

## ***Integrative Review on Silicone Breast Implants and ASIA Syndrome: What is the relationship?***

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### **REVIEW**

#### **ABSTRACT**

**OBJECTIVE:** The study aims to indicate the correlation between breast implants and the occurrence of ASIA Syndrome. **METHODOLOGY:** The articles were selected from the PubMed database, published between 2016 and 2021. The research used the Health Science Descriptors (DeCS) and their synonyms, in English: breast implants, silicones, autoimmune diseases and rheumatic diseases. **RESULTS:** Despite the divergent results between the studies analyzed, in most cases the correlation is evident between breast implants and the occurrence of autoimmune diseases. **DISCUSSION:** ASIA syndrome is involved as an adjuvant factor for the development of autoimmunity, as there is an exacerbation of the immunological response, with the release of cytokines and defense cells in the body with the presence of breast implants. The diagnosis is made based on the patient's symptoms and past history, in which there are characteristic symptoms. The main treatment is the extraction of breast implants. There is an important correlation between low vitamin D levels and ASIA syndrome, in addition to the presence of other autoimmune diseases. **CONCLUSION:** Breast implants can be an adjuvant for the occurrence of ASIA syndrome, being reaffirmed by the improvement factors after silicone removal.

**Keywords:** ASIA, Silicones, Breast implants, Autoimmune syndrome, Adjuvants

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## 1 INTRODUÇÃO

Initially described in 2011 by Shoenfeld et al, adjuvant-induced autoimmune-inflammatory syndrome (ASIA) already has more than 4,400 reported cases<sup>1</sup>, it consists of the development of autoimmune diseases in genetically predisposed individuals as a result of exposure to adjuvants, causing a reduction in quality of life and involvement in occupational, social and personal activities.<sup>2</sup> As for its causes due to different adjuvants, hormones, vaccines, aluminum and silicone implants stand out. These external stimuli result in hyperstimulation of the immune system in individuals with genetic predisposition (mainly HLA-DRB1 and PTPN22 genes), which may occasionally result in autoimmune diseases.<sup>1</sup> Silicone breast implants were introduced in 1962 and since their implementation studies have been carried out in order to discover the real impacts that these substances can have on the human body.<sup>3</sup>

In 1990, a segment was published suggesting that these implants were causing autoimmune diseases,<sup>4</sup> this publication had repercussions at the time, leading to the non-use of these types of prostheses in some places. However, in 2000 silicone breast implants returned and are currently widely used. In 2020, in the United States, they were present in 300,000 breast augmentation procedures and 100,000 breast reconstruction procedures. Although the silicone breast implant is related to ASIA syndrome, it is one of the most commonly performed surgical procedures.<sup>3</sup>

The diagnosis of the pathology is made using the Shoenfeld criteria, which can be classified into “major” and “minor”. The major criteria correspond to the typical clinical presentation of the syndrome, that is, symptoms such as myalgia, muscle weakness, arthralgia and/or arthritis, chronic fatigue, sleep disorders, fever and dry mouth, in addition to neurological and cognitive manifestations; minor ones: immunological changes and/or other clinical manifestations.<sup>5</sup>

Over the years there have been changes in the composition of silicone implants, however this remains an adjuvant that stimulates the immune system, which may result in the appearance of ASIA.<sup>6</sup>

In view of the notorious number of procedures with silicone prosthesis implants, the need for studies on this syndrome is highlighted, in order to contribute to the scientific community to clarify the pathology, epidemiology and ratify the diagnostic criteria, which appear in the literature. specific. Therefore, the present study aimed to investigate the scientific evidence, with the purpose of correlating the occurrence of ASIA Syndrome with silicone breast implants. Based on this guideline, we proposed to contribute to the medical-scientific community with updated evidence and make knowledge accessible to patients.

## 2 METODOLOGIA

This is an integrative literature review, based on the guiding question “What is the relationship between breast implants and ASIA Syndrome?”. A comprehensive manual search was carried out in the Medical Literature and Retrieval System Online (MEDLINE/PubMed) database, during the months of March and April 2021, using the Health Science Descriptors (DeCS) and their synonyms, in English: breast implants, silicones, autoimmune diseases and rheumatic diseases. The Boolean operators “AND” and “OR” were used to create combinations between the descriptors. The inclusion

criteria for analyzing the articles were: English language, publications made from 2016 onwards and that mention ASIA syndrome or Shoenfeld syndrome. Repeated articles, which only addressed other specific rheumatological diseases, animal experiments and case reports were excluded. Clinical trials, literature reviews and meta-analyses were selected, totaling 31 articles. Of these, after exploratory reading, 14 studies were included to answer the guiding question.

### **3 RESULTADOS e DISCUSSÃO**

From reading the pre-selected articles, divergent results were observed regarding the causal relationship between silicone breast implants and ASIA. In the study "Silicone gel breast implant rupture, extracapsular silicone and health status in a population of women" carried out by SL Brown et al., in 2001, it was demonstrated, through an observational study, that silicone can act as an immunological adjuvant for increased specific immune response to the antigen, which can spread to lymph nodes, lungs, liver and other tissues.<sup>6</sup> Colaris et al. conducted a study in Maastricht, Netherlands in 2014, showing that 34 breast implant patients were diagnosed with an autoimmune disease.<sup>5</sup>

In the study "ASIA syndrome and endocrine autoimmune disorders", the clinical case of a 51-year-old woman was described, who, 20 years after undergoing breast implant surgery, presented with a left thyroid nodule and developed subacute thyroid. The treatment resulted in total thyroidectomy and silicone explantation. Two other cases reported by the same study presented autoimmune Hashimoto's thyroiditis after silicone implantation. The first clinical situation reports a 51-year-old woman who, 15 years after undergoing silicone implant surgery, presented symptoms such as fatigue, arthralgia, morning stiffness and Sjögren's syndrome. Laboratory tests performed revealed the presence of antinuclear autoantibodies in a titer of 1/640, and antimicrosomal thyroid autoantibodies in a titer of 1/256,000.

Treatment with Levothyroxine and silicone explantation was performed. The second case reported, a 55-year-old woman, 11 years after undergoing silicone implant surgery, presented with pain and sensitivity of the thyroid gland. Laboratory tests reported positive for anti-thyroglobulin autoantibodies, antinuclear autoantibodies at a titer of 1/200. The treatment carried out was the use of steroids and removal of the silicone.<sup>7</sup> Such results are confirmed in some studies that reaffirmed that silicone breast implants can cause ASIA. <sup>2,5,8,9,10</sup>

In 2001, Fryzek J P, et al. published a study called "Self-reported symptoms among women after cosmetic breast implant and breast reduction" which compared the frequency of the appearance of rheumatological symptoms among 2500 patients who underwent silicone breast implants and 3500 others who underwent removal of the previously performed implant, pointing out as a result, patients with implants have a 57% greater chance of developing such symptoms.<sup>11</sup>

Another of them is a study done by Luis J Jara; et al. in 2016, called "Severe manifestation of autoimmune syndrome by induced adjuvants (Shoenfeld's syndrome)" which points out that, of 4479 cases of ASIA, 305 were considered serious and may have been caused by the silicone implant.<sup>12</sup> Another study "Women with silicone breast implants and unexplained systemic symptoms: a descriptive cohort study", carried out by MC Majers; et al. in 2013, it was found that 36 out of 52 women reported a

significant improvement in the symptoms of autoimmune diseases after removing the implants, with 9 of them reporting a complete disappearance of symptoms.<sup>13</sup>

Finally, an analysis of 11 case reports and 12 case series by M de Boer; et al. in "Is explantation of silicone breast implants useful in patients with complaints?" addressed that 75% (469) of the patients evaluated reported improvement in rheumatological, neurological symptoms, sleep disorders and Raynaud's disease, after explantation compared to those who did not undergo explantation.<sup>14</sup> However, there are studies that show the opposite of such research. A study carried out by the International League of Rheumatology Associations in 2015 in Mexico reported that, although two of the six cases of patients with silicone breast implants and who presented rheumatological symptoms showed improvement after removal of the implant, two did not.<sup>15</sup>

Another study done by Slavica Pavlov-Dolijanovic; et al. called "Women with silicone breast implants and autoimmune inflammatory syndrome induced by adjuvants: description of three patients and a critical review of the literature", of 3 patients with autoimmune inflammatory response induced by adjuvants and the breast implant removed, no improvement was observed after removal, influencing other research participants not to remove their silicone implants.<sup>15</sup> One of the studies, however (Vitamin D deficiency as a risk factor for the development of autoantibodies in patients with ASIA and silicone breast implants: a cohort study and review of the literature, by Maartje J L Colaris; et al., carried out in 2017), proved that vitamin D levels in patients with breast implants are inversely related to antibody levels, which suggests a good treatment for women with breast implants. silicone.<sup>16</sup>

#### **4 CONCLUSÃO**

ASIA Syndrome is a disorder that involves multiple autoimmune responses, triggered by an adjuvant. In this context, the silicone implant, together with several other substances, can be considered an adjuvant, therefore it can be a cause of ASIA, characterized mainly by fatigue, cognitive impairment, arthralgias, myalgia and concomitant occurrence of other autoimmune diseases. This possible relationship is further reinforced by the improvement in symptoms after implant removal. However, there are literary divergences regarding the establishment of a causal relationship between the syndrome and implants, since there are only retrospective studies carrying out this analysis.

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