

## Dental Implant Failure as a Risk Factor for Selective Serotonin Reuptake Inhibitors: A Study of Clinical History

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### Abstract

Antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), have seen an exponential rise in popularity in recent decades in Europe and the United States. This retrospective study wanted to find out if there was a link between taking SSRIs and dental implant (DI) failure or survival, and secondarily, how other systemic and local factors affected it. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) observational study guidelines were followed in this retrospective cohort study. 573 DIs were given to 170 patients altogether. The reported failure rate for DI was 6.11 percent. 18.31 percent of these failed in patients who were prescribed SSRIs, while 4.38 percent failed in patients who were not. In particular, the multivariate analysis revealed 3.70 times higher adjusted risk and a 4.53 times higher hazard ratio for DI failure when these drugs were used. These patients also had a lower rate of DI survival at 90 months compared to those who did not take them. With the restrictions of the current review, it tends to be certified that there is a connection between the admission of SSRIs and DI disappointment, as well as a lower endurance rate in these patients.

**Keywords:** Failure of dental implants; Difficulties with dental implants; Implants for teeth; Inhibitors of the serotonin reuptake system; SSRI; Antidepressant

### Introduction

Although certain risk factors may predispose to lower success rates, dental implants (DIs) are the most predictable treatment option for the total or partial replacement of missing teeth. Recently, it has been suggested that taking antidepressants can increase the likelihood of DI failure [1]. The prescription of antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), increased by 20% annually in Europe.<sup>2</sup> According to data published by the Norwegian Institute of Public Health, there was a 107% increase in the consumption of these medications in Europe. In the past year, 7.20 percent of adults in the United States had experienced a major depressive episode, and 13.20 percent had been prescribed antidepressants in the previous 30 days.

People who have recovered from acute COVID-19 appear to have lower mental health quality, elevated levels of anxiety, depression, and post-traumatic stress disorder. Nearly one in five COVID-19 survivors, including 5.80% of those with new-onset conditions, were found to have received a psychiatric diagnosis within three months of their COVID-19 diagnosis in a recent US cohort analysis [2]. In fact, the risk of receiving a new psychiatric disorder diagnosis was more than twice as high as the risk of other health events.<sup>5</sup> Despite this, oral issues persisted throughout the initial months of the pandemic, and the fear of spreading the disease led a significant number of patients (24.50 percent) to avoid going to the dentist. The population's oral health has suffered as a result of these factors. Additionally, the use of antidepressants has been linked to dry mouth as a side effect of psychiatric disorders and poor oral health as a result of lifestyle and dietary changes. Particularly, these patients have a 1.21- and 1.22-fold increased risk of tooth decay and loss [3]. DIs will be required to replace missing teeth in an increasing number of antidepressant patients for all of these reasons.

The purpose of this study was twofold: first, to assess the impact of SSRI use on DI failure, and second, to assess the impact of other systemic and local factors.

For restoring edentulous areas, dental implants are increasingly

becoming the treatment of choice. According to data from the National Health and Nutrition Examination Survey, the prevalence of dental implants increased from 0.7% to 5.7%, according to a study [4]. If the current rate of growth in the number of dental implants is maintained, it was anticipated that the prevalence of dental implants would reach 17% by the year 2026.

Cone-beam computed tomography (CBCT) imaging of the implant site in three dimensions is one of the most important tools for implant treatment planning and placement. Cross-sectional pictures created from CBCT, alongside embed arranging programming programs, help in assessing the embed site for bone levels and closeness to critical designs like the floor of the sinus and the sub-par alveolar nerve. This lets the doctor plan the procedure to make sure the implant is in the right place and won't touch any important anatomical structures that are close by.

Due to their mechanical properties, high resistance to corrosion, and biocompatibility, titanium or titanium alloys are typically used in the fabrication of traditional dental implants. However, using metallic implants comes with a number of drawbacks [5]. Esthetically, titanium implants frequently cause gingival discoloration, which can be particularly noticeable in patients with a high smile line or a thin gingival biotype. Additionally, titanium-based dental implants may not be available to patients who are allergic to titanium.

In particular in the anterior esthetic zone, ceramic implants have been increasingly regarded as viable alternatives to titanium implants

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over the past ten years. The survival, success, and bone loss rates of ceramic implants and traditional titanium implants were found to be comparable. The metallic artifact that is produced when CBCT images titanium implants is one of their radiographic drawbacks.

## Materials and Procedures

All 170 patients who received 573 DIs and were then treated with implant-supported prostheses (ISP) were included in this retrospective cohort study. Consistent with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) observational study guidelines, the study was carried out in accordance with the Declaration of Helsinki's guidelines. The inclusion and exclusion criteria for the patient sample are listed below.

### Inclusion criteria

Patients of both sexes over the age of 18 who were fully or partially edentulous, had undergone maxillary or mandibular rehabilitation with DIs, and met the inclusion criteria [6]. They were type I or type II patients according to the American Society of Anesthesiologists (ASA) classification, had at least a one-year follow-up following ISP loading, and smoked less than ten cigarettes per day. Patients taking SSRIs ought to have been on treatment for somewhere around one year before the arrangement of the DIs.

Patients with severe systemic disease, untreated or uncontrolled periodontal disease, pregnant women, medical conditions related to altered bone metabolism, and patients who were not maintaining their implants were excluded. also patients with immunosuppression, patients who smoke less than 10 cigarettes per day, patients who are currently receiving head and/or neck radiotherapy or chemotherapy treatment, and patients who had such treatment less than two years ago.

### Exclusion criteria

Surgical phase of the clinical protocol A preliminary study using orthopantomography and cone-beam computed tomography (CBCT) for radiological diagnosis and planning was carried out on each case. Without the use of intravenous sedation, local anesthesia was used [7]. In patients with sufficient bone, DIs were inserted. Six months prior to DI placement, horizontal guided bone regeneration was carried out for transverse bone deficits. In cases requiring a sinus lift, this procedure was carried out eight months prior. Particulate bone grafts of heterologous origin and resorbable collagen barrier membranes were the materials used in bone regeneration. This study did not include more complicated regenerative methods.

### Postoperative period

The patients were rinsed twice daily for 14 days with 0.20 percent chlorhexidine digluconate. Amoxicillin 750 mg three times daily for seven days was given, and azithromycin 500 mg daily for three days was given to penicillin-sensitive patients. 14 days after the procedure, the sutures were removed. One and a half months after surgery, a clinical checkup with radiographic (periapical) control was done. Clinically, osseointegration was assessed at three months. DIs that had at least one of the following problems were deemed unsuccessful: apical peri-implantitis, suppuration, exfoliation of the ID, pain, mobility, radiographic bone loss that is equivalent to one third of the length of the DI, or pain.

Patients were checked once a year after the ISP was installed at one, three, and six months for the first year. Radiological control (periapical), periodontal maintenance, and oral hygiene technique

reinforcement were all carried out at each annual checkup. Patients were kept in the loop until one of the following happened: Failure of the DI, the patient's death, or the patient's exclusion from the study due to treatment withdrawal; or the study period came to an end.

## Statistical analyses

IBM SPSS Statistics 28 and R software were utilized for statistical analysis. The qualitative variables' absolute and relative values, as well as quantitative variables' measures of central tendency and variability, were analyzed using descriptive statistics [8]. The Kolmogorov-Smirnov test, which was used to define non-parametric tests, was used to confirm that assumptions of normality for quantitative variables were correct. The chi-squared test for ordinal variables and the Mann-Whitney test for continuous variables were utilized in bivariate analyses in inferential statistics to establish a correlation between variables and the condition of failure or not of the DI. The log-rank test (Mantel-Cox) was used to compare the curves for DI survival analysis. Cox regression was used to estimate the risk of DI failure, taking into account the significance of the survival curves for SSRIs, diabetes, smoking, and length. Univariate and multivariate analysis of these variables was also done.

## Results

### Characteristics of the patients and the DIs placed

There were a total of 170 patients included, and 573 DIs were applied to them. The DI failure rate was 6.11 percent, with late failures accounting for 68.57% and early failures for 31.43% [9]. The standard deviation (SD) ranges from 12 to 18 weeks; the median time to early DI failure was 13 weeks, and the median time between symptoms and explantation was two weeks. Mobility was the most common indicator of DI failure, followed by pain, bone loss, suppuration, apical peri-implantitis (8.57%), and DI exfoliation. the patients' and DIs' characteristics.

### Influence of systemic factors on DI failure

We looked at how systemic factors affected the rate of DI failure. When SSRI-treated patients were compared to untreated patients, there was a statistically significant increase in DI failure [10]. Additionally, these patients had significantly more DI exfoliation than the general population.

Patients with hyperlipidemia did not have significantly higher failure rates than patients with adequate lipid values or arterial hypertension (AH). When compared to nonsmokers, failure rates were higher among smokers. There were significant differences in the proportion of DI failures between diabetic and non-diabetic patients.

DIs with late-stage failure were subjected to survival analysis in patients taking SSRIs. In particular, patients who did not take SSRIs had a survival rate of 96%, whereas DI patients had a survival rate of 84.30%.

## Discussion

The World Health Organization (WHO) has estimated that depression affects over 350 million people worldwide. Serotonin, also known as 5-hydroxytryptamine (5-HT), is a monoamine that plays a role in fostering feelings of happiness and well-being [11]. Depression can result from low levels or difficulty using this neurotransmitter. SSRIs are now the most commonly prescribed antidepressant in the world because of their effectiveness in treating depression. SSRIs may have an impact on the digestive, cardiovascular, and skeletal systems

due to the presence of serotonin receptors in peripheral tissues like the digestive tract, platelets, and bones, in addition to nervous tissue. Additionally, it has been discovered that these drugs concentrate more strongly in the bone marrow than in the blood or brain. Serotonin, in particular, causes a complex cascade of signals to be sent to osteoblasts and osteoclasts by binding to receptors and 5-HTTs in bone cells. This is because SSRIs inhibit 5-HTTs in bone cells, which has negative effects on bone metabolism and formation, increases osteoclast differentiation, and slows osteoblast proliferation. SSRIs reduce bone mass and bone mineral density (BMD) as a result.

It is interesting to note that taking an SSRI medication simultaneously reduces osteoblast marker genes like alkaline phosphatase, osterix, and osteocalcin and significantly reduces osteogenic differentiation and mineralization [12]. This suggests that the medication may have an effect on how bone metabolism is controlled. As a result, these cellular findings would be consistent with the findings of those who demonstrated an increased risk of DI failure in patients taking SSRIs. Additionally, it is important to take into account the possibility that a patient's psychological state rather than their use of SSRIs may play a role in their increased risk of DI failure. As a result of epigenetic changes, depression as a whole has a negative impact on oral health by making people less likely to cooperate with dental treatments and practice good oral hygiene [13]. The likelihood of developing periodontal disease and, consequently, peri-implant diseases is raised by these factors. Additionally, the pathological activation of various molecules of the adrenergic signaling axis by depression has an impact on the organism's physiological homeostasis. SSRIs, on the other hand, influence the onset and severity of sleep bruxism, acting as a factor of functional overload of the DI system, and causing mechanical complications that may lead to DI failure. This generates a cascade of hormonal, biologically active peptides and cytokines that are neurobiologically associated with depression, as well as possibly even periodontitis and peri-implantitis.

Analyzing a sample of 2056 patients with 5302 DIs using the available systematic reviews and meta-analyses, we discovered a risk ratio (RR) for DI failure linked to the use of these drugs. An odds ratio (OR) for DI failure in the experimental group versus failure in the control group was calculated using the fixed effects model in another study. 3.00 was the outcome of the random-effects model. The fixed-effects and random-effects models, on the other hand, estimated a difference in DI failure of 7.48 percent ( $p = 0.01$ ) and 7.50 percent ( $p = 0.01$ ), respectively, with higher DI failure rates in the experimental group (SSRIs) than in the control group and an OR of DI failure of 3.00 ( $p = 0.36$ ) in the SSRI group [14]. As a result, a significant effect of SSRIs was found. Both the univariate and multivariate analyses yielded HRs, which are consistent with the findings of the current study. In a similar vein, patients who did not take SSRIs had a survival rate of 96% compared to 84.30% in patients who did. This rate is lower than what is reported in other studies.

## Limitation

The fact that the doses and patterns, as well as the time of intake prior to and following the placement of the DI, are not recorded in patients treated with SSRIs is the primary limitation of this study as well as previous research in the literature.

## Future research directions

The goal of future research directions ought to be to investigate the connection between the ability of several neurotransmitters to be modulated and brand-new antidepressants with multimodal

action, as well as the effect of depression on the survival of DIs that is independent of SSRIs [15]. It would be prudent to conduct studies with larger samples and methodological rigor in order to generate guidelines for action in these patients based on the active ingredient, dosage, and treatment duration.

## Conclusion

Despite the limitations of this study, it can be concluded that taking SSRIs increases one's risk of DI failure and increases one's risk of depression. The use of these drugs has been linked to a DI failure rate that is 4.53 times higher. What's more, a lower endurance rate at 90 months follow-up was seen in these patients contrasted and those not consuming these medications.

## Acknowledgement

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## Conflict of Interest

None

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