

# Breast Tuberculosis in Iran: A Comprehensive Review

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## Abstract

Tuberculosis (TB) remains a significant global health concern and kills millions of people every year. While TB can affect any organ in the body, breast TB is relatively uncommon. This study presents a comprehensive review of literature spanning 23 years, with a focus on cases of breast TB in Iran. Among the 96 cases found, the majority (89.6%) fell within the age range of 20–60, with a striking prevalence among women (98.9%). Common symptoms included pain and palpable mass, each presenting in approximately 60.4% of cases. Notably, only a quarter of patients had a confirmed history of exposure to a known TB case. Left breast involvement was more prevalent (58.3%), with ipsilateral lymph node enlargement observed in 40.6% of cases. Given the clinical presentation of breast TB, which often leads to misdiagnosis, a significant proportion of cases (68.7%) were diagnosed through excisional biopsy. Following a standard 6-month regimen of anti-TB drugs, relapse occurred in only 4.2% of cases. This study highlights the need for heightened awareness and vigilance in diagnosing breast TB, especially in regions with a high burden. Although breast TB poses diagnostic challenges, with prompt identification and treatment, the prognosis is generally favorable, with a low incidence of relapse.

**Keywords:** Breast disease, granulomatosis, mastitis, tuberculosis

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## INTRODUCTION

Any organ can be affected by tuberculosis (TB), but the breast is an uncommon site.<sup>[1]</sup> Studies have shown that breast is involved in 0.6%–3.6% of all cases of TB and chest wall TB accounts for 1%–5% of all cases of extrapulmonary TB. In developed countries, breast TB is the cause of <0.1% of all breast diseases, but in developing countries, 0.3%–0.5% of breast lesions are caused by TB.<sup>[2]</sup>

Although breast TB is relatively rare in the 21<sup>st</sup> century, awareness of this disease, which is often confused with breast cancer, is essential because most patients, despite presenting as a mass and with a malignant appearance, require nonsurgical management.<sup>[3]</sup> Unfortunately, breast TB does not have a pathogenomic characteristic and there are limited studies in the medical literature regarding its clinical features, diagnostic methods, treatment modalities, and outcome. Considering that the characteristics of infectious diseases may be varied in different regions, national and local epidemiological studies can be important.<sup>[4]</sup>

In this article, we review this disease in the cases reported from Iran in more than two decades.

## METHODS

We reviewed the literature for articles about breast TB from Iran in the period of 2000–2023. First, the keywords were determined: “breast tuberculosis,” “tuberculous mastitis,” “TB mastitis,” “mamillary tuberculosis,” and “Iran.” Then, international databases (PubMed, Scopus, and Google Scholar) and also Iranian resources (Irandoc, SID, ISC, Magiran, CIVILICA, and Elmnet) were searched with keywords and case reports and case series studies of breast TB from Iran

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were selected. We reviewed the articles carefully and the reported cases were extracted and duplicates were removed. Demographics, clinical characteristics, methods of diagnosis, and outcome of treatment were extracted and integrated.

This article was done with the approval of the research ethics committee and its code: IR.MAZUMS.REC.1400.13813.

## RESULTS

We found 18 articles that reported a total of 95 patients with tuberculous mastitis, and with the case, we had in Mazandaran University of Medical Sciences, a total of 96 cases [Table 1].

In general, 95 (98.9%) of reported cases were women and one was a man (1.1%). The highest prevalence of the disease was in the age group of 20–40 years (58.3%), then 41–60 years (31.3%). Nine people (9.3%) were over 60 years old and one person (1%) was under 20 years old. There was no significant relationship between breastfeeding history and the occurrence of TB. The left breast was affected in 56 (58.3%) and the right side in 36 (37.5%) cases. In four cases (4.2%) bilateral involvement was diagnosed.

The most common clinical symptoms and signs were mastalgia 58 (60.4%), thickening and/or discoloration of the skin 54 (56.3%), swelling and skin ulcers 47 (49%), solitary palpable mass 46 (47.9%), axillary lymphadenopathy 39 (40.6%), constitutional symptoms 35 (36.5%), nipple discharge 21 (21.9%), and multiple palpable masses 12 (12.5%), respectively.

While 49 (51%) cases had no contact with a known case of TB, 24 (25%) cases reported the presence of an infected person near them before the onset of the disease, and 23 (24%) reported inconclusive or suspicious reports of contact history.

Apart from the breast, the other organs involved in TB were lymph nodes 39 (40.6%), lungs 6 (6.3%), and chest wall 3 (3.1%). In 48 (50%) cases, no other part of the body was affected by TB.

Tissue biopsy and/or histopathological studies were necessary to diagnose TB in most cases 66 (68.7%). A bacteriological study (smear and culture) of secretions was helpful just in 30 cases (31.3%).

In 25 people (26.1%) no surgical intervention was necessary for diagnosis and treatment, but a combination of surgery and anti-tubercular drugs was necessary in diagnosing or controlling the complications of breast TB such as failure of treatment, and management of abscess or fistula in 71 (73.9%) cases. In 92 cases (95.8%) 6 months of anti-tubercular therapy was curative without any recurrence, but in 4 cases (4.2%) a recurrence was observed in 1 year of follow-up.

Table 2 summarizes the demographic and clinical characteristics of 96 cases of breast TB reported from Iran.

## DISCUSSION

*Mycobacterium tuberculosis* can reach the breast in three ways: through the hematogenous spread, by direct inoculation to the

**Table 1: The summary of reported cases of breast tuberculosis from Iran**

Serial number	Reported cases	Report period	Gender		Clinical presentation	References
			Female	Male		
1	1	2000	1		Concurrent prolactinoma	[5]
2	1	2001	1		Breast mass suspected to carcinoma	[6]
3	2	2003	2		Ulcer and purulent secretion - mass	[7]
4	1	2005	1		Erythema of skin and mass	[8]
5	4	2007	4		Erythema of skin and ulceration	[9]
6	8	2004–2008	8			[10]
7	1	2008	1		Breast swelling and axillary sinus tract	[11]
8	7	2005–2010	7		Chronic ulcer	[12]
9	1	2010	1		Mass in the breast with chronic cough and lobar consolidation in CXR	[13]
10	1	2010	1		Painful lump, swelling, and retraction of the skin and nipple suspected to carcinoma	[14]
11	22	2002–2012	22			[15]
12	1	2011	1		Abscess formation	[16]
13	9	2011	9			[17]
14	1	2013	1		Pregnant, unilateral mass and galactorrhea	[18]
15	1	2014	1		Mass	[19]
16	1	2017	1		Painful mass (TB and carcinoma simultaneously)	[20]
17	32	2008–2018	31	1	Solitary breast mass	[21]
18	1	2017	1		Breast swelling in pregnancy	[22]
19	1	2022	1		Erythema, pain, tenderness, and ulcer	Author's case
Total	96	2000–2022	95	1		

TB: Tuberculosis, CXR: Chest X-ray

skin, or through extension from the adjacent tissues such as lymph nodes.<sup>[23]</sup> Breast TB is called the “Great Masquerader” because it is easily mistaken for breast cancer.<sup>[24]</sup> Indeed, due to the variation in the expression of breast TB, frequently it is misdiagnosed as cancer, granulomatous mastitis, sarcoidosis, cellulitis, or pyogenic abscess.<sup>[4]</sup> Since the symptoms are not specific and the prevalence of the disease is not high, it is less thought about, and therefore the diagnosis is delayed, and it often happens that unnecessary and expensive diagnostic procedures and inappropriate treatment measures are performed before a definitive diagnosis is made.<sup>[25]</sup> The most

common clinical manifestation is a mass in the breast that may be painful or painless, with or without discharge, and ipsilateral lymphadenopathy may be present.<sup>[26-28]</sup> This mass can be found just like a malignant lesion with an indistinct margin and adhesion to adjacent tissues.<sup>[29]</sup> Other clinical manifestations include diffuse nodularity, breast swelling, nipple inversion or skin retraction, fistula, recurrent abscess, or chronic ulcers.<sup>[3,27,30]</sup>

The risk of developing breast TB in men is low, but diagnosis can be difficult and diagnostic delays are common. In a systematic review, Quaglio *et al.* reported 26 cases of male breast TB, with a mean age of 56.5 years. In about 90% of them, the mass was unilateral, along with axillary lymphadenitis (27.8%) and skin inflammation (33.3%). The most common symptoms were pain (64.7%) and fever (35.3%). Cytologic and culture studies of fine needle aspirates were the most common diagnostic methods (61.5%). The overall prognosis was good after a standard anti-TB regimen with or without surgical intervention like incision or drainage.<sup>[30]</sup>

Imaging investigations such as mammography, ultrasonography, computed tomography scan, or magnetic resonance imaging (MRI) do not give sensitive and specific conclusive results<sup>[31]</sup> but can give some diagnostic clues.<sup>[32,33]</sup>

For example, sonography can show a heterogeneous mass containing fluid with or without a moving internal echo. Also, axillary or intra-mammary lymphadenopathy, calcifications, and cutaneous sinus tracts may be found. On mammography, a tuberculous abscess appears as a dense duct that connects a breast mass to a superficial skin thickening.<sup>[34]</sup> MRI shows a breast lesion with high signal intensity in T2-weighted images, with smooth or irregular margins and an increase in the edge in the postcontrast sequence. However; these findings are nonspecific for tuberculous abscesses. Also, an MRI may show involvement of the chest wall or a fistula with the pleura.<sup>[35]</sup>

The gold standard for diagnosis of breast TB is the detection of *M. tuberculosis* by special staining (most common is Ziehl–Neelsen staining) for acid-fast bacteria or organism isolation from the lesion on culture. In most cases the number of bacilli compared to those observed in pulmonary infections is low, so it is difficult to isolate *M. tuberculosis* from the lesions.<sup>[36]</sup> Fine needle aspiration (FNA) cytology and Pathological findings on biopsy specimens besides polymerase chain reaction are other diagnostic alternatives.<sup>[31,37]</sup>

Definite diagnosis of breast TB in biopsy specimens is challenging for pathologists. Histologically, breast TB is a type of granulomatous inflammation and can be diagnosed by the detection of epithelioid cell granulomas, Langhans’ giant cells, and lymphohistiocytic aggregates, with or without caseous necrosis. Granulomatous inflammation can be detected in FNA samples in approximately 73% of cases.<sup>[31]</sup> What challenges a definitive diagnosis is the fact that other systemic or breast diseases like sarcoidosis, idiopathic granulomatous mastitis (IGM), granulomatosis with polyangiitis, foreign body reaction, traumatic fat necrosis, and some other infections such

**Table 2: Demographic data and clinical manifestations of 96 reported cases of breast tuberculosis from Iran**

Variables	n (%)
Age categories (years)	
<20	1 (1)
20–40	56 (58.3)
41–60	30 (31.3)
>60	9 (9.3)
Gender	
Female	95 (98.9)
Male	1 (1.1)
History of contact with TB patient	
No	49 (51)
Yes	24 (25)
Suspicious	23 (24)
Clinical symptoms	
Mastalgia	58 (60.4)
Skin thickening or discoloration	54 (56.3)
Swelling and skin ulceration	47 (49)
Solitary palpable mass	46 (47.9)
Axillary lymphadenopathy	39 (40.6)
Constitutional symptoms	35 (36.5)
Nipple discharge	21 (22.9)
Skin fistula	18 (18.8)
Nipple retraction	14 (14.6)
Multiple palpable masses	12 (12.5)
Location	
Left side	56 (58.3)
Right side	36 (37.5)
Bilateral	4 (4.2)
Other organ involvement	
Lymph node	39 (40.6)
Pulmonary	6 (6.3)
Chest wall	3 (3.1)
No other organ found	48 (50)
Diagnosis confirmation	
Histopathology	66 (68.7)
Smear and culture of secretions	30 (31.2)
Management	
Medical and surgical intervention	71 (73.9)
Just medical therapy	25 (26.1)
Outcome	
Complete cure	92 (95.8)
Relapse	4 (4.2)

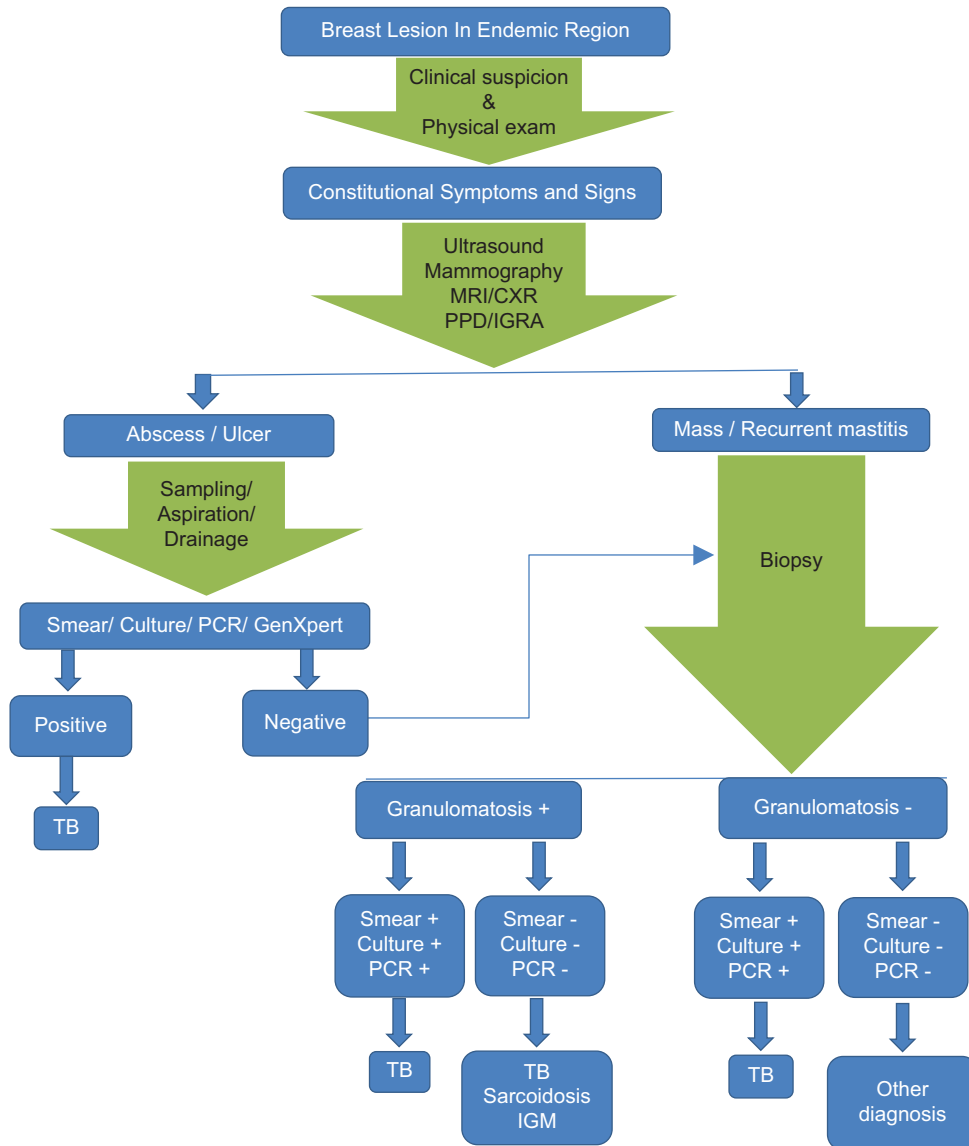
TB: Tuberculosis

as actinomycosis and fungal infections may show a pathologic pattern indistinguishable or very difficult to differentiate from TB.<sup>[31,38]</sup> The most important and challenging differential diagnoses are sarcoidosis and lobular granulomatous mastitis. IGM is an inflammatory reaction characterized by lobulocentric nonnecrotizing granulomas sometimes including neutrophilic infiltration with organized micro abscess formation. In IGM granulomas are bounded by breast lobules, compared to TB mastitis which most granulomas are around the ducts rather than lobules. The presence of necrotizing granulomas favors the diagnosis of TB mastitis<sup>[39-41]</sup> while the presence of well-formed nonnecrotizing granulomas limited to lobules increases the probability of breast sarcoidosis.<sup>[42]</sup> Traumatic fat necrosis is limited to ruptured fat globules in the histologic examination. The presence of sulfur granules at the sites of infection is a typical histopathological feature of actinomycosis.<sup>[43,44]</sup>

The proposed algorithmic diagnostic approach to breast lesions, when TB mastitis is suspected, is given in Figure 1.

This study analyzed all cases of breast TB in Iran that were reported in nearly a quarter of a century and found epidemiologic and clinical aspects of breast TB in Iran. The study also highlighted the diagnostic challenges of breast TB due to its varied clinical manifestations and similarities with breast cancer. Although the diagnosis of breast TB does not necessarily require surgery, it is often diagnosed after surgical intervention and excisional biopsy. A significant proportion of cases (68.7%) were diagnosed through excisional biopsy, which suggests that there is a possibility of misdiagnosis with breast malignancies. However, With prompt identification and treatment, the prognosis for breast TB was generally favorable, with a low incidence of relapse posttreatment.

What is certain is that not all cases of TB mastitis in Iran have been reported, suggesting that the actual number of cases in



**Figure 1:** An algorithmic approach for diagnosis of breast tuberculosis. TB: Tuberculosis, PCR: Polymerase chain reaction, IGM: Idiopathic granulomatous mastitis, MRI: Magnetic resonance imaging, CXR: Chest X-ray, PPD: Purified protein derivative test, IGRA: Interferon-gamma release assays

Iran is higher. Some cases may not have been diagnosed or may be treated empirically, creating uncertainty in diagnosis. Therefore, the true number is probably greater than reported.

Although we did not have any case of TB mastitis in the context of HIV infection among the reported cases from Iran, HIV co-infection is a major risk factor for extra-pulmonary TB including breast TB.<sup>[45]</sup>

## CONCLUSION

Breast TB poses diagnostic challenges due to its varied clinical manifestations, underscoring the importance of a thorough evaluation process. Due to its paucibacillary nature, it is difficult to detect mycobacteria in a smear, so culture and pathologic studies are good tools for diagnosis. The treatment of breast TB is the same as the standard treatment of pulmonary TB. Relapse is uncommon. With prompt identification and treatment, the prognosis for breast TB is generally favorable, with a low incidence of relapse posttreatment. The result of this study may help to fill a knowledge gap, inform clinical practice, and contribute to the development of effective strategies for the prevention, diagnosis, and treatment of breast TB.

## Limitation of the study

Not all cases of TB mastitis in Iran have been reported in the literature. In addition, no long-term follow-up of the patients is available.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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