



# Association of anxiety and depression with breast implant illness syndrome (BII): a prospective observational cross-sectional study

Maria Eduarda Guelfi Pinto<sup>1\*</sup>, Jesselina Francisco dos Santos Haber<sup>2</sup>,  
Daniel De Bortoli Teixeira<sup>3</sup>

<sup>1</sup> Student of the Undergraduate Medicine course at the University of Marília. Volunteer for the Scientific Initiation Program: PIIC/UNIMAR, Marília, Brazil.

<sup>2</sup> University of Marília (UNIMAR) and Postgraduate of Health and Aging Program, Faculty of Medicine of Marília, Marília, Brazil.

<sup>3</sup> Professor of the Undergraduate Medicine course at the University of Marília. Advisor of the Scientific Initiation Program: PIIC/UNIMAR, Marília, Brazil.

\*Corresponding author: Maria Eduarda Guelfi Pinto.

Student of the Undergraduate Medicine course at the University of Marília. Volunteer for the Scientific Initiation Program: PIIC/UNIMAR, Marília, Brazil.

E-mail: [duda\\_guelfi@icloud.com](mailto:duda_guelfi@icloud.com)

DOI: <https://doi.org/10.54448/mdnt24304>

Received: 04-17-2024; Revised: 03-30-2024; Accepted: 07-06-2024; Published: 07-12-2024; MedNEXT-id: e24304

**Editor:** Idiberto José Zotarelli Filho, MSc., Ph.D., Post-Doctoral.

## Abstract

**Introduction:** Breast Implant Illness syndrome (BII), popularly known as “silicone disease”, has no defined pathophysiology or recognition by the WHO. It consists of systemic symptoms such as joint pain, muscle pain, confusion, memory loss/cognitive problems, chronic fatigue, and immune diseases. In some more recent studies, anxiety and depression have been observed as an incident characteristic of the syndrome. **Objective:** It was to relate the appearance of anxiety and depression pathologies with the development of Breast Implant Illness syndrome in women with breast implants. **Methods:** To prepare the following prospective observational cross-sectional study, 132 women who had breast implants were interviewed and answered an online questionnaire with 18 questions about the breast implant that was disseminated through social networks. To obtain the data, questions about pre-operative and post-operative signs and symptoms were crossed, this data was subsequently struck and finally, another cross was carried out with the other unknown, symptoms were diagnosed by doctors. **Results:** The validation analysis of the questionnaire proposed in this study using Cronbach's alpha ( $\alpha$ ) statistical technique showed that the reliability rating was high, with alpha ( $\alpha$ )=0.82. It was noted that 31%

of women who did not have any characteristic signs and symptoms presented after placement and of these 22 women were diagnosed by doctors. And at the other intersection, it was clear that 25% presented depression after the placement of the breast implant and 23 of these women were diagnosed by doctors. **Conclusion:** It can be stated that anxiety and depression are pathologies associated with Breast Implant Illness syndrome.

**Keywords:** Anxiety. Depression. Breast Implant Illness Syndrome.

## Introduction

Breast implant surgery is the most common surgery worldwide [1], as silicone implants are the most used and studied medical devices in the world, however, in recent times, several patients have been seeking the removal of such prostheses. These reasons are due to some systemic symptoms that are related to the breast implant illness (BII), popularly known as “silicone disease” [2-5]. There is still no consensus regarding the pathophysiology of the disease, but there are several theories, one of which is that BII Syndrome, is caused by chemical and heavy metal toxicity, immunological dysfunction, and other theories considered focus on psychological factors. and social [2,6].

Among the symptoms of BII, a series of systemic symptoms stand out, such as joint pain, muscle pain, confusion, memory loss/cognitive problems, chronic fatigue, and immune diseases [7]. Furthermore, anxiety and depression are also present in the Breast Implant Illness syndrome, in the study carried out by Newby et al, 2021 [1], which included analysis of data from women with self-reported BII and implants still in place (n=51), self-reported BII who had explanted (n = 60), and women with implants implanted without BII (n = 58), it was clear that women with BII, regardless of whether they had undergone explant surgery, reported more severe somatic symptoms, greater depression, health anxiety and anxiety, and worse physical health than women without BII. Despite all the signs and symptoms, BII is not yet an accepted disease in the WHO classification, and there are no specific tests to diagnose it, nor is there a specific technique for removing silicone [8].

Therefore, the present study aimed to analyze the incidence of anxiety and depression in women after breast implant placement, as well as identify whether anxiety and depression were diagnosed by doctors, relating the appearance of anxiety and depression with the development of breast implant illness syndrome.

## Methods

### Study Design

The study followed the prospective observational cross-sectional, quantitative, and descriptive study model, following the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) rules. Available at: <https://www.strobe-statement.org/checklists/>. Accessed on 04/11/2024.

### Eligibility

The inclusion criteria considered Brazilian women over 18 years of age who had silicone implants placed in their breasts. Exclusion was applied in cases of incomplete questionnaires and non-acceptance of signing the consent form.

### Ethical Approval

The study included the participation of women who signed the Free and Informed Consent Form, the research participants were interviewed using an online questionnaire approved by the Ethics and Research Committee of UNIMAR - Marília, São Paulo, under the number 5.324.797.

### Research Instrument - Questionnaires

Questions were asked regarding depression and anxiety, being raised when they occurred, that is,

whether the pathologies occurred pre-surgery or post-surgery and whether they were diagnosed by doctors, the questionnaire lasted an average of 03 minutes to be answered and It has 18 objective questions on the subject. The questionnaire was published from May to July 2022, on social networks such as Instagram, Facebook, and WhatsApp groups for free through the link: <https://tinyurl.com/projetoBII>.

### Settings

132 responses were received, therefore a statistical analysis was carried out to determine the responses of pre-operative diseases/symptomatology and another investigation of post-operative diseases/symptomatology. Then, a statistical analysis was carried out with data crossing to understand whether women presented anxiety and depression before the implantation of the prosthesis or after the insertion of the silicone breast prosthesis. Finally, the data obtained through the first crossing was crossed with the unknown whether they were diagnosed by a doctor and the final data for this research was obtained.

### Statistical Analysis

In describing the data, absolute (n) and relative frequencies (%) were used for qualitative variables and measures of central tendency and dispersion for quantitative variables. Normality was identified by the Shapiro-Wilk test. The existence of an association was assessed using the Pearson or Fisher chi-square test, when necessary. To compare mean values, the Mann-Whitney test was used (non-parametric data). The significance level used in the research was 5% ( $p < 0.05$ ). The validation of the questionnaire proposed in this study was determined using the statistical technique of Cronbach's alpha ( $\alpha$ ), to know the reliability and measure of internal consistency. The calculation of Cronbach's alpha coefficient ( $\alpha$ ) required the administration of just one test to provide a single estimate of the reliability of the entire survey. The reliability of Cronbach's alpha coefficient varies between 0 and 1 as standard. The Cronbach's alpha coefficient reliability classification obeyed the following limits: A.  $\alpha \leq 0.30$  – Very low; B.  $0.30 < \alpha \leq 0.60$  – Low; C.  $0.60 < \alpha \leq 0.75$  – Moderate; D.  $0.75 < \alpha \leq 0.90$  – High; E.  $\alpha > 0.90$  – Very high [Bland JM, Altman DG. Statistics notes: Cronbach's alpha. British Medical Journal, 1997, v.314, n. 7080, p. 572]. The Excel program was used to create the database and the Stata 16.1 software (STATA, 2019) [9] for data analysis. Information was collected from 170 women. Data from 167 women who filled out the research form were analyzed.

## Results

The exclusions occurred due to one case of current age being less than 18 years old, one case of implausible current age (three years), and one case of non-acceptance of the ICF. The validation analysis of the questionnaire proposed in this study using Cronbach's alpha ( $\alpha$ ) statistical technique showed that the reliability rating was high, with alpha ( $\alpha$ )=0.82, considering  $0.75 < \alpha \leq 0.90$ . In this research, a total of 167 women who underwent at least one surgery for silicone breast implants were evaluated.

The average age at the time of completing the survey was 35.58 (Standard Deviation – SD: 9.09) years and ranged from 18 to 67 years. Of these, 95.81% were classified as adults (20 - 59 years old) 3.59% as adolescents (< 20 years old), and one (0.60%) as elderly ( $\geq 60$  years old). Data on age at the time of surgery were available for 162 women and the mean identified was 26.72 (SD: 7.58) years and ranged from 15 to 54 years. Of these, 83.33% were classified as adults (20-59 years old) and 16.67% as adolescents (<20 years old).

It was found that the technique most commonly used for silicone implantation was above the muscle (49.70%), followed by the technique below the muscle (32.93%) and other techniques (5.39%). In 11.98% of the forms this information was not answered. For statistical purposes, only the two prevalent categories were included in the analysis.

Analysis of the volume of the implanted prosthesis showed that 59.28% of women used 100 to 299 mL, 38.32% used 300 to 500 mL, and, in 2.40% of the forms, this data was not available. For statistical purposes, only the two prevalent categories were included in the analysis. Table 1 identifies the description of the sociodemographic and clinical characteristics of women who underwent breast implants, according to the research outcomes, which are age group, surgical technique, and implant volume.

Considering the age group outcome, there was a statistically significant association ( $p < 0.05$ ) with the

variables, family history of any of the symptoms evaluated, existence of symptoms after insertion of the prosthesis, psychological support before surgery, and receipt of information before surgery about BII syndrome. Adolescents had a statistically higher frequency than adults of family history of the symptoms assessed (66.67% vs 42.22%), previous psychological support (40.00% vs 5.15%), and receipt of information about BII syndrome before surgery (18.52% vs 4.44%). On the other hand, adults had a higher frequency than adolescents of the presence of symptoms assessed after insertion of the prosthesis (70.37% vs 37.04%) (Table 1).

Considering the outcome of the surgical technique performed, there was a statistically significant association ( $p=0.024$ ) with the variable reason for surgery. Women with the surgical technique under the muscle had a statistically higher frequency than those who underwent the technique above the muscle, for surgical reasons related to the disease (7.27% vs 0.00%). Considering the outcome volume of the prosthesis used, there was a statistically significant association ( $p=0.024$ ) with the variable reason for surgery. Women who placed a prosthesis volume of 300-500 mL had a statistically higher frequency, than those who placed 100-300 mL, of reasons related to the disease (7.81% vs 1.01%).

It was observed, in the 110 women with available data, that the onset of symptoms after insertion of the prosthesis had a median of 10 (P25: 4; P75: 36) months and varied between zero and 300 months. There was no association between the median time and the age group ( $p=0.3786$ ), the surgical technique ( $p=0.8393$ ), or the volume of the prosthesis ( $p=0.8508$ ).

**Table 1.** Description of number, percentage, and significance of women who underwent silicone implants in their breasts, according to sociodemographic and clinical characteristics and outcomes, age range, surgical technique performed, and volume of the prosthesis used. Marília, 2023.

Variables	<u>Age range</u> (N=162)				*p-value	<u>Surgical technique</u> (N=138)				*p-value	<u>Volume (mL)</u> <u>prosthesis</u> (N=163)				*p-value
	<u>Adult</u>		<u>Adolescent</u>			<u>Under</u>		<u>Over</u>			<u>100-299</u>		<u>300-500</u>		
	N	%	N	%		N	%	N	%		N	%	N	%	
<b>The age range at the surgery</b>															
Adult	-	-	-	-	-	45	84.91	66	81.48	0.607	79	80.61	54	88.52	0.190
Adolescent	-	-	-	-		8	15.09	15	18.52		19	19.39	7	11.48	
<b>Surgical technique</b>															
Under	45	40.54	8	34.78	0.607	-	-	-	-	-	30	35.71	25	46.30	0.215
Over	66	59.46	15	65.22		-	-	-	-		54	64.29	29	53.70	
<b>Volume used</b>															
100-299mL	79	59.40	19	73.08	0.190	30	54.55	54	65.06	0.215	-	-	-	-	-
300-500mL	54	40.60	7	26.92		25	45.45	29	34.94		-	-	-	-	

Prosthetic motif															
Aesthetics	130	96.30	26	96.30	1.000	51	92.73	83	100.00	0.024 <sup>¥</sup>	98	98.99	59	92.19	0.024
Illness	5	3.70	1	3.70		4	7.27	-	-		1	1.01	5	7.81	
Post-surgical complication															
No	109	80.74	20	74.07	0.432	42	76.36	66	79.52	0.660	75	75.76	55	85.94	0.114
Yes	26	19.26	7	25.93		13	23.64	17	20.48		24	24.24	9	14.06	
Time to change the prosthesis															
Up to 10 years	17	30.91	13	15.66	0.118	18	18.18	18	28.13	0.053	34	25.19	2	7.41	0.053
More than 10 years	12	21.82	28	33.73		32	32.32	13	20.31		31	22.96	12	44.44	
Uninformed	8	14.55	17	20.48		24	24.24	9	14.06		29	21.48	4	14.81	
Didn't happen	18	32.73	25	30.12		25	25.25	24	37.50		41	30.37	9	33.33	

**Caption:** N: number; %: percentage; \*: Pearson's chi-square test; ¥: Fisher's exact test. Source: Own Authorship.

**Table 1 (Continued 1).** Description of the number, percentage, and significance of women who underwent silicone implants in their breasts, according to sociodemographic and clinical characteristics and outcomes, age range, surgical technique performed, and volume of the prosthesis used. Marília, 2023.

Variables	<u>Age range</u> (N=162)				*p-value	<u>Surgical technique</u> (N=138)				*p-value	<u>Volume (mL)</u> <u>prosthesis</u> (N=163)				*p-value
	<u>Adult</u>		<u>Adolescent</u>			<u>Under</u>		<u>Over</u>			<u>100-299</u>		<u>300-500</u>		
	N	%	N	%		N	%	N	%		N	%	N	%	
<b>Symptoms prior to prosthesis</b>															
No symptoms	64	47.41	14	51.85	0.673	24	43.64	46	55.42	0.175	50	50.51	29	45.31	0.517
With 1 or more	71	52.59	13	48.15		31	56.36	37	44.58		49	49.49	35	54.69	
<b>Family history of symptoms</b>															
No	78	57.78	9	33.33	0.020	31	56.36	43	51.81	0.599	58	58.59	30	46.88	0.143
Yes	57	42.22	18	66.67		24	43.64	40	48.19		41	41.41	34	53.13	
<b>Presented symptoms after the prosthesis</b>															
No	40	29.63	17	69.96	0.001	23	41.82	25	30.12	0.158	41	41.41	18	28.13	0.085
Yes	95	70.37	10	37.04		32	58.18	58	69.88		58	58.59	46	71.88	
<b>Medical diagnostic</b>															
No	91	67.41	22	81.48	0.146	39	70.91	58	69.88	0.897	68	68.69	45	70.31	0.826
Yes	44	32.59	5	18.52		16	29.09	25	30.12		31	31.31	19	29.69	
<b>Did follow-up</b>															
No	92	94.85	6	60.00	<0.0001	31	91.18	53	91.38	0.973	52	88.14	46	97.87	0.059
Yes	5	5.15	4	40.00		3	8.82	5	8.62		7	11.86	1	2.13	
<b>The silicone was removed</b>															
No	60	61.86	6	60.00	0.909	22	64.71	33	56.90	0.461	38	64.41	26	55.32	0.342
Yes	37	38.14	4	40.00		12	35.29	25	43.10		21	35.59	21	44.68	

**Caption:** N: number; %: percentage; \*: Pearson's chi-square test; ¥: Fisher's exact test. Source: Own Authorship.

**Table 1 (Continued 2).** Description of the number, percentage, and significance of women who underwent silicone implants in their breasts, according to sociodemographic and clinical characteristics and outcomes, age range, surgical technique performed, and volume of the prosthesis used. Marília, 2023.

Variables	<u>Age range</u> (N=162)				*p-value	<u>Surgical technique</u> (N=138)				*p-value	<u>Volume (mL) prosthesis</u> (N=163)				*p-value
	<u>Adult</u>		<u>Adolescent</u>			<u>Under</u>		<u>Over</u>			<u>100-299</u>		<u>300-500</u>		
	N	%	N	%		N	%	N	%		N	%	N	%	
<b>If yes, there was an improvement in symptoms</b>															
Did not remove	60	64.52	6	60.00	0.777	22	68.75	33	57.89	0.312	38	67.86	26	56.52	0.239
Yes	33	35.84	4	40.00		10	31.25	24	42.11		18	32.14	20	43.48	
<b>Have you heard about BII syndrome?</b>															
No	44	32.59	7	25.93	0.496	22	40.00	23	27.71	0.132	31	31.31	23	35.94	0.540
Yes	91	67.41	20	74.07		33	60.00	60	72.29		68	68.69	41	64.06	
<b>You were told you might have BII syndrome</b>															
No	129	95.56	22	81.48	<b>0.008</b>	54	91.18	75	90.36	0.069	92	92.93	59	92.19	0.859
Yes	6	4.44	5	18.52		1	1.82	8	9.64		7	7.07	5	7.81	

**Caption:** N: number; %: percentage; \*: Pearson's chi-square test; ¥: Fisher's exact test. Source: Own Authorship.



## Discussion

With the statistical analysis of the data, it was noted that 31.06% (41 women) had anxiety after the placement of a breast prosthesis, and they did not have any symptoms before the placement, based on this information and the other question of whether the symptoms were diagnosed by doctors, it was identified that 53.6% of women had a medical diagnosis. According to a study carried out by Newby et al., 2021 [1], that was investigating Breast Implant Illness syndrome, used the Hospital Anxiety and Depression Scale (HADS) to evaluate anxiety symptoms, a cutoff score was obtained of 8 on the anxiety subscales of the HADS, thus achieving ideal sensitivity and specificity in detecting anxiety.

In another analysis, the diagnosis of depression in women after the placement of breast implants became clear. Analyzing the data, it was found that 25% of women who answered the questionnaire and had nothing suggestive of depression after having the prosthesis placed began to experience depression after having the prosthesis placed. Of these women who experienced depression after having a prosthesis, 23 of them were diagnosed by doctors. According to a query of the MDR database for all reports published between January 1, 2008, and April 1, 2022, regarding a breast prosthesis made by the FDA, and subsequently, the note that was released by reporting systemic symptoms in women with breast implants, depression is one of the pathologies reported by patients [6].

Thus, patients with self-reported BII have reported systemic symptoms that they attribute to the use of breast implants, such as fibromyalgia, chronic fatigue syndrome, autoimmune disorders, and hypothyroidism that often produce fatigue, joint and muscle pain, "brain fog," anxiety or depression, and falling of hair [10]. The possibility that patients with breast implants have an undiagnosed chronic illness unrelated to breast implants should be considered, as well as other factors that may produce similar symptoms [11].

Finally, a recent retrospective case-control study carried out by authors Nagy et al. (2024) [12] analyzed the possible association between BII and mast cell activation syndrome (MCAS), which often manifests an increase in mast cells (MCs) in various tissues and may explain the symptoms of BII. We retrospectively analyzed 20 implanted patients who underwent explantation and total capsulectomy; 15 reported preoperatively that they had BII (subject group); 5 thought not (control group 1 (CG1)). Five prophylactic mastectomized patients constituted control group 2 (CG2). With CD117 staining, the mean and maximum mast cell counts (MCCs) in the resected tissues were

determined. The mean BII symptom score at 2 weeks post-explant was reduced by 77% and 85% at 9 months. The analysis also suggested BII in CG1 patients, who improved similarly. Among patients in GC2, healthy breast tissue showed a mean and maximum CCM of 5.0/CGA and 6.9/CGA. The mean and maximum MCCs in capsules in BII patients were 11.7/hpf and 16.3/hpf, a.6/hpf and 13.3/hpf in GC1 patients. All intergroup comparisons were significantly different. Thus, CCMs in peri-implant capsules in BII patients are increased.

## Conclusion

Given the above, it was noted that one of the pathologies associated with BII syndrome is anxiety and depression. However, there are still few studies relating to BII syndrome. Therefore, more studies on this syndrome are necessary.

## CRedit

Author contributions: **Conceptualization** - Maria Eduarda Guelfi Pinto, Jesselina Francisco dos Santos Haber, Daniel De Bortoli Teixeira; **Data curation**- Maria Eduarda Guelfi Pinto, Jesselina Francisco dos Santos Haber; **Formal Analysis**- Maria Eduarda Guelfi Pinto, Jesselina Francisco dos Santos Haber, Daniel De Bortoli Teixeira; **Investigation** - Maria Eduarda Guelfi Pinto, Daniel De Bortoli Teixeira; **Methodology** - Maria Eduarda Guelfi Pinto, Jesselina Francisco dos Santos Haber, Daniel De Bortoli Teixeira; **Project administration** - Maria Eduarda Guelfi Pinto; **Supervision** - Daniel De Bortoli Teixeira; **Writing - original draft** - Maria Eduarda Guelfi Pinto, Jesselina Francisco dos Santos Haber, Daniel De Bortoli Teixeira; **Writing-review & editing**- Maria Eduarda Guelfi Pinto, Jesselina Francisco dos Santos Haber, Daniel De Bortoli Teixeira.

## Acknowledgment

Not applicable.

## Ethical Approval

The study included the participation of women who signed the Free and Informed Consent Form, the research participants were interviewed using an online questionnaire approved by the Ethics and Research Committee of UNIMAR - Marília, São Paulo, under the number 5.324.797.

## Informed Consent

It was applicable.

## Funding

Not applicable.

## Data Sharing Statement

No additional data are available.

## Conflict of Interest

The authors declare no conflict of interest.

## Similarity Check

It was applied by Ithenticate®.

## Peer Review Process

It was performed.

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## References

1. Newby J, Tang S, Faasse K, Sharrock M, Adams. Commentary on: Understanding Breast Implant Illness. *Aesthetic Surgery Journal*, 2021, v.41, n.12, p.e 1367–1379.
2. Tervaert JWC, Shoenfeld Y, Cruciani C, Scarpa C, Bassetto F. Breast implant illness: Is it causally related to breast implants? *Autoimmun Rev*. 2024 Jan;23(1):103448. doi: 10.1016/j.autrev.2023.103448.
3. Cohen Tervaert JW, Mohazab N, Redmond D, van Eeden C, Osman M. Breast implant illness: scientific evidence of its existence. *Expert Rev Clin Immunol*. 2022 Jan;18(1):15-29. doi: 10.1080/1744666X.2022.2010546.
4. Atiyeh B, Emsieh S. Breast Implant Illness (BII): Real Syndrome or a Social Media Phenomenon? A Narrative Review of the Literature. *Aesthetic Plast Surg*. 2022 Feb;46(1):43-57. doi: 10.1007/s00266-021-02428-8.
5. Kaplan J, Rohrich R. Breast implant illness: a topic in review. *Gland Surg*. 2021 Jan;10(1):430-443. doi: 10.21037/gs-20-231.
6. FDA – US Food and Drug Administration. Medical Device Reports for Systemic Symptoms in Women with Breast Implants. US Food and Drug Administration, 2020. Disponível em: <<https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-systemicsymptoms-women-breast-implants>>. Acesso em: 5 , outubro, 2022.
7. Lee M, Ponraja G, Mcleod K, Chong S. Breast Implant Illness: A Biofilm Hypothesis. *Plastic and Reconstructive Surgery – Global Open*, 2020, v.8, n.4, p.e2755.
8. SBCP – Sociedade Brasileira de Cirurgia Plástica. Nota de Esclarecimento. Sociedade Brasileira de Cirurgia Plástica, 2021. Disponível em: <http://www2.cirurgioplastica.org.br/2021/02/03/nota-de-esclarecimento-4/>>. Acesso em: 5, outubro, 2022.
9. StataCorp. 2019. Stata: Release 16. Statistical Software. College Station, TX: StataCorp LLC.
10. Wee CE, Younis J, Isbester K, Smith A, Wangler B, Sarode AL, Patil N, Grunzweig K, Boas S, Harvey DJ, Kumar AR, Feng LJ. Understanding Breast Implant Illness, Before and After Explantation: A Patient-Reported Outcomes Study. *Annals of Plastic Surgery*, 2020, v.85, n.1, p.82-86.
11. Bresnick SD. Self-Reported Breast Implant Illness: The Contribution of Systemic Illnesses and Other Factors to Patient Symptoms. *Aesthet Surg J Open Forum*. 2023 Mar 27;5:ojad030. doi: 10.1093/asjof/ojad030.
12. Nagy ÈS, Westaway M, Danieleto S, Afrin LB. Breast Implant Illness May Be Rooted in Mast Cell Activation: A Case-Controlled Retrospective Analysis. *Ann Surg Open*. 2024 Mar 13;5(1):e398. doi: 10.1097/AS9.0000000000000398.