

Clinical Characteristics of ASIA Syndrome in Patients with Silicone Breast Implants: A Scoping Review

Ospina-Gómez Juan Esteban^{1*}, Latorre-Arévalo María Gabriela¹, Ayala-Gutierrez María Camila¹, Monsalve-Suárez Edgar Felipe¹, Amaya-Muñoz María Camila¹, Caceres-Ramírez Catalina¹, Alviar-Rueda Juan Darío¹, Camacho-López Paul Anthony¹

1. Research Department, FOSCAL,
Floridablanca, Colombia

ABSTRACT

Background: Adjuvant-induced autoimmune syndrome (ASIA), described in 2011, includes autoimmune reactions triggered by environmental adjuvants, such as silicone breast implants (SBI). Symptoms include fatigue, sleep disturbances, appetite changes, muscle pain, fever, among others, with pathophysiology involving a combination of genetic predisposition and adjuvant exposure, leading to abnormal immune responses. We aimed to define clinical profiles and outcomes of patients with SBI, clarify ASIA's clinical implications, and guide future research.

Methods: Using the PRISMA-ScR framework, a scoping review was conducted to identify clinical profiles, preexisting conditions, prosthetic anomalies, and outcomes of patients with ASIA syndrome associated with SBI. Searches were performed in Medline, Scopus, Lilacs, and Google Scholar to locate relevant studies.

Results: Of 35 selected studies, 21 were case reports, 6 case series, and 8 cohort studies, identifying 848 patients, predominantly from the Netherlands (n=513), with an average age of 45-47 yr. Common medical histories included autoimmune diseases and breast cancer, while frequent implant-related anomalies were capsular contracture and rupture. Musculoskeletal symptoms and fatigue were the most prevalent, and implant explantation was the primary treatment, resulting in symptom improvement for most patients.

Conclusion: This review highlights the clinical features of ASIA syndrome in patients with SBI, particularly musculoskeletal symptoms, fatigue, and the presence of positive antinuclear antibody as a potential marker. However, the relationship between SBI and ASIA remains controversial. Despite limitations in current evidence, ongoing clinical monitoring and further research are crucial to better understanding and managing ASIA syndrome in patients with SBI.

KEYWORDS

Adjuvant-induced autoimmune syndrome (ASIA); ASIA syndrome; Breast implants; Plastic surgery; Scoping review

*Corresponding Author:

Juan Esteban Ospina-Gómez,
Research Department, FOSCAL,
Floridablanca, Colombia.

Email:

juanestebanospina98@gmail.com

Received: ***

Accepted: ***

Please cite this paper as:

Juan Esteban OG, María Gabriela LA, María Camila AG, Edgar Felipe MS, María Camila AM, Catalina CR, Juan Darío AR, Paul Anthony CL Clinical Characteristics of ASIA Syndrome in Patients with Silicone Breast Implants: A Scoping Review. World J Plast Surg. 2025;14(2):1-10.
doi: 10.61186/wjps.14.2.**

INTRODUCTION

The autoimmune/inflammatory syndrome induced by adjuvants (ASIA), first described in 2011, includes a range of autoimmune reactions triggered by environmental adjuvants, such as silicone, used in breast implants (SBI). ASIA is characterized by symptoms like fatigue, memory disturbances, muscle and joint pain, fever, lymphadenopathy, and the presence of antibodies. It encompasses various diagnoses, including siliconosis and Gulf War syndrome¹.

ASIA syndrome is a complex disorder resulting from a combination of genetic predisposition and environmental factors, particularly exposure to adjuvants, which are substances that enhance the immune response². Theories suggest that immune overstimulation and activation of transcription factors by adjuvants lead to cytokine and chemokine production, driving immune response expansion³. There is growing concern about the association between silicone breast implants (SBI) and ASIA syndrome, given the increasing use of SBI in cosmetic and reconstructive surgeries.

Initially thought to be biologically inert when introduced in 1960⁴, silicone has had various immunological effects⁵, raising concerns about long-term safety and autoimmune risks. Millions of procedures have been performed, yet many women have reported complications and systemic symptoms aligning with ASIA syndrome⁶, prompting requests for implant removal.

The diagnosis of ASIA syndrome is challenging due to its heterogeneous presentation and overlap with other autoimmune disorders, alongside a variable latency period between implant placement and symptom onset.

We aimed to characterize the clinical profiles, medical records, prosthetic abnormalities, clinical manifestations, laboratory abnormalities, and outcomes of patients diagnosed with ASIA syndrome related to SBI. By synthesizing available data, the review seeks to improve understanding of ASIA syndrome's clinical implications and inform future research directions.

METHODS

We chose a scoping review methodology in line with the Arksey and O'Malley framework⁷ and reported

according to the PRISMA-ScR guidelines⁸. The aim was to explore the characteristics of research on ASIA syndrome in patients with SBI and their clinical features.

A systematic search was conducted in the databases Medline (PubMed), Scopus, Lilacs, Google Scholar using Medical Subject Headings (MeSH), Health Sciences Descriptors (DeCS), and free terms in both Spanish and English (Supplementary 1). Two independent reviewers (JEOG and MGLA) conducted the searches, and discrepancies were resolved by consensus with a third researcher (CCR). Articles discussing ASIA syndrome and SBI, published up to the search date (2011- 01/19/2024) were included. Exclusions were based on secondary source studies, animal studies, conferences, books, book chapters, conference reviews, notes, errata, editorials, letters to the editor, and other non-scientific documents. Subsequently, all full-text documents were reviewed by the researchers, and those not addressing our research question were excluded.

An electronic matrix was designed for data extraction using Google Sheets. The following variables were extracted: patient characteristics, clinical manifestations, diagnoses, laboratory abnormalities, treatments, and outcomes. Articles were categorized into case reports/series or cohorts/other studies for better data presentation. Based on the extracted data, an inductive content analysis of the information was conducted. The synthesis of results was presented in the form of tables, according to the objective and research question.

RESULTS

Selection of articles

Figure 1 presents the PRISMA diagram for article selection in this review. Initially, 193 articles were identified from databases, and 82 duplicates were removed using the Rayyan QCRI platform⁹. Subsequently, titles and abstracts were screened, excluding 69 articles that did not meet the inclusion criteria (not addressing ASIA syndrome, SBI, reviews, or not available). Forty-two articles were selected for full-text review, and seven were excluded for not meeting criteria.

General characteristics of the articles

Of the 35 selected articles, most were case reports

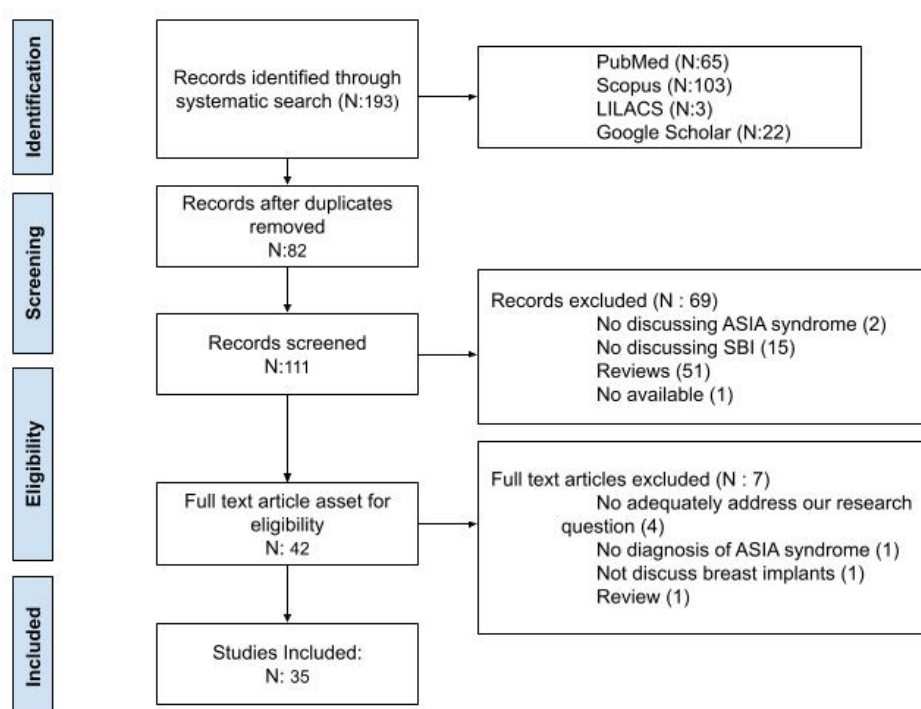


Figure 1: PRISMA flowchart illustrating the study selection process. The diagram outlines the number of studies identified, screened, assessed for eligibility, and included in the review, along with the reasons for exclusion at each stage

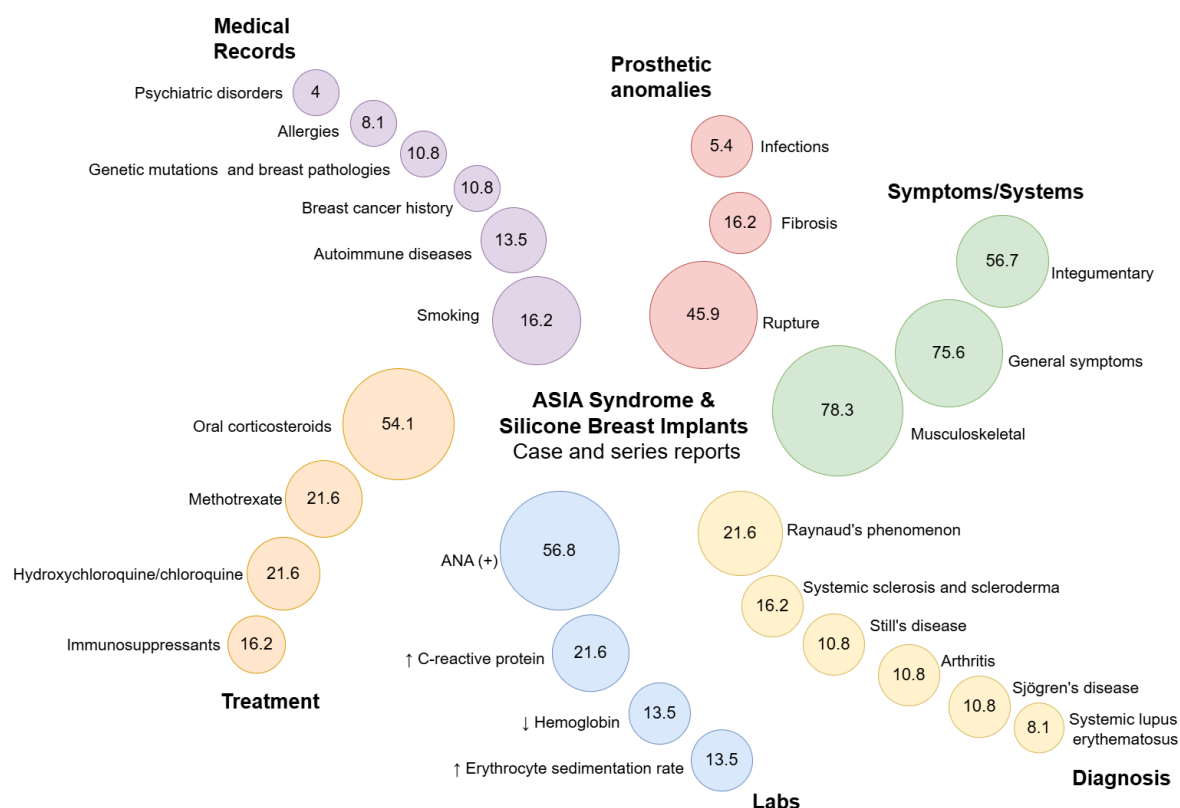


Figure 2: Summary of the findings from the case reports and case series. The circles represent the main categories. Each color represents a category, and the size of each circle is proportional to the percentage described inside it

(21)^{10–30} and case series (6)^{31–36}, followed by cohorts and other studies (8)^{37–44}. A summary of the findings from the case reports and case series is presented in Figure 2. Only one field study and one cross-sectional study were found. Detailed characteristics of each study are presented in Supplementary material (Supplementary 2).

Patient demographics

The study included 848 patients, with 37 from case reports and series, and 811 from cohorts and other studies. The Netherlands had the highest number of patients (513), followed by Israel (168), the United States (100), Brazil (31), and Argentina (14). The mean age in case reports and series was 45.1 yr (23–64 yr), while the age range in cohorts and other studies was 17–83 yr, with a range between 17–83 yr old.

Medical records

In case reports, the most common medical history was smoking (16.2%), followed by autoimmune diseases such as Sjögren's syndrome and lupus (13.5%), and breast cancer history (10.8%). Preventive mastectomies due to genetic mutations or breast pathologies were reported in another 10.8% of patients. Allergies (8.1%), psychiatric disorders (4%), and other conditions were also noted. Some patients (14) had no history or it was unreported. In the cohort data, allergies were the most prevalent medical history, affecting 60% of cases in one cohort⁴², 40.7% in another³⁷, and were also reported in a third cohort⁴³. Thyroid diseases were found in two cohorts^{37,42}, with a prevalence of 30% and 7.9%. Autoimmune diseases were common, affecting 30% and 7.9% of patients in different cohorts^{37,42}. Malignant tumors were reported in 9% of one cohort⁴⁰, while benign tumors were noted in 15.5% of cases. Other histories included chronic diseases, psychiatric disorders, cardiovascular diseases, and chronic fatigue. Three cohorts did not mention any personal histories.

Prosthetic anomalies

Prosthetic abnormalities were reported in 27 of the 37 (72%) patients from case reports and series. Among these, 17 patients had SBI rupture, six had fibrosis and two had infections. Less frequent abnormalities included prosthetic displacement,

capsulitis, with only one case each.

In cohort studies, capsular contracture was the most frequent complication, reported across three cohorts^{37,40,43}. The Colaris cohort⁴⁰ documented 29 cases of capsular contracture, while Bird³⁷ reported a 25.7% prevalence. Implant rupture was also significant, with Colaris noting 25 cases, and Bird reporting a 14.2% rupture rate. Silicone leakage was seen in 13 cases in the Colaris cohort. Additional complications in the Bird cohort included implant discoloration (12.9%), excess fluid around the implant (4.3%), and implant malposition or rotation (1.4%). Less common issues were excess scar tissue or calcification (2.8%), intraoperative rupture (2.1%), siliconoma (1.4%), and a volume decrease greater than 50 cc (1.4%). Four cohorts did not report any prosthetic anomalies.

Time to symptom onset

The average time from implantation to symptom onset in case reports and series was 5.58 yr, ranging from 6 wk to 20 yr. In the included cohorts, the time to symptom onset ranged from 5 d to 40 yr.

Symptoms

The main symptoms observed across case reports, series, and cohort studies were musculoskeletal symptoms such as polyarthralgia, myalgia, arthritis, and pain. These were present in 78.37% of cases (29 cases) and in all eight cohorts. Fatigue, fever, malaise, and weight loss were also common, appearing in 75.67% of case reports (28 cases) and all cohorts. Integumentary symptoms, including erythema, rosacea, cyanosis, telangiectasia, and rashes, were noted in 56.75% of case reports (21 cases), but only in three of the eight cohorts^{38,40,42} and other studies. Neurological symptoms, such as memory loss and cognitive issues, ranked third in the cohorts, and were present in 10 case reports. Ophthalmological manifestations were reported in five cohorts. Less frequently affected systems included the auditory system⁴¹, and the gynecological^{25,32,36} and urinary system^{13,19,22,40}.

Diagnoses

In the review of case reports and series, the most frequent diagnosis was Raynaud's phenomenon,

present in eight cases (21.6%), followed by systemic sclerosis and scleroderma in six cases (16.2%). Other notable diagnoses included Still's disease, arthritis, and Sjögren's syndrome (10.8% each), and systemic lupus erythematosus (8.1%). Less common diagnoses, each with a single report (2.7%), included Takayasu's arteritis, sarcoidosis, and myofibrillar myopathy, among others.

In cohort studies, Raynaud's phenomenon was also the most common diagnosis, appearing in three cohorts^{38,40,44}. Connective tissue diseases were reported in 18% of patients⁴⁰, while systemic autoimmune diseases were present in 53.1% of patients³⁹. Sjögren's syndrome and limited systemic scleroderma were documented too³⁸, along with vasculitis (5%) and granulomatous disease (3%)⁴⁰.

Labs

In the case reports, the most frequent laboratory finding was the presence of antinuclear antibodies (ANA), including variants such as anticentromere, anti-Ro, anti-RP155, and anti-CenpB, observed in 21 out of 37 cases (56.8%). Elevated C-reactive protein (CRP) was noted in eight cases (21.6%), while low hemoglobin and increased erythrocyte sedimentation rate (ESR) were each identified in five cases (13.5%). Elevated lactate dehydrogenase (LDH) was found in four cases (10.8%), and antineutrophil cytoplasmic antibodies (ANCA) were positive in five cases (13.5%). Other abnormalities, such as increased eosinophils and creatine kinase were reported, among others.

In the cohorts, ANA positivity was also the most common finding, present in 60% of patients³⁸ and 19.38%⁴⁰. Acute phase reactants were elevated in 40% of cases in Cavallasca's cohort. The Colaris cohort reported increased immunoglobulins in 15.5% of patients and decreased levels in 21.2%. The Cohen cohort found decreased immunoglobulins in 46.8% of cases. Rheumatoid factor was positive in 7.7% of Colaris cohort cases. Five cohorts did not report any lab results.

Treatment

In the review of case reports and series, oral corticosteroids, particularly prednisone and prednisolone, were the most frequently used treatments, prescribed in 54.1% of cases (20 out of

37). These were often combined with methotrexate or hydroxychloroquine/chloroquine, each used in 21.6% of cases (8 cases). Immunosuppressants like azathioprine and cyclophosphamide were administered in 16.2% of cases (4 cases each). Additional therapies included NSAIDs, opioids, vitamin D3 supplements, and cytotoxic agents like rituximab. Combined therapies included ACE inhibitors, aspirin, and vitamins C and E. Explantation of breast implants was a key treatment in 56.7% of cases (21 reports), leading to symptom improvement in most patients.

In cohort studies, explantation was the primary treatment in 6 cohorts^{37,40-44}. In De Miranda et al.'s cohort, all patients showed symptom improvement after explantation, whereas in Colaris et al.'s cohort, only 50% of patients improved. Other treatments were limited, except in Cavallasca's cohort, where prednisone, hydroxychloroquine, and calcium channel blockers were used, leading to symptom improvement. Cohen et al.'s cohort did not clearly document treatment outcomes. Most cohorts focused on explantation as the main therapeutic approach.

DISCUSSION

Relationship between ASIA syndrome and SBI

SBIs, first developed in 1963, consist of silicone gel within a silicone shell⁴. In 1982, safety concerns emerged due to complications like gel leakage, capsular contracture, and autoimmune diseases (e.g., lupus, rheumatoid arthritis) following implantation⁴. However, expert evaluations in 2000 by the European Parliament⁴⁵ and U.S. courts⁴⁶ found no scientific evidence linking SBIs to cancer or autoimmune diseases, though they acknowledged common local complications such as implant rupture.

Shoenfeld and Agmon-Levin introduced the concept of autoimmune/inflammatory syndrome induced by adjuvants (ASIA), proposing that silicone in implants could trigger inflammatory and autoimmune diseases⁴⁷. ASIA diagnostic criteria were established, but their validity remains controversial due to the nonspecific nature of symptoms, leading to concerns about overdiagnosis. Social media has exacerbated patient fears, with misinformation contributing to symptom misinterpretation as autoimmune disease.

To address this, healthcare professionals must provide accurate, evidence-based information to mitigate the effects of misinformation and prevent unnecessary diagnoses based on nonspecific symptoms.

Age and medical record

Age is a crucial factor in ASIA syndrome development related to SBI, influencing susceptibility and symptom progression. Studies show it mainly affects middle-aged individuals; for example, Watad et al.'s international registry reported an average onset age of 37.6 yr (range: 4-82)⁴⁸. In our review, most patients were aged 18-83, with an average onset of 46.89 yr. This suggests a link between surgical age and ASIA onset, as Becherer et al.'s registry showed augmentation procedures between ages 31-36 and reconstruction between 41-49⁴⁹, aligning with our findings.

Medical records highlight genetic predisposition as a key factor. Watad et al. found immune susceptibility in 20.3% of cases, supporting genetics' role in ASIA onset. Our review also noted a high prevalence of autoimmune diseases (13.5%) like Sjögren's syndrome and lupus, and allergies (8.1%). Kappel et al.'s case series described three sisters with BRCA1 mutations developing ASIA post-breast reconstruction³⁴, emphasizing genetic predisposition's impact on ASIA risk.

Most common prosthetic abnormalities associated with ASIA Syndrome

This review found a high prevalence of prosthetic abnormalities in patients with SBI, especially in case studies and series, emphasizing the need for close monitoring. Silicone leakage can trigger immune responses, fibrosis, and granuloma formation^{35,50}. The body forms a fibrous capsule around the implant, and ruptures can be intracapsular (contained) or extracapsular (leaking outside)⁵¹. Although rupture types were often unspecified, extracapsular ruptures are hypothesized to be more strongly linked to ASIA syndrome.

Onset time of symptoms

The onset of ASIA syndrome symptoms varies widely. Puerta et al reported an average onset of

seven years for ASIA caused by biopolymers and silicone implants⁵². In contrast, symptoms appeared three weeks after COVID-19 infection in a patient with biopolymer injection⁵³, and two weeks after receiving the AstraZeneca vaccine in a case of subacute thyroiditis⁵⁴. Factors such as adjuvant type, exposure route, and immune response likely influence this variability in symptom onset.

Associated symptoms

Significant similarities were observed in symptoms between ASIA cases related to vaccines and SBI, despite different adjuvants. Musculoskeletal symptoms, such as polyarthralgia and myalgia, were prevalent in both groups; in our study, these symptoms were present in 78.37% of cases, while in the vaccine-induced ASIA study, myalgia and arthralgia were reported in 50.8% and 73.8% of patients, respectively. Fatigue was also prevalent, affecting 75.67% of implant patients and 65.6% of vaccinated individuals. Neurological symptoms, including memory and concentration issues, were present in both, with a 35% prevalence in vaccinated patients. Raynaud's phenomenon was the most common diagnosis, suggesting a shared immunological mechanism, despite variations in adjuvants. These findings underscore the notion that ASIA symptoms are nonspecific and challenging to quantify, contributing to ongoing controversy surrounding its diagnosis and management. This highlights the urgent need for further studies to explore this association in greater depth⁵⁵.

Associated diagnoses

Comparing ASIA syndrome diagnoses from SBI to those induced by cosmetic injections⁵⁶, Raynaud's phenomenon (21.6%) was the most frequent in our study, followed by systemic sclerosis (16.2%) and Sjögren's syndrome (10.8%). These findings align with similar autoimmune diagnoses in ASIA cases related to injectable materials. Despite differing adjuvants (silicone vs. mineral oil), both studies suggest that immune activation by external adjuvants triggers autoimmune responses. This highlights the nonspecificity of ASIA symptoms and diagnoses, reinforcing the idea that different adjuvants can lead to similar autoimmune mechanisms and conditions.

Paraclinical tests

Laboratory results in ASIA syndrome highlight its autoimmune and autoinflammatory nature. ANAs are the most frequently altered biomarker, found in 51.7% of patients from the international ASIA registry ⁴⁶, consistent with our findings. While ANAs detect autoantibodies across many autoimmune diseases, their low specificity means they can also appear in healthy individuals ⁵⁷, indicating a potential predisposition in susceptible patients.

Additionally, elevations in acute phase reactants like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were observed in 21.6% and 13.5% of cases, respectively, suggesting a systemic inflammatory pattern in ASIA ⁵⁸. However, biomarkers such as ANCA and elevated muscle enzymes (CK and LDH) were less common. These variations indicate heterogeneity in the serological profiles of ASIA syndrome, reflecting differences in disease severity or individual immune responses to adjuvants. Overall, while common inflammatory markers are consistent, variability in less frequent biomarkers underscores the complexity of ASIA syndrome.

Effects of explantation on ASIA Syndrome symptoms

Analysis of ASIA syndrome criteria reveals that symptom improvement following the removal of adjuvants, specifically SBI, is a key indicator of recovery. In 21 case reports, most patients experienced symptom relief after explantation. Spit et al ⁵⁹ have compared symptom improvement in patients who underwent explantation to those who did not. They found that 30% of women explanted experienced significant improvement, particularly those who had their implants for over 10 years. Conversely, patients who did not undergo explantation demonstrated only a 12% improvement (OR = 2.86; CI 1.31-6.24, with a statistically significant *P*-value).

Although ASIA syndrome's exact pathophysiology is unclear, removing silicone breast implants leads to significant clinical improvement. This occurs by reducing chronic immune activation, halting molecular mimicry that produces autoantibodies, and eliminating silicone particles that increase antigenic load. These mechanisms restore immune balance, decrease inflammation, and alleviate symptoms. Explantation effectively addresses these

triggers, leading to symptom improvement ³.

Study limitations

This review has limitations, including reliance on case reports and case series, which may introduce publication bias. The variability in patients' clinical presentations complicates generalization of findings, and the lack of detailed treatment data limits the ability to establish specific therapeutic recommendations.

Future directions

Future studies should involve larger, well-defined cohorts to validate findings and improve understanding of ASIA syndrome in breast implant patients. Research on treatment effectiveness and the link between prosthetic characteristics and symptom onset is also crucial for clinical management.

CONCLUSION

This scoping review provides a comprehensive overview of the clinical characteristics of patients with ASIA syndrome and SBI. Musculoskeletal symptoms and fatigue are prevalent, and the presence of positive ANAs can be an important marker of the disease. The link between SBI and ASIA syndrome remains unclear, and the syndrome itself is controversial, with limited robust evidence from primary studies. Nevertheless, these findings underscore the necessity for ongoing clinical surveillance and additional research to enhance patient management and outcomes.

ACKNOWLEDGEMENTS

The authors did not receive any financial support.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AVAILABILITY OF SUPPLEMENTARY DATA

All supplementary data are accessible via sending email to the corresponding author based on reasonable application.

REFERENCES

- Rosenblum H, Shoenfeld Y, Amital H. The common immunogenic etiology of chronic fatigue syndrome: from infections to vaccines via adjuvants to the ASIA syndrome. *Infect Dis Clin North Am* 2011;**25**(4):851-863. <https://doi.org/10.1016/j.idc.2011.07.012>
- Israeli E, Agmon-Levin N, Blank M, Shoenfeld Y. Adjuvants and autoimmunity. *Lupus* 2011;**18**(13):1217-1225. <https://doi.org/10.1177/0961203309345724>
- Perricone C, Colafrancesco S, Mazor RD, Soriano A, Agmon-Levin N, Shoenfeld Y. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 2013: Unveiling the pathogenic, clinical and diagnostic aspects. *J Autoimmun* 2013;**47**:1-16. <https://doi.org/10.1016/j.jaut.2013.10.004>
- Deva AK, Cuss A, Magnusson M, Cooter R. The "Game of Implants": A Perspective on the Crisis-Prone History of Breast Implants. *Aesthet Surg J* 2019;**39**:S55-S65. <https://doi.org/10.1093/asj/sjy310>
- Cohen Tervaert JW, Colaris MJ, Van Der Hulst RR. Silicone breast implants and autoimmune rheumatic diseases: myth or reality. *Curr Opin Rheumatol* 2019;**29**(4):348-354. <https://doi.org/10.1097/BOR.0000000000000391>
- FDA. Medical Device Reports of Systemic Symptoms in Women with Breast Implants. U.S. Food and Drug Administration; 2023 [cited 2024 Oct 7]. Available from: <https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-systemic-symptoms-women-breast-implants>.
- Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;**8**(1):19-32. <https://doi.org/10.1080/1364557032000119616>
- Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med* 2018;**169**(7):467-473. <https://doi.org/10.7326/M18-0850>
- Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev* 2016;**5**(1):210. <https://doi.org/10.1186/s13643-016-0384-4>
- Araujo Santiago E, De Paula IB. Autoimmune / Inflammatory Syndrome Induced by Adjuvants (Asia Syndrome) Associated with Silicone Breast Implant Rupture. *Arch Breast Cancer* 2021;**15**:156-161. <https://doi.org/10.32768/abc.202182156-161>
- Bolaños Aguilar MA, Celis Vera KD, Barragán Garfias JA, Orrantia Vértiz M, Duarte Mote J. Kikuchi-Fujimoto disease in presentation with silicosis. *Med Interna México* 2018;**34**(2):335-341. <https://doi.org/10.24245/mim.v34i2.1565>
- Caldeira M, Ferreira AC. Siliconosis: autoimmune/inflammatory syndrome induced by adjuvants (ASIA). *Isr Med Assoc J* 2012;**14**(2):137-8
- Carrera Muñoz C, González Rodríguez J, Abó Rivera A, Estarán E, Roig Cárcel J, Segarra Medrano A. Systemic sclerosis and microscopic polyangiitis after systemic exposure to silicone. *Clin Kidney J* 2021;**14**(7):1848-1850. <https://doi.org/10.1093/ckj/sfab058>
- Dagan A, Kogan M, Shoenfeld Y, Segal G. When uncommon and common coalesce: adult onset Still's disease associated with breast augmentation as part of autoimmune syndrome induced by adjuvants (ASIA). *Clin Rheumatol* 2016;**35**(6):1643-1648. <https://doi.org/10.1007/s10067-015-2869-2>
- De Stefano L, Volpi N, De Stefano P, Ginanneschi F, Frati E, Rossi A. Sporadic late-onset nemaline myopathy in a patient with silicone breast implants. *Clin Neurol Neurosurg* 2020;**196**:105999. <https://doi.org/10.1016/j.clineuro.2020.105999>
- Del Giacco SR, Firinu D, Piludu G, Settembrini AM, Tulli M, Pirari P, et al. Raynaud's Phenomenon and Scleroderma Associated with Silicone Gel Breast Implants: An Example of Asia Syndrome. *Eur J Inflamm* 2012;**10**(2):233-238. <https://doi.org/10.1177/1721727X1201000209>
- Herrero-Ruiz SP, Garrido-Ríos AA, Fernández de la Fuente L, Baeza-Hernández G, Echeverría-García B, Borbujo J. A case of systemic lupus erythematosus in the context of ASIA syndrome because of silicone breast implants. *Int J Dermatol* 2023;**62**(12):1549-1550. <https://doi.org/10.1111/ijd.16866>
- Hoteit B, Pinsolle V, Delgove A, Dannepond A, Michot A. Siliconosis with rheumatoid polyarthritis following a breast implant rupture: Case report and literature review. *Ann Chir Plast Esthet* 2023;**68**(4):368-372. <https://doi.org/10.1016/j.anplas.2023.03.001>
- Jara LJ, Medina G, Gómez-Bañuelos E, Saavedra MA, Vera-Lastra O. Still's disease, lupus-like syndrome, and silicone breast implants. A case of "ASIA" (Shoenfeld's syndrome). *Lupus* 2012;**21**(2):140-145. <https://doi.org/10.1177/0961203311430970>
- Kivity S, Katz M, Langevitz P, Eshed I, Olchovski D, Barzilai A. Autoimmune syndrome induced by adjuvants (ASIA) in the Middle East: morphea followingsiliconeimplantation. *Lupus* 2012;**21**(2):136-139. <https://doi.org/10.1177/0961203311429551>
- Maldonado G, Guerrero R, Intriago M, Rios C. Autoinflammatory/Autoimmunity Syndrome Induced By Adjuvants (ASIA) Due to Silicone Incompatibility Syndrome. *Case Rep Rheumatol* 2021;**2021**:5595739. <https://doi.org/10.1155/2021/5595739>

22. Mir TH, Khan AK, Parvaiz MO, Rath PD, Sharma A. ASIA syndrome with severe lupus - A case report. *Lupus* 2022;**31**(12):1532-1535. <https://doi.org/10.1177/09612033221124424>
23. Moling O, Piccin A, Tauber M, Marinello P, Canova M, Casini M, et al. Intravascular large B-cell lymphoma associated with silicone breast implant, HLA-DRB1*11:01, and HLA-DQB1*03:01 manifesting as macrophage activation syndrome and with severe neurological symptoms: a case report. *J Med Case Rep* 2016;**10**(1):254. <https://doi.org/10.1186/s13256-016-0993-5>
24. Pineda JC, Díaz JC, Agualimpia A, García JF. Autoimmune/inflammatory syndrome induced by adjuvants causing myositis and pulmonary fibrosis. *Isr Med Assoc J* 2013;**15**(11):720-1.
25. Plavsic A, Arandjelovic S, Dimitrijevic M, Kusic N, Tomic Spiric V, Popovic B, et al. Autoimmune/inflammatory syndrome induced by adjuvants in a woman with Hashimoto thyroiditis and familial autoimmunity: a case report and literature review. *Front Immunol* 2023;**14**:1139603. <https://doi.org/10.3389/fimmu.2023.1139603>
26. Posso-Osorio I, Méndez-Rayó T, Jimenez CA, Escobar D, Sepúlveda M, Navarro EP, et al. Hepatic infiltration by silicone in a patient with ASIA syndrome. *Hepatology* 2018;**67**(1):444-5. <https://doi.org/10.1002/hep.29274>
27. Simeonova D, Georgiev T, Shivacheva T. Takayasu arteritis associated with autoimmune/inflammatory syndrome induced by adjuvants: a case-based review. *Rheumatol Int* 2023;**43**(5):975-81. <https://doi.org/10.1007/s00296-023-05309-2>
28. Van Assche S, Parmentier H, Varkas G, Peene I, Herdewyn S. Progressive sensory ataxia and breast implant rupture, an uncommon presentation of a debated concept: a case report. *BMC Neurol* 2022;**22**(1):368. <https://doi.org/10.1186/s12883-022-02894-w>
29. Wroński J, Bonek K, Stanisławska-Biernat E. Scleroderma-like syndrome in a woman with silicone breast implants: case report and critical review of the literature. *Reumatologia* 2019;**57**(1):55-8. <https://doi.org/10.5114/reum.2019.83241>
30. Vercelli L, Averó P. Actualización en enfermedad autoinmune/inflamatoria inducida por adyuvantes (síndrome ASIA). *Rev Argent Microbiol* 2017;**49**:334-41.
31. David PR, Dagan A, Colaris M, de Boer M, Cohen Tervaert JW, Shoenfeld Y. Churg-Strauss syndrome: Singulair or silicone (or both)? *Isr Med Assoc J* 2016;**18**(3-4):168-70.
32. de Carvalho JF, de Oliveira CBA, Boas RV, Matias MFV, Bastos LMC. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) with postural orthostatic tachycardia syndrome after silicone breast implantation: Case report. *Eur J Rheumatol* 2023;**10**(1):23-25. <https://doi.org/10.5152/eurjrheum.2022.21108>
33. Fenoglio R, Cecchi I, Roccatello D. ASIA Syndrome Following Breast Implant Placement. *Isr Med Assoc J* 2018;**20**(11):714-716.
34. Kappel RM, Cohen Tervaert JW, Pruijn GJM. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) due to silicone implant incompatibility syndrome in three sisters. *Clin Exp Rheumatol* 2014;**32**(2):256-258.
35. Nesher G, Soriano A, Shlomai G, Iadgarov Y, Shulimzon TR, Borella E, et al. Severe ASIA syndrome associated with lymph node, thoracic, and pulmonary silicone infiltration following breast implant rupture: experience with four cases. *Lupus* 2015;**24**(4-5):463-468. <https://doi.org/10.1177/0961203314562622>
36. Pavlov-Dolijanovic S, Vujasinovic Stupar N. Women with silicone breast implants and autoimmune inflammatory syndrome induced by adjuvants: description of three patients and a critical review of the literature. *Rheumatol Int* 2017;**37**(8):1405-1411. <https://doi.org/10.1007/s00296-017-3731-4>
37. Bird GR, Niessen FB. The effect of explantation on systemic disease symptoms and quality of life in patients with breast implant illness: a prospective cohort study. *Sci Rep* 2022;**12**(1):21073. <https://doi.org/10.1038/s41598-022-25300-4>
38. Cavallasca JA, Musuruana JL, Maliandi MDR. Clinical manifestations, laboratory features, and evolution in patients with autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA). *Rev Colomb Reumatol (Engl Ed)*. 2024;**S2444440524001328**. <https://doi.org/10.1016/j.rcrue.2024.08.006>
39. Cohen Tervaert JW, Kappel RM. Silicone implant incompatibility syndrome (SIIS): a frequent cause of ASIA (Shoenfeld's syndrome). *Immunol Res* 2013;**56**(2-3):293-298. <https://doi.org/10.1007/s12026-013-8401-3>
40. Colaris MJL, de Boer M, van der Hulst RR, Cohen Tervaert JW. Two hundreds cases of ASIA syndrome following silicone implants: a comparative study of 30 years and a review of current literature. *Immunol Res* 2017;**65**(1):120-128. <https://doi.org/10.1007/s12026-016-8821-y>
41. Greenbaum A, Halpert G, Dotan A, Shivatzki S, Heidecke H, Kaplan Neeman R, et al. The Prevalence of Hearing Impairments in Women with Silicone Breast Implants. *Dis (Basel)* 2023;**11**(1):31. <https://doi.org/10.3390/diseases11010031>
42. Miranda RED. En bloc explant of silicone breast prostheses and quality of life and evolution of

- ASIA syndrome symptoms. *Rev Bras Cir Plást* 2020;**35**(4):427-431. <https://doi.org/10.5935/2177-1235.2020RBCP0076>
43. Miseré RML, Colaris MJL, Tervaert JWC, van der Hulst RRWJ. The Prevalence of Self-Reported Health Complaints and Health-Related Quality of Life in Women With Breast Implants. *Aesthet Surg J* 2021;**41**(6):661-668. <https://doi.org/10.1093/asj/sjaa207>
 44. Peradotto B, Dezoti Micheletti VC, Da Silva Pierotto AA, Oliveira Rodrigues De Carvalho K, Pasquotto Batista ME, Ramos Araújo BL, et al. Síndrome autoimune induzida por adjuvantes (ASIA): sinais e sintomas experienciados por mulheres. *Rev SOBECC* 2023;**28**:E2328874. <https://doi.org/10.5327/Z1414-4425202328874>
 45. European Parliament. The impact of endocrine disruptors on human health and wildlife. European Parliament Think Tank. 2000. [https://www.europarl.europa.eu/thinktank/sk/document/IPOL-JOIN_ET\(2000\)471573](https://www.europarl.europa.eu/thinktank/sk/document/IPOL-JOIN_ET(2000)471573). Accessed 7 October 2024.
 46. Hulka BS, Kerkvliet NL, Tugwell P. Experience of a Scientific Panel Formed to Advise the Federal Judiciary on Silicone Breast Implants. *N Engl J Med* 2000;**342**(11):812-815. <https://doi.org/10.1056/NEJM200003163421111>
 47. Shoenfeld Y, Agmon-Levin N. "ASIA" - autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun* 2011;**36**(1):4-8. <https://doi.org/10.1016/j.jaut.2010.07.003>
 48. Watad A, Quaresma M, Bragazzi NL, Cervera R, Tervaert JWC, Amital H, et al. The autoimmune/inflammatory syndrome induced by adjuvants (ASIA)/Shoenfeld's syndrome: descriptive analysis of 300 patients from the international ASIA syndrome registry. *Clin Rheumatol* 2018;**483-493**. <https://doi.org/10.1007/s10067-017-3748-9>
 49. Becherer BE, Hopper I, Cooter RD, Couturaud B, von Fritschen U, Mullen E, et al. Comparing 200,000 Breast Implants and 85,000 Patients over Four National Breast Implant Registries. *Plast Reconstr Surg* 2023;**152**(2):307-318. <https://doi.org/10.1097/PRS.00000000000010208>
 50. De Backer H, Darquennes K, Dooms C, Yserbyt J, Coolen J, Verschakelen J, et al. The inner and outer of our thorax: silicone breast implants and pulmonary alveolar proteinosis. *Acta Clin Belg* 2015;**70**(5):384-386. <https://doi.org/10.1179/2295333715Y.00000000035>
 51. Swezey E, Shikhman R, Moufarrege R. Breast Implant Rupture. *StatPearls* [Internet]. <https://www.ncbi.nlm.nih.gov/books/NBK459308>. Accessed 07 Oct 2024.
 52. Puerta Sarmiento GE, Modragón I, Echeverri A, Sua LF, Bonilla-Abadía F, Aguirre-Valencia D. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA), medical treatment of severe systemic compromise: case report. *Colomb Med (Cali)* 2023;**54**(1):e5004625. <https://doi.org/10.25100/cm.v54i1.4625>
 53. Aguilera-Fernandez P, Navarro-Saez MDC, Feijoo-Massó C, Esteve-Valverde E, Calzado Isbert S, Parra Parente T. The "autoimmune/inflammatory syndrome induced by adjuvants" (ASIA) after COVID-19 infection: A case report. *Reumatol Clin* 2023;**19**(10):593-595. <https://doi.org/10.1016/j.reuma.2023.06.002>
 54. Das L, Bhadada SK, Sood A. Post-COVID-vaccine autoimmune/inflammatory syndrome in response to adjuvants (ASIA syndrome) manifesting as subacute thyroiditis. *J Endocrinol Invest* 2022;**45**(2):465-467. <https://doi.org/10.1007/s40618-021-01681-7>
 55. Watad A, Bragazzi NL, McGonagle D, Adawi M, Bridgwood C, Damiani G, et al. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) demonstrates distinct autoimmune and autoinflammatory disease associations according to the adjuvant subtype: Insights from an analysis of 500 cases. *Clin Immunol* 2019;**203**:1-8. <https://doi.org/10.1016/j.clim.2019.03.007>
 56. Kushida-Contreras BH, Gómez-Calva B, Mendoza-Ramírez B, Gaxiola-García MA. Autoimmune Autoinflammatory Syndrome Induced by Adjuvants (ASIA) After Injection of Foreign Materials for Cosmetic Purposes: Retrospective Analysis of 1027 Cases. *Aesthetic Plast Surg* 2024;**48**(3):491-500. <https://doi.org/10.1007/s00266-023-03670-y>
 57. Pashnina IA, Krivolapova IM, Fedotkina TV, Ryabkova VA, Cheresheva MV, Churilov LP, et al. Antinuclear Autoantibodies in Health: Autoimmunity Is Not a Synonym of Autoimmune Disease. *Antibodies*. 2021;**10**(1):9. <https://doi.org/10.3390/antib10010009>
 58. Guerrissi JO. Asia Syndrome: Diagnosis and Surgical Approach. *Austin J Surg* 2017;**4**(1):1093.
 59. Spit KA, Scharff M, De Blok CJ, Niessen FB, Bachour Y, Nanayakkara PW. Patient-reported systemic symptoms in women with silicone breast implants: a descriptive cohort study. *BMJ Open* 2022;**12**(6):e057159. <https://doi.org/10.1136/bmjopen-2021-057159>