the psychological impact of cancer diagnosis during reproductive years [2,11]. The implications extend beyond immediate medical concerns to encompass fertility preservation, genetic counseling, and long-term survivorship issues.

In North Africa, particularly Morocco, breast cancer incidence has been steadily increasing, representing 35.8% of female cancers in the Greater Casablanca region [12]. However, comprehensive data on breast cancer characteristics in young Moroccan women remains limited. Understanding the specific epidemiological and clinical patterns in this population is crucial for developing appropriate screening strategies, treatment protocols, and support systems.

This study aims to characterize the epidemiological, clinical, pathological, and therapeutic features of breast cancer in women under 40 years treated at a major Moroccan cancer center, providing insights into local disease patterns and treatment outcomes that may inform clinical practice and public health strategies.

Methods:-

Study Design and Setting

We conducted a retrospective descriptive study at the Mohamed VI Oncology Center of Ibn Rochd University Hospital, Casablanca, Morocco. This tertiary cancer center serves as a major referral facility for the Greater Casablanca region and surrounding areas.

Patient Selection

All women diagnosed with breast cancer between January 1, 2023, and December 31, 2024, were identified from the institutional database. Inclusion criteria were: (1) age ≤40 years at diagnosis, (2) histologically confirmed breast cancer, and (3) complete medical records available for analysis. Exclusion criteria included: (1) incomplete medical records, (2) patients lost to follow-up before histological confirmation, and (3) age >40 years at diagnosis.
From 1,663 total breast cancer cases during the study period, 153 patients met the inclusion criteria for final analysis.

Data Collection:-

Comprehensive clinical data were extracted from medical records using standardized data collection forms. Variables included:

Demographics and Risk Factors:

Age at diagnosis, menarche age, marital status, parity, breast feeding history, contraceptive use, family history of breast/ovarian cancer, and body mass index.

Clinical Presentation:
Mode of discovery, consultation delay, tumor characteristics (size, location, consistency, mobility), skin changes, lymph node involvement, and bilateral breast examination findings.

Diagnostic Workup:
Mammography (ACR classification), breast ultrasound, magnetic resonance imaging when performed, and biopsy methods (core needle biopsy, vacuum-assisted biopsy, surgical biopsy).

Pathological Characteristics:
Histological type, tumor grade (Scarff-Bloom-Richardson), tumor size, multifocality, lymphovascular invasion, surgical margins, lymph node involvement, hormone receptor status (estrogen and progesterone receptors), HER2 status, and Ki-67 proliferation index.

Staging and Extension:
Clinical and pathological TNM staging according to the 8th edition AJCC guidelines, imaging studies for metastatic workup (chest CT, abdominal ultrasound/CT, bone scintigraphy, PET-CT when available), and tumor markers (CA 15-3).

Treatment Details:
Surgical procedures (breast-conserving surgery vs. mastectomy, axillary lymph node dissection vs. sentinel lymph node biopsy), neoadjuvant and adjuvant chemotherapy regimens, radiation therapy (indication, dose, fractionation), hormone therapy protocols, and targeted therapy administration.

Outcomes:
Local and distant recurrence, overall survival, treatment-related complications, and follow-up duration.

Molecular Classification
Tumors were classified into molecular subtypes based on immunohistochemistry results **[9]**:

- Luminal A: ER+ and/or PR+, HER2-, Ki-67 <14%
- Luminal B HER2-negative: ER+ and/or PR+, HER2-, Ki-67 ≥14%
- Luminal B HER2-positive: ER+ and/or PR+, HER2+
- HER2-enriched: ER-, PR-, HER2+
- Triple-negative: ER-, PR-, HER2-

Statistical Analysis
Descriptive statistics were used to characterize the study population. Continuous variables were expressed as means with standard deviations or medians with ranges, as appropriate. Categorical variables were presented as frequencies and percentages. Statistical analyses were performed using statistical software. Survival analysis was calculated using the Kaplan-Meier method for the subset of patients with available follow-up data **[13]**.

Ethical Considerations
This study was conducted in accordance with the Declaration of Helsinki. Patient anonymity and confidentiality were maintained throughout the data collection and analysis process. Institutional review board approval was obtained from the local ethics committee.

Results:-

Patient Characteristics and Epidemiology
During the 2-year study period, 153 women aged ≤40 years were diagnosed with breast cancer, representing 9.2% of all female breast cancer cases (n=1663). The annual distribution showed 83 cases in 2023 (8.96% of 927 total cases) and 70 cases in 2024 (9.51% of 736 total cases).

The mean age at diagnosis was 35.07 years (range 21-39 years), with the 36-39 years age group being most affected (62.75%, n=96). Age distribution showed 28.76% (n=44) in the 21-35 years group and 8.49% (n=13) in the 21-25 years subgroup.

Risk Factors and Reproductive History

Regarding reproductive factors, menarche data were available for 110 patients, with a mean age of 12.2 years. Early menarche (≤12 years) was observed in 60.9% (n=67) of patients. Marital status distribution showed 66.01% married (n=101), 26.8% single (n=41), 6.54% divorced (n=10), and 0.65% widowed (n=1).

Parity analysis revealed nulliparity in 32.68% (n=50), while pauciparous women represented 33.99% (n=52), multiparous in 30.07% (n=46), and grand multiparousin 3.27% (n=5). Among parous women, the mean age at first pregnancy was 23.24 years (range 16-36 years, n=34). Breastfeeding was practiced by 73.78% (n=76) of non-nulliparous women, with a mean duration of 19.50 months (range 10 days to 3 years).

Contraceptive use was reported by 56.86% (n=87) of patients, primarily oral contraceptives, with a mean duration of 4 years (range 2 months to 10 years). Body mass index data were available for 80 patients, showing overweight in 46.25% (n=37), normal weight in 28.75% (n=23), and obesity in 13.75% (n=11).

Family history of breast cancer was present in 19.60% (n=30) of patients, including 4 first-degree relatives, 5 second-degree relatives, and 13 third-degree relatives.

Clinical Presentation

The median consultation delay was 6.44 months (range 1.5-15 months), with 33.99% (n=52) consulting within 3-6 months of symptom onset. Self-palpation of a breast mass was the most common mode of discovery (82.35%, n=126), followed by mastalgia (5.22%, n=8) and inflammatory signs (3.26%, n=5).

Tumor location showed right breast predominance (56.86%, n=87) and bilateral involvement in 3.26% (n=5). The upper outer quadrant was the most frequent site (42.48%, n=65). Mean tumor size was 4.05 cm (range 1-12 cm), with 58.82% (n=90) measuring 2-5 cm.

Physical examination revealed firm consistency in 69.93% (n=107) of palpable masses, with mobility in 75.81% (n=116). Skin changes were present in 25.49% (n=39) of cases, including “peaud'orange” (7.18%), nipple retraction (6.53%), and skin inflammation (6.53%). Axillary lymphadenopathy was palpable in 58.16% (n=89) of patients.

Imaging Characteristics

Mammography was performed in all patients, showing stellate opacity in 79.73% (n=122) and ACR 5 classification in 61.43% (n=94). Breast ultrasound, available in 141 patients, demonstrated hypoechoic/heterogeneous lesions in 77.30% (n=109). Magnetic resonance imaging was performed in 48.36% (n=74) of patients, primarily for discordant radio-clinical findings.

Pathological Characteristics

Tissue diagnosis was obtained through core needle biopsy in 58.82% (n=90), vacuum-assisted biopsy in 20.26% (n=31), and surgical methods in the remainder. Invasive ductal carcinoma (IDC) was the predominant histological type (91.5%, n=140), followed by invasive lobular carcinoma (3.26%, n=5).

Histological grading showed grade II in 58.96% (n=79) and grade III in 39.55% (n=53) of 134 evaluable cases. Hormone receptor analysis (n=133) revealed ER and PR positivity in 85.71% (n=114), dissociated receptors in 6.76% (n=9), and hormone receptor negativity in 7.51% (n=10).

HER2 overexpression was observed in 25% (n=33) of 134 tested patients. Ki-67 proliferation index was >14% in 95.31% (n=122) of 128 evaluable cases. Lymphovascular invasion was present in 58.75% (n=47) of 80 assessed cases.

Molecular Classification

Molecular subtyping (n=133) showed Luminal B HER2-negative as the most common subtype (52.63%, n=70), followed by Triple-negative (18.04%, n=24), HER2-enriched (10.52%, n=14), Luminal B HER2-positive (14.28%, n=19), and Luminal A (4.51%, n=6).

Staging and Metastatic Disease

TNM staging revealed T2 tumors in 44.4% (n=68), T1 in 25.49% (n=39), and T4 in 20.25% (n=31). Nodal involvement showed N1 in 56.8% (n=87), N0 in 31.38% (n=48), and N2-N3 in 11.76% (n=18). Notably, 30% (n=46) presented with metastatic disease (M1) at diagnosis.

UICC staging distribution showed Stage IV (30%), Stage IIA (17.64%), and Stage IIB (16.9%) as the most frequent presentations.

Treatment Patterns
Surgical treatment was performed in 56.2% (n=86) of patients. Among surgical patients, breast-conserving surgery was performed in 52.32% (n=45) and mastectomy in 47.67% (n=41). Axillary lymph node dissection was performed in all surgical patients, with sentinel lymph node biopsy in 19.76% (n=17).

Pathological examination of surgical specimens confirmed lymph node metastases in 67.44% (n=58) of operated patients, with >3 involved nodes in 23.5% and extracapsular extension in 20.93%.
Systemic therapy included neoadjuvant chemotherapy in 26.14% (n=40), adjuvant chemotherapy in 28.75% (n=44), and palliative chemotherapy in 10.45% (n=16). Radiation therapy was administered to 47.71% (n=73) of patients, with curative intent in 87.67% (n=64).

Hormone therapy was prescribed to 75.43% (n=86) of hormone receptor-positive patients, primarily tamoxifen with or without LHRH agonists. Targeted therapy was administered to 54% (n=18) of HER2-positive patients, and CDK4/6 inhibitors were used in 8.5% (n=13) of patients with metastatic hormone receptor-positive disease.

Outcomes and Survival
Follow-up data were available for 53 patients with a median follow-up of 24 months. Local recurrence occurred in 2 patients (3.8%) at 7 months post-treatment. Locoregional recurrence was observed in 1 patient (1.9%) at 6.4 months. Distant metastases developed in 7 patients (13.2%). Five deaths (9.4%) were recorded, all due to progressive metastatic disease. The 2-year overall survival rate was 90.6% in this subset.

Discussion:-
This study provides comprehensive insights into breast cancer characteristics among young women in Morocco, revealing several important findings that align with international literature while highlighting regional specificities.

Epidemiological Patterns
The proportion of young women (9.2%) in our breast cancer population is consistent with reports from other developing countries but higher than most Western series (2-5%) **[5,6,7]**. This finding reflects the younger demographic profile of North African populations and possibly earlier age at breast cancer diagnosis in this region. The mean age of 35.07 years aligns with previous Moroccan studies and emphasizes the significant burden of breast cancer in the reproductive age group **[14]**.

Clinical Presentation and Diagnostic Challenges
The predominance of self-detection (82.35%) underscores the critical importance of breast awareness education in young women **[15]**. The substantial consultation delay (mean 6.44 months) represents a significant challenge that may contribute to advanced disease presentation. This delay likely reflects multiple factors including low cancer awareness in young women, attribution of symptoms to benign conditions, and healthcare system factors.

The large mean tumor size (4.05 cm) and high rate of locally advanced disease indicate that many patients present at advanced stages, possibly due to diagnostic delays and more aggressive tumor biology **[4,16]**. The frequent involvement of the upper outer quadrant (42.48%) is consistent with the known anatomical distribution of breast cancer.

Pathological and Molecular Characteristics
The predominance of invasive ductal carcinoma (91.5%) and high-grade tumors (grade II-III: 98.51%) confirms the aggressive nature of breast cancer in young women **[8,17]**. The high Ki-67 proliferation index (>14% in 95.31%) further supports this aggressive phenotype.
Interestingly, our study revealed a high proportion of hormone receptor-positive tumors (85.71%), which contrasts with some international studies showing higher rates of triple-negative breast cancer in young women **[18,19]**. This finding may reflect genetic, environmental, or lifestyle factors specific to the Moroccan population and warrants further investigation.

The molecular subtype distribution with Luminal B predominance (66.91%) is clinically significant, as these tumors typically require both chemotherapy and hormone therapy **[9,20]**. The relatively high HER2 overexpression rate (25%) aligns with international data and highlights the importance of HER2 testing and targeted therapy availability.

Advanced Disease at Presentation

The exceptionally high rate of metastatic disease at diagnosis (30%) is alarming and significantly higher than reported in most developed countries (3-10%) [21,22]. This finding has several important implications:

1. **Public Health Impact**: The high metastatic rate suggests inadequate early detection strategies and emphasizes the urgent need for enhanced breast cancer awareness and screening programs targeted at young women **[23]**.
2. **Healthcare System Considerations**: This pattern may reflect limitations in healthcare access, diagnostic capabilities, or patient education in the region.
3. **Treatment Implications**: The high proportion of advanced disease necessitates robust palliative care services and multidisciplinary treatment approaches [24].

Treatment Patterns and Outcomes

The equal distribution between breast-conserving surgery and mastectomy (52.32% vs. 47.67%) reflects contemporary surgical practices balancing oncological safety with cosmetic outcomes **[25]**. However, the high rate of lymph node involvement (67.44%) among surgical patients underscores the advanced nature of disease even in those deemed operable.

The comprehensive use of multimodal therapy, including high rates of systemic therapy administration, demonstrates adherence to international treatment guidelines **[16,24]**. The availability of targeted therapies (HER2-directed therapy in 54% of eligible patients) indicates reasonable access to modern treatments, though room for improvement remains.

Survival Outcomes

The 2-year overall survival rate of 90.6% in the followed cohort is encouraging, though limited by short follow-up duration and potential selection bias. Longer-term follow-up will be essential to determine true survival outcomes and late recurrence patterns in this population **[26]**.

Clinical Implications

These findings have several important clinical implications:

1. **Screening Strategies**: The high disease burden in young women suggests the need for risk-stratified screening approaches, particularly for those with family history or other risk factors.
2. **Awareness Programs**: Intensive breast cancer awareness campaigns targeting young women could potentially reduce diagnostic delays.
3. **Treatment Protocols**: The aggressive disease characteristics support the use of intensive multimodal treatment approaches in young women.
4. **Genetic Counseling**: The high proportion of young women with breast cancer warrants expanded genetic counseling and testing programs.

Limitations:-

Several limitations should be acknowledged. The retrospective design introduces potential selection and information bias. The relatively short follow-up period limits survival analysis and late outcome assessment. Single-center design may limit generalizability, though our institution serves as a major regional referral center. Missing data for some variables, particularly molecular markers, may affect the completeness of molecular classification.

The lack of genetic testing data represents a significant limitation, as hereditary breast cancer syndromes are more common in young women and would influence treatment and family counseling decisions.

Future Directions:-

Future research should focus on several key areas:

1. **Prospective Studies**: Larger prospective multicenter studies would provide more robust data on outcomes and treatment patterns.
2. **Genetic Analysis**: Comprehensive genetic testing and family history assessment would inform hereditary cancer risk in this population.

3. **Biomarker Research**: Investigation of novel prognostic and predictive biomarkers specific to young women with breast cancer.
4. **Health System Interventions**: Evaluation of interventions to reduce diagnostic delays and improve early detection.
5. **Survivorship Studies**: Long-term studies examining fertility, quality of life, and late effects in young breast cancer survivors.

This study demonstrates that breast cancer in young Moroccan women presents with aggressive features and advanced stages, highlighting the urgent need for enhanced prevention strategies, earlier detection methods, and optimized treatment approaches tailored to this vulnerable population **[23,24]**.

Conclusion:-

Breast cancer in young women under 40 years represents a significant clinical challenge in Morocco, accounting for 9.2% of all breast cancer cases in our institutional series. These patients present with distinctly aggressive disease characteristics, including large tumor sizes, high histological grades, and an alarming 30% rate of metastatic disease at diagnosis **[21,22]**.

The predominance of Luminal B molecular subtype (66.91%) and high Ki-67 proliferation indices underscore the biological aggressiveness of breast cancer in this population **[9,20]**. Despite the availability of multimodal treatment approaches and reasonable 2-year survival rates (90.6%), the substantial proportion of advanced disease at presentation represents a critical public health concern.

Key findings include the predominance of self-detection as the mode of discovery (82.35%), significant diagnostic delays (mean 6.44 months), and the high prevalence of hormone receptor-positive disease (85.71%). These observations highlight the urgent need for enhanced breast cancer awareness programs, risk-stratified screening strategies, and improved healthcare access for young women in Morocco **[23,27]**.

The clinical implications extend beyond immediate patient care to encompass broader public health initiatives, including targeted education campaigns, genetic counseling services, and healthcare system strengthening **[24,27]**. Future research priorities should include prospective multicenter studies, comprehensive genetic analysis, and evaluation of interventions to reduce diagnostic delays and improve early detection in this high-risk population.

List of key Figures:

Table 1:- Annual frequency distribution of breast cancer in our series.

Year	Number of cases < 40 years	Total number of cases	Percentage (%)
2023	83	927	8,96 %
2024	70	736	9,51 %
Total	153	1663	9,2 %

Table 2:- Distribution according to histological types.

Histological type	**Number**	**Percentage %**
Infiltrating ductal carcinoma	**140**	**91.5%**
Infiltrating lobularcarcinoma	**5**	**3.26%**
Ductal carcinoma in situ	**1**	**0.65%**
Papillarycarcinoma	**4**	**2.63%**
Mucinous carcinoma	**2**	**1.3%**
Total	**152**	**100%**

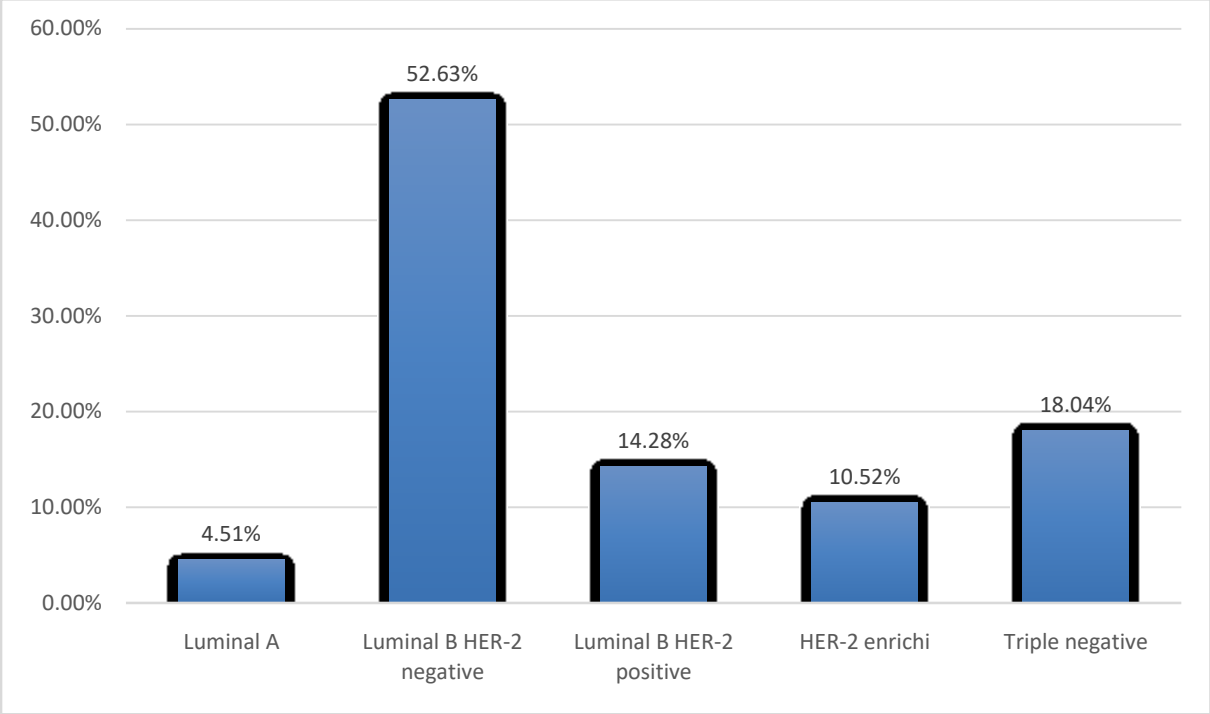
Table 3:- Distribution of Patients According to Lymph Node Involvement.

Lymph Node Status	**Number**	**Percentage (%)**
Positive	**58**	**67.44%**
Negative	**28**	**32.55%**
Total	**86**	**100%**

Table 4:- Distribution of Patients According to Therapeutic Schemes.

Treatment Modality	Type	Number	Percentage (%)
Surgery	Radical	41	26.79%
	Conservative	45	29.41%
Chemotherapy	Neoadjuvant	40	26.14%
	Adjuvant	44	28.75%
Radiotherapy		64	41.83%
Hormone Therapy		73	47.71%
Targeted Therapy		15	9.8%
Immunotherapy		1	0.65%

Table 5:- Distribution of patients according to molecular classification.



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