Review Article

Breast Tuberculosis in Women: A Systematic Review

Gianluca Quaglio,^{1,2,3*} Damiano Pizzol,⁴ Petros Isaakidis,⁵ Arianna Bortolani,² Francesca Tognon,² Claudia Marotta,² Francesco Di Gennaro,⁶ Giovanni Putoto,² and Piero L. Olliaro^{7,8}

¹European Parliamentary Research Services (EPRS), European Parliament, Brussels, Belgium; ²Operational Research Unit, Doctors with Africa, Collegio Universitario Aspiranti e Medici Missionari (CUAMM), Padua, Italy; ³Department of International Health, Care and Public Health Research Institute (CAPHRI), Faculty of Health, Medicine, and Life Sciences, University of Maastricht, Maastricht, The Netherlands; ⁴Operational Research Unit, Doctors with Africa CUAMM, Beira, Mozambique; ⁵Médecins Sans Frontières, Southern Africa Medical Unit (SAMU), Cape Town, South Africa; ⁶Department of Infectious Diseases, University of Bari, Bari, Italy; ⁷Special Programme for Research and Training in Tropical Diseases, World Health Organization (WHO/TDR), Geneva, Switzerland; ⁸Nuffield Department of Medicine, Centre for Tropical Medicine and Global Health, University of Oxford, Oxford, United Kingdom

Abstract. Breast tuberculosis (TB) is rarely reported and poorly described. This review aims to update the existing literature on risk factors, clinical presentations, constitutional symptoms, diagnostic procedures, and medical and surgical treatments for breast TB. In all, 1,478 cases of breast TB were collected. Previous history of TB was reported in 19% of cases. The most common clinical appearance of the lesion was breast lump (75%). The most common associated finding was axillary lymphadenitis (33%) followed by sinus or fistula (24%). The most common symptoms were pain and fever, reported in 42% and 28% of cases, respectively. The most used diagnostic method was fine-needle aspiration cytology (32%), followed by biopsy (27%), acid-fast bacteria Ziehl–Neelsen stain (26%), culture (13%), and polymerase chain reaction (2%). These tested positive in 64%, 93%, 27%, 26%, and 58% of cases, respectively. The majority (69%) of patients received a 6-month anti-TB treatment (isoniazid, rifampicin, pyrazinamide, and ethambutol). Surgery consisted of excision in 39% of cases, drainage in 23%, and mastectomy in 5%. The great majority of patients had a positive outcome. It often mimics breast cancer, which makes it difficult to diagnose. Most patients, when diagnosed in time, respond to antitubercular therapy alone.

INTRODUCTION

Globally, tuberculosis (TB) is now the number one killer infectious disease. More than 95% of TB deaths occur in low- and middle-income countries (LMICs), where TB is among the top three causes of death for women aged 15 to 44.¹ Any organ can be affected by TB, but the breast is an uncommon extrapulmonary TB site.² The first case of breast TB was described by Cooper in 1829 as, “scrofulous swelling of the bosom of young women,”³ but the first detailed description of the disease was not reported until the end of the 19th century by Richet⁴ and Powers.⁵ It is generally believed that the infection of the breast is usually secondary to a primary site elsewhere in the body, which may or may not be clinically apparent^{6,7}; however, breast TB may be the primary site when no demonstrable tuberculous focus exists elsewhere. Lymphatic spread by retrograde extension from the axillary lymph nodes is considered the most common way the disease spreads. Propagation from cervical and mediastinal lymph nodes has occasionally been reported.²

There are no well-defined clinical features suggestive of breast TB. Because of its protean clinical presentations, establishing a diagnosis is difficult. For instance, it may be confused with breast carcinoma or pyogenic abscess.^{2,8} The diagnostic delay can last months, and patients often undergo numerous investigations and unsuccessful treatments before a definitive diagnosis is made.^{9,10} The most common clinical presentation is a lump, with or without a duct, painful or not.⁶ The lump can mimic carcinoma, being hard, with irregular borders, and fixed to either the skin or the muscle or even to the chest wall.^{8,11} Other presentations

include diffuse breast swelling and edema, diffuse nodularity, nipple retraction, fistulization, multiple sinuses, skin ulcers, and recurrent abscess with or without axillary involvement.^{12–15}

There are different ways to diagnose and follow up breast TB, although none are ideal because of a combination of technical limitations and no or limited availability, particularly in LMICs. The gold standard for diagnosis is the detection of *Mycobacterium tuberculosis* by acid-fast bacteria Ziehl–Neelsen stain (AFB) or the isolation of the organism from the lesion on culture, but the former lacks sensitivity in paucibacillary samples, and the latter is relatively expensive and impractical in some low-resource settings.^{2,8} An alternative is polymerase chain reaction (PCR) to identify the *M. tuberculosis* genetic material, but it is rarely used.¹⁵ Fine-needle aspiration cytology (FNAC)—which detects the presence of epithelioid cell granulomas and necrosis—is often used instead, but has drawbacks—differential diagnosis is difficult in cases of granulomatous mastitis and sarcoidosis, for instance.^{16,17} Histopathology on biopsy identifies a chronic granulomatous inflammation (with caseous necrosis and Langhans-type giant cells).⁸ Investigations such as ultrasonography, mammography, computed tomography, and magnetic resonance imaging do not give a conclusive diagnosis and, once again, are not widely available in LMICs.^{12,15,18–21} Treatment generally involves anti-TB medications with or without surgery.^{2,6} Medical treatment often consists of an intensive four-drug, 2-month phase with isoniazid, rifampicin, pyrazinamide, and ethambutol, followed by a two-drug, 6-month (or longer) continuation phase with isoniazid and rifampicin.

Despite several published literature reviews of breast TB,^{7,10,18,22,23} a systematic review has not been conducted. Therefore, we aimed to update and expand the existing evidence base by systematically reviewing the English, Spanish, and French literature about risk factors and clinical, diagnostic, and therapeutic aspects of breast TB in women.

* Address correspondence to Gianluca Quaglio, European Parliamentary Research Services (EPRS), European Parliament, Rue Wiertz 60, Brussels B-1047, Belgium. E-mail: gianluca.quaglio@europarl.europa.eu

METHODS

Searches were undertaken in PubMed, Embase, and Web of Science. A search strategy was developed using a combination of free-text and predetermined terms, adapted for each database. We used the following search strategy: (tuberculosis OR TB) AND (breast OR mammary OR mastitis) AND (women OR female). Included were reports of studies published in English, Spanish, and French between 1990 and March 2018. Additional studies were identified by contacting the authors and by searching the reference lists of primary studies. The process of study selection is summarized in Figure 1. Title and abstracts identified through the searches were reviewed independently by two reviewers (G. Q. and D. P.). If there were duplicate publications of the same study, the most recent publication which reported full data was included. Full-text copies of the selected studies were retrieved and independently reviewed against the inclusion criteria by two reviewers from a team of three (G. Q., D. P., and G. P.).

With respect to study designs, we included any retrospective and prospective analyses of medical records and case reports. Outcome measures included 1) risk factors for breast TB, 2) clinical appearance of the lesion and clinical presentations, 3) constitutional symptoms, 4) diagnostic procedures, and 5) anti-TB and surgical treatments. The inclusion criterion was articles published in English, French, and Spanish from 1990 to March 2018. The exclusion criteria were articles published in languages other than English, French, and Spanish; cases of breast TB described in association with other mammary diseases (cancer, granulomatous mastitis, etc.); and male case reports; however, articles which described cases of male TB within a large number of TB female cases were instead included. Purely qualitative studies were excluded.

Each of the included studies was coded with a predetermined rating sheet with relevant data extracted and recorded by two reviewers. Data extracted included name of the first author, year of publication, country where the study was conducted, prevalence (entente as the number of breast

TB among the total number of mammary conditions treated in the centers reporting case series), general participant characteristics (age and gender), risk factors (multiparity, pregnancy, lactation, HIV+, and previous history of TB), breast affected (right, left, and bilateral), breast quadrant affected (superior, inferior, and peri-areolar), clinical appearance of the lesion (lump, abscess, and disseminated), clinical presentations (sinus or fistula, skin ulceration, nipple retraction, and discharging sinus), constitutional symptoms (fever, decreased appetite, decreased weight, and pain), duration of symptoms, previous empirical antibiotic treatment, chest X-ray results (negative, positive (active TB), and features of previously healed TB), diagnostic procedure (biopsy, FNAC, AFB, culture, and PCR), type and duration of anti-TB treatment, and, finally, surgical treatment (none, excision, incision and drainage, and mastectomy).

We generated a summary of the results in a table to describe the characteristics and results of each of the included studies. The review collected series and individual case reports. Most of the articles featuring series were included in the database as a single study. However, some series, typically those with few cases, have described these cases in a very detailed way; for these articles, each case was included independently in the database. Because of the heterogeneity in the presentations of case reports and series, a decision was made not to perform meta-analysis, but instead to summarize the results as simple averages in tables. Age was calculated as a weighted mean to account for sample size heterogeneity across studies. Between-test agreement was calculated using the Cohen's kappa coefficient. Because this is a systematic review of non-analytical studies, that is, case series and case reports, the assessment of publication bias might not be practically applicable.²⁴ The Grading of Recommendations, Assessment, Development, and Evaluation and the approach by the Agency for Healthcare Research and Quality are not suitable for our systematic review of nonanalytical studies. For this reason, we have not performed a formal evaluation of the quality of the included studies.²⁴

FIGURE 1. Flow diagram for study selection.

RESULTS

We identified 512 potentially eligible citations from the database searches and 95 studies from hand searching and screening of bibliographies. We screened the titles and abstracts of the 402 remaining articles after removing duplicates and selected 237 publications for full-text screening, from which 180 articles were included in the final analysis (Figure 1). Only one prospective patient recruitment study was identified.²⁵ The final list of 180 relevant articles reported a total of 1,458 (98.6%) cases of breast TB in women and 20 (1.4%) in men. Of these 180 articles, 107 were single-case reports,^{8,9,21,26–129} 38 reported between two and nine cases,^{10,11,14,15,19,23,130–161} and 35 reported 10 or more cases^{6,7,12,13,17,18,20,22,25,162–187} (Supplemental Appendix 1). The 10 articles with the largest series (ranging from 42 to 160 cases) reported 693 (46.9%) of the total 1,478 cases included in these 180 articles.^{6,12,13,23,25–27,29,31,34} The amounts of information collected on different variables differ, as the publications did not provide full information on each variable. For the following variables: 1) breast affected, 2) breast quadrant affected, 3) clinical appearance of lesion, 4) chest X-ray, 5) antitubercular treatment, and 6) surgical treatment, the parameters were calculated for the population in which all variables were known. The majority of subjects (1,002, 67.9%) were from Asia, mainly India and Pakistan, followed by Africa with 249 (16.8%) of the cases, South America with 79 (5.3%), mostly from Peru and Brazil, Europe with 71 (4.8%) mainly from the United Kingdom, the Middle East with 69 (4.7%), mainly from Iran, and the United States with eight (0.5%). Where described, the prevalence of breast TB among the total number of breast cases examined ranged from 0.2% to 6.8%, with an average of 1.7%.

Risk factors and clinical presentations. As described in Table 1, the mean age of included patients was 29 years (range 12–89 years). Among 185 single cases described, 125 (67.5%) were in the reproductive age range (14–45 years). Twenty-nine (4.5%) patients were pregnant, and 167 (14.7%) were lactating mothers. Multiparity was reported in 362 cases (70.2%). The HIV status was described in 211 cases, and 45 (21.3%) of them were HIV positive. Previous history of TB was reported in 111 cases (18.7%).

The most common clinical appearance of the lesion was breast lump (877, 74.9%) and breast abscess (174, 14.9%). Nearly half of the patients (431, 48.4%) presented with an involvement of the right breast. Bilateral localization was rare (38 subjects, 4.2%). The most common site was the superior quadrant (237, 60.4%). The most common associated finding was axillary lymphadenitis (377, 32.6%), followed by sinus or fistula (217, 23.9%), skin ulceration (103, 23.5%), and nipple retraction (83, 16.7%). The most common constitutional symptoms were pain, reported in 314 (42.5%) of the cases, and fever, reported in 175 (28.2%). The average duration of symptoms before seeking medical care was highly variable: on average, the delay in diagnosis was 7.1 months.

Diagnosis, treatment, and outcomes. Overall, 2,663 tests were reportedly applied to these 1,478 cases. As described in Table 2, the most common diagnostic method was FNAC, carried out in 842 cases (31.6%), followed by biopsy (723, 27.1%), AFB (687, 25.8%), culture (344, 12.9%), and PCR (67, 2.5%). Respectively, positive results were found in 64.1%, 92.8%, 26.6%, 25.9%, and 58.2% of the methods used

TABLE 1

Risk factors, signs, and symptoms in 1,478 patients with breast TB

Variable	N (%)
Gender	
Female	1,458/1,478 (98.6%)
Male	20/1,478 (1.4%)
Age (years)	
Mean	29
Range	12–89
Risk factors	
Multiparity	362/516 (70.2%)
HIV+	45/211 (21.3%)
Previous history of TB	111/592 (18.7%)
Active breastfeeding	167/1,137 (14.7%)
Pregnancy at the time of diagnosis	29/641 (4.5%)
Breast affected*	
Right	431/891 (48.4%)
Left	422/891 (47.4%)
Bilateral	38/891 (4.2%)
Breast quadrant affected*,†	
Superior	237/392 (60.4%)
Inferior	118/392 (30.1%)
Peri-areolar	68/392 (17.3%)
Clinical appearance of the lesion*	
Lump	877/1,171 (74.9%)
Abscess	174/1,171 (14.9%)
Disseminated	120/1,171 (10.2%)
Clinical findings	
Axillary lymphadenopathy	377/1,157 (32.6%)
Sinus or fistula	217/909 (23.9%)
Skin ulceration	103/438 (23.5%)
Discharging sinus	138/743 (18.6%)
Nipple retraction	83/497 (16.7%)
Constitutional symptoms	
Pain	314/739 (42.5%)
Fever	175/621 (28.2%)
Decreased appetite	119/497 (23.9%)
Decreased weight	137/507 (27%)

TB = tuberculosis.

* Parameters were calculated for population in which all variables were known.

† The total is more than 100% because in some cases, the lesion involved more quadrants.

(percentage of positivity found on the total of each test performed). Additional details were extracted for 412 cases, which were found positive on at least one of the tests they had been submitted to (1 test = 15% of cases, 2 tests = 32%, 3 tests = 30%, 4 tests = 18%, and 5 tests = 5%); they are shown in Table 3. In individual tests, biopsy was used in 29% of cases and found positive in 90%; AFB in 25%, positive in 59%; FNAC in 23%, positive in 59%; culture in 17%, positive in 56%; and PCR in 7%, positive in 61%. A single test was positive in 15% of cases. When two or more tests were combined, the sample was confirmed by two tests being positive in roughly half of the cases (59%, 55%, 46%, and 50% with two, three, four, and five tests, respectively). Diagnosis involved variable combinations of tests, most commonly between AFB and FNAC ($n = 59$), biopsy ($n = 62$), or culture ($n = 69$). As described in Table 4, the between-test agreement was low or very low. A chest X-ray was carried out in 1,026 subjects: 100 (9.7%) had a chest X-ray positive for active TB and 28 (2.7%) showed sequelae of past TB.

Of the 1,478 patients in this review, information on treatment—medical and/or surgical—was provided for 1,087 (73.5%). Of these, 1,050 patients (96.6%) received medical treatment; for the remaining 37, only surgical treatment was reported, whereas information on medical treatment was missing. Of 1,050 patients with anti-TB treatment, 733 (69.8%) received the standard 6-month anti-TB treatment (2 months of

TABLE 2
Diagnosis and treatments in patients with breast TB

Variable	N (%)
Delay in diagnosis	
Mean (months)	7.1
Range	0.25–78
Previous empirical antibiotic treatment	85/251 (33.8%)
Chest X-ray*	
Negative	855/983 (87.1%)
Positive (active TB)	100/983 (10.2%)
Sequelae findings of past TB†	28/983 (2.7%)
Method of diagnosis‡	
Biopsy	671/723 (92.8%)
Fine-needle aspiration cytology	540/842 (64.1%)
Acid-fast bacteria Ziehl–Neelsen	183/687 (26.6%)
Culture	89/344 (25.9%)
Polymerase chain reaction	39/67 (58.2%)
Type of antitubercular treatment*	
Two months of isoniazid, rifampicin, pyrazinamide, and ethambutol + 4 months of isoniazid and rifampicin	733/1,050 (69.8%)
Other antitubercular regimen§	207/1,050 (30.2%)
Antitubercular treatment duration	
Mean (months)	6.1
Range	2–24
Surgical treatment*	
None	350/977 (35.8%)
Excision	377/977 (38.6%)
Incision and drainage	226/977 (23.1%)
Mastectomy (partial or total)	45/977 (4.6%)

TB = tuberculosis.

* Parameters were calculated for population in which all variables were known.

† Calcified parenchymal nodules, calcified radiological scars, calcified hilar lymph nodes, etc.

‡ Percentage of positivity found on the total of each test performed.

§ Other antitubercular regimen: different from the standard treatment in terms of type of used drugs.

|| The total is more than 100% because some patients received more than one treatment.

HRZE isoniazid, rifampicin, pyrazinamide, and ethambutol, and 4 months of HR) and 317 (30.2%) received a modified anti-TB treatment in terms of type and duration. The average treatment duration was 6.1 months, ranging 2–24 months. Among the 1,050 cases with medical treatment, 491 (47%) received medical treatment only and 559 (53%) also underwent surgery (excision, incision, and mastectomy). Surgery consisted in excision in 377/559 cases (67.4%), drainage in 226 (40.4%), and mastectomy in 45 (8%); 63 patients underwent two different surgical interventions. Information relating to previous antibiotic treatment was reported for 251 subjects, of whom 85 (33.8%) received empirical antibiotic treatment before the final diagnosis of breast TB was made. The treatment outcome was reported for 792 (67.9%) subjects: 762 (96.3%) were cured, with the others lost to follow-up.

DISCUSSION

The present review identified 1,478 breast TB cases reported in the literature. To our knowledge, this is the first time a systematic review has been carried out of the risk factors and

clinical, diagnostic, and treatment aspects of breast TB. The average reported prevalence was 1.7%, ranging from 0.2%²⁰ to 6.8%.³⁵ The prevalence in Western countries is less than 0.1%.^{2,6} Breast TB more commonly affects women of child-bearing age (average age 29 years in this review). Elderly women may also be affected,^{8,38,63} whereas the disease is very rare under the age of 18.^{62,96,172} Tuberculosis of the male breast is an extremely rare condition.^{12,63,170,188} Lilleng et al, in a study of 809 cases of male breast mass, did not find a single case of TB.¹⁸⁹

In pregnant and lactating women, the increased vascularity of the breast with dilated ducts predispose to infection.¹⁹⁰ Pregnancy suppresses the T-helper 1 pro-inflammatory response, which may increase susceptibility to a new infection or reactivation of TB.¹⁹¹ It is difficult to understand from this review whether this might be the case: on the one hand, a small percentage were either pregnant or lactating, and on the other hand, more than 70% were multiparous, and, considering the long diagnostic delays, breast TB might have been triggered by a previous pregnancy. HIV infection carries an increased risk for primary TB, for reactivation of previous TB, and for second episodes of TB from exogenous reinfection.^{192–194} Breast TB as a presenting manifestation of HIV is extremely rare.^{33,195} In the present study, the HIV status was described in 211 cases, and approximately one in five were positive.

The clinical presentation of breast TB is generally poorly described in the literature, and clinically important features are not uniformly reported or not reported at all. The average duration of symptoms before diagnosis is highly variable, spanning from a few weeks in Europe^{93,96,154} to more than 7 months in India and sub-Saharan Africa.^{12,14,170} This includes both patient and health system delays, and reflects the range of cultural, psychological, and economic components, as well as the diagnostic challenges. One-third of the patients about whom this information was collected received empirical antibiotic therapy at some point during their clinical history, typifying the challenges to the final diagnosis. The disease is generally mono-lateral and can equally affect either breast.^{67,94,159} A lump is the most common presentation, with other less common forms being cold abscess and diffuse breast inflammation. Breast lumps are mostly misdiagnosed as fibroadenoma, malignancy, or breast abscess. One-third of the cases also have axillary lymph nodes. The rate of nipple–areola involvement in the present review is 17.3%. For comparison, in the carcinoma literature, studies showed a rate of gross nipple areola involvement of 12.5% (41/326 cases) in Laronga et al.¹⁹⁶ and 8% (99/1,291 consecutive cases) in Santini et al.¹⁹⁷

This review shows a low prevalence of constitutional symptoms. This, combined with the low presence of concomitant active pulmonary TB (less than one in 10 was chest X-ray positive), or previous history of TB (less than one in five),

TABLE 3
Cases positive on at least one of the diagnostic test

Test	No. tested	% tested	No. positive	% positive	1 test	2 tests	3 tests	4 tests	5 tests
Fine-needle aspiration cytology	93	23%	55	59%	17	32	25	15	4
Biopsy	119	29%	107	90%	36	37	26	16	4
Culture	68	17%	38	56%	4	21	27	12	4
Acid-fast bacteria Ziehl–Neelsen stain	104	25%	61	59%	4	39	38	19	4
Polymerase chain reaction	28	7%	17	61%	0	3	7	14	4
Total (%)	412	–	–	–	61 (15)	132 (32)	123 (30)	76 (18)	20 (5)

TABLE 4
Test agreement between different diagnostic tests

Test		Polymerase chain reaction	AFB	Culture	Biopsy
Fine-needle aspiration cytology	Tested	18	59	36	34
	Concordance	39%	63%	72%	26%
	Kappa	-0.11	-0.06	-0.62	0.00
Biopsy	Tested	18	62	56	—
	Concordance	50%	42%	21%	—
	Kappa	-0.11	-0.06	-0.62	—
Culture	Tested	12	69	—	—
	Concordance	58%	45%	—	—
	Kappa	0.29	-0.01	—	—
AFB	Tested	25	—	—	—
	Concordance	48%	—	—	—
	Kappa	0.00	—	—	—

AFB = acid-fast bacteria Ziehl-Neelsen stain.

further contributes to the diagnostic delay. Pain is the most common constitutional symptom. Typically, its manifestation is a noncyclical mastalgia, that is, not linked to the menstrual cycle (as in fibrocystic disease, periductal mastitis, or breast abscess). Localized pain is very rare in breast cancer.¹⁹⁸

As mentioned previously, the protean presentation of breast TB leads to significant diagnostic delay. This is compounded by multiple possible differential diagnoses, especially in resource-limited settings. The main differential diagnoses to be considered are fibroadenoma^{199,200}; breast cancer; inflammatory diseases, such as idiopathic granulomatous mastitis, sarcoidosis, Wegener's granulomatosis, and giant cell arteritis^{187,201–203}; and other infectious diseases, such as brucellosis, actinomycosis, mycotic infections, and fat necrosis.^{199,204,205} The coexistence of carcinoma and breast TB is rare. The clinical situations include the presence of carcinoma and breast TB, carcinoma in the breast with axillary tuberculous adenitis, or both.^{73,206,207} In the absence of a gold standard, the main question regarding the diagnosis of breast TB is whether it requires the detection of the microorganism or whether distinctive pathological changes suffice. The two most common diagnostic techniques are FNAC and biopsy, which in this review were positive in approximately 64% and 93% of cases, respectively.

With the proviso that a relatively small proportion of cases underwent more than one test, this review allowed for the comparison of diagnostic agreement between tests, which was very low. Using PCR or culture as standards by default, no test has satisfactory sensitivity and limited specificity. Of the *M. tuberculosis* detection methods, microscopy with AFB has, probably, the best balance between sensitivity (~80%) and specificity (35–65%). Biopsy has the best sensitivity (90% or more) but very low specificity, whereas FNAC has low sensitivity and specificity. However, the use of culture or PCR as standards might be questioned. One caveat is that it is not clear whether evidence of the presence of *M. tuberculosis* is mandatory to confirm the diagnosis of breast TB, especially if in the presence of definitive histological/cytological changes.⁶ It has been argued²⁰⁸ that the low sensitivity of direct detection techniques (especially in paucibacillary lesions) may cause delays in diagnosis and underdiagnosis. In the articles reviewed here, culture was positive only in about one in four cases, and PCR in just over half. By contrast, in various series included in this review,^{17,22,141,162,166,167,182} in most cases, the diagnosis was made based on pathology and confirmed ex juvantibus as they responded to anti-TB therapy.

Therefore, generally, pathological examination appears to be of more practical use than bacteriology, especially considering that both culture and PCR are technically challenging and cannot be applied in many settings in LMICs. This conclusion, however, is challenged by the very low agreement (29%) and concordance (kappa = 0.02) between FNAC and biopsy in the 34 cases in which both tests were conducted. To our knowledge, GeneXpert has not been tested on breast TB. A Cochrane systematic review and meta-analysis of the use of GeneXpert on extrapulmonary TB found variable sensitivities and specificities against culture depending on the type of specimen. When tested on lymph nodes, sensitivity and specificity ranged widely (56–100% and 39–100%, respectively); pooled sensitivity and specificity (95% credible intervals) were 87.6% (range 81.7–92.0%) and 86.0% (range 78.4–91.5%), respectively.²⁰⁹

Breast TB overall has a good prognosis. No specific guidelines are available for chemotherapy of breast TB; the most common approach is the standard TB treatment with 2 months of isoniazid, rifampicin, pyrazinamide, and ethambutol, followed by 4 months of isoniazid and rifampicin. Some authors prefer the 9-month regimen (2 months of isoniazid, rifampicin, pyrazinamide, and ethambutol, and 7 months of isoniazid and rifampicin) because of a lower relapse rate in general.^{13,166} Infection with multidrug-resistant TB has been reported.^{47,123} The continuation phase may be extended, commonly to 12 months, but up to 18 months in cases with slow clinical response. In general, complete resolution is obtained in most patients.^{2,143} Only 4.6% of the cases required radical surgical treatment (subtotal or total mastectomy). A minority of patients needed a combination of minor surgical procedures such as cold abscess aspiration and resection of sinus formation or necrotic tissue (63/559, 11.3%). Most cases which underwent surgical treatments went to a clinician several months after the development of their first symptoms; because of this delay at presentation, the lesion had already been complicated by abscess or sinus formation, for which surgical intervention proved necessary. Of all surgical cases, 38.6% underwent lump excision. However, as most of the series were retrospectively reviewed, in many cases, these procedures were performed as an initial step during the workup of the patient diagnosis, and as a consequence, they cannot be fully intentionally included in the treatment plan.^{12,13}

To the best of our knowledge, this is the first study which attempts to review prevalence, risk factors, symptoms,

diagnosis, and therapy of breast TB in a systematic manner. However, our review is not without its limitations. Inevitably, as there is only one prospective study, there was an element of poor recall in each report, particularly for the case series. The main difficulty was dealing with a wide range of different study objectives, methods, and results presentations leading to a high, but heterogeneous, number of cases reported. Moreover, the different presentations of results, sometimes as cumulative findings, made it very difficult to standardize analyses; hence, the denominators change for different variables as the information for each of them was not fully available from all studies.

To improve future research on breast TB, there is a need for standardization in data collection as part of routine monitoring and evaluation. There is also a need for more prospective studies. Ideally, such data should capture information on possible risk factors, symptoms, and clinical presentations for a better differential diagnosis with other breast diseases, mainly granulomatous mastitis and carcinoma. Qualitative studies should be considered to clarify the reasons for the delay in diagnosis. Finally, diagnostic algorithms that could be applied in LMICs should be investigated, comparing different diagnostic approaches systematically.

Received January 21, 2019. Accepted for publication April 11, 2019.

Published online May 20, 2019.

Note: Supplemental appendix appears at www.ajtmh.org.

Acknowledgments: We thank James Dean for his help with proofreading.

Disclaimer: The views expressed in this publication are the sole responsibility of the authors and do not necessarily reflect the views of the affiliated organizations.

Authors' addresses: Gianluca Quaglio, European Parliamentary Research Services, European Parliament, Brussels, Belgium, E-mail: gianluca.quaglio@europarl.europa.eu. Damiano Pizzol, Operational Research Unit, Doctors with Africa CUAMM, Beira, Mozambique, E-mail: d.pizzol@cuamm.org. Petros Isaakidis, Médecins Sans Frontières, Southern Africa Medical Unit (SAMU), Cape Town, South Africa, E-mail: petros.isaakidis@joburg.msf.org. Arianna Bortolani, Francesca Tognon, Claudia Marotta, and Giovanni Putoto, Operational Research Unit, Doctors with Africa CUAMM, Padua, Italy, E-mails: a.bortolami@cuamm.org, f.tognon@cuamm.org, marotta.claudia@gmail.com, and g.putoto@cuamm.org. Francesco Di Gennaro, Department of Infectious Diseases, University of Bari, Bari, Italy, E-mail: cicciodigennaro@yahoo.it. Piero Luigi Olliaro, Special Programme for Research and Training in Tropical Diseases, World Health Organization (WHO/TDR), Geneva, Switzerland, E-mail: olliarop@who.int.

REFERENCES

- World Health Organisation (WHO), 2018. *Global Tuberculosis Report*. Available at: https://www.who.int/tb/publications/global_report/en/. Accessed January 17, 2019.
- Baharoon S, 2008. Tuberculosis of the breast. *Ann Thorac Med* 3: 110–114.
- Cooper A, 1829. *Illustration of the Diseases of the Breast. Part I. Longmans*. London, United Kingdom: Orme, Brown and Green.
- Richet M, 1880. Tumeur rare du sein; sarcome kystique. *Gaz Hop LIII*: 553.
- Powers CA, 1894. Tuberculosis of the breast. *Ann Surg* 20: 159–164.
- Tewari M, Shukla HS, 2005. Breast tuberculosis: diagnosis, clinical features and management. *Indian J Med Res* 122: 103–110.
- Da Silva BB, Lopes-Costa PV, Pires CG, Pereira-Filho JD, Santos AR, 2009. Tuberculosis of the breast: analysis of 20 cases and a literature review. *Trans R Soc Trop Med Hyg* 103: 559–563.
- Marinopoulos S, Lountou D, Gatzionis T, Dimitrakakis C, Papaspyrou I, Antsaklis A, 2012. Breast tuberculosis: diagnosis, management and treatment. *Int J Surg Case Rep* 3: 548–550.
- Da Silva BB, dos Santos LG, Costa PV, Pires CG, Borges AS, 2005. Primary tuberculosis of the breast mimicking carcinoma. *Am J Trop Med Hyg* 73: 975–976.
- Akçay MN, Sağlam L, Polat P, Erdoğan F, Albayrak Y, Povoski SP, 2007. Mammary tuberculosis—importance of recognition and differentiation from that of a breast malignancy: report of three cases and review of the literature. *World J Surg Oncol* 5: 67.
- Jah A, Mulla R, Lawrence FD, Pittam M, Ravichandran D, 2004. Tuberculosis of the breast: experience of a UK breast clinic serving an ethnically diverse population. *Ann R Coll Surg Engl* 86: 416–419.
- Khanna R, Prasanna GV, Gupta P, Kumar M, Khanna S, Khanna AK, 2002. Mammary tuberculosis: report on 52 cases. *Postgrad Med J* 78: 422–424.
- Shinde SR, Chandawarkar RY, Deshmukh SP, 1995. Tuberculosis of the breast masquerading as carcinoma: a study of 100 patients. *World J Surg* 19: 379–381.
- Elsiddig KE, Khalil EA, Elhag IA, Elsafi ME, Suleiman GM, Elkhidir IM, Hussein AM, El Hassan AM, 2003. Granulomatous mammary disease: ten years' experience with fine needle aspiration cytology. *Int J Tuberc Lung Dis* 7: 365–369.
- Bani-Hani KE, Yaghan RJ, Matalaka II, Mazahreh TS, 2005. Tuberculous mastitis: a disease not to be forgotten. *Int J Tuberc Lung Dis* 9: 920–925.
- Martinez-Parra D, Nevado-Santos M, Meléndez-Guerrero B, García-Solano J, Hierro-Guilmain CC, Pérez-Guillermo M, 1997. Utility of fine-needle aspiration in the diagnosis of granulomatous lesions of the breast. *Diagn Cytopathol* 17: 108–114.
- Gupta D, Rajwanshi A, Gupta SK, Nijhawan R, Saran RK, Singh R, 1999. Fine needle aspiration cytology in the diagnosis of tuberculous mastitis. *Acta Cytol* 43: 191–194.
- Meerkotter D, Spiegel K, Page-Shipp LS, 2011. Imaging of tuberculosis of the breast: 21 cases and a review of the literature. *J Med Imaging Radiat Oncol* 55: 453–460.
- Makanjuola D, Murshid K, Al Sulaimani S, Al Saleh M, 1996. Mammographic features of breast tuberculosis: the skin bulge and sinus tract sign. *Clin Radiol* 51: 354–358.
- Sakr AA, Fawzy RK, Fadaly G, Baky MA, 2004. Mammographic and sonographic features of tuberculous mastitis. *Eur J Radiol* 51: 54–60.
- Romero C, Carreira C, Cereceda C, Pinto J, Lopez R, Bolanos F, 2000. Mammary tuberculosis: percutaneous treatment of a mammary tuberculous abscess. *Eur Radiol* 10: 531–533.
- Al-Marri MR, Almosleh A, Almosmani Y, 2000. Primary tuberculosis of the breast in Qatar: ten year experience and review of the literature. *Eur J Surg* 166: 687–690.
- Sen M, Gorpelioglu C, Bozer M, 2009. Isolated primary breast tuberculosis: report of three cases and review of the literature. *Clinics (Sao Paulo)* 64: 607–610.
- Institute of Medicine (US), 2011. Committee on standards for systematic reviews of comparative effectiveness research. Eden J, Levit L, Berg A, Morton S, eds. *Finding What Works in Health Care: Standards for Systematic Reviews*. Washington, DC: National Academies Press (US).
- Pinto Paz ME, Piazza LR, Garcia FB, Santa Cruz E, Carrera Palao D, 2014. Mastitis crónica granulomatosa tuberculosa. Diagnóstico y tratamiento en 28 casos. *Rev Senol Patol Mamar* 27: 27–33.
- Domingo C, Ruiz J, Roig J, Texido A, Aguilar X, Morera J, 1990. Tuberculosis of the breast: a rare modern disease. *Tubercle* 71: 221–223.
- Collins P, Clancy L, Barnes L, 1991. Erythema induratum (Bazin's disease). *Ir Med J* 84: 96–98.
- Amir H, 1991. Tuberculosis of the breast presenting as mammary carcinoma. *Cent Afr J Med* 37: 53–56.
- Thakore V, 1994. Tuberculous mastitis. *Trop Doct* 24: 171.
- Estrin J, Bernstein M, 1994. Tuberculous mastitis. *South Med J* 87: 1151–1152.

31. Roy PM, Cornu P, Lebas FX, Bertrand G, Bergere A, 1996. Une cause rare de tumefaction pseudoneoplasique du sein: la tuberculose mammaire. *Rev Med Interne* 17: 173–175.
32. Frouge C, Miquel A, Cochran-Priollet B, Adrien C, Blery M, 1995. Breast mass due to rib tuberculosis. *Eur J Radiol* 19: 118–120.
33. Fred HL, 1995. An enlarging breast mass in an HIV-seropositive woman. *Hosp Pract* 30: 31–32.
34. Abboud P, Banchéri F, Bajolet-Laudinat O, Béguinot I, Wahl P, Quéreux C, 1997. Breast tuberculosis. A case of a diffuse inflammatory form. *J Gynecol Obstet Biol Reprod (Paris)* 26: 822–824.
35. Goyal M, Sharma R, Sharma A, Chumber S, Sawhney S, Berry M, 1998. Chest wall tuberculosis simulating breast carcinoma: imaging appearance. *Australas Radiol* 42: 86–87.
36. Gach O, Corhay JL, Lousberg L, Bartsch P, 1999. Breast abscess and pregnancy toxemia revealing multidrug resistant tuberculosis. *Rev Mal Respir* 16: 842–845.
37. Arslan A, Ciftçi E, Yildiz F, Cetin A, Demirci A, 1999. Multifocal bone tuberculosis presenting as a breast mass: CT and MRI findings. *Eur Radiol* 9: 1117–1119.
38. Zandrino F, Monetti F, Gandolfo N, 2000. Primary tuberculosis of the breast. A case report. *Acta Radiol* 41: 61–63.
39. Pardo J, Galindo I, Navarro LM, Querol R, 2000. Bilateral tuberculosis mastitis in a woman with human immunodeficiency virus infection. *Enferm Infecc Microbiol Clin* 18: 98–99.
40. Yilmaz F, Yagmur Y, Uzunlar AK, 2000. Tuberculosis in an intramammary lymph node. *Eur J Surg* 166: 267–268.
41. Lucht F, Cazorla C, Plat D, 2001. Tuberculose mammaire et infection par le virus de l'immunodéficience humaine. *Mal Infect* 31: 449–451.
42. Daryanani A, Sundeep P, Rodrigues G, Kumar S, Kudva R, 2002. Tuberculous mastitis masquerading as carcinoma breast. *Internet J Trop Med* 1: 1–4.
43. Chellaoui M, Taleb A, Chat L, Achaabane F, Alami D, Najid A, Benamour-Ammar H, 2002. Tuberculosis of the breast: a case report. *J Radiol* 83: 742–744.
44. Hernández Fernández M, Gutiérrez Guzmán MT, González Pablos E, 2002. Tuberculous mastitis: presentation of a new case. *An Med Interna* 19: 437–438.
45. Eroglu A, Kurkcuglu C, Karaoglanoglu N, Kaynar H, 2002. Breast mass caused by rib tuberculosis abscess. *Eur J Cardiothorac Surg* 22: 324–326.
46. Yuen JHF, Lam TPW, Leong L, 2003. Primary tuberculosis of the breast. *JHK Coll Radiol* 6: 33–35.
47. Kumar P, Sharma N, 2003. Primary MDR-TB of the breast. *Indian J Chest Dis Allied Sci* 45: 63–65.
48. Carrillo Casas E, Rodríguez Carballeira M, Sanjaume M, Martínez Lacasa J, Vives P, Garau J, 2003. Mammary, cutaneous and nodal tuberculosis without pulmonary affection in patient without apparent immunosuppression. *Rev Clin Esp* 203: 312–313.
49. Ben Ghorbel I, Ben Massoud M, Khanfir M, Mrad K, Lamloum M, Houman MH, Ben Rhomdhane K, Miled M, 2003. Association of a pulmonary, breast and cerebral tuberculosis. *Rev Med Interne* 24: 815–818.
50. Bodur H, Erbay A, Bodur H, Yilmaz O, Kulacoglu S, 2003. Multifocal tuberculosis presenting with osteoarticular and breast involvement. *Ann Clin Microbiol Antimicrob* 2: 6.
51. Miles G, Walters TK, Shee CD, 2003. Periprosthetic tuberculous breast infection. *J R Soc Med* 96: 556–557.
52. Filippou DC, Rizos S, Nissiotis A, 2003. Primary breast tuberculosis. A case report. *Radiol Oncol* 37: 1–3.
53. Salem A, Mnif N, Karray M, Kribi L, Ellouze T, Hamza R, 2004. Double location of breast and spine tuberculosis. A case report. *J Gynecol Obstet Biol Reprod* 33: 148–150.
54. Shelat VG, Pandya GJ, Dixit R, 2005. Tuberculous mastitis with rib erosion. *J Indian Acad Clin Med* 6: 82–85.
55. Chauhan A, Kakkar S, Mahapatra S, 2006. Mammary tuberculosis. A case report. *Med J Armed Forces India* 62: 385–386.
56. Kervancioğlu S, Kervancioğlu R, Özkur A, Şirikç A, 2005. Primary tuberculosis of the breast. *Diagn Interv Radiol* 11: 210–212.
57. Fellah L, Leconte I, Weynand B, Donneze J, Berlière M, 2006. Breast tuberculosis imaging. *Fertil Steril* 86: 460–461.
58. Godara R, Ahuja V, Dhingra A, Sen J, Singh R, 2006. Tubercular mastitis masquerading as carcinoma: a case report. *Internet J Surg* 13: 1.
59. Sklair-Levy M, Muggia-Sulam M, Mally B, 2006. Primary breast tuberculosis diagnosed by sonographically guided core-needle biopsy. *J Ultrasound Med* 25: 1357–1360.
60. Bakaris S, Yuksel M, Ciragil P, Guven MA, Ezberci F, Bulbuloglu E, 2006. Granulomatous mastitis including breast tuberculosis and idiopathic lobular granulomatous mastitis. *Can J Surg* 49: 427–430.
61. Ozol D, Bozer M, Bayrak R, 2006. Breast tuberculosis. *Saudi Med J* 27: 1066–1068.
62. Indumathi CK, Alladi A, Dinakar C, Rout PL, 2007. Tuberculosis of the breast in an adolescent girl: a rare presentation. *J Trop Pediatr* 53: 133–134.
63. Luh SP, Hsu JD, Lai YS, Chen SW, 2007. Primary tuberculous infection of breast: experiences of surgical resection for aged patients and review of literature. *J Zhejiang Univ Sci B* 8: 580–583.
64. Kant S, Dua R, Goel MM, 2007. Bilateral tubercular mastitis. *Lung India* 24: 90–93.
65. Mandal S, Jain S, 2007. Purulent nipple discharge—a presenting manifestation in tuberculous mastitis. *Breast J* 13: 205.
66. Sriram KB, Moffatt D, Stapledon R, 2008. Tuberculosis infection of the breast mistaken for granulomatous mastitis: a case report. *Cases J* 1: 273.
67. Van Keirsbilck J, Riphagen I, Struyven H, Van den Eeckhout A, Cornelis A, Neven P, Amant F, Vergote I, 2008. Bilateral mammary tuberculosis associated with a borderline ovarian tumor. *Breast Care* 3: 200–203.
68. Borens-Fefer B, Engohan-Aloghe C, Noël JC, Simon P, Bucella D, Boutemy R, 2008. Primary mammary tuberculosis presenting as a voluminous abscess. *JBR-BTR* 91: 54–57.
69. Bianco SR, Gurgel RL, Tavares Mde A, 2009. Radiological aspects of primary tuberculosis in the breast: a case report and review of the literature. *Rev Soc Bras Med Trop* 42: 203–205.
70. Maroulis I, Spyropoulos C, Zolota V, Tzorakoleftherakis E, 2008. Mammary tuberculosis mimicking breast cancer: a case report. *J Med Case Rep* 2: 34.
71. Madhusudhan KS, Gamanagatti S, 2008. Primary breast tuberculosis masquerading as carcinoma. *Singapore Med J* 49: e3–e5.
72. Das CJ, Kumar R, Balakrishnan VB, Chawla M, Malhotra A, 2008. Disseminated tuberculosis masquerading as metastatic breast carcinoma on PET-CT. *Clin Nucl Med* 33: 359–361.
73. Alzarraa A, Dalal N, 2008. Coexistence of carcinoma and tuberculosis in one breast. *World J Surg Oncol* 6: 29.
74. Abu-Rumman I, Mahafza S, Khamaiseh K, Shdefat S, 2008. Acute primary tuberculous mastitis: a case report. *J R Med Serv* 15: 50–52.
75. Jain S, Shrivastava A, Chandra D, 2009. Breast lump, a rare presentation of costochondral junction tuberculosis: a case report. *Cases J* 2: 7039.
76. Ochoa Aguilar MA, Ortiz Martinez JD, 2009. Tuberculosis of the breast. A case report. *Ginecol Obstet Mex* 77: 282–286.
77. Thp T, Gh H, Chaturverdi A, Bkj K, 2009. Tuberculosis of the chest wall: unusual presentation as a breast lump. *Singapore Med J* 50: e97–e99.
78. Islam A, Gafur MA, Khan SA, Karim MR, Mohiuddin M, Jahan S, 2010. A young lady with secondary tuberculosis of breast. *Mymensingh Med J* 19: 618–621.
79. Chowdri NA, Paray FQ, Dar RA, Malik AA, Mushtaque M, Malik RA, 2010. Tubercular mastitis—a rare presentation. *Int J Surg* 8: 398–400.
80. Farrokh D, Rezaii F, Rastegar YF, 2010. Primary breast tuberculosis mimicking carcinoma: a case report. *Iran J Clin Inf Dis* 5: 242–245.
81. Kao PT, Tu MY, Tang SH, Ma HK, 2010. Tuberculosis of the breast with erythema nodosum: a case report. *J Med Case Rep* 4: 124.
82. Dickson JK, Sarginson J, Moonesamy V, Oliver D, 2010. Onco-reconstructive techniques in the treatment of tuberculosis of the breast. *J Plast Reconstr Aesthet Surg* 63: e397–e399.

83. Haque MM, Badruddoza SM, Haque MM, Nazneen A, Rahman S, 2011. Primary tuberculosis of breast. *Mymensingh Med J* 20: 320–322.
84. Azarkar T, Zardast M, Ghanbarzadeh N, 2011. Tuberculosis of the breast: a case report. *Acta Med Iran* 49: 124–126.
85. Tauro LF, Martis JS, George C, Kamath A, Lobo G, Rathnakar Hegde B, 2011. Tuberculous mastitis presenting as breast abscess. *Oman Med J* 26: 53–55.
86. De Sousa R, Patil R, 2011. Breast tuberculosis or granulomatous mastitis: a diagnostic dilemma. *Ann Trop Med Public Health* 4: 122–125.
87. Wani I, Lone AM, Malik R, Wani KA, Wani RA, Hussain I, Thakur N, Snabel V, 2011. Secondary tuberculosis of breast: case report. *ISRN Surg* 2011: 529368.
88. Naghshin R, Yahyapour F, Moghaddam PZ, Ghourchian S, 2011. Breast tuberculosis in a postmenopausal woman with an insidious manner: a case report. *Med J Islam Repub Iran* 25: 47–51.
89. Termos S, Sbeity E, Oweidat M, Korban ZR, Abi Saad GS, 2011. Primary breast tuberculosis. *JBR-BTR* 94: 98.
90. Peiris L, Alam N, Agrawal A, 2012. Tuberculosis of the breast masquerading as breast cancer. *J Surg Case Rep* 10: 1.
91. Gupta R, Singal RP, Gupta A, Singal S, Shahi SR, Singal R, 2012. Primary tubercular abscess of the breast—an unusual entity. *J Med Life* 5: 98–100.
92. Kachewar S, Sankaye S, 2012. Primary tubercular mastopathy. *Australas Med J* 5: 436–439.
93. Meggiorini ML, Vitolo D, Russo A, Trinchieri V, De Felice C, 2011/2012. Breast tuberculosis: rare but still present in Italy. A case of mycobacterium breast infection. *Breast Dis* 33: 177–182.
94. Ruiz-Moreno JL, Peña-Santos G, 2012. Bilateral tuberculous mastitis nulliparous patient, initially treated as idiopathic granulomatous mastitis. *Ginecol Obstet Mex* 80: 228–231.
95. Stears L, Ismail F, Holl J, 2011/2012. Primary tuberculosis of the breast: a rare cause of a breast lump. *Breast Dis* 33: 133–137.
96. Green M, Millar E, Merai H, O'Shea M, Dedicoat M, Inglea H, 2012/2013. Mammary tuberculosis in the young: a case report and literature review. *Breast Dis* 34: 39–42.
97. Wagner VD, Huitron S, King CS, 2012. The clinical picture. A 26-year-old woman with a lump in her chest. *Cleveland Clin J Med* 79: 177–178.
98. Lall M, Sahni AK, 2013. Polymerase chain reaction: the panacea for diagnosing tubercular breast disease? *Ann Trop Med Public Health* 6: 131–133.
99. Gon S, Bhattacharyya A, Majumdar B, Kundu S, 2013. Tubercular mastitis—a great masquerade. *Turk Patoloji Derg* 29: 61–63.
100. Singal R, Guta J, Bala S, Gojal S, Mahajal NC, Chwala Aneet, 2013. Primary breast tuberculosis presenting as a lump: a rare modern disease. *Ann Med Health Sci Res* 3: 110–112.
101. Singal R, Dalal AK, Dalal U, Attri AK, 2013. Primary tuberculosis of the breast presented as multiple discharge sinuses. *Indian J Surg* 75: 66–67.
102. Singhai M, Rawat V, Joshi V, Jain P, 2013. Nipple discharge: an uncommon presentation of a common disease, tuberculosis. *J Pharm BioAllied Sci* 5: 80.
103. Khandelwal R, Jain I, 2013. Breast tuberculosis mimicking a malignancy: a rare case report with review of literature. *Breast Dis* 34: 53–55.
104. Kumar M, Tanwar P, Radhika S, Dey P, 2013. Fine needle aspiration cytology of primary mucormycosis of the breast in a young immunocompetent pregnant woman. *Cytopathology* 24: 411–412.
105. Cuervo SI, Bonilla DA, Murcia MI, Hernández J, Gómez JC, 2013. Mastitis tuberculosa. *Biomedica* 33: 36–41.
106. Gulpinar K, Ozis SE, Ozdemir S, Korkmaz A, 2013. Primary breast tuberculosis: report of a case. *Surg Sci* 4: 68–71.
107. Pandit GA, Dantkale SS, Thakare NV, Pudale SS, 2013. Tuberculous mastitis: a case report. *J Krishna Inst Med Sci Univ* 2: 123–126.
108. Brouwer A, Degrieck N, Rasschaert M, Lockefeer F, Huizing M, Tjalma W, 2014. Tuberculous mastitis presenting as a lump: a mimicking disease in a pregnant woman case report and review of literature. *Acta Clin Belg* 69: 389–394.
109. Merlet A, Dauchy FA, Creux H, Dupon M, 2014. Breast ulceration in a teenager. *Infection* 42: 449–450.
110. Prathima S, Kalyani R, 2014. Primary tubercular mastitis masquerading as malignancy. *J Nat Sci* 5: 184–187.
111. Bakhshi GD, Shenoy SS, Jadhav KV, Tayade MB, Rawoot SS, Jain K, 2014. Tuberculous osteomyelitis of sternum secondary to primary tuberculous mastitis. *Clin Pract* 4: 656.
112. Challa VR, Srivastava A, Dhar A, 2014. Scrofulous swelling of the bosom masquerading as cancer. *Indian J Med Microbiol* 32: 82–84.
113. Pal P, Patra SK, Ray S, 2014. An unusual cause of breast lump: isolated tuberculosis of the breast. *Am J Trop Med Hyg* 90: 788–789.
114. Lazrak F, Abourazzak FE, Elouzzani FE, Benzagmout M, Harzy T, 2014. A rare location of sacral tuberculosis: a report of three cases. *Eur J Rheumatol* 1: 78–80.
115. Bazi-Fontes F, Zanetti G, Marchiori E, 2015. Pulmonary and breast tuberculosis: an unusual association. *Arch Bronconeumol* 51: 598–599.
116. Chikkannaiah P, Vani BR, Benachinmardi K, Murthy VS, 2016. Axillary lymph node tuberculosis masquerading as inflammatory breast carcinoma in an immune-compromised patient. *Int J STD AIDS* 27: 149–151.
117. Robbins HL, Hetzel M, Mungall S, Cawthorn SJ, 2015. Interferon gamma release assay in the diagnosis of tuberculous mastitis. *Ann R Coll Surg Engl* 97: e1–e2.
118. Sabageh D, Afolabi Amao E, Ayo-Aderibigbe A, Olukemi Sabageh A, 2015. Tuberculous mastitis simulating carcinoma of the breast in a young Nigerian woman: a case report. *Pan Afr Med J* 21: 125.
119. Orerah GI, Wasike RW, 2016. Tuberculosis of the breast. *Clin Oncol* 1: 1068.
120. Adeiza MA, Yusuf R, Liman AA, Abur P, Bello F, Abba AA, 2016. Tuberculosis of the breast: an initial presentation of the metabolic syndrome with type 2 diabetes mellitus in a young Nigerian woman. *Case Rep Inf Dis* 15: 548586.
121. Al Shibli N, 2017. Tuberculosis of the breast—diagnosis, management, and treatment. *Int J Pharm Sci Res* 8: 3962–3965.
122. Bawany MA, Kumari K, Ali Shah SZ, Karim I, Ali Qutrio Baloch Z, 2017. Secondary tuberculosis of breast: case report. *Indo Am J Pharm Sci* 4: 3733–3735.
123. Giri VP, Giri P, Kumawat P, 2017. Primary multidrug-resistant tuberculosis of the breast—a rare presentation. *Ann Med Health Sci Res* 7: 70–72.
124. Gupta A, Gupta M, Gupta J, 2017. Unusual case of bilateral tubercular mastitis. *Cureus* 9: e1383.
125. Houssem R, Abir A, Abdrahmen D, Najeh B, 2017. Breast tuberculosis: a diagnosis often unknown: a case report. *J Tuberc Ther* 2: 109.
126. Kumar R, Kshetrimayum S, Kumar S, Garg R, 2017. Primary tuberculosis of breast: a rare presentation. *J Case Rep* 7: 127–129.
127. Murthy C, Ramu R, Patil A, 2017. Tuberculous mastitis masquerading as anti-bioma. *RGUHS J Med Sci* 7: 129–131.
128. Natraj M, Irfan Ismail A, Dhanasekar T, Rajagopalan B, 2017. Primary tuberculous mastitis. *Scholars J Med Case Rep* 5: 652–654.
129. Quilles MB, Balbo PAM, Benez MF, Nicoletti LP, Barbosa RNW, Siqueira FPC, Zutin ITM, 2017. Abscess in primary tuberculosis of breast: case report. *J Tuberc Res* 5: 161–167.
130. Hussain Naqvi SQ, Memon JM, Akhund AA, Taqi T, 2007. Tuberculosis of the breast: a cytomorphological study of nine cases. *Pak J Surg* 23: 237–241.
131. Raza MA, Mukherjee S, Mohan M, Mohan N, Zahid M, 2016. Breast tuberculosis—experience of cases in a tertiary care institute. *IJSS J Surg* 2: 1–7.
132. Supe AN, Prabhu RY, Priya H, 2002. Role of computed tomography in the diagnosis of rib and lung involvement in tuberculous retromammary abscesses. *Skeletal Radiol* 31: 96–98.
133. Fadaei-Araghi M, Geranpayeh L, Irani S, Matloob R, Kuraki S, 2008. Breast tuberculosis: report of eight cases. *Arch Iran Med* 11: 463–465.

134. Hawilo A et al., 2012. Tuberculosis of the breast: a rare often unrecognized diagnosis. *Méd Sante Trop* 22: 292–296.
135. Atamanalp SS, Gündoğdu C, Polat P, Öztürk G, Aydinli B, Ören D, Başoğlu M, Yildirgan MI, 2010. Clinical presentation of breast tuberculosis in eastern Anatolia. *Türk J Med Sci* 40: 293–297.
136. Çakar B, Çiledağ A, 2016. Retrospective analysis of seven breast tuberculosis cases. *Exp Ther Med* 12: 3053–3057.
137. Popli MB, 1999. Tuberculosis of the breast. *Indian J Radiol Imaging* 9: 127–132.
138. Gupta PP, Gupta KB, Yadav RK, Agarwal D, 2003. Tuberculous mastitis: a review of seven consecutive cases. *Indian J Tuberc* 50: 47–50.
139. Marrakchi C, Kilani B, Kanoun F, Abdelmalek R, Tiouiri H, Goubontini A, Zouiten F, Chaabane TB, 2004. La tuberculose mammaire (à propos de 6 cas). *Méd Mal Infect* 34: S130–S169.
140. Gill M, Chhabra S, Sangwan M, 2012. Tuberculous mastitis. A great mimicker. *Asian Pac J Trop Dis* 2: 348–351.
141. Kalaç N, Ozkan B, Bayiz H, Dursun AB, Demirağ F, 2002. Breast tuberculosis. *Breast* 11: 346–349.
142. Chung Soo Y, Yang Ik, Bae Sang H, Yul L, Park Hai J, Kim Hak H, Im Jung G, 1996. Tuberculous abscess in retromammary region: CT findings. *J Comput Assist Tomogr* 20: 766–769.
143. Mirsaeidi SM, Masjedi MR, Mansouri SD, Velayati AA, 2007. Tuberculosis of the breast: report of 4 clinical cases and literature review. *East Mediterr Health J* 13: 670–676.
144. Bouti K, Soualhi M, Marc K, Zahraoui R, Benamor J, Bourkadi JE, Iraqi G, 2012. Postmenopausal breast tuberculosis—report of 4 cases. *Breast Care* 7: 411–413.
145. Ndungu BM, Tharao MK, Githaiga JW, Radia K, 2008. Breast tuberculosis in outpatient practice: case reports. *Ann Afr Surg* 3: 30–33.
146. Kumar M, Chand G, Nag VK, Maurya AK, Rao RN, Agarwal S, Babu SS, Dhole TN, 2012. Breast tuberculosis in immunocompetent patients at tertiary care center: a case series. *J Res Med Sci* 17: 199–202.
147. Seker D, Kaya O, Seker GE, 2010. Tuberculosis of the breast: medical treatment. *Acta Chir Belg* 110: 614–615.
148. Zouhal A, Outifa M, Filali A, El Amrani N, Bensaid F, Fehri S, Alaoui MT, 2000. Les tumeurs pseudoneoplasiques du sein: la tuberculose mammaire. A propos de 2 cas. *Méd Maghreb* 82: 11–14.
149. Escobedo L, Ramírez E, Martín J, Reveles M, Cicero R, 2000. Tuberculosis de mama. Reporte de dos casos y revisión de la literatura. *Neumol Cirugia Torax* 59: 115–118.
150. Chalazonitis AN, Tsimitselis G, Tzovara J, Chronopoulos P, 2003. Tuberculosis of the breast. *Breast J* 9: 327–329.
151. Rakoto-Ratsimba HN, Samison LH, Razafimahandry HJ, Rakototiana AF, Imbiki Z, Ranaivozanany A, 2005. Two cases of breast tuberculosis in Madagascar. *Med Trop (Mars)* 65: 355–358.
152. Gupta V, Mohan H, Jain P, Singh S, Singla N, 2006. Tuberculous mastitis: a report of two cases in elderly females. *Jpn J Infect Dis* 59: 279–280.
153. Morino GF, Rizzardi G, Gobbi F, Baldan M, 2007. Breast tuberculosis mimicking other diseases. *Trop Doct* 37: 177–178.
154. Soto C, Vizcaino I, Isarria S, Pastor MR, 2008. Tuberculosis of the breast: imaging findings in two patients. *Radiologia* 50: 518–521.
155. Khair M, El Hafidy K, Ghalloudi A, Hermas S, Samouh N, 2010. La tuberculose mammaire: à propos de trois cas. *Espérance Méd* 17: 498–501.
156. Kapan M, Toksöz M, Bakır S, Erdal Sak M, Evsen MS, Bozkurt Y, Önder A, 2010. Tuberculosis of breast. *Eur J Gen Med* 7: 216–219.
157. Hafidi MR, Kouach J, Hamidi LA, Achenani M, Benchakroun K, Salek G, Zoubir Y, Moussaoui RD, Dehayni M, 2011. Tuberculose mammaire, a propos de deux cas. *Mali Med* 26: 58–61.
158. Zida M, Ouedraogo S, Ouangr E, Traor S, 2011. The breast tuberculosis in teaching hospital Yalgado Ouédraogo: 2 cases report. *Revue en Sciences Médicales* 14: 169–173.
159. Yanamandra U, Pathak N, Naithani N, Grover N, Nair V, 2012. Tuberculosis of breast: unusual manifestation of tuberculosis. *J Infect Chemother* 18: 109–111.
160. Al-Roomi E, Jamal W, Al-Mosawi A, Rotimi VO, 2009. *Mycobacterium tuberculosis* breast infection mimicking pyogenic abscesses in Kuwait. *Med Princ Pract* 18: 245–247.
161. Efares B, Sidibé IS, Erregad F, Hammas N, Chbani L, El Fatemi H, 2017. Breast tuberculosis: a report of five cases. *Trop Med Health* 45: 40.
162. Kakkar S, Kapila K, Singh MK, Verma K, 2000. Tuberculosis of the breast. A cytomorphicologic study. *Acta Cytol* 44: 292–296.
163. Ben Hassouna J et al., 2005. Mammary tuberculosis: a retrospective study of 65 cases. *Gynecol Obstet Fertil* 33: 870–876.
164. Ramaema DP, Buccimazza I, Hift RJ, 2015. Prevalence of breast tuberculosis: retrospective analysis of 65 patients attending a tertiary hospital in Durban, South Africa. *S Afr Med J* 105: 866–869.
165. Mehta G, Mittal A, Verma S, 2010. Breast tuberculosis. Clinical spectrum and management. *Indian J Surg* 72: 433–437.
166. Jalali U, Rasul S, Khan A, Baig N, Khan A, Akhter R, 2005. Tuberculous mastitis. *J Coll Physicians Surg Pak* 15: 234–237.
167. Khan MR, Barua A, Tarek N, Rouf A, Karim A, Bhiyan NH, Bhattacharjee T, Nizamuddin M, 2014. Mammary tuberculosis: a clinical experience on 50 cases. *Chattagram Maa-O-Shishu Hosp Med Coll J* 13: 42–46.
168. Kilic MO, Sağlam C, Ağca FD, Terzioğlu SG, 2016. Clinical, diagnostic and therapeutic management of patients with breast tuberculosis: analysis of 46 cases. *Kaohsiung J Med Sci* 32: 27–31.
169. Puneet S, Tiwary SK, Ragini R, Singh S, Gupta SK, Shukla VK, 2004. Breast tuberculosis: still common in India. *Internet J Trop Med* 2: 1–4.
170. Harris SH, Khan MA, Khan R, Haque F, Syed A, Ansari MM, 2006. Mammary tuberculosis: analysis of thirty-eight patients. *ANZ J Surg* 76: 234–237.
171. Longman CF, Campion T, Butler B, Suaris TD, Khanam A, Kunst H, Tiberi S, O'Keeffe SA, 2017. Imaging features and diagnosis of tuberculosis of the breast. *Clin Radiol* 72: 217–222.
172. Afridi SP, Memon A, Rehman SU, Memon A, Baig N, 2009. Spectrum of breast tuberculosis. *J Coll Physicians Surg Pak* 19: 158–161.
173. Gonzales Muro DJ, Siccha GC, Gutiérrez RR, 2013. Características clínicas de la tuberculosis mamaria en pacientes atendidas en un servicio de ginecoobstetricia, 2002–2011. *Rev Peruana Ginecol Obstet* 59: 107–113.
174. Tanrikulu AC, Abakay A, Abakay O, Kapan M, 2010. Breast tuberculosis in southeast Turkey: report of 27 cases. *Breast Care (Basel)* 5: 154–157.
175. Lin TL, Chi SY, Liu JW, Chou FF, 2010. Tuberculosis of the breast: 10 years' experience in one institution. *Int J Tuberc Lung Dis* 14: 758–763.
176. Tandon M, Chintamani, Panwar P, 2014. Breast tuberculosis at a tertiary care centre: a retrospective analysis of 22 cases. *Breast Dis* 34: 127–130.
177. Khodabakhshi B, Mehravar F, 2014. Breast tuberculosis in northeast Iran: review of 22 cases. *BMC Womens Health* 14: 72.
178. Mehmood N, Zeeshan HK, Ali Khan U, Nawaz A, Irfan AM, Iqbal Khan M, 2009. Tuberculous mastitis. Presentation and outcome in our setup. *Ann Pak Inst Med Sci* 5: 245–250.
179. Basarkod SI, Lamanl YP, Emmi SM, Kalburgi B, Dombale V, Vishwanath G, Chetan VN, 2012. Tuberculosis of the breast: a review of 16 cases. *J Clin Diagn Res* 6: 69–71.
180. Ben Ibrahim H, Loussaief C, Haddad A, Toumi A, Ben Romdhane F, Sakouhi M, Zakhama A, Bouzouaia N, Chakroun M, 2008. Breast tuberculosis: study of 15 cases. *Rev Tun Infectiol* 2: 31–34.
181. Bhatti Y, Baloch I, Saleem Shaikh M, Shaikh S, Deenari RA, 2010. Is tuberculosis of breast a common problem? *Med Channel* 16: 172–174.
182. Morsad F, Ghazli M, Boumzgou K, Abbassi H, El Kerroumi M, Matar N, Belabidia B, Aderdour M, El Mansouri A, 2001. Mammary tuberculosis: a series of 14 cases. *J Gynecol Obstet Biol Reprod (Paris)* 30: 331–337.
183. Ahmed R, Sultan F, 2006. Granulous mastitis: a review of 14 cases. *J Ayub Med Coll Abbottabad* 18: 52–54.
184. Mhetre SC, Rathod CV, Katti TV, Chennappa Y, 2011. Tuberculous mastitis: not an infrequent malady. *Ann Niger Med* 5: 20–23.

185. Chandanwale SS, Buch AC, Gore CR, Ramanpreet KC, Jadhav P, 2012. Fine needle aspiration cytology in breast tuberculosis: diagnostic difficulties—study of eleven cases. *Indian J Tuberc* 59: 162–167.
186. Zekri H, Boufettal H, Bennani O, Laghzaoui M, Bouhya S, 2010. La tuberculose mammaire. À propos de 10 cas. *J Marocain Sci Méd* 17: 19–23.
187. Seo HR et al., 2012. Differential diagnosis in idiopathic granulomatous mastitis and tuberculous mastitis. *J Breast Cancer* 15: 111–118.
188. Quaglio GL, Pizzolo D, Bortolani A, Manenti F, Isaakidis P, Putoto G, Olliaro PL, 2018. Breast tuberculosis in men: a systematic review. *PLoS One* 13: e0194766.
189. Lilleng R, Paksoy N, Vural G, Langmark F, Hagmar B, 1995. Assessment of fine needle aspiration cytology and histopathology for diagnosing male breast masses. *Acta Cytol* 39: 877–881.
190. Walker M, 2008. Conquering common breast-feeding problems. *J Perinat Neonatal Nurs* 22: 267–274.
191. Mathad JS, Gupta A, 2012. Tuberculosis in pregnant and postpartum women: epidemiology, management, and research gaps. *Clin Infect Dis* 55: 1532–1549.
192. Sharma SK, Kadiravan T, Banga A, Goyal T, Bhatia I, Saha PK, 2004. Spectrum of clinical disease in a series of 135 hospitalised HIV-infected patients from north India. *BMC Infect Dis* 4: 52.
193. Corbett EL, Steketee RW, ter Kuile FO, Latif AS, Kamali A, Hayes RJ, 2002. HIV-1/AIDS and the control of other infectious diseases in Africa. *Lancet* 359: 2177–2187.
194. Korenromp EL, Scano F, Williams BG, Dye C, Nunn P, 2003. Effects of human immunodeficiency virus infection on recurrence of tuberculosis after rifampin-based treatment: an analytical review. *Clin Infect Dis* 37: 101–112.
195. Hartstein M, Leaf HL, 1992. Tuberculosis of the breast as a presenting manifestation of AIDS. *Clin Infect Dis* 15: 692–693.
196. Laronga C, Kemp B, Johnston D, Robb GL, Singletary SE, 1999. The incidence of occult nipple-areola complex involvement in breast cancer patients receiving a skin-sparing mastectomy. *Ann Surg Oncol* 6: 609–613.
197. Santini D, Taffurelli M, Gelli MC, Grassigli A, Giosa F, Marrano D, Martinelli G, 1989. Neoplastic involvement of nipple-areolar complex in invasive breast cancer. *Am J Surg* 158: 399–403.
198. Iddon J, Dixon JM, 2013. Mastalgia. *BMJ* 347: 3288.
199. Olu-Eddo AN, Ugiagbe EE, 2011. Benign breast lesion in an African population. *Niger Med J* 52: 211–216.
200. Amin AL, Purdy AC, Mattingly JD, Kong AL, Termuhlen PM, 2013. Benign breast disease. *Surg Clin North Am* 93: 299–208.
201. Nicholson BT, Mills SE, 2007. Sarcoidosis of the breast: an unusual presentation of a systemic disease. *Breast J* 13: 99–100.
202. Mathew M, Siwawa P, Misra S, 2015. Idiopathic granulomatous mastitis: an inflammatory breast condition with review of the literature. *BMJ Case Rep* 2015: bcr2014208086.
203. Korkut E, Akcay MN, Karadeniz E, Subasi ID, Gursan N, 2015. Granulomatous mastitis: a ten-year experience at a university hospital. *Eurasian J Med* 47: 165–173.
204. Nemenqani D, Yaqoob N, 2009. Fine needle aspiration cytology of inflammatory breast lesions. *J Pak Med Assoc* 59: 167–170.
205. Kataria SP, Sharma J, Singh G, Kumar S, Malik S, Kumar V, 2016. Primary breast mucormycosis: FNAC diagnosis of a rare entity. *Diagn Cytopathol* 44: 761–763.
206. Tulasi NR, Raju PC, Damodaran V, Radhika TS, 2006. A spectrum of coexistent tuberculosis and carcinoma in the breast and axillary lymph nodes: report of five cases. *Breast* 15: 437–439.
207. Akbulut S, Sogutcu N, Yagmur Y, 2011. Coexistence of breast cancer and tuberculosis in axillary lymph nodes: a case report and literature review. *Breast Cancer Res Treat* 130: 10371–11042.
208. Ozol D, 2006. Bacteriology or pathology for tuberculosis mastitis. *Int J Tuberc Lung Dis* 10: 824.
209. Kohli M, Schiller I, Dendukuri N, Dheda K, Denkinger CM, Schumacher SG, Steingart KR, 2018. Xpert® MTB/RIF assay for extra-pulmonary tuberculosis and rifampicin resistance. *Cochrane Database Syst Rev* 8: CD012768.