UNIVERSIDADE DO ESTADO DE AMAZONAS
FUNDAÇÃO DE MEDICINA TROPICAL DR. HEITOR VIEIRA DOURADO
PROGRAMA DE PÓS-GRADUAÇÃO EM MEDICINA TROPICAL
MESTRADO EM DOENCIAS TROPICAIS E INFECCCIOSAS

MASTITE INFECCIOSA NAS AMÉRICAS: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE DA LITERATURA

VICTOR COSTA MORAIS DE OLIVEIRA

MANAUS

2019

VICTOR COSTA MORAIS DE OLIVEIRA

MASTITE INFECCIOSA NAS AMÉRICAS: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE DA LITERATURA

Projeto de dissertação apresentada ao Programa de Pós-Graduação em Medicina Tropical da Universidade do Estado do Amazonas em Convênio com a Fundação de Medicina Tropical Dr. Heitor Vieira Dourado**,** como requisito parcial para obtenção grau de *Mestre em Doenças Tropicais e Infecciosas.*

Orientador: Prof. Dr. Fernando Fonseca del Almeida e Val

Co-orientadores:

Prof. Dr. Marcus Vinícius Guimarães de Lacerda

Prof. Dr. Marcelo Cordeiro dos Santos

MANAUS

2019

Ficha Catalográfica

Oliveira, Victor Costa Morais de

Mastite infecciosa: uma revisão sistemática nas Américas. Victor Costa Morais de Oliveira. -- Manaus, Amazonas, 2019.

XII, 51f

Dissertação (Mestrado) –Universidade do Estado do Amazonas.

Programa de Pós-graduação em Medicina Tropical

Título em inglês: Infectious Mastitis in the Americas: a systematic review and meta-analysis.

1. Non-puerperal mastitis. 2. Granulomatous Mastitis. 3. *Mycobacterium tuberculosis*. 4. Nontuberculous Mycobacteria. 5. Epidemiology

FOLHA DE JULGAMENTO

MASTITE INFECCIOSA NAS AMÉRICAS: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE DA LITERATURA

VICTOR COSTA MORAIS DE OLIVEIRA

"Esta Dissertação foi julgada adequada para obtenção do Título de Mestre em Doenças Tropicais e Infecciosas, aprovada em sua forma final pelo Programa de Pós-Graduação em Medicina Tropical da Universidade do Estado do Amazonas em convênio com a Fundação de Medicina Tropical Dr. Heitor Vieira Dourado".

Banca Julgadora:

_____

Presidente

_____

Membro

_____

Membro

DEDICATÓRIA

Dedico este trabalho a meu avô materno Manoel Vieira da Costa, todas as minhas conquistas acadêmicas e profissionais refletem na sua dedicação e trabalho ao longo da sua vida, assim como meus pais Lúcio Flávio Morais de Oliveira e Sônia Maria da Costa que me proporcionaram um ambiente propício para dedicação aos estudos.

AGRADECIMENTOS

Agradeço as instituições: Universidade Estadual do Amazonas (UEA); Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (FMT-HVD); Superintendência da Zona Franca de Manaus (SUFRAMA); Fundação de Amparo á Pesquisa do Estado do Amazonas (FAPEAM); Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES); Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), pelo apoio e fornecimento da estrutura necessária para o desenvolvimento deste trabalho.

Gostaria de deixar meu profundo agradecimento aos Drs. Marcus Vinícius Guimarães de Lacerda e Marcelo Cordeiro dos Santos, que foram uma grande influência na minha formação acadêmica, como exemplo de profissionais pelo conhecimento teórico e pela relação perante os pacientes e com os demais profissionais da área da saúde.

Estendo meus agradecimentos a Dra. Izabella Picinin Safe, que sempre demonstrou apoio e incentivo profissional e acadêmico, a quem guardo junto aos demais grande admiração.

Ao meu orientador Dr. Fernando Fonseca de Almeida e Val e à colaboradora Nadia Carolina Cubas Vega, que foram fundamentais para realização deste trabalho, a quem devo todos os méritos para sua finalização devido o suporte fornecido no momento de maior dificuldade para sua conclusão.

DECLARAÇÃO DAS AGÊNCIAS FINANCIADORAS

Este trabalho não contou com financiamento específico de instituições ou órgãos nos setores públicos, privados ou sem fins lucrativos.

RESUMO

A mastite infecciosa é uma doença inflamatória benigna da mama, com uma apresentação clínica variada que pode atrasar o diagnóstico específico e perpetuar tratamentos ineficazes. Esta revisão sistemática teve como objetivo ampliar o conhecimento existente sobre a apresentação clínica, principais agentes infecciosos, bem como procedimentos diagnósticos, manejo terapêutico e taxas de recaída de diferentes casos notificados. Um total de 36 artigos foram incluídos resultando em 69 casos. Dados demográficos, clínicos, radiográficos, histopatológicos, tratamento e desfecho da doença foram revisados. A pesquisa resultou em 65 casos de infecção de mama em mulheres e 4 casos em homens, com idade média de 40,3 anos. Os sintomas mais prevalentes foram nódulo mamário (39.1%), fístula, abscesso e descarga papilar em 34,8, 18,8 e 17,4%, respectivamente; treze casos foram considerados suspeitos de câncer de mama. Sessenta e quatro pacientes (92,7%) receberam tratamento farmacológico, 32 (46,3%), acompanhados de procedimento cirúrgico. Quatro (5,9%) casos apresentaram recidiva. *Mycobacterium tuberculosis* foi o agente etiológico de mastite infecciosa mais comum; as mulheres foram a população mais afetada por essa entidade, embora existam casos raros em homens. Foi encontrada uma diferença entre o tempo para concluir o diagnóstico entre os países americanos de alta renda per capita e aqueles com baixa renda, sendo no primeiro grupo um número maior de ressecções cirúrgicas realizadas. Diagnóstico adequado e tratamento oportuno parecem ser a chave para uma recuperação satisfatória.

Palavras Chaves: Mastite não-puerperal, Mastite granulomatosa, *Mycobacterium tuberculosis*, Micobactéria não tuberculosa, Epidemiologia.

ABSTRACT

Infectious mastitis is a benign inflammatory breast disease with a varied clinical presentation that can delay specific diagnosis and perpetuate ineffective treatments. This systemic review aimed to expand the existing knowledge on the clinical presentation, main infectious agents as well as diagnostic procedures, therapeutic management and relapse rates of different reported cases. A total of 36 articles were included resulting in 69 cases. Demographic, clinical, radiographic, histopathological data, treatment and disease outcome were reviewed. The search yielded 65 cases of breast infection in women and 4 cases in men, median age 40.3 years. Most prevalent symptoms were breast lump (39.1%), fistula, abscess and nipple discharge in a 34.8, 18.8 and 17.4%, respectively; thirteen cases were considered as breast cancer suspicious. Sixty-four patients (92.7%) received pharmacological treatment, 32 (47.1%), accompanied by surgical procedure. Four (5.9%) cases presented recurrence. Mycobacterium tuberculosis was the commonest infectious mastitis etiological agent; women were the most affected population by this entity, although there are very rare cases in men. A difference between the time to conclude the diagnosis between the high per capita American countries and those with low income was found, being in the first group a greater number of surgical resections performed. Appropriate diagnosis and timely treatment seem to be the key to a satisfactory recovery. The lack of systematic reports of the included studies makes a comprehensive and exhaustive data analysis difficult.

Keywords: Non-puerperal mastitis, Granulomatous Mastitis, *Mycobacterium tuberculosis*, Nontuberculous Mycobacteria, Epidemiology.

RESUMO LEIGO

A doença da mama tem diferentes causas, afetando homens e mulheres, independentemente da idade. Uma de suas principais causas são infecções, seja por bactérias, vírus, fungos ou parasitas. Para uma cura satisfatória e definitiva dos pacientes, é necessário conhecer as características dos sintomas de nossa população e assim fazer um diagnóstico adequado e rápido. Uma revisão foi feita de 36 artigos científicos com casos de infecção de mama em pacientes que vivem no continente Americano, 69 pacientes foram encontrados afetados por esta doença, principalmente mulheres adultas. O sintoma mais frequente relatado pelos pacientes foi massa ou nódulo com muitos dias ou semanas de aparecimento. Para fechar o diagnóstico em quase todos os pacientes foram necessários aproximadamente 5 meses, mais do 90% deles receberam tratamento com remédios e quase a metade teve que passar por uma cirurgia para curar sua doença. Um pequeno número de pessoas teve a infecção de mama mais de uma vez.

LISTA DE TABELAS

LISTA DE QUADROS

LISTA DE FIGURAS

LISTA DE ABREVIATURAS, SÍMBOLOS E UNIDADES DE MEDIDA

IM: mastite infecciosa
TB: tuberculose
spp: espécies

SUMÁRIO

1. INTRODUÇÃO

A mastite é uma doença inflamatória não maligna da mama, que pode ou não estar acompanhada de infecção, capaz de afetar qualquer estrutura anatômica da glândula mamária [1–3]. Pode ser classificada de acordo com sua apresentação clínica (clínica ou subclínica), evolução (aguda, subaguda, crônica ou recorrente), em mulheres, de acordo com sua fase no processo reprodutivo (lactacional ou não-lactacional) e conforme etiologia entre infecciosa, não infecciosa e maligna. [4,5]

1.1. Epidemiologia e etiologia

A mastite infecciosa (IM) ocorre mais comumente em mulheres em idade reprodutiva, amamentando ou não [3,6]; no entanto, pode ocorrer em pessoas de ambos os sexos em qualquer idade [7–9]. A prevalência da doença varia de acordo com o grupo populacional estudado, entre 1-33% em mulheres que amamentam e 5 a 9% e mulheres não lactantes [10], os dados em homens, crianças e adolescentes são mais limitados. Se a mastite infecciosa não for tratada, pode desenvolver complicações graves, como abscesso, fístulas, sepse ou até mesmo casos fatais; o abscesso mamário ocorre em 3 a 11% das mulheres com mastite e em até 50% das crianças com mastite neonatal (1,10). Enquanto as fístulas mamárias são apresentadas em menor porcentagem, com 1-2%.[11]

Alguns fatores de risco têm sido descritos para o desenvolvimento da mastite infecciosa, dentre eles estão o tabagismo, diabetes mellitus, lesões em mamilo e aréolas, doenças imunossupressoras, multiparidade e técnicas inadequadas de amamentação.[4,12]

Os agentes etiológicos mais comuns da mastite infecciosa não puerperal estão listados no Quadro 1.

Quadro 1. Principais agentes infecciosos etiológicos da mastite não puerperal (13,14)

Bacteria
Tuberculose
Micobactéria não tuberculosa
Actinomicose
Corynebacterium
Fungo (pouco frequente)
Candida
Criptococose
Histoplasmose
Parasitas e vírus (muito raro)
Filariose

A mastite tuberculosa apesar de ser considerada uma causa rara de doença da mama, representando 0,025 – 4% dependendo da localização

geográfica, representa uma das principais causas infecciosas de mastite crônica não puerperal, sendo descrita pela primeira vez em 1829 por Sir Astley Cooper. O tempo médio entre a apresentação clínica e o diagnóstico pode variar entre 1 a 12 meses ou mais, sendo o mesmo estabelecido através de exame histopatológico com lesão granulomatosa, havendo baixa positividade nos resultados de cultura (12,15,16). Já os casos de mastite não tuberculosa estão quase que na sua totalidade associados a procedimentos cirúrgicos da mama, não raramente ocasionando surtos em determinada região ou hospital (17).

Infecções por *Corynebacterium* spp. já foram descritas como tendo possível associação na fisiopatologia da mastite granulomatosa idiopática, o que a tornaria um agente etiológico mais relevante do que a tuberculose mamária nos casos de mastite não puerperal, porém essa hipótese ainda não foi bem estabelecida (18), estas mastites também são denominadas como mastite granulomatosa cística neutrofílica devido características analisadas no histopatológico.(19)

1.2. Características clínicas, diagnóstico e abordagem terapêutica

As principais características clínicas das mastites infecciosas estão apresentadas no Quadro no.2 e apresentam sinais e sintomas semelhantes aos casos de mastite não infecciosa. Estudos de imagem podem auxiliar no diagnóstico ou definir a extensão da lesão, sendo a ultrassonografia uma ferramenta útil na abordagem inicial para avaliar complicações quando se suspeita de um abscesso mamário, podendo ser usada para realizar a aspiração com agulha fina da lesão. A mamografia pode ser inadequada devido aos achados limitados causados pela densidade da mama na faixa etária mais prevalente, além de ser dolorosa e desconfortável para as pacientes. Há casos em que a realização de uma biópsia pode ser considerada necessária, principalmente quando a resposta ao tratamento inicial se dá de forma inadequada ocasionando recidiva das lesões, ou especialmente nos casos em que se suspeita de uma entidade neoplásica uma vez que em muitos pacientes a mastite infecciosa pode imitar um tumor maligno da mama, principalmente pelas características radiológicas.(4,15,20-21)

O tratamento na suspeita de mastite infecciosa deve ser iniciado o mais breve possível. Todos os pacientes devem receber tratamento sintomático com analgésicos e meios locais (compressas feitas com água quente); a terapia antimicrobiana adequada é essencial e geralmente é suficiente para que o controle da infecção. Os medicamentos mais utilizados são as penicilinas antiestafilocócicas (flucloxaxilina, dicloxacilina), cefalosporina de primeira geração (cefalexina, cefazolina), antibióticos não beta-lactâmicos (amoxicilina + ácido clavulânico ou, nos casos mais graves, vancomicina intravenosa), macrolídeos (eritromicina ou claritromicina) ou lincosamidas (clindamicina) (1,14,22). Qualquer abscesso mamário deve sempre ser drenado, se necessário em várias ocasiões, seja por aspiração ou por um procedimento ligeiramente mais invasivo, acompanhado de antibioticoterapia; as fístulas também têm uma intervenção cirúrgica. (11,22)

Quadro 2. Sinais e sintomas de mastite infecciosa [2,3]

Mastite
Dor mamária/Mastalgia
Vermelhidão da mama
Calor dos seios
Firmeza / dureza da mama
Inchaço mamário
Aumento dos linfonodos axilares
Outros sintomas: mal-estar, febre, mialgia, dor de cabeça.
Complicações (além dos sinais e sintomas anteriores)
Absceso: massa ou nódulo
Fístula: orifício fistuloso com supuração ativa

2. OBJETIVOS

2.1 Objetivo geral

Caracterizar o perfil etiológico, clínico, diagnóstico e terapêutico de pacientes com mastite infecciosa não puerperal no continente americano.

2.2 Objetivos específicos

1. Descrever os aspectos epidemiológicos, clínicos e de estudos de imagem destas populações.
2. Verificar se há associação entre a apresentação clínica, tempo de diagnóstico e abordagem terapêutico com a recorrência da doença.
3. Realizar uma comparação entre os parâmetros estudados dos países considerados de alta renda com aqueles de baixa e média renda.

3. PRODUTO DA DISSERTAÇÃO

ARTIGO

A primeira versão do manuscrito encontra-se abaixo. Consiste em uma revisão sistemática da literatura com meta-análise de casos de mastite de etiologia infecciosa em países das américas. Pretende-se publicação na revista “The Breast”, fator de impacto 2018: 3.494 (© Clarivate Analytics Journal Citation Reports 2019).

Manuscript

Title: Infectious mastitis in the Americas: a systematic review and meta-analysis of the literature

Authors:
Victor Costa Morais de Oliveira[1,2,3], Nadia Carolina Cubas Vega[1,3], Izabella Picinin Safe[1,3], Marcelo Cordeiro dos Santos[1,3,4], Marcus Vinícius Guimarães de Lacerda[1,5], Fernando Val[1,3],

Filiations:

1. Fundação de Medicina Tropical Dr. Heitor Vieira Dourado, Av. Pedro Teixeira 25, Dom Pedro, Manaus-AM, Brazil, 69040-000.
2. Fundação Hospital Adriano Jorge, Av. Carvalho Leal, 1778, Cachoeirinha, Manaus-AM, Brazil, 69065-001.
3. Universidade do Estado do Amazonas, Av. Carvalho Leal, 1777, Cachoeirinha, Manaus-AM, Brazil, 69065-001
4. Universidade Nilton Lins, Av. Prof. Nilton Lins, 3259, Flores, Manaus-AM, Amazonas, Brazil, 69058-030
5. Instituto Leônidas e Maria Deane, FIOCRUZ-AM, Rua Terezina, 476, Adrianópolis, Manaus-AM, Brazil, 69057-070

Corresponding author:
Dr. Fernando Val
E-mail address: ffaval@gmail.com
Full postal address: Fundação de Medicina Tropical Doutor Heitor Vieira Dourado. Av. Pedro Teixeira, número 25. Bairro Dom Pedro, Manaus, Amazonas, Brazil. ZIP-Code: 69040-000

Abstract

Infectious mastitis is a benign inflammatory breast disease with a varied clinical presentation that can delay specific diagnosis and perpetuate ineffective treatments. This systemic review aimed to expand the existing knowledge on the clinical presentation, main infectious agents as well as diagnostic procedures, therapeutic management and relapse rates of different reported cases. A total of 36 articles were included resulting in 69 cases. Demographic, clinical, radiographic, histopathological data, treatment and disease outcome were reviewed. The search yielded 65 cases of breast infection in women and 4 cases in men, median age 40.3 years. Most prevalent symptom was breast lump (39.1%), fistula, abscess and nipple discharge in a 34.8, 18.8 and 17.4%, respectively; thirteen cases were considered as breast cancer suspicious. Sixty-four patients (92.7%) received pharmacological treatment, 32 (47.1%), accompanied by surgical procedure. Four (5.9%) cases presented recurrence. Mycobacterium tuberculosis was the commonest infectious mastitis etiological agent; women were the most affected population by this entity, although there are very rare cases in men. A difference between the time to conclude the diagnosis between the high per capita American countries and those with low income was found, being in the first group a greater number of surgical resections performed. Appropriate diagnosis and timely treatment seem to be the key to a satisfactory recovery. The lack of systematic reports of the included studies makes a comprehensive and exhaustive data analysis difficult.

Keywords: Non-puerperal mastitis, Granulomatous Mastitis, *Mycobacterium tuberculosis*, Nontuberculous Mycobacteria, Epidemiology.

Introduction

Mastitis is a nonmalignant inflammatory breast disease, which may or may not be accompanied by infection, that can affect any anatomical structure of the mammary gland [1–3]. It can be classified according to its clinical presentation (clinical or subclinical), evolution (acute, subacute, chronic or recurrent) and, in women, according to their stage in the reproductive process (lactational or non-lactational) [4].

Infectious mastitis (IM) may be caused by bacteria, fungus, parasites or virus; higher prevalence occur in women of reproductive age, breastfeeding or not [3,6,15]. However, it can occur in people of both sexes at any age [8,9,16,17]. Risk factors include smoking, diabetes mellitus, lesions in nipple and areolas, chronic diseases, disseminated tuberculosis, multiparity and inadequate breastfeeding techniques [3,12,18]. The clinical features of IM are very similar to the non-IM, which include breast pain, redness, warmth, tenderness, swelling and enlargement of axillary lymph nodes; flu-like symptoms as fever, myalgia and headache may also be present [2,13].

Imaging techniques, as ultrasound, may assist diagnosis and help defining lesion extent. In many patients IM can mimic a malignant breast tumor, therefore, a biopsy may be necessary [11,19,20]. Treatment should start as soon as possible. Adequate antimicrobial therapy is essential and is usually sufficient for the infection to subside [1,5,21,22]. Breast abscess should always be drained, if necessary on multiple occasions, either by aspiration or more invasive procedures, accompanied by antibiotic therapy [3,11].

Infectious mastitis is an important public health problem. Nonetheless, little is known in regard to clinical presentation, main infectious agents, diagnostic procedures, therapeutic management and relapse rates in the Americas. Therefore, the main objective of this study was to review these aspects in reports originating from countries in this geographical region.

Methods

A systematic review addressing IM was conducted using Preferred Reporting items for Systematic Reviews and Meta-Analysis guidelines [23]. We systematically identified studies reporting cases presenting mastitis of infectious etiology in the Americas using a pre-defined search strategy (**Table 1**). The last search was performed in February 2019. All studies with primary data were included. No restrictions regarding language and date were applied.

Title and abstracts were reviewed for data regarding studies with humans and confirmation of a non-puerperal mastitis infection diagnosis. Only case reports presenting mastitis of infectious origin from countries of the Americas were included. All included studies were assessed for eligibility through full-text review and excluded when reported non-human studies, inconclusive data upon mastitis and experimental and basic research designs. All reviews were performed by two independent researchers and disagreements were resolved by consensus. References from the included studies were assessed in order to identify those not originally detected. The process of study selection is summarized in **Figure 1**.

The following data were extracted: publication metadata (authors, year of publication), geographical location, demographical and epidemiological characteristics (age, time to reach diagnosis, clinical presentation, treatment length, side and quadrant of the breast compromised, culture results, Ziehl-Neelsen, possible risk factors, gestational history, ultrasonographic and mammographic bi-rads classification, histopathological pattern, x-ray description, treatment and relapse rate). In addition, a comparison was made between the characteristics of patients from countries with low, low-middle and upper middle income (Latin American countries) and those from high income countries (United States [US] and Canada) according to the World Bank classification based in the gross national income (GNI) per capita of each nation [24]. All the extracted data was entered into an Excel datasheet. Descriptive statistics was used to describe data. Difference in proportions were tested by Chi squared test (corrected by Fisher's test if necessary). Statistical analyses were performed using independent t tests, Wilcoxon Mann–Whitney or $\chi 2$ tests to compare variables across groups. Significance was set as $p < 0.05$. Analysis was performed using STATA software, version 14 (Texas, USA).

Results

The original search yielded a total of 4539 potentially eligible studies from the database search, of which 3377 (74.4%) were excluded due to be non-human studies. After eliminating duplicates and assessing inclusion and exclusion criteria, a total of 33 studies remained. Three additional records were identified and included through reference search, being a total of 36 studies included. (**Figure 1).**

A total of 69 patients resulted from the included studies. Characteristics of all patients are summarized in **Table 2**. The cases were reported in eight different countries, being Brazil the country with the highest number of cases, 34 (49.3%). Of the total number of patients, only 4 (5.8%) were men. The majority, therefore, was female (n= 65, 94.2%) and the median age was 40.3 years (range, 15 days – 78 years). (**Table 3)**

At first, thirteen cases (19.1%) were considered as breast cancer suspicious. Location was reported as unilateral (n: 60, 86.9%), being the right breast the most committed, with 52.2% (n= 36). The most prevalent complaints were breast lump (n=27, 39.1%), fistula (n= 24, 34.8%), abscess (n=13, 18.8%) and nipple discharge (n= 12, 17.4%). One patient was asymptomatic. In six out of 68 symptomatic patients (8.8%), the breast lump was accompanied by either nipple discharge (n=3, 4.4%), fistula (n=2, 2.9%) or abscess (n=1, 1.5%). Other signs and symptoms are described in **Table 4**.

The etiological agent could be determined in 67 patients. Treatment was prescribed mainly based on epidemiological risk or after biopsy results. Bacteria was the most prevalent etiology (n=61, 88.4%) followed by four (5.8%) cases of fungal infection and one case (1.4%) described for each, viral and parasitic origin. Among bacterial diagnosis, 30 (43.5%) cases presented *M*. *tuberculosis*; 12 (17.4%) were caused by non-tuberculous mycobacteria and an equal number by *Corynebacterium sp*.

Time between the onset of symptoms and the definitive diagnosis was reported for 50 cases and was highly variable, ranging from 1 day to 13 years

with a median of 32.5 weeks. Different diagnostic methods were used alone or combined; breast ultrasound, mammography, chest x-rays, culture, PPD and biopsy were reported. Among 69 cases, 36, 3 and 2 patients were reported findings in x-rays, ultrasound and mammography, respectively; amongst these, 10 patients had abnormal chest x-rays and three were classified as BIRAD IV or V, two of them were part of the breast cancer suspicious group. Culture was performed in 65 patients, 26 (40%) were positive; 57 patients underwent biopsy. Findings are presented in **Supplementary Table 1.**

Thirty-two patients (47%) underwent surgery, all combined with pharmacological treatment; median treatment time was 22.6 weeks (range 1-60). Fifty-six (81.1%) cases reported complete remission. Four recurrences were described, of which three underwent surgical treatment. Follow up was missing in nine cases.

When comparing the two groups of countries categorized by their annual GNI per capita, a statistically significant similarity was stablished in term of most affected gender by IM. Patients from the US/Canada group presented a shorter diagnostic time when compared to the Latin American group (p=0.002) and were subjected to a greater number of surgical resections. There was no significant statistical difference of time of treatment of patients, initial clinical malignancy suspicious or in the presence of relapses. Further data regarding country differences of selected variables are presented in Table 5.

Discussion

To our knowledge this is the first systemic review of reported cases on IM in the American continent that involves different etiological agents and that also compares the behavior of distinct health indicators between two population groups. In a study performed in the Asian continent AbdelHadi and Bukharie reported *S. aureus* as the main etiologic cause of non-lactating breast infections [6], and in the African continent the fungal infection caused by *Candida sp*. It seems, although very rare, a cause of complaint of women who are breastfeeding [25]. However, in this review *Mycobacterium tuberculosis* was found responsible for 40% of cases, which indicates the persistence of tuberculosis as a public health problem. Despite these observed differences, it is not surprising that this bacteria is an important cause of IM, since a large number of original articles in the Americas are focused on tuberculous or granulomatous mastitis [9,19,26]. In addition, IM may be caused by other mycobacteria, as already reported in India and England [27,28], as different species of Corynobacterium gram positive bacillus [29,30], also described in this review.

In Asia and Europe it has been shown that the prevalence of breast infections is higher in women [22,31,32], and even in many articles, male patients are initially excluded. The findings in this study, coincide with the behaviors in these two continents, with a greater number of cases in the female sex, and only 5.8% (four cases, all due to bacteria) of male patients. Infectious mastitis most frequently affects females in reproductive age and is characterized by the presence of local inflammatory symptoms and a breast mass, usually unilateral, which may be confused with a malignant tumor lesion. Most cases were found to be of young adults, with more than a third presenting unilateral breast lump, also considered suspicious of malignancy. A case series study conducted in Turkey

by Kilic et.al. showed a prevalence of 34.8% of the cases with suspicious initial tumor. [12]

The duration of signs and symptoms prior to diagnosis may vary greatly. The duration found in this study was higher than studies from Europe and Africa [9,12,25]. The diagnostic methods and treatment approaches both medical and surgical were very similar to those described by other European authors [9,12,22].

In Africa the recurrence of mastitis in lactating women was studied, it was found that 6.9% of mothers had at least 1 episode of recurrence [33]. The recurrence rate in our study was very similar, approximately 7%, of which three patients needed surgical treatment; higher recurrence rates have been characterized in follow-ups performed in hospital in Italy and Greece [8,34]. No significant differences were found in the clinical characteristics, auxiliary examinations. and treatment approaches between those who had a favorable evolution and those who had persistence or clinical recurrence.

Only studies containing IM were included, which may increase prevalence rates of such presentations. Furthermore, unfrequented clinical presentations are more likely to be published, leading to a publication bias. Also, assessing disease prevalence or clinical outcomes among several reports of different authors from different geographical regions and dates may lead to a lack of data standardization, which is an expected limitation. These may also affect case management, which may have further influenced the results of the present study. The lack of systematic reporting from the included studies hampers broad data analysis and completeness.

Conclusion

Breast tuberculosis seems to be a very common cause of IM. Although consisting of a non-frequent inflammatory benign pathology of the breast, it has been increasingly described in the literature in the last years. Since IM has a great variety of causes, the length to reach a final diagnosis is still a long and daunting task. Acute or chronic inflammatory processes have a negative psychological effect, especially in women. Investigational techniques such as ultrasonography, cytological and histological analysis should be fully utilized to rule out the specific cause of a breast infectious, along with a detailed clinic and laboratorial approach. Important inferences were described between the health systems of the countries with greater economic income and those with lower income levels, with one of the most important findings being the time to elucidate the diagnosis of IM. The analysis suggested that the countries belonging to the first group have a better performance than those who do not have access to health systems of such high quality. As our understanding of the infectious mastitis process grows, it can establish well-defined diagnostic and management protocols that are appropriate for each case and thus avoid close or future clinical complications. Our review is limited by the lack of some detailed information in some cases reports, some studies were focus on radiological or histopathological descriptions without therapy or follow up narrative. Prospective and controlled studies are needed to better study IM in the future.

Conflict of interest/disclosure: The authors declare that they do not have financial or other conflicts of interest in relation to this publication.

References

[1] Amir LH. ABM Clinical Protocol #4: Mastitis, Revised March 2014. Breastfeed Med 2014;9:239–43. doi:10.1089/bfm.2014.9984.

[2] Inch S, Xylander S, Savage F. Mastitis causes and Mangaement. vol. WHO/FCH/CA. 2000.

[3] Boakes E, Woods A, Johnson N, Kadoglou N. Breast Infection: A Review of Diagnosis and Management Practices. Eur J Breast Heal 2018:136–43. doi:10.5152/ejbh.2018.3871.

[4] Contreras GA, Rodríguez JM. Mastitis: comparative etiology and epidemiology. J Mammary Gland Biol Neoplasia 2011;16:339–56. doi:10.1007/s10911-011-9234-0.

[5] Angelopoulou A, Field D, Ryan CA, Stanton C, Hill C, Ross RP. The microbiology and treatment of human mastitis. Med Microbiol Immunol 2018;207:83–94. doi:10.1007/s00430-017-0532-z.

[6] AbdelHad M, Bukharie H. Breast Infections in non-lactating Women. J Family Community Med 2005;12:133–7.

[7] Conde DM. Treatment approach for breast abscess in nonlactating adolescents. Int J Gynecol Obstet 2015;128:72–3. doi:10.1016/j.ijgo.2014.08.009.

[8] Michala L, Tsigginou A, Zacharakis D, Dimitrakakis C. Breast Disorders in Girls and Adolescents. Is There a Need for a Specialized Service? J Pediatr Adolesc Gynecol 2015;28:91–4. doi:10.1016/j.jpag.2014.05.011.

[9] Quaglio G, Pizzol D, Isaakidis P, Bortolani A, Tognon F, Marotta C, et al. Breast Tuberculosis in Men: A Systematic Review. Am J Trop Med Hyg 2019:1–11. doi:10.4269/ajtmh.19-0061.

[10] Miltenburg DM, Speights VO. Benign Breast Disease. Obstet Ginecol Clin North Am 2008;35:285–300. doi:10.1016/j.ogc.2008.03.008.

[11] Lam E, Chan T, Wiseman SM. Breast abscess: Evidence based management recommendations. Expert Rev Anti Infect Ther 2014;12:753–62. doi:10.1586/14787210.2014.913982.

[12] Kilic MO, Sałlam C, Ałca FD, Terziołlu SG. Clinical, diagnostic and therapeutic management of patients with breast tuberculosis: Analysis of 46 Cases. Kaohsiung J Med Sci 2016;32:27–31. doi:10.1016/j.kjms.2015.12.005.

[13] Cusack L, Brennan M. Lactational mastitis and breast abscess: Diagnosis and management in general practice. Aust Fam Physician 2011;40:976–9.

[14] Dixon JM, Macaskill EJ. Management of Benign Breast Disease. In: Riker A, editor. Breast Dis, New York: Springer; 2015, p. 51–77. doi:10.1007/978-1-4939-1145-5.

[15] Dreyer G, Brandão AC, Amaral F, Medeiros Z, Addiss D. Detection by ultrasound of living adult Wuchereria bancrofti in the female breast. Mem

Inst Oswaldo Cruz 1996;91:95–6. doi:10.1590/S0074-02761996000100016.

[16] Palmieri A, D'Orazi V, Martino G, Frusone F, Crocetti D, Amabile MI, et al. Plasma cell mastitis in men: A single-center experience and review of the literature. In Vivo (Brooklyn) 2016;30:727–32. doi:10.21873/invivo.10987.

[17] Mohr EL, Berhane A, Zora JG, Suchdev PS. Acinetobacter baumannii neonatal mastitis: a case report. J Med Case Rep 2014;8:318. doi:10.1186/1752-1947-8-318.

[18] C. M, Lockie F, Lynn W. The challenge of mastitis. Arch Dis Child 2003;88:818–21.

[19] Tafur K, Cáceres J, Accinelli R. Características clínicas y anatomo-patológicas de las pacientes que ingresaron al Programa de Control de Tuberculosis con diagnóstico de tuberculosis de mama. Rev Medica Hered 2016;25:215. doi:10.20453/rmh.2014.2180.

[20] Asoglu O, Ozmen V, Karanlik H, Tunaci M, Cabioglu N, Abdullah I, et al. Feasibility of Surgical Management in Patients with. Breast J 2005;11:108–14.

[21] Barreto DS, Sedgwick EL, Nagi CS, Benveniste AP. Granulomatous mastitis: etiology, imaging, pathology, treatment, and clinical findings. Breast Cancer Res Treat 2018;171:527–34. doi:10.1007/s10549-018-4870-3.

[22] Aghajanzadeh M, Hassanzadeh R, Alizadeh Sefat S, Alavi A, Hemmati H, Esmaeili Delshad MS, et al. Granulomatous mastitis: Presentations, diagnosis, treatment and outcome in 206 patients from the north of Iran. The Breast 2015;24:456–60. doi:10.1016/j.breast.2015.04.003.

[23] Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6:e1000097. doi:https://doi.org/10.1371/journal.pmed.1000097.

[24] The World Bank. World Bank Country and Lending Groups 2019.

[25] Bland RM, Becquet R, Rollins NC, Coutsoudis A, Coovadia HM, Newell ML. Breast Health Problems Are Rare in Both HIV-Infected and HIV-Uninfected Women Who Receive Counseling and Support for Breast-Feeding in South Africa. Clin Infect Dis 2007;45:1502–10. doi:10.1086/523320.

[26] Denys Janet Gonzales Muro;, Gerardo Campos Siccha;, Raulins Ramírez Gutiérrez. Características clínicas de la tuberculosis mamaria en pacientes atendidas en un servicio de ginecoobstetricia, 2002- 2011. Rev Peru Ginecol y Obstet 2013;59:107–14.

[27] Yasar K, Pehlivagohlu F, Sengoz G, Cabioglu N. Successfully treated Mycobacterium abscessus mastitis: A rare cause of breast masses. Indian J Med Microbiol 2011;29:425–7.

[28] Cooke F, Friedland J. Spontaneous Breast Abscess Due to

Mycobacterium fortuitum. Clin Infect Dis 1998;26:760–1. doi:https://doi.org/10.1086/517117.

[29] Stone N, Gillett P, Burge S. Breast abscess due to Corynebacterium striatum. Br J Dermatol 1997;137:623–5. doi:10.1111/j.1365-2133.1997.tb03799.x.

[30] Riegel P, Liégeois P, Chenard MP, Mathelin C, Monteil H. Isolations of Corynebacterium kroppenstedtii from a breast abscess. Int J Med Microbiol 2004;294:413–6. doi:10.1016/j.ijmm.2004.07.013.

[31] Tse GMK, Poon CSP, Ramachandram K, Ma TKF, Pang LM, Law BKB, et al. Granulomatous mastitis: A clinicopathological review of 26 cases. Pathology 2004;36:254–7. doi:10.1080/00313020410001692602.

[32] Bing AU, Loh SF, Morris T, Hughes H, Dixon JM, Helgason KO. Actinomyces Species Isolated from Breast Infections. J Clin Microbiol 2015;53:3247–55. doi:10.1128/jcm.01030-15.

[33] Zadrozny S, Westreich D, Hudgens MG, Chasela C, Jamieson DJ, Martinson F, et al. Effect of Postnatal HIV Treatment on Clinical Mastitis and Breast Inflammation in HIV-Infected Breast-feeding Women. Paediatr Perinat Epidemiol 2017;31:134–43. doi:10.1111/ppe.12337.

[34] Taffurelli M, Pellegrini A, Santini D, Zanotti S, Di Simone D, Serra M. Recurrent periductal mastitis: Surgical treatment. Surg (United States) 2016;160:1689–92. doi:10.1016/j.surg.2016.06.048.

[35] García-Lozano T. Lesiones vesículo-ampollosas en un paciente oncológico inmunodeprimido Vesiculobullous lesions in an immunocompromised cancer patient. Rev Argent Microbiol 2012;31:46009.

[36] Cuervo, Sonia; Bonilla, Diego; Murcia, Martha; Hernández, Johana; Gómez J. Mastitis tuberculosa. Biomédica 2013;33:36–41. doi:http://dx.doi.org/10.7705/biomedica.v33i1.1426.

[37] Sánchez-Miño JI, Ortíz AM, Orozco L, Venegas B, Yepez F, Escalona-Rabaza M. Tuberculosis de mama: Reporte de un Caso. Rev Peru Med Exp Salud Publica Tuberc 2018;35:333–7. doi:10.17843/rpmesp.2018.352.3131. 333.

[38] Palmero DJ, Ambroggi MG, Poggi SE, Muñiz HFJ, Aires B. Mastitis por Mycobacterium fortuitum en una paciente HIV negativa. Medicina (B Aires) 2004;64:529–32.

[39] Chambô Filho A, Borges FLL, Cintra LC, Martins RM. Mastite por Paracoccidioidomicose: Relato de Caso. Rev Bras Ginecol e Obs 2000;22. doi:10.1590/S0100-72032000000900009.

[40] Ramos-barbosa S, Guazzelli LS. Criptococose mamária manifesta após corticoterapia Cryptococcal mastitis after corticosteroid therapy. Rev Soc Bras Med Trop 2004;37:65–6.

[41] Wajnberg GB, Basile VVD, Prado LGM, Faria J de, Radwanski HN, Pitanguy I. Mycobacteriosis in patients with breast implants: a case

review from the Ivo Pitanguy Institute. Rev Bras Cir Plástica 2011;26:482–7. doi:10.1590/s1983-51752011000300019.

[42] Lizaso D, García M, Aguirre A, Esposto A. Infección protésica mamaria por Mycobacterium fostuitum em una paciente con lupus eritematoso sistémico. Rev Chil Infectología 2011;28:474–8. doi:http://dx.doi.org/10.4067/S0716-10182011000600013.

[43] Fred HL. An Enlarging Breast Mass in an HIV-Seropositive Woman. Hosp Pract 1995;30:31–2. doi:10.1080/21548331.1995.11443196.

[44] Al-Qattan, M.; M. B.; Robertson, G.A.; Phil M. FRCS. Bilateral Chronic Infection of the Lactosebaceous Glands of Montgomery. Ann Plast Surgey 1990;25:491–3.

[45] Reyes C V., Thompson KS, Jensen J. Fine Needle Aspiration Biopsy of Mastitis Secondary to Empyema Necessitatis. Acta Cytol 1999;43:873–6. doi:10.1159/000331307.

[46] Thompson K, Donzelli J, Jense J, Pachucki C, M A, Reyes C. Breast and cutaneous mycobacteriosis: diagnosis by fine-needle aspiration biopsy. Diagn Cytopathol 1997;17:45–9. doi:http://dx.doi.org/10.1002/%28SICI%291097-0339%28199707%2917:1%3C45::AID-DC9%3E3.0.CO;2-O.

[47] Stary CM, Lee YS, Balfour J. Idiopathic granulomatous mastitis associated with corynebacterium sp. Infection. Hawaii Med J 2011;70:99–101.

[48] Renshaw AA, Derhagopian RP, Gould EW. Cystic neutrophilic granulomatous mastitis: an underappreciated pattern strongly associated with gram-positive bacilli. Am J Clin Pathol 2011;136:424–7. doi:10.1309/AJCP1W9JBRYOQSNZ.

[49] Johnson MG, Leal S, Plongla R, Leone PA, Gilligan PH. The Brief Case: Recurrent Granulomatous Mastitis Due to Corynebacterium kroppenstedtii. J Clin Microbiol 2016;54:1938–41. doi:10.1128/JCM.03131-15.

[50] Silva WA, Pinheiro AM, Jahns B, Bögli-Stuber K, Droz S, Zimmerli S. Breast abscess due to Actinomyces europaeus. Infection 2011;39:255–8. doi:10.1007/s15010-011-0119-3.

[51] Castello, L.; Bou, M.; Bazzana, M. S.; Predari SC. Absceso mamario no puerperal por Finegoldia magna. Rev Argent Microbiol 2007;39:95–8.

[52] Payne S, Kim S, Das K, Mirani N. A 36-Year-Old Woman With a Unilateral Breast Mass. Arch Pathol Lab Med 2006;130:1–2.

[53] Gamblin TC, Nobles-James C, Bradley RA, Katner HP, Dale PS. Cat scratch disease presenting as breast mastitis. Can J Surg 2005;48:254–5.

[54] Scott Soo, Mary; Ghate S. Herpes Simplex Virus Mastitis. Am J Roentgenol 2000;174:1087–8.

[55] Moreira MAR, de Freitas, Jr. R, Gerais BB. Granulomatous Mastitis

Caused by Sparganum. Acta Cytol 1997;41:859–62. doi:10.1159/000332717.

[56] Goldman M, Pottage JC. Cryptococcal infection of the breast. Clin Infect Dis 1995;21:1166–9. doi:10.1093/clinids/21.5.1166.

[57] Cunningham CO, Selwyn PA. Case Report: Mastitis Due to Mycobacterium avium Complex in an HIV-Infected Woman Taking Highly Active Antiretroviral Therapy. AIDS Patient Care STDS 2003;17:547–50. doi:10.1089/108729103322555935.

[58] Trupiano JK, Sebek BA, Goldfarb J, Levy LR, Hall GS, Procop GW. Mastitis Due to Mycobacterium abscessus after Body Piercing. Clin Infect Dis 2001;33:131–4. doi:10.1086/320885.

[59] Brickman M, Parsa AA, Parsa FD. Mycobacterium cheloneae infection after breast augmentation. Aesthetic Plast Surg 2005;29:116–8. doi:10.1007/s00266-004-0023-7.

[60] Pereira LH, Sterodimas A. Autologous fat transplantation and delayed silicone implant insertion in a case of mycobacterium avium breast infection. Aesthetic Plast Surg 2010;34:1–4. doi:10.1007/s00266-009-9357-5.

[61] Kamyab A. Granulomatous lobular mastitis secondary to Mycobacterium fortuitum . World J Clin Cases 2016;4:409. doi:10.12998/wjcc.v4.i12.409.

[62] Shoyele O, Vidhun R, Dodge J, Cheng Z, Margules R, Nee P, et al. Cystic neutrophilic granulomatous mastitis: A clinicopathologic study of a distinct entity with supporting evidence of a role for Corynebacterium-targeted therapy. Ann Diagn Pathol 2018;37:51–6. doi:10.1016/j.anndiagpath.2018.08.005.

[63] Qiao Y, Hayward JH, Balassanian R, Ray KM, Joe BN, Lee AY. Tuberculosis mastitis presenting as bilateral breast masses. Clin Imaging 2018;52:28–31. doi:10.1016/j.clinimag.2018.02.013.

[64] Lehman, Trang; Damania, Zubin; Tschetter, Clifford; Lehman N. Case Report. J Fam Pract 2017;66:38–41. doi:10.1016/s0267-3649(02)00716-1.

[65] Da Silva BB, Dos Santos LG, Costa PVL, Pires CG, Borges AS. Clinical case report: Primary tuberculosis of the breast mimicking carcinoma. Am J Trop Med Hyg 2005;73:975–6.

[66] Hale JA, Peters GN, Cheek JH. Tuberculosis of the breast: Rare but still extant. Am J Surg 1985;150:620–4. doi:10.1016/0002-9610(85)90450-7.

[67] Bhatty O, Waters D, Wilka N, Samuel S, Horne J, Vivekanandan R. A Rare Manifestation of Tuberculosis Presenting in the United States. Case Rep Infect Dis 2016;2016:1–4. doi:10.1155/2016/8216040.

[68] da Silva BB, Lopes-Costa P V., Pires CG, Pereira-Filho JD, dos Santos AR. Tuberculosis of the breast: analysis of 20 cases and a literature review. Trans R Soc Trop Med Hyg 2009;103:559–63. doi:10.1016/j.trstmh.2009.02.005.

Supplementary Table 1– Clinical ad demographical characteristics of patients that developed mastitis of infectious etiology from Latin America.

Ref.	Country	Age	Pregnancy history	Risk factors	Time to close diagnosis (Weeks)	Signs and symptoms	Treatment time (Weeks)	Biopsy	Etiology	BAAR/ culture	Surgical resection	Treatment	Relapse
García-Lozano, 2012 [35]	Argentina	53	N/A[1]	Type 1 DM/ Leiomyosarcoma	N/A	Blisters + Fever	N/A	Vasculitis	*Aeromonas hydrophila*	N/A	N/A	N/A	N/A
Cuervo, 2013 [36]	Colombia	34	N/A	None	16	Fistula + Fever	24	Granuloma	*Mycobacterium tuberculosis* (PCR+)	-	No	RIPE	No
Sánchez-Miño, 2018 [37]	Equador	45	N/A	None	2	Breast lump + Fistula	24	Non caseating Granuloma and necrosis	*Mycobacterium tuberculosis*	+	Yes	RIPE	No
Palmero, 2004 [38]	Argentina	39	N/A	DM	96	Breast lump + Nipple discharge + Fistula	60	N/A	Non-tuberculous Mycobacteria: *M. fortuitum*	-	No	Kanamycin + Doxycycline + Ciprofloxacin	Yes
Chambô Filho, 2000 [39]	Brazil	72	N/A	None	N/A	Abscess	48	Granuloma and yeast infection	*Paracoccidioides brasiliensis*	-	No	TPM/SMX[3]	No
Ramos-Barbosa, 2004 [40]	Brazil	46	N/A	Cortic. Therapy	24	Nipple discharge	48	Granuloma	*Criptococo neoformans*	N/A	Yes	Ketoconazole	No
Wajnberg, 2011 [41]	Brazil	23	N/A	Breast implant	N/A	Abscess	N/A	N/A	Non-tuberculous Mycobacteria: *M. abscessos*	-	Yes	Ciprofloxacin	No
Wajnberg, 2011 [41]	Brazil	31	N/A	Breast implant	N/A	Fistula	16	Necrotizing granuloma	Non-tuberculous Mycobacteria	-	Yes	Clarithromycin	No

Wajnberg, 2011 [41]	Brazil	34	N/A	Breast implant	N/A	Abscess	12	N/A	Non-tuberculous Mycobacteria	+	Yes	Clarithromycin + Ciprofloxacin	No
Wajnberg, 2011 [41]	Brazil	23	N/A	Breast implant	N/A	Abscess	24	N/A	Non-tuberculous Mycobacteria	-	Yes	Clarithromycin + Ciprofloxacin	No
Wajnberg, 2011 [41]	Brazil	24	N/A	Breast implant	N/A	Breast implant exhibition	24	N/A	Non-tuberculous Mycobacteria	-	Yes	Clarithromycin + Ciprofloxacin	No
Lizaso, 2011 [42]	Argentina	50	N/A	Breast implant/ SLE	N/A	Abscess	28	N/A	Non-tuberculous Mycobacteria: *M. fortuitum*	-	Yes	Ciprofloxacin + TMP/SMX + Amikacin	No
Conde, 2015 [7]	Brazil	12	0	None	1	Breast lump + Abscess	2	N/A	Acutte mastitis (N/A)	N/A	No	Cefadroxil	No
Conde, 2015 [7]	Brazil	12	0	None	1	Abscess	2	N/A	Acutte mastitis: *S. haemolyticus*	N/A	No	Cefadroxil	No
Fred, 1995 [43]	USA	37	N/A	HIV/ Previous TB	3	Breast lump + Fever	N/A	Granuloma	*Mycobacterium tuberculosis*	+	No	RIPE[4]	No
Al-Qattan, 1990 [44]	Canada	36	N/A	N/A	13 years	Abscess + Fistula	N/A	Inflam. and cystic degeneration	Cronic mastites (N/A)	N/A	Yes	Dicloxacilin + Topical antibiotics	No
Mohr, 2014 [17]	USA	15 ds.	N/A	N/A	1 day	Abscess + Fever	1	N/A	Acutte mastites: *Acinetobacter baumani*	N/A	No	Ceftazidime	No
Reyes, 1999 [45]	USA	68	N/A	N/A	4	Breast lump	24	N/A	Empyema necessitatis: *Mycobacterium tuberculosis*	+	Yes	Rifampin + Isoniazid	No
Reyes, 1999 [45]	USA	47	N/A	IV drug user	4	Breast lump	6	N/A	Empyema necessitatis:	-	No	Penicillin	No

									Actinomyces israeli				
Thompson, 1997 [46]	USA	58	N/A	Previous TB/ Lung squa. cell carcino.	4	Breast lump + Fever	N/A	Acute inflam. exudate	*Mycobacterium tuberculosis*	+	Yes	Anti-tuberculous drugs (Not specified)	No
Stary, 2011 [47]	USA	33	Yes	N/A	2	Fistula	4	Granuloma and necrosis	*Corynebacterium*	-	Yes	TMP/SMX + Penicillin and Vancomycin + Doxycycline	N/A
Renshaw, 2011 [48]	USA	54	N/A	N/A	N/A	Breast lump	4	Granuloma	*Corynebacterium*	-	Yes	Tetracycline	No
Renshaw, 2011 [48]	USA	22	N/A	Nipple piercing	2	Breast lump	2	Granuloma	*Corynebacterium*	_	No	Doxycycline	No
Renshaw, 2011 [48]	USA	27	N/A	N/A	N/A	Abscess	4	Neutrofilic cystic inflam.	*Corynebacterium*	-	Yes	Tetracycline	No
Johnson, 2016 [49]	Mexico	34	N/A	N/A	56	Breast lump + Fistula	4	Granuloma and fat necrosis	*Corynebacterium*	-	Yes	Doxycycline + Clindamycin + Amoxicillin/ Clavulanic + Linezolid + ciprofloxacin	Yes
Silva, 2011 [50]	Brazil	67	N/A	Aortic surgery	1	Fistula + Abscess	40	Necrosis	*Actinomyces europaeus*	-	Yes	Amoxicillin/ Clavulanic	No
Castello, 2007 [51]	Argentina	32	N/A	Breast reduct. surgery	1	Abscess	2	N/A	*Finegoldia magna*	-	Yes	Cefadroxil	No
Payne, 2006 [52]	Brazil	36	N/A	HIV/ HBV/ HCV	20	Breast lump	N/A	Necrotizing granuloma	*Histoplasma sp.*	-	Yes	Amphotericin	No

Gamblin, 2005 [53]	USA	36	N/A	Cat scratch	6	Fistula	3	Granuloma	Gram - bacterias	-	Yes	Ciprofloxacin	No
Soo, 2000 [54]	USA	50	0	Multiple cyst aspirat.	4	Nipple discharge	1	Herpectic dermatitis	*H. simplex* (biopsy + antigen)	-	No	Aciclovir	No
Moreira1997 [55]	Brazil	64	N/A	N/A	N/A	Breast lump	N/A	Necrotizing granuloma	*Sparganum* (histological)	N/A	Yes	Surgery	No
Goldman, 1995 [56]	USA	59	N/A	N/A	1	Breast lump	12	Macrophages and yeast inclusion inflammation	*Criptococos* (biopsy)	-	Yes	Surgery + Fluconazol	No
Cunningham, 2003 [57]	USA	48	N/A	HIV/ Previous TB/ HCV/ IV Drug user	8	Breast lump	24	Caseous necrotizing granuloma	Non-tuberculous Mycobacteria: *Mycobacterium avium*	+	No	Rifampin + Isoniazid + Ethambutol + Azithromycin	No
Trupiano, 2001 [58]	USA	17	N/A	Nipple Piercing	8	Breast lump	N/A	Caseous necrotizing granuloma	Non-tuberculous Mycobacteria: *M. abscessus*	-	Yes	Surgery	N/A
Brickman, 2005 [59]	Hawaii/ USA	32	N/A	Breast Implant	7	Breast hardness	24	Granulation tissue	Non-tuberculous Mycobacteria: *M. chelonae*	-	Yes	Clarythromycin + TMP/SMX	N/A
Pereira, 2010 [60]	Brazil	48	N/A	Breast Implant	12	Nipple discharge + Abscess	48	Granuloma	Non-tuberculous Mycobacteria: *M. avium*	-	Yes	Clarythromycin + Ethambutol	Yes
Kamyab, 2016 [61]	USA	29	Yes	None	8	Breast lump	N/A	Granuloma	Non-tuberculous Mycobacteria: *M. fortuitum*	-	Yes	Ciprofloxacin + TMP/SMX + Linezolid + Prednisone	Yes

Shoyele et al., 2018 [62]	USA	28	Yes	Nipple piercing	N/A	Breast lump	44	Neutrofilic cystic granuloma	*Corynebacterium*	-	Yes	Surgery and antibiotics	No
Shoyele, 2018 [62]	USA	36	Yes	Previous mastitis	N/A	Breast lump	N/A	Neutrofilic cystic granuloma	*Corynebacterium*	-	No	Topical anti inflammatory	Yes
Shoyele, 2018 [62]	USA	53	Yes	None	N/A	None	N/A	Neutrofilic cystic granuloma	*Corynebacterium*	-	No	Expectant treatment	N/A
Shoyele, 2018 [62]	USA	41	Yes	None	N/A	Breast lump + Nipple discharge	36	Neutrofilic cystic granuloma	*Corynebacterium*	-	Yes	Dalbavancin + Daptomycin + Cefuroxime + Prednisone + Methotrexate + Hydroxychloroquine	N/A
Shoyele, 2018 [62]	USA	46	Yes	None	N/A	Breast lump + Nipple discharge	40	Neutrofilic cystic granuloma	*Corynebacterium*	-	Yes	Antibiotics + Drainage	N/A
Shoyele, 2018 [62]	USA	36	Yes	None	N/A	Breast lump	24	Neutrofilic cystic granuloma	*Corynebacterium*	-	Yes	Antibiotics + Prednisone + Methotrexate	N/A
Shoyele, 2018 [62]	USA	45	No	None	N/A	Breast lump	44	Neutrofilic cystic granuloma	*Corynebacterium*	-	Yes	Antibiotics + Prednisone + Methotrexate	N/A
Qiao, 2018 [63]	USA	49	N/A	Rheumat Arthritis	20	Breast lump	24	Necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Lehman, 2017 [64]	USA	44	N/A	DM	44	Breast lump	2	Caseous necrotizing granuloma	*Mycobacterium tuberculosis* (PCR+)	+	Yes	RIPE	No
Da Silva, 2005 [65]	Brazil	73	Yes	N/A	32	Breast lump	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	+	No	RIPE	No

Hale, 1985 [66]	USA	31	N/A	Previous TB	20	Breast lump + Nipple Discharge	24	Granuloma	*Mycobacterium tuberculosis*	+	Yes	Rifampin + Isoniazid	No
Bhatty, 2016 [67]	USA	64	N/A	N/A	N/A	Breast lump	N/A	Granuloma	*Mycobacterium tuberculosis*	+	No	RIPE	No
Da Silva, 2009 [68]	Brazil	19	N/A	N/A	24	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	+	No	RIPE	No
Da Silva, 2009 [68]	Brazil	54	N/A	N/A	40	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	36	N/A	N/A	28	Nipple Discharge	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	73	N/A	N/A	20	Nipple Discharge	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	42	N/A	N/A	24	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	32	N/A	N/A	48	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	53	N/A	N/A	32	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	72	N/A	N/A	28	Nipple Discharge	25	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	40	N/A	N/A	32	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No

Da Silva, 2009 [68]	Brazil	28	N/A	N/A	32	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	24	N/A	N/A	28	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	78	N/A	N/A	36	Nipple Discharge	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	25	N/A	N/A	40	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	23	N/A	N/A	24	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	22	N/A	N/A	44	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	32	N/A	N/A	28	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	23	N/A	N/A	28	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	70	N/A	N/A	32	Nipple Discharge	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	22	N/A	N/A	32	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No
Da Silva, 2009 [68]	Brazil	34	N/A	N/A	12	Fistula	24	Caseous necrotizing granuloma	*Mycobacterium tuberculosis*	-	No	RIPE	No

[1]N/A: No information available. [2] SLE: Systemic lupus erythematosus. [3] TMP/SMX: Trimethoprim/Sulfamethoxazole. [4] RIPE: Rifampin, Isoniazid, Pyrazinamide, Ethambutol

Table 1. Search strategy

Database	Search strategy
Scielo	Mastitis
Medline/Pubmed Lilacs	Mastitis AND (Americas OR Latin America OR North America OR South America OR Central America OR Antilles OR Anguilla OR Antigua OR Aruba OR Argentina OR Barbuda OR Belize OR Bahamas OR Barbados OR Bolivia OR Bonaire OR Brazil OR Canada OR Caribbean OR Chile OR Colombia OR Costa Rica OR Cuba OR Curacao OR Dominica OR Dominican Republic OR Ecuador OR El Salvador OR Grenada OR Grenadines OR Guadeloupe OR Guatemala OR Guyana OR Haiti OR Honduras OR Jamaica OR Martinique OR Mexico OR Montserrat OR Nevis OR Nicaragua OR Panama OR Paraguay OR Peru OR Puerto Rico OR Saint Kitts OR Saint Lucia OR Saint Vincent OR Suriname OR Surinam OR Trinidad OR Tobago OR United States of America OR USA OR Uruguay OR Venezuela)

Figure 1 – Flow chart of the inclusion of case reports regarding mastitis of infectious origin in Latin American studies.

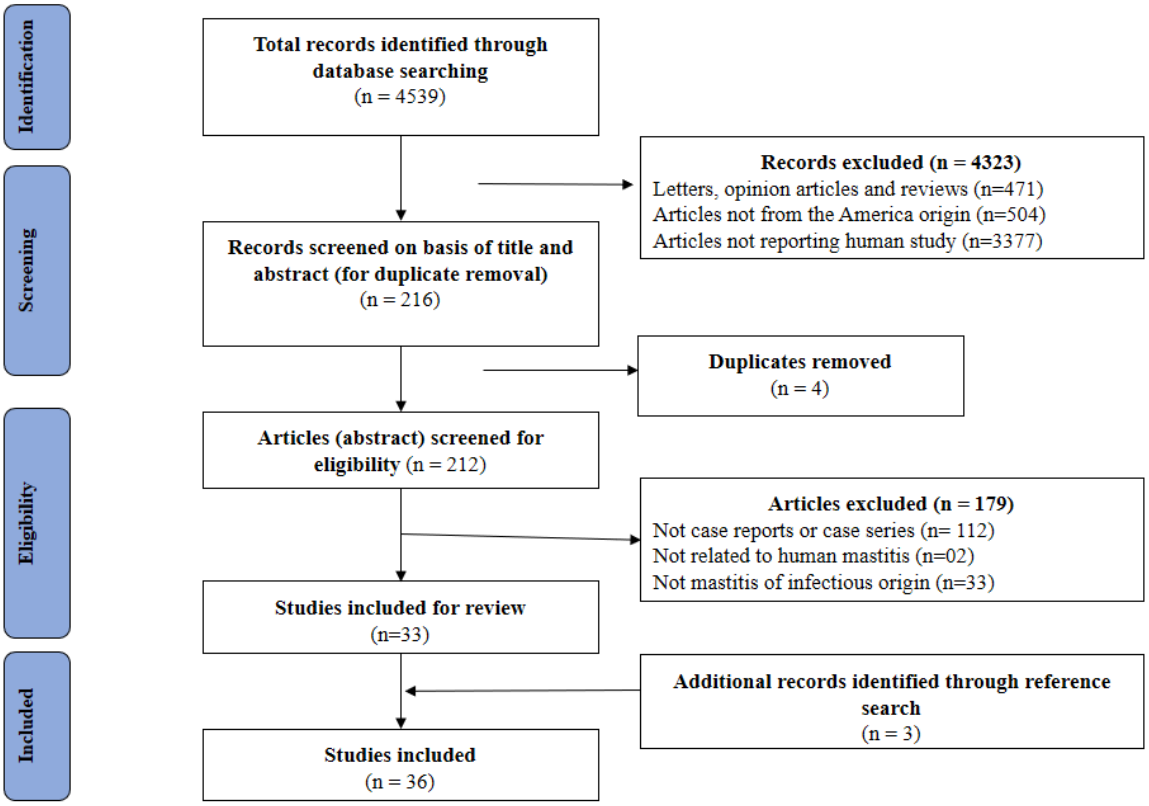

Table 2 – Baselines characteristics of cases

Variables	**Total (n = 69)**	**Completeness* N (%)**
Demographics		
Sex F n(%)	65 (94.2)	69 (100)
Age (median years, IQR)	36 (28-51)	69 (100)
Pregnancy history n(%)	11 (15.9)	18 (26.1)
Country of origin n(%)		69 (100)
Brazil	34 (49.3)	
USA	26 (37.7)	
Argentina	4 (5.8)	
Canada	1 (1.4)	
Colombia	1 (1.4)	
Ecuador	1 (1.4)	
Hawaii	1 (1.4)	
Mexico	1 (1.4)	
Risk factors n(%)	27 (39.1)	38 (55.07)

completeness of data in 100%.

Table 3 –

Variables	Total # (n = 69)
Signs and symptoms previous to hospitalization	
Abscess n(%)	13 (18.8)
Blisters n(%)	1 (1.4)
Breast hardness n(%)	1 (1.4)
Breast implant exhibition n(%)	1 (1.4)
Breast lumps n(%)	27 (39.1)
Fever n(%)	5 (7.2)
Fistula n(%)	24 (34.8)
Nipple discharge n(%)	12 (17.4)
Ulcer n(%)	0 (0)
None n(%)	1 (1.4)
Breast of occurence	
Left n(%)	24 (34.8)
Right n(%)	36 (52.2)
Bilateral n(%)	4 (5.8)
Not described n(%)	5 (7.3)
Breast quadrant	
Upper-outer n(%)	5 (7.3)
Upper-inner n(%)	1 (1.4)
Lower-outer n(%)	3 (4.4)
Lower-inner n(%)	4 (5.8)
More than one quadrant n(%)	2 (2.9)
Not described n(%)	54 (78.3)

completeness of data in 100%.

Table 4– Population characteristics according to high and middle/low income countries

Variables	All (n=68)	USA/Canada (n=27)	Latin-Americans Countries (n=41)	Completeness	p-value
Demographics					
Sex F n(%)	65 (94.2)	24 (88.9)	41 (100)	68 (100)	0.029*
Age (median years, IQR)	36 (28.5-51.5)	41 (32-50)	34 (24-53)	68 (100)	0.414
Pregnancy history n(%)	11 (16.2)	9 (33.3)	2 (4.9)	14 (100)	0.099
Risk factors n(%)	27 (39.7)	14 (51.9)	13 (31.7)	38 (55.9)	0.880
Signs and symptoms previous to hospitalization					
Abscess n(%)	12 (17.7)	2 (7.4)	10 (24.4)	68 (100)	0.072
Blisters n(%)	1 (1.5)	0 (0)	1 (2.4)	68 (100)	0.414
Breast hardness n(%)	1(1.5)	1 (3.7)	0 (0)	68 (100)	0.214
Breast implant exhibition n(%)	1 (1.5)	0 (0)	1 (2.4)	68 (100)	0.414
Breast lumps n(%)	27 (39.7)	20 (74.1)	7 (17.1)	68 (100)	0.000*
Fever n(%)	4 (5.9)	2 (7.4)	2 (4.8)	68 (100)	0.664
Fistula n(%)	24 (35.3)	3 (11.1)	21 (51.2)	68 (100)	0.001*
Nipple discharge n(%)	12 (17.7)	4 (14.8)	8 (19.5)	68 (100)	0.619
Ulcer n(%)	0 (0)	0 (0)	0 (0)	68 (100)	-
None n(%)	1 (1.5)	1 (3.7)	0 (0)	68 (100)	0.214
Cancer suspicious n(%)	13 (19.1)	4 (14.8)	9 (22.0)	59 (86.8)	0.787
Diagnosis and treatment					
Time to close diagnosis (median weeks, IQR)	20 (4-32)	6 (4-8)	28 (18.32)	49 (72.1)	0.002*
Treatment time (mean ± SD)	23 ± 13.4	19.1 ± 15.1	24.9 ± 12.2	54 (79.4)	0.157

Abnormal Chest X-ray n(%)	10 (14.7)	7 (25.9)	3 (7.3)	35 (52.5)	0.000*
Abnormal breast ultrasound n(%)	3 (4.4)	2 (7.4)	1 (2.4)	3 (4.4)	-
Abnormal mammography n (%)	2 (2.94)	2 (7.4)	0 (0)	2 (2.9)	-
Biopsy n(%)	57 (83.8)	25 (92.6)	32 (78.0)	68	0.111
Culture n(%)	26 (38.2)	13 (48.1)	13 (31.7)	65	0.118
Surgical resection n(%)	32 (47.1)	18 (26.5)	14 (34.1)	67	0.011*
Relapse n(%)	4 (5.9)	2 (7.4)	2 (4.8)	59	0.430

4. LIMITAÇÕES E PERSPECTIVAS DO TRABALHO

Nossa revisão é limitada pela falta de algumas informações detalhadas em alguns relatos de casos. À medida que nossa compreensão do processo de mastite infecciosa cresce, podem-se estabelecer protocolos diagnósticos e de manejo apropriados para a população vulnerável e, assim, evitar complicações clínicas próximas ou futuras. Estudos prospectivos devem ser realizados com a finalidade de possuir dados mais precisos.

5. CONCLUSÃO

Em conclusão esta revisão sistemática encontrou: **i)** reportes de casos de mastite infecciosa foram documentados em sua maioria no contexto brasileiro, o que é de grande importância no contexto do nosso sistema de saúde e reflete o quadro endêmico de tuberculose no país; **ii)** todos os casos descritos de mastite por corynebacterium foram da América do Norte, podendo refletir a diferença na estrutura hospitalar devido a complexidade laboratorial para se isolar este agente etiológico**; iii)** a heterogeneidade foi encontrada na maioria dos estudos em termos de descrições dos casos clínicos, sendo possível observar que existem lacunas de dados em diferentes publicações, o que indica a necessidade de discussão entre os especialistas na área, a fim de padronizar a descrição de relatos e séries de casos, permitindo conclusões mais precisas.; **iv)** os resultados apresentados nesta revisão sustentam a existência de uma lateralidade de gênero na prevalência de mastite infecciosa.; **v)** sugeriu-se a superioridade nos sistemas de saúde dos países com alta renda per capita, o que deixa como reflexo a melhoria ainda em falta, e possível, da maioria dos sistemas de saúde nos países da América Latina.

6. REFERÊNCIAS BIBLIOGRÁFICAS

[1] Amir LH. ABM Clinical Protocol #4: Mastitis, Revised March 2014. Breastfeed Med 2014;9:239–43. doi:10.1089/bfm.2014.9984.

[2] Inch S, Xylander S, Savage F. Mastitis causes and Mangaement. vol. WHO/FCH/CA. 2000.

[3] Boakes E, Woods A, Johnson N, Kadoglou N. Breast Infection: A Review of Diagnosis and Management Practices. Eur J Breast Heal 2018:136–43. doi:10.5152/ejbh.2018.3871.

[4] Contreras GA, Rodríguez JM. Mastitis: comparative etiology and epidemiology. J Mammary Gland Biol Neoplasia 2011;16:339–56. doi:10.1007/s10911-011-9234-0.

[5] Angelopoulou A, Field D, Ryan CA, Stanton C, Hill C, Ross RP. The microbiology and treatment of human mastitis. Med Microbiol Immunol 2018;207:83–94. doi:10.1007/s00430-017-0532-z.

[6] AbdelHad M, Bukharie H. Breast Infections in non-lactating Women. J Family Community Med 2005;12:133–7.

[7] Conde DM. Treatment approach for breast abscess in nonlactating adolescents. Int J Gynecol Obstet 2015;128:72–3. doi:10.1016/j.ijgo.2014.08.009.

[8] Michala L, Tsigginou A, Zacharakis D, Dimitrakakis C. Breast Disorders in Girls and Adolescents. Is There a Need for a Specialized Service? J Pediatr Adolesc Gynecol 2015;28:91–4. doi:10.1016/j.jpag.2014.05.011.

[9] Quaglio G, Pizzol D, Isaakidis P, Bortolani A, Tognon F, Marotta C, et al. Breast Tuberculosis in Men: A Systematic Review. Am J Trop Med Hyg 2019:1–11. doi:10.4269/ajtmh.19-0061.

[10] Miltenburg DM, Speights VO. Benign Breast Disease. Obstet Ginecol Clin North Am 2008;35:285–300. doi:10.1016/j.ogc.2008.03.008.

[11] Lam E, Chan T, Wiseman SM. Breast abscess: Evidence based management recommendations. Expert Rev Anti Infect Ther 2014;12:753–62. doi:10.1586/14787210.2014.913982.

[12] Kilic MO, Sałlam C, Ałca FD, Terziołlu SG. Clinical, diagnostic and therapeutic management of patients with breast tuberculosis: Analysis of 46 Cases. Kaohsiung J Med Sci 2016;32:27–31. doi:10.1016/j.kjms.2015.12.005.

[13] Cusack L, Brennan M. Lactational mastitis and breast abscess: Diagnosis and management in general practice. Aust Fam Physician 2011;40:976–9.

[14] Dixon JM, Macaskill EJ. Management of Benign Breast Disease. In: Riker A, editor. Breast Dis, New York: Springer; 2015, p. 51–77. doi:10.1007/978-1-4939-1145-5.

[15] Dreyer G, Brandão AC, Amaral F, Medeiros Z, Addiss D. Detection by ultrasound

of living adult Wuchereria bancrofti in the female breast. Mem Inst Oswaldo Cruz 1996;91:95–6. doi:10.1590/S0074-02761996000100016.

[16] Palmieri A, D'Orazi V, Martino G, Frusone F, Crocetti D, Amabile MI, et al. Plasma cell mastitis in men: A single-center experience and review of the literature. In Vivo (Brooklyn) 2016;30:727–32. doi:10.21873/invivo.10987.

[17] Mohr EL, Berhane A, Zora JG, Suchdev PS. Acinetobacter baumannii neonatal mastitis: a case report. J Med Case Rep 2014;8:318. doi:10.1186/1752-1947-8-318.

[18] C. M, Lockie F, Lynn W. The challenge of mastitis. Arch Dis Child 2003;88:818–21.

[19] Tafur K, Cáceres J, Accinelli R. Características clínicas y anatomo-patológicas de las pacientes que ingresaron al Programa de Control de Tuberculosis con diagnóstico de tuberculosis de mama. Rev Medica Hered 2016;25:215. doi:10.20453/rmh.2014.2180.

[20] Asoglu O, Ozmen V, Karanlik H, Tunaci M, Cabioglu N, Abdullah I, et al. Feasibility of Surgical Management in Patients with. Breast J 2005;11:108–14.

[21] Barreto DS, Sedgwick EL, Nagi CS, Benveniste AP. Granulomatous mastitis: etiology, imaging, pathology, treatment, and clinical findings. Breast Cancer Res Treat 2018;171:527–34. doi:10.1007/s10549-018-4870-3.

[22] Aghajanzadeh M, Hassanzadeh R, Alizadeh Sefat S, Alavi A, Hemmati H, Esmaeili Delshad MS, et al. Granulomatous mastitis: Presentations, diagnosis, treatment and outcome in 206 patients from the north of Iran. The Breast 2015;24:456–60. doi:10.1016/j.breast.2015.04.003.

[23] Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6:e1000097. doi:https://doi.org/10.1371/journal.pmed.1000097.

[24] The World Bank. World Bank Country and Lending Groups 2019.

[25] Bland RM, Becquet R, Rollins NC, Coutsoudis A, Coovadia HM, Newell ML. Breast Health Problems Are Rare in Both HIV-Infected and HIV-Uninfected Women Who Receive Counseling and Support for Breast-Feeding in South Africa. Clin Infect Dis 2007;45:1502–10. doi:10.1086/523320.

[26] Denys Janet Gonzales Muro;, Gerardo Campos Siccha;, Raulins Ramírez Gutiérrez. Características clínicas de la tuberculosis mamaria en pacientes atendidas en un servicio de ginecoobstetricia, 2002- 2011. Rev Peru Ginecol y Obstet 2013;59:107–14.

[27] Yasar K, Pehlivagohlu F, Sengoz G, Cabioglu N. Successfully treated Mycobacterium abscessus mastitis: A rare cause of breast masses. Indian J Med Microbiol 2011;29:425–7.

[28] Cooke F, Friedland J. Spontaneous Breast Abscess Due to Mycobacterium fortuitum. Clin Infect Dis 1998;26:760–1. doi:https://doi.org/10.1086/517117.

[29] Stone N, Gillett P, Burge S. Breast abscess due to Corynebacterium striatum. Br J Dermatol 1997;137:623–5. doi:10.1111/j.1365-2133.1997.tb03799.x.

[30] Riegel P, Liégeois P, Chenard MP, Mathelin C, Monteil H. Isolations of Corynebacterium kroppenstedtii from a breast abscess. Int J Med Microbiol 2004;294:413–6. doi:10.1016/j.ijmm.2004.07.013.

[31] Tse GMK, Poon CSP, Ramachandram K, Ma TKF, Pang LM, Law BKB, et al. Granulomatous mastitis: A clinicopathological review of 26 cases. Pathology 2004;36:254–7. doi:10.1080/00313020410001692602.

[32] Bing AU, Loh SF, Morris T, Hughes H, Dixon JM, Helgason KO. Actinomyces Species Isolated from Breast Infections. J Clin Microbiol 2015;53:3247–55. doi:10.1128/jcm.01030-15.

[33] Zadrozny S, Westreich D, Hudgens MG, Chasela C, Jamieson DJ, Martinson F, et al. Effect of Postnatal HIV Treatment on Clinical Mastitis and Breast Inflammation in HIV-Infected Breast-feeding Women. Paediatr Perinat Epidemiol 2017;31:134–43. doi:10.1111/ppe.12337.

[34] Taffurelli M, Pellegrini A, Santini D, Zanotti S, Di Simone D, Serra M. Recurrent periductal mastitis: Surgical treatment. Surg (United States) 2016;160:1689–92. doi:10.1016/j.surg.2016.06.048.

[35] García-Lozano T. Lesiones vesículo-ampollosas en un paciente oncológico inmunodeprimido Vesiculobullous lesions in an immunocompromised cancer patient. Rev Argent Microbiol 2012;31:46009.

[36] Cuervo, Sonia; Bonilla, Diego; Murcia, Martha; Hernández, Johana; Gómez J. Mastitis tuberculosa. Biomédica 2013;33:36–41. doi:http://dx.doi.org/10.7705/biomedica.v33i1.1426.

[37] Sánchez-Miño JI, Ortíz AM, Orozco L, Venegas B, Yepez F, Escalona-Rabaza M. Tuberculosis de mama: Reporte de un Caso. Rev Peru Med Exp Salud Publica Tuberc 2018;35:333–7. doi:10.17843/rpmesp.2018.352.3131. 333.

[38] Palmero DJ, Ambroggi MG, Poggi SE, Muñiz HFJ, Aires B. Mastitis por Mycobacterium fortuitum en una paciente HIV negativa. Medicina (B Aires) 2004;64:529–32.

[39] Chambô Filho A, Borges FLL, Cintra LC, Martins RM. Mastite por Paracoccidioidomicose: Relato de Caso. Rev Bras Ginecol e Obs 2000;22. doi:10.1590/S0100-72032000000900009.

[40] Ramos-barbosa S, Guazzelli LS. Criptococose mamária manifesta após corticoterapia Cryptococcal mastitis after corticosteroid therapy. Rev Soc Bras Med Trop 2004;37:65–6.

[41] Wajnberg GB, Basile VVD, Prado LGM, Faria J de, Radwanski HN, Pitanguy I. Mycobacteriosis in patients with breast implants: a case review from the Ivo Pitanguy Institute. Rev Bras Cir Plástica 2011;26:482–7. doi:10.1590/s1983-51752011000300019.

[42] Lizaso D, García M, Aguirre A, Esposto A. Infección protésica mamaria por

Mycobacterium fostuitum em una paciente con lupus eritematoso sistémico. Rev Chil Infectología 2011;28:474–8. doi:http://dx.doi.org/10.4067/S0716-10182011000600013.

[43] Fred HL. An Enlarging Breast Mass in an HIV-Seropositive Woman. Hosp Pract 1995;30:31–2. doi:10.1080/21548331.1995.11443196.

[44] Al-Qattan, M.; M. B.; Robertson, G.A.; Phil M. FRCS. Bilateral Chronic Infection of the Lactosebaceous Glands of Montgomery. Ann Plast Surgey 1990;25:491–3.

[45] Reyes C V., Thompson KS, Jensen J. Fine Needle Aspiration Biopsy of Mastitis Secondary to Empyema Necessitatis. Acta Cytol 1999;43:873–6. doi:10.1159/000331307.

[46] Thompson K, Donzelli J, Jense J, Pachucki C, M A, Reyes C. Breast and cutaneous mycobacteriosis: diagnosis by fine-needle aspiration biopsy. Diagn Cytopathol 1997;17:45–9. doi:http://dx.doi.org/10.1002/%28SICI%291097-0339%28199707%2917:1%3C45::AID-DC9%3E3.0.CO;2-O.

[47] Stary CM, Lee YS, Balfour J. Idiopathic granulomatous mastitis associated with corynebacterium sp. Infection. Hawaii Med J 2011;70:99–101.

[48] Renshaw AA, Derhagopian RP, Gould EW. Cystic neutrophilic granulomatous mastitis: an underappreciated pattern strongly associated with gram-positive bacilli. Am J Clin Pathol 2011;136:424–7. doi:10.1309/AJCP1W9JBRYOQSNZ.

[49] Johnson MG, Leal S, Plongla R, Leone PA, Gilligan PH. The Brief Case: Recurrent Granulomatous Mastitis Due to Corynebacterium kroppenstedtii. J Clin Microbiol 2016;54:1938–41. doi:10.1128/JCM.03131-15.

[50] Silva WA, Pinheiro AM, Jahns B, Bögli-Stuber K, Droz S, Zimmerli S. Breast abscess due to Actinomyces europaeus. Infection 2011;39:255–8. doi:10.1007/s15010-011-0119-3.

[51] Castello, L.; Bou, M.; Bazzana, M. S.; Predari SC. Absceso mamario no puerperal por Finegoldia magna. Rev Argent Microbiol 2007;39:95–8.

[52] Payne S, Kim S, Das K, Mirani N. A 36-Year-Old Woman With a Unilateral Breast Mass. Arch Pathol Lab Med 2006;130:1–2.

[53] Gamblin TC, Nobles-James C, Bradley RA, Katner HP, Dale PS. Cat scratch disease presenting as breast mastitis. Can J Surg 2005;48:254–5.

[54] Scott Soo, Mary; Ghate S. Herpes Simplex Virus Mastitis. Am J Roentgenol 2000;174:1087–8.

[55] Moreira MAR, de Freitas, Jr. R, Gerais BB. Granulomatous Mastitis Caused by Sparganum. Acta Cytol 1997;41:859–62. doi:10.1159/000332717.

[56] Goldman M, Pottage JC. Cryptococcal infection of the breast. Clin Infect Dis 1995;21:1166–9. doi:10.1093/clinids/21.5.1166.

[57] Cunningham CO, Selwyn PA. Case Report: Mastitis Due to Mycobacterium avium Complex in an HIV-Infected Woman Taking Highly Active Antiretroviral Therapy. AIDS Patient Care STDS 2003;17:547–50. doi:10.1089/108729103322555935.

[58] Trupiano JK, Sebek BA, Goldfarb J, Levy LR, Hall GS, Procop GW. Mastitis Due to Mycobacterium abscessus after Body Piercing. Clin Infect Dis 2001;33:131–4. doi:10.1086/320885.

[59] Brickman M, Parsa AA, Parsa FD. Mycobacterium cheloneae infection after breast augmentation. Aesthetic Plast Surg 2005;29:116–8. doi:10.1007/s00266-004-0023-7.

[60] Pereira LH, Sterodimas A. Autologous fat transplantation and delayed silicone implant insertion in a case of mycobacterium avium breast infection. Aesthetic Plast Surg 2010;34:1–4. doi:10.1007/s00266-009-9357-5.

[61] Kamyab A. Granulomatous lobular mastitis secondary to Mycobacterium fortuitum . World J Clin Cases 2016;4:409. doi:10.12998/wjcc.v4.i12.409.

[62] Shoyele O, Vidhun R, Dodge J, Cheng Z, Margules R, Nee P, et al. Cystic neutrophilic granulomatous mastitis: A clinicopathologic study of a distinct entity with supporting evidence of a role for Corynebacterium-targeted therapy. Ann Diagn Pathol 2018;37:51–6. doi:10.1016/j.anndiagpath.2018.08.005.

[63] Qiao Y, Hayward JH, Balassanian R, Ray KM, Joe BN, Lee AY. Tuberculosis mastitis presenting as bilateral breast masses. Clin Imaging 2018;52:28–31. doi:10.1016/j.clinimag.2018.02.013.

[64] Lehman, Trang; Damania, Zubin; Tschetter, Clifford; Lehman N. Case Report. J Fam Pract 2017;66:38–41. doi:10.1016/s0267-3649(02)00716-1.

[65] Da Silva BB, Dos Santos LG, Costa PVL, Pires CG, Borges AS. Clinical case report: Primary tuberculosis of the breast mimicking carcinoma. Am J Trop Med Hyg 2005;73:975–6.

[66] Hale JA, Peters GN, Cheek JH. Tuberculosis of the breast: Rare but still extant. Am J Surg 1985;150:620–4. doi:10.1016/0002-9610(85)90450-7.

[67] Bhatty O, Waters D, Wilka N, Samuel S, Horne J, Vivekanandan R. A Rare Manifestation of Tuberculosis Presenting in the United States. Case Rep Infect Dis 2016;2016:1–4. doi:10.1155/2016/8216040.

[68] da Silva BB, Lopes-Costa P V., Pires CG, Pereira-Filho JD, dos Santos AR. Tuberculosis of the breast: analysis of 20 cases and a literature review. Trans R Soc Trop Med Hyg 2009;103:559–63. doi:10.1016/j.trstmh.2009.02.005.

7. ANEXOS E APÊNDICES

Prisma Check-List do Artigo

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	18
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	19
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	20
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	20
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	20
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	20
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	20
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	20, 36
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	20, 37
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	20

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	20
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	21
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	21
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	21, 37
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	21,22, 29-35
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	21-22, 38-41
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	23
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	23

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.