Review Article

Implant survival in patients with neuropsychiatric, neurocognitive, and neurodegenerative disorders: A meta-analysis

ABSTRACT

Neurologic disorders impede oral hygiene measures and routine clinical follow-up, along with the various drugs used may jeopardise oral health and the peri- implant tissue health. A total of 7 studies were considered eligible for the current systematic review. The overall estimated effect was categorized as significant where $P < 0.05$. Funnel plot was used to assess the publication bias within the studies. Difference in means was used as principal summary measure. P value <0.05 was considered as statistically significant. 1069 implants survived in test group and 4677 implants survived in control group (odds ratio: 2.58, 95% CI: 1.93-3.43) indicating significant success in patient without any disorders or taking medications for these disorders. Subgroup analysis was done to check the implant survival rate in patients taking selective serotonin reuptake inhibitors (SSRI) compared with SSRI non-users. Subgroup analysis showed that SSRI non-users had higher implant survival rate than patients taking SSRI (odds ratio: 2.45, 95% CI: 1.82-3.31). Serotonin significantly inhibits bone mineralization and osteoblast differentiation. The presence of any form of neuropsychiatric or neuromuscular disorders precludes proper oral hygiene and may contribute towards implant failure.

Keywords: Implant survival, implants and neurologic patients, neuropsychiatric disorders

INTRODUCTION

Rationale

Tooth loss has a major influence on oral health in geriatric patients. Inability to masticate food adequately due to tooth loss can lead to decreased nutrition and affect general health in edentulous patients.[1,2] Dental implants are becoming one of the most predictable treatment modalities to combat edentulism.[3,4] The prevalence rate of neuropsychiatric and neurocognitive disorders (NDs) among individuals is increasing in recent times. Various neuropsychiatric symptoms, such as agitation, depression, apathy, delusions, and hallucinations, are highly prevalent in older adults with dementia or milder forms of cognitive impairment. These symptoms can lead to a higher risk of functional decline.[5-10] In a recent cross-sectional analysis in US individuals, it was found that depression was the most common individual symptom in those with normal cognition (12%), cognitive impairment, not demented (30%), and mild dementia (25%), whereas apathy (42%) and agitation (41%) were most common in those with severe dementia.[11] Cognitive impairment (CI) is one of the natural outcomes of the progression of Alzheimer's disease (AD) and other NDs. Studies based on clinical data report showed an increase in the prevalence of AD and other NDs leading to dementia.[12] The Alzheimer's Association recently reported that there

Rathindra Nath Bera, Richik Tripathi, Bappaditya Bhattacharjee[1], Akhilesh Kumar Singh, Shweta Kanojia, Vikram Kumar[1]

Departments of Oral and Maxillofacial Surgery and [1]Prosthodontics, Faculty of Dental Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Address for correspondence: Dr. Rathindra Nath Bera, E-10, Aurobindanagar, Judges Court, Midnapore - 721 101, West Bengal, India.
E-mail: rathin12111991@gmail.com

Received: 20 October 2020, **Revised:** 25 November 2020, **Accepted:** 28 January 2021, **Published:** 15 July 2021

Access this article online	
Website: www.njms.in	Quick Response Code
DOI: 10.4103/njms.NJMS_230_20	

How to cite this article: Bera RN, Tripathi R, Bhattacharjee B, Singh AK, Kanojia S, Kumar V. Implant survival in patients with neuropsychiatric, neurocognitive, and neurodegenerative disorders: A meta-analysis. Natl J Maxillofac Surg 2021;12:162-70.

is an overall increased number of NDs in the last 25 years despite a decrease in the last 3–4 years.[13] Prosthodontic rehabilitation in patients with neurological disorders needs a specific approach because these patients belong to a class with special needs. Progression of the neurological disease and the side effects of the neurological medication on the oral cavity can modulate maintenance of oral hygiene and professional care during the recall system (follow-up) for this group of patients.[14] The implant survival rate is dependent on the maintenance of oral hygiene in patients having dental implants and plaque index and other periodontal indices. Serotonin (5-hydroxytryptamine) is a monoamine neurotransmitter that modulates well-being and happiness in any individual. Depression can be caused by lower levels of serotonin and blockage in its circulatory pathway.[15] Selective serotonin reuptake inhibitors (SSRIs) such as Celexa, Paxil, Lexapro, Prozac, and Zoloft have become widely used antidepressants by inhibiting the reuptake of serotonin and boost its levels to treat depression.[16] Deranged metabolism of peri-implant bone in healing period is one of the reasons of implant failures.[17-19] Various pharmacological therapies either directly or indirectly modulate bone metabolism.[20]

Objectives

The purpose of this present systematic review (SR) is to evaluate how implant survival rate changes in patients suffering from neuropsychiatric or NDs or any medications used in these disorders.

METHODS

Protocol

The current SR has been prepared according to the equator guidelines (https://www. equator-network.org) and Prisma Statement (http://prisma-statement.org/).[21] The study is registered with Prospero (https://www.crd.york.ac.uk/PROSPERO/) ID: CRD42020201520.

Eligibility criteria

The Patient, Intervention, Comparison, Outcome, and Study Questionnaire[22,23] has been used to assess the eligibility of the studies.

Focus question: What is the effect of neurodegenerative, neurocognitive, and neuromuscular disorders on survival of dental implants?

Inclusion criteria

1. Studies evaluating the dental implant survival in patients with neurodegenerative, neurocognitive, neuromuscular disorders and patients on antidepressant drugs
2. Human studies
3. Randomized and nonrandomized clinical trials and observational studies.

Exclusion criteria

1. Isolated case reports
2. Animal studies
3. Inadequate follow-up.

Information sources

Electronic database: MEDLINE (PubMed), https://www.ncbi.nlm.nih.gov/pubmed/; EMBASE, https://www.embase.com/; and Cochrane database http://www.cochranelibrary.com.

Others: Hand searches were done where articles or abstracts were not available electronically.

Search terms

Population: # (Adults) or (elderly) or (edentulous) or (antidepressants) or (SSRIs) or (Parkinson) or (Alzheimer) or (psychiatric) or (neurocognitive) or (neurodegenerative) or (neuromuscular).

Intervention: # (dental implants) or (implants) or (prosthesis).

Comparator: # (healthy adults) or (normal adults) or (healthy individuals).

Outcome: # (implant failure) or (survival rate) or (survival) or (failure) or (marginal bone loss) or (complications).

Study Design: # (Randomized clinical trial) or (nonrandomized trials) or (prospective) or (retrospective).

Filters

- Language – Not applied
- Species – Human
- Ages – middle aged, young, aged, and older
- Journal categories – Dental, oral surgery, implant dentistry, and dentistry
- Search dates – 1986–June 2020.

Study selection

Two reviewers (RNB and BB) screened all identifiable titles and abstracts independently. In addition, the reference lists of the subsequently selected abstracts and the bibliographies of the SRs, human randomized and nonrandomized controlled trials (RCTs), and prospective and retrospective cohort studies were searched manually. For studies appearing to meet the inclusion criteria, or for which insufficient data in the title and abstract were available, the full text was obtained. Disagreements were solved through discussion between the reviewers. The inter-rater reliability was assessed using

Cohen's kappa; values ≤0 indicated no agreement, 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as perfect agreement. Regarding the translation of studies from other languages, two independent translators blinded to the outcome translated the entire manuscript into English. Disagreements were again sought with discussion, and kappa statistics was used to assess inter-rater reliability.[24] Finally, the full-text evaluation of the remaining publications was done using the above-listed inclusion and exclusion criteria.

Data extraction

Two reviewers (RNB and BB) independently extracted data from the included studies. Disagreements were again resolved through discussion. With respect to the listed question of our SR, data were sought for predictor variables, i.e., dental implants in patients with neurodegenerative, neurocognitive, neuromuscular disorders and patients taking antidepressants. Both reviewers evaluated the primary outcome of the study and the survival of dental implants. The secondary outcomes assessed were implant-related complications.

Quality of the studies

The quality assessment of the selected studies was executed by the Newcastle–Ottawa Scale.

Stars were awarded such that the highest quality studies were awarded up to nine stars. The oxford level of evidence 2011 was used to assess the strength of each study. The levels of evidence of our selected studies were of III and IV categories.

The Oxford 2011 Levels of Evidence[25,26]

Level category of evidence:

I SR (with homogeneity) of RCT
- Individual RCT.

II SR (with homogeneity) of cohort studies
- Individual cohort study (including low-quality RCT, for example, <80% follow-up)
- "Outcome" research and ecological studies.

III SR (with homogeneity) of case–control studies
- Individual case–control study.

IV Case series and poor-quality cohort and case–control studies

V Expert opinion without explicit critical appraisal, or based on physiology, bench research, or first principles.

Statistical analysis

Statistical software RevMan (Review Manager [Computer program], version 5.3, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for meta-analysis. The overall estimated effect was categorized as significant where $P < 0.05$. Chi-square test and I^2 were used to measure heterogeneity among the studies. A value of <25% indicated a lack of heterogeneity. A funnel plot was used to assess the publication bias within the studies. Difference in means was used as a principal summary measure. Z-test was used to measure the statistical significance. $P < 0.05$ was considered statistically significant.

RESULTS

Study selection

The literature search yielded a total of 344 articles from PubMed electronic database ($n = 344$). In addition to this, a hand search of references mentioned in articles was done. After removal of the duplicates ($n = 72$), initial screening of titles and abstracts was performed by two independent reviewers (RB and BB). Eighteen articles were selected for full-text reading, seven studies were included for qualitative and quantitative analysis,[27-33] and eleven studies were excluded [Figure 1]. Any disagreements between reviewers during study selection process were solved by discussion. Kappa statistics was used to assess the inter-rater reliability among the reviewers. A coefficient value between 0.61 and 0.80 indicated substantial agreement. Non-English articles were translated by two independent translators, and Cohen's kappa was used to address the reliability. A kappa value of 1.00 indicated definitive agreement.

Study characteristics

The characteristics of the included studies are shown in Table 1. The common baseline characteristics of the included

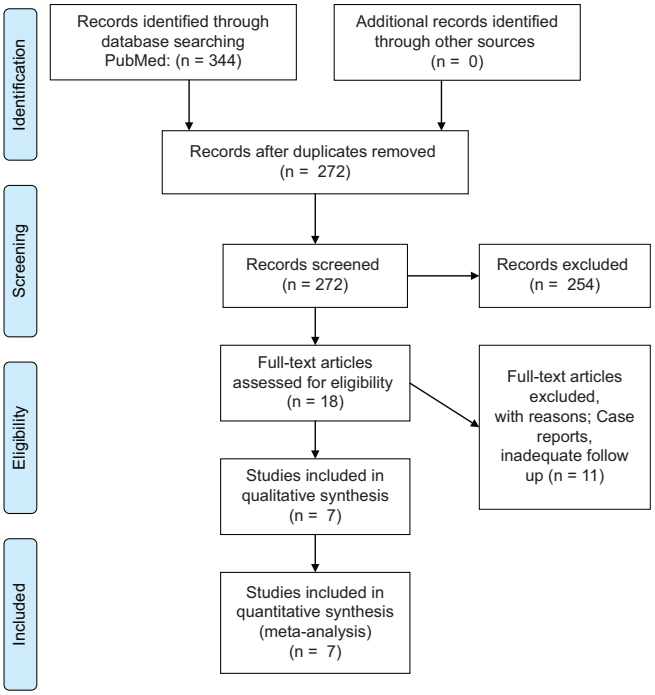

Figure 1: Study selection according to Prisma guidelines

Table 1: Characteristics of included studies

Study	Study design	Country	Sample characteristics	Intervention	Follow-up
Packer *et al*. (2009)[27]	Prospective	United Kingdom	Sample size - nine individuals Gender - male (9), female (0) Age range - 54-77 years (mean 63 years)	Nine patients who were definitively diagnosed suffering from Parkinson's disease were included in the study and implant placement was done "The DIDL assessment" assessed on the 3rd and 12th month after placing provisional final prosthesis DIDL composed of two components - The OH-QoL inventory and the SROH and functional status	Third and 12th month after completion of treatment
Ekfeldt *et al*. (2013)[28]	Prospective	Norway	Sample size: Twenty-seven individuals Gender - Male (14), female (13) Age - 19 to 80 years (mean - 46 years)	Patients with various neurological disabilities were included in the study. After completion of implant placement in all the patients, five patients died during observation period. Twelve implant-supported crowns and 17 implant-supported fixed prostheses were fabricated. Implant survival rate, bleeding on probing was measured during 5-10 years follow up	5-10 years
Wu *et al*. (2014)[29]	Retrospective	Canada	Sample size - Four hundred and ninety patients Gender - male (198), female (292) Age - 17-93 years averaging 56.4±13.7 years	This retrospective cohort study was conducted on patients treated with dental implants from January 2007 to January 2013. A total number of 916 dental implants were placed in the included patients, out of which 94 implants were placed in SSRI users whereas 822 implants were in SSRI nonusers. Implant survival rate calculated in both the groups during the follow-up period	3-67 months after completion of treatment
Chrcanovic *et al*. (2017)[30]	Retrospective	Sweden	Sample size - Three hundred patients Gender and age - 145 men (mean age 55.9±18.5, range 15.9-82.6 years), 155 women (mean age 56.0±17.8 years, range 14.9-90.8 years)	Patients treated with implant supported prostheses in between 1980 and 2014 at one specialist clinic (clinic for prosthodontics, center of dental specialist care, Malmo¨, Sweden) were included in the study. Patients who took SSRI type of medication during the presurgery appointment that was scheduled 1-2 weeks prior to implant placement categorized as SSRI users The outcome variable in this study was implant failure. Signs and symptoms which led to implant removal, including lack or loss of osseointegration, implant mobility, continuous pain, advanced marginal bone loss, and refractory infection, were considered as implant failure	Within 6 months after the final implant-supported/ retained restoration
Altay *et al*. (2018)[31]	Retrospective	Turkey	Sample size - Six hundred and thirty-one patients Gender and age - female (339), 51 years (18-84 years) Male (292), 50.57±14.18 years, range: 17-87 years	Patients who were treated with dental implants between May 2012 and March 2017 were included in the study Inclusion criteria were patients with no systemic conditions and not taking any other medications except SSRI for psychiatric disorders An SSRI user was defined as a patient who reported taking any type of SSRI medication perioperatively Osseointegration failure was the outcome variable in this study, which was considered as the condition leading to early implant removal before prosthetic loading due to implant mobility and advanced peri-implant bone loss	Median duration of follow-up was 21.5 (4-56) months for SSRI users and 23 (3-60) months for nonusers
Deepa *et al*. (2018)[32]	Retrospective	India	Sample size - Three hundred and fifty-two patients Gender - male (150), female (204) Age - >50 years (95), <50 years (257)	Three hundred and fifty-two patients of both genders were included in this retrospective study who were rehabilitated with a total of 680 dental implants. Included patients were divided into two groups: Group I (110 patients, 230 dental implants) was on SSRI users, while Group II (242 patients, 450 dental implants) was non-SSRI users Implant survival rate defined by analyzing the following factors fracture of implant, prosthesis screw fracture, and loosening of screw, and features of peri-implantitis, such as radiolucency around implant apex and bone loss around implants	Not mentioned

Contd...

Table 1: Contd...

Study	Study design	Country	Sample characteristics	Intervention	Follow-up
Carr *et al*. (2019)[33]	Retrospective	USA	Sample size - 5456 patients Gender - female (3143) (58%), male (2313) (42%) Age - median age 53 years (interquartile range 40-64 years)	Patients who underwent first implant placement in Mayo Clinic (Rochester, MN) from January 1, 1995, through December 31, 2014, were included in this study. Inclusion of patients was done after assessing their history of SSRI use, active SSRI use, and SSRI use during follow-up with implant failure. Cox proportional hazards regression models were used to check associations between demographic characteristics and SSRI use with implant failure, and outcomes were summarized with HRs and 95% CIs	The median duration of follow-up was 5.3 years (interquartile range, 2.3-10.2 years)

DIDL: Dental impact on daily living, OH-QoL: Oral health quality of life, SROH: Self-reported assessment of oral health, BOP: Bleeding on probing, SSRI: Selective serotonin reuptake inhibitor, HRs: Hazard ratios, CIs: Confidence intervals

Table 2: Implant characteristics of the included studies

Study	Implant system	Number of implants placed	Number of implants survived	Loading protocol	Prosthesis type
Packer *et al*. (2009)[27]	Astra-Tech implants	28	23	Conventional	Implant-supported/retained fixed prosthesis, single crown, overdentures
Ekfeldt *et al*. (2013)[28]	Nobel Biocare	70	58	Conventional loading protocol in 23 patients, early loading period in 3 patients, and immediate loading in 1 patient	Implant-supported/retained fixed prosthesis, single crown, overdentures
Wu *et al*. (2014)[29]	Nobel Biocare	Test group - 94, control group - 822	Test group - 84, control group - 784	Conventional	Not mentioned
Chrcanovic *et al*.[30] (2017)	TiUnite, Nobel Biocare AB	Test group - 48, control group - 883	Test group - 42, control group - 854	Conventional	Not mentioned
Altay *et al*. (2018)[31]	TPS or sand-blasted acid-etched surfaces	Test group - 109, control group - 1946	Test group - 107, control group - 1935	Delayed	Not mentioned
Deepa *et al*. (2018)[32]	Nobel Biocare	Test group - 230, control group - 450	Test group - 205, control group - 429	Conventional	Not mentioned
Carr *et al*. (2019)[33]	Nobel Biocare, TiUnite system	613	550	Not mentioned	Not mentioned

TPS: Titanium plasma sprayed

studies were study, study design, country, sample description, intervention, and follow-up. Implant characteristics and prosthesis type used in different studies are tabulated in Table 2.

Quality analysis

The quality of the included studies was determined by the Newcastle–Ottawa Scale. Among the included studies, seven studies were of good quality according to predetermined mentioned criteria. All the studies selected the nonexposed cohort from the same source. Deepa *et al*.[32] did not mention about the duration of follow-up in the study (two stars in outcome/exposure domain). The qualities of the included studies are shown in Table 3.

Data synthesis

Meta-analysis was done of seven included studies using fixed-effect model. To identify study heterogeneity, I^2 test statistics was applied ($I^2 < 25\%$ – no heterogeneity, I^2 value 50%–75% – serious heterogeneity), and $P < 0.05$ was considered significant statistically. Forest plots were produced for the outcome variables with 95% confidence interval and overall treatment effects and subgroup effects at a significance level of 0.05. Funnel plot asymmetry was checked to report any publication bias. A total of 1192 implants were placed in patients suffering from neuropsychiatric/NDs or taking any medications for these disorders, and a total of 4812 implants were placed in the control group. Of these, 1069 implants survived in the test group and 4677 implants survived in the control group (odds ratio: 2.58, 95% CI: 1.93–3.43) indicating significant success in patients without any disorders or taking medications for these disorders. I^2 value was 0% in this analysis, and Chi-square value was less than degree of freedom showing low heterogeneity in this study [Figure 2]. Subgroup analysis was done to check the implant survival rate in patients taking SSRIs compared with SSRI nonusers. Subgroup analysis [Figure 3] showed that SSRI nonusers had a higher implant survival rate than patients taking SSRI (odds ratio: 2.45, 95% CI: 1.82–3.31). Tests for

Table 3: Newcastle-Ottawa Scale for quality rating of included studies

Study	Representativeness of the exposed cohort (star)	Selection of the nonexposed cohort (star)	Ascertainment of exposure (star)	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for confounders (star)	Assessment of outcome (star)	Was follow-up long enough for outcomes to occur (star)	Adequacy of follow-up of cohorts (star)
Packer *et al.* (2009)[27]	1	1	1	-	1	1	1	1
Ekfeldt *et al.* (2013)[28]	1	1	1	-	1	1	1	1
Wu *et al.* (2014)[29]	1	1	1	-	1	1	1	1
Chrcanovic *et al.* (2017)[30]	1	1	1	-	1	1	1	1
Altay *et al.* (2018)[31]	1	1	1	-	1	1	1	1
Deepa *et al.* (2018)[32]	1	1	1	-	1	1	-	1
Carr *et al.* (2019)[33]	1	1	1	-	1	1	1	1

funnel plot asymmetry [Figure 4] showing both positive and negative studies were included in this study as studies are present on both sides of the vertical line.

DISCUSSION

Removable prosthesis manipulation demands a well neuromuscular coordination from the edentulous patients. There is an important role of neuromuscular coordination in functioning of dental prosthesis. It is therefore obvious that neuropsychiatric/NDs can create severe obstacles to the serviceability of the removable dentures. The tremulous muscle motion and lessened muscular power characterizing Parkinson's disease or other movement disorders render the use of dentures very difficult. Therefore, it is better to rehabilitate these patients with some fixed alternatives. Furthermore, the anticholinergic agents and antidepressants used in these disorders can cause severe xerostomia and burning of dry and emaciated mucosa. Reduced salivation also causes more accumulation of plaque and other debris which can be responsible for postoperative periodontal problems in case of fixed prosthesis.[34] There is little scientific evidence till now for the use of implants in neurological conditions. Previously, one report based on three cases of edentulous people with Parkinson's disease rehabilitated with implant-supported dentures showed a positive impact on general health of patients.[35] Another study used magnets as an attachment system for an implant-supported overdenture.[36] Implant-retained complete dentures have also been used in patients with cerebral palsy.[37] Implant survival rate or postoperative complications in patients with these disorders cannot be predicted depending on these case reports. There are a very few number of prospective and retrospective studies available which evaluated implant survival rate in patients with neuropsychiatric/NDs. SSRIs are one of the commonly used groups of drugs in these neurological disorders in recent times. Nam *et al*.[38] showed in an animal study that serotonin has a significant role in reducing osteogenic differentiation and mineralization of cells. Serotonin also reduced the expression of osteoblast marker genes including Alpl (alkaline phosphatase), Sp7 (osterix), and Bglap (osteocalcin) and significantly inhibits β-tricalcium phosphate-induced bone regeneration.[39] Receptor activator of nuclear factor-kappa B ligand-induced osteoclast-like cells generally shows increased expression of serotonin receptor (5-HTT). Fluoxetine, an inhibitor of 5-HTT, showed reduced osteoclast differentiation in the result of the study. Results from the study showed that there may be a role for 5-HTT in osteoclast function and antidepressive agents may affect bone metabolism.[39] Another study demonstrated that the SSRI group of drugs has a detrimental effect on

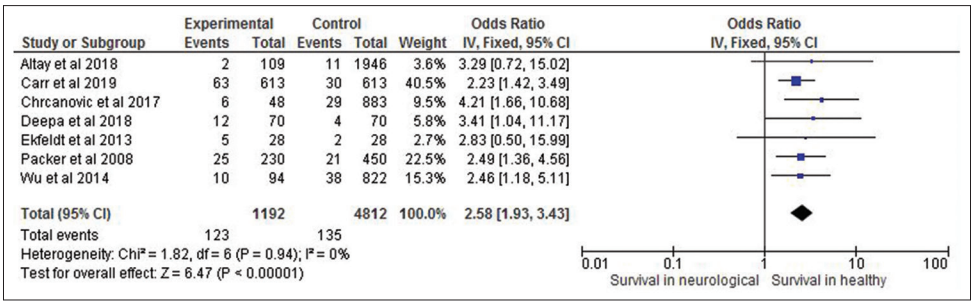

Figure 2: Forest plot indicating the significant success of dental implants in the control group

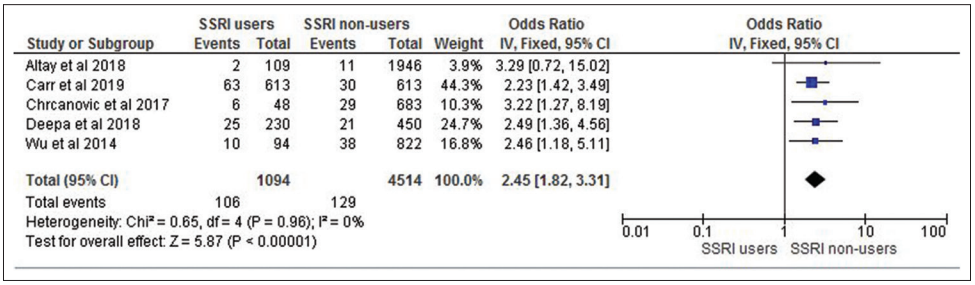

Figure 3: Forest plot for subgroup analysis

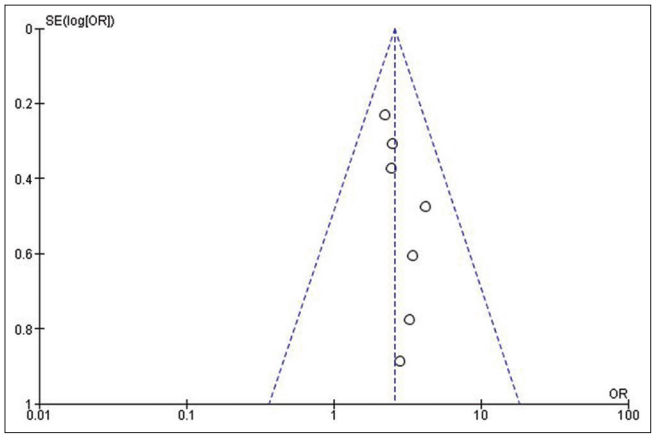

Figure 4: Funnel plot showing publication bias

bone mineral density and trabecular microarchitecture.[40] Endocrine, autocrine/paracrine, and neuronal pathways are responsible for the effect of SSRIs on bone metabolism. Previous data from *in vitro*, *in vivo* studies indicate that SSRIs have a negative effect on the bone at the therapeutic dose levels used for the treatment of neurological disorders.[41]

Wu *et al*.[29] conducted a retrospective cohort study on patients rehabilitated with dental implants, in which there were two groups. One group of patients was SSRI users, and the other group consisted of SSRI nonusers. After follow-up period, implants with at least one of the following complications were defined as failures: pain on function, mobility, radiographic bone loss equivalent to one-half of the implant length, uncontrolled exudate, or implant no longer in the mouth. Overall failure rates were 4.6% for SSRI nonusers and 10.6% for SSRI users. The authors concluded that this result supports the antianabolic effect of SSRI on bone metabolism. Deepa *et al*.[32] similarly selected patients with a history of depression and SSRI medication in a retrospective study. Patients with dental implants were divided into two groups depending on SSRI usage. SSRI user group showed a greater number of implant failures than the other group. Chrcanovic *et al*.[30] also showed that implant failure rate was 12.5% for SSRI users compared to 3.3% for nonusers ($P = 0.007$). Implant failure criteria were the same as in previous studies. In another study by Altay *et al*.,[31] 2 out of 36 SSRI users had one failed implant each, and the failure rate was 5.6%. Eleven nonusers out of 595 individuals also had one failed implant each, and the failure rate was 1.85% which was lower than the other group. Statistically, the odds of implant failure were 3.123 times greater for SSRI users compared to nonusers. Overall, the patients using SSRIs were found to be 3.005 times more prone to experience implant failure than the patients not using SSRIs. A retrospective review conducted by Carr *et al*.[33] evaluated all patients who received at least 1 dental implant placed in their mouth. The implant failure rate was assessed with their history of SSRI use, active SSRI use, and SSRI use during follow-up. Six different SSRI medications were assessed with implant failure, and only those patients who had a history of sertraline use showed a greater failure rate. Active users of this medication or those patients taking this medication after implant placement did not show any significantly higher failure rate. The authors stated that these results indicate long-term use of medications may lead to a sufficient blood

concentration of SSRI that may interfere with bone healing dynamics. All the studies included support the fact.

Packer *et al*.[27] rehabilitated nine patients with Parkinson's disease (with an age range of 54–77 years) with either implant-supported removable/fixed prosthesis. The implant success rate was 85% and 81% in the maxilla and mandible compared to the success rate of 85%–90% in the maxilla and 95% in the mandible in normal individuals. Various postinsertion problems aroused in this study during follow-up period such as fracture of overdentures, difficulty in removing appliances due to dexterity problem, and gingival hyperplasia under the attachment systems. Ekfeldt *et al*.[28] used patients suffering from various neurological disorders such as down syndrome, Asperger syndrome, mental retardation, and cerebral palsy as a test group. These patients also showed complications such as fracture of porcelain (due to extreme parafunctional movements), fracture of abutment, and implant due to self-destructive behavior. The overall implant failure rate was higher in these patients compared to healthy patients (12 out of 88 implants loosed).

Limitations

The limitations of this study were as follows: nonavailability of randomized controlled clinical trials and a smaller number of prospective and retrospective studies on influence of neuropsychiatric/NDs.

Generalizability

Overall data from included studies in this review signify the fact that there is always a chance of increased implant failures in patients with neuropsychiatric/NDs or patients taking any medication for these disorders.

CONCLUSION

Patients with neuropsychiatric, neurocognitive and neurodegenerative disorders are at an increased risk for implant failures.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Alvarenga MO, Ferreira RD, Magno MB, Fagundes NC, Maia LC, Lima RR. Masticatory dysfunction by extensive tooth loss as a risk factor for cognitive deficit: A systematic review and meta-analysis. Front Physiol 2019;10:832.
2. Bortoluzzi MC, Traebert J, Lasta R, Rosa TN, Capella DL, Presta AA. Tooth loss, chewing ability and quality of life. Contemp Clin Dent 2012;3:393-7./
3. Guillaume B. Dental implants: A review. Morphologie 2016;100:189-98.
4. Pjetursson BE, Heimisdottir K. Dental implants are they better than natural teeth? Eur J Oral Sci 2018;126 Suppl 1:81-7.
5. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment. JAMA 2002;288:1475-83.
6. Gonza´lez-Salvador MT, Arango C, Lyketsos CG, Barba AC. The stress and psychological morbidity of the Alzheimer patient caregiver. Int J Geriatr Psychiatry 1999;14:701-10.
7. Logsdon RG, Teri L, McCurry SM, Gibbons LE, Kukull WA, Larson EB. Wandering: A significant problem among community-residing individuals with Alzheimer's disease. J Gerontol B Psychol Sci Soc Sci 1998;53:294-9.
8. Lyketsos CG, Steele C, Baker L, Galik E, Kopunek S, Steinberg M, *et al*. Major and minor depression in Alzheimer's disease: Prevalence and impact. J Neuropsychiatry Clin Neurosci 1997;9:556-61.
9. Scarmeas N, Brandt J, Albert M, Hadjigeorgiou G, Papadimitriou A, Dubois B, *et al*. Delusions and hallucinations are associated with worse outcome in Alzheimer disease. Arch Neurol 2005;62:1601-8.
10. Scarmeas N, Brandt J, Blacker D, Albert M, Hadjigeorgiou G, Dubois B, *et al*. Disruptive behavior as a predictor in Alzheimer disease. Arch Neurol2007;64:1755-61.
11. Okura T, Plassman BL, Steffens DC, Llewellyn DJ, Potter GG, Langa KM. Prevalence of neuropsychiatric symptoms and their association with functional limitations in older adults in the United States: The aging, demographics, and memory study. J Am Geriatr Soc 2010;58:330-7.
12. Akushevich I, Yashkin AP, Kravchenko J, Ukraintseva S, Stallard E, Yashkin AI. Time trends in the prevalence of neurocognitive disorders and cognitive impairment in the United States: The effects of disease severity and improved ascertainment. J Alzheimers Dis 2018;64:137-48.
13. Alzheimer's Association. 2016 Alzheimer's disease facts and figures. Alzheimers Dement 2016;12:459-509.
14. Badea M, Muresanu DF. Dental care for patients with neurological disorders. Roman J Neurol 2008;1:10-3.
15. Krishnan V, Nestler EJ. The molecular neurobiology of depression. Nature 2008;455:894-902.
16. Liu B, Anderson G, Mittmann N, To T, Axcell T, Shear N. Use of selective serotonin-reuptake inhibitors or tricyclic antidepressants and risk of hip fractures in elderly people. Lancet 1998;351:1303-7.
17. Guobis Z, Pacauskiene I, Astramskaite I. General diseases influence on peri-implantitis development: A systematic review. J Oral Maxillofac Res 2016;7:e5.
18. Donos N, Calciolari E. Dental implants in patients affected by systemic diseases. Br Dent J 2014;217:425-30.
19. Marder MZ. Medical conditions affecting the success of dental implants. Compend Contin Educ Dent 2004;25:739-42, 744, 746.
20. Ouanounou A, Hassanpour S, Glogauer M. The influence of systemic medications on osseointegration of dental implants. J Can Dent Assoc 2016;82:7.
21. Moher D, Liberati A, Tetzlaff J, Altman DG; The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6:e1000097.
22. Eriksen MB, Frandsen TF. The impact of patient, intervention, comparison, outcome (PICO) as a search strategy tool on literature search quality: A systematic review. J Med Libr Assoc 2018;106:420-31.
23. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: A key to evidence-based decisions. ACP J Club 1995;123:A12-3.
24. McHugh ML. Interrater reliability: The kappa statistic. Biochem Med (Zagreb) 2012;22:276-82.
25. OCEBM Levels of Evidence Working Group. The Oxford Levels of Evidence 2. Oxford Centre for Evidence-Based Medicine. Available

from: https://www.cebm.net/index.aspx?o=5653. [Last accessed on 2020 Oct 02].
26. Howick J, Chalmers I, Glasziou P, Greenhalgh T, Heneghan C, Liberati A, *et al.* The 2011 Oxford CEBM levels of evidence (introductory document).
27. Packer M, Nikitin V, Coward T, Davis DM, Fiske J. The potential benefits of dental implants on the oral health quality of life of people with Parkinson's disease. Gerodontology 2009;26:11-8.
28. Ekfeldt A, Zellmer M, Carlsson GE. Treatment with implant-supported fixed dental prostheses in patients with congenital and acquired neurologic disabilities: A prospective study. Int J Prosthodont 2013;26:517-24.
29. Wu X, Al-Abedalla K, Rastikerdar E, Abi Nader S, Daniel NG, Nicolau B, *et al*. Selective serotonin reuptake inhibitors and the risk of osseointegrated implant failure: A cohort study. J Dent Res 2014;93:1054-61.
30. Chrcanovic BR, Kisch J, Albrektsson T, Wennerberg A. Is the intake of selective serotonin reuptake inhibitors associated with an increased risk of dental implant failure? Int J Oral Maxillofac Surg 2017;46:782-8.
31. Altay MA, Sindel A, Özalp Ö, Yildirimyan N, Kader D, Bilge U. Does the intake of selective serotonin reuptake inhibitors negatively affect dental implant osseointegration? A retrospective study. J Oral Implantol 2018;44:260-5.
32. Deepa, Mujawar K, Dhillon K, Jadhav P, Das I, Singla YK. Prognostic implication of selective serotonin reuptake inhibitors in osseointegration of dental implants: A 5-year retrospective study. J Contemp Dent Pract 2018;19:842-6.
33. Carr AB, Gonzalez RL, Jia L, Lohse CM. Relationship between selective serotonin reuptake inhibitors and risk of dental implant failure. J Prosthodont 2019;28:252-7.
34. Langer A. Prosthodontic failures in patients with systemic disorders. J Oral Rehabil 1979;6:13-9.
35. Heckmann SM, Heckmann SG, Weber PH. Clinical outcomes of three Parkinson's disease patients treated with mandibular implant overdentures. Clin Oral Implants Res 2000;11:566-71.
36. Chu FC, Deng FL, Siu AS, Chow TW. Implant-tissue supported, magnet retained mandibular overdenture for an edentulous patient with Parkinson's disease: A clinical report. J Prosthet Dent 2004;91:219-22.
37. Rogers JO. Implant-stabilised complete mandibular denture for a patient with cerebral palsy. Dent Update 1995;22:23-6.
38. Nam SS, Lee JC, Kim HJ, Park JW, Lee JM, Suh JY, *et al*. Serotonin inhibits osteoblast differentiation and bone regeneration in rats. J Periodontol 2016;87:461-9.
39. Battaglino R, Fu J, Späte U, Ersoy U, Joe M, Sedaghat L, *et al*. Serotonin regulates osteoclast differentiation through its transporter. J Bone Miner Res 2004;19:1420-31.
40. Kahl KG, Greggersen W, Rudolf S, Stoeckelhuber BM, Bergmann-Koester CU, Dibbelt L, *et al*. Bone mineral density, bone turnover, and osteoprotegerin in depressed women with and without borderline personality disorder. Psychosom Med 2006;68:669-74.
41. Tsapakis E, Gamie Z, Tran G, Adshead S, Lampard A, Mantalaris A, *et al*. The adverse skeletal effects of selective serotonin reuptake inhibitors. Eur Psychiatry 2012;27:156-69.