# REVIEW ARTICLE

# Global prevalence of Candida species diversity in oral cavity of denture wearing patients- A systematic review and meta analysis

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## ABSTRACT

### Aim

in order to give current evidence regarding the diversity of candida species in individuals who have dentures or who suffer from denture stomatitis (DS).

### Methods

The study was registered in PROSPERO and followed the PRISMA guidelines for systematic reviews and meta-analyses. Patients with dentures or denture stomatitis were the subjects of a comprehensive literature search that spanned the years 2000–2023. The goal was to find studies that measured the prevalence of multiple species of candida that colonise denture patients. In order to determine the studies' quality, the Newcastle Ottawa scale (NOS) was used. Employing a random-effect model with a significance level set at $p<0.05$, the summary statistic measure was the odds ratio (OR) and the risk ratio (RR).

### Results

The criteria were met by fifteen papers, twelve of which were included in the meta-analysis, and all of them underwent qualitative synthesis. All studies were thoroughly evaluated because their quality assessments showed a moderate to low risk of bias. Among 15 studies, seven studies were from American continent, five studies from Asian continent and three studies from European continent showing a wide range of candida diversity in these population. Meta-analysis revealed that American, Asian and European population with denture stomatitis (DS) had a strong association and risk of acquiring candida colonisation and infection ($p<0.05$). Funnel plot did not reveal presence of any publication bias in meta-analysis.

### Conclusion

there is a need for comprehensive oral health care for denture wearing patients or denture stomatitis (DS) to monitor the candida colonization and by targeting proper preventive measures so as to improve and maintain the oral hygiene of patient.

## Keywords

candida albicans; denture infection; denture stomatitis; fungal colonization, non-albicans;systematic review

## INTRODUCTION

Denture wear can significantly alter the oral cavity's microenvironment, leading to mechanical irritation, inflammation, and increased susceptibility to fungal infections, particularly Candida albicans [1]. However, other Candida species, such as Candida glabrata, are also commonly found on dentures and underlying tissues [2]. Factors like oral hygiene practices, denture characteristics, and colonizing Candida species influence Candida colonization and

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biofilm formation[3-5].

Stomatitis affects more than 60% of people who wear dentures. It may not cause any symptoms at all but can lead to other issues such erythema, angular cheilitis, leukoplakia, and pseudomembrane formation.[6-8] Structural variables pertaining to dentures, such as their height and the strength of the material, influence the spread of stomatitis and yeast colonisation[9,10].

Despite the dominance of Candida albicans, non-albicans Candida species such as C. glabrata,

C. krusei, and C. tropicalis are on the rise[11]. Of the more than 200 Candida species known, 95% of instances of oral candidiasis are caused by Candida albicans [12]. However, infections of the mouth can also be caused by species that aren't albicans[13].

Even while Candida is a normal, beneficial member of the oral cavity's flora, there are situations in which it can cause disease[13]. Dentures provide an optimal setting for the retention and proliferation of germs[14]. Thus, denture stomatitis can develop when Candida biofilm forms, which can be accelerated by the use of dentures, which adds to the risk factors already associated with increased Candida colonisation[15].

The rising incidence of candidiasis necessitates understanding local Candida epidemiology and antifungal susceptibility profiles to enhance therapeutic management and reduce recurrent infections [16]. The purpose of this meta-analysis is to present the most recent findings regarding Candida species diversity in patients who wear dentures.

## Methodology Protocol development

This review was abided by preferred reporting items for systematic review and meta-analysis(PRISMA) 2020 statement[16] and PROSPERO registration was done- CRD42024506928.

## Study design

The focused research question was proposed "What are the various diversity of candida species that colonize among denture wearing patients or patients with denture stomatitis (DS)?" in the format mentioned below

**P (Participants) –** individuals from worldwide population, diagnosed or at risk of DS.

**E (Exposure) –** presence of C. albicans and non-albicans in Denture Stomatitis individuals within worldwide population.

**C (Comparison) –** individuals not suffering from DS or not colonized by C. albicans and nonalbicans from same population

**O (Outcome) –** prevalence, presence and severity of DS in the population associated with C.albicans and non- albicans colonization

## Eligibility Criteria:

### a) Inclusion Criteria:

1) Published studies in English language
2) Published studies from January 2000 – December 2023 and having pertinent adequate data on the prevalence of various diversity of candida species that colonize among denture wearing patients or patients with denture stomatitis
3) cohort study and cross-sectional studies
4) Open access journals studies
5) Reported articles with study outcomes in terms of frequency

### a) Exclusion Criteria:

1) Studies performed before the year 2000
2) Articles in language other than English
3) Editorials, letter to the editor, animal studies and in vitro studies
4) Non-open access journal articles

## Search Strategy

An electronic search was carried out on published research within last 23 years (from 2000 to 2023), till December 2023 utilizing the PubMed, google scholar and EBSCO databases to retrieve articles in English using proper keywords with Boolean operators like AND/OR.

## Screening Process

To find the right articles, two writers used a strict two-stage screening procedure. At first, we looked over the titles and abstracts to make sure nothing irrelevant was included. Following this, the identical reviewers worked separately to conduct full-text reviews, and any disagreements were settled via panel discussion. When consensus wasn't achieved, a third reviewer was contacted.

## Data extraction

All research that were considered had their author(s), nation, year, sample size, and detected candida species recorded and graphed.

## Methodological quality evaluation

The Newcastle Ottawa Scale (NOS), a 9-point grading system, was used to evaluate the listed studies[17]. A maximum of four points were allotted for selection, two for comparability, and three for the evaluation of the exposure or outcome. Study quality is defined as follows: 7–9 =excellent quality, 4–6 = moderate quality, and 0–3 = low quality or extremely high risk of bias.

## Statistical analysis

RevMan 5.3 was employed for statistical analysis with odds ratio (OR) and risk ratio (RR) serving as summary measure [18]. Significance was determined at the threshold of p < 0.05.

## Assessment of heterogeneity

Cochranes test for heterogeneity was employed to assess the significance of any differences in treatment effect estimations among trials [19]. Heterogeneity was deemed statistically significantif the P-value was less than 0.01

## Investigation of publication bias

Begg's funnel plot was used to assess publication bias, which plots the effect size againststandard error. An asymmetric funnel plot may imply potential publication bias [20].

## RESULTS

### Study Selection

The reference lists of the included research were screened after the duplicates were removed,which led to the deletion of certain studies. After that, after reviewing the complete texts of the

articles, we eliminated those that did not fit our inclusion criteria. Figure 1 shows that fifteen publications were considered for the review, and twelve research were considered for the meta-analysis.

### Study Characteristics

Data was assessed from seven studies[27-33] of from an aggregate of total of 687 denture stomatitis from American continent. Among the included studies, one study[27] was from Canadawhile six studies[28-33] were from Brazil. All the included studies evaluated the various candida species diversity in American population as shown in Table 2.

Data was evaluated from five studies[34-38] from an aggregate of total of 560 denture stomatitis from Asian continent. Among the included studies, three studies[34-36]

was from Turkey while one study[37] was from Yemen and one study[38] from India. All the included studies evaluated thevarious candida species diversity in Asian population as depicted in Table 2.

Data evaluated from three studies[39-41] from an aggregate of total of 1360 denture stomatitis from European continent. Among the included studies, one study each was conducted in Italy[39],Poland[40] and Serbia [41]. All the included studies evaluated the various candida species diversityin European population as in Table 2.

## Quality assessment of included studies

For studies, only four studies[24,28,32,33] reached the maximum score and had maximum score in selection criteria while twelve studies[21,23,24,26-33,35] as shown in Figure 5, had a perfect score on the comparability objective and was thought to have a little risk of bias. Additionally, every study had a partial score on the exposure outcome.

## Meta-analysis results

The quantitative synthesis was performed for assessing the prevalence of candida species in denture wearing patients in American, Asian and European population are depicted in **Figures2**, **Figure 3 and Figure 4.**

On evaluation of six studies[21-26] containing data on 1040 denture stomatitis (DS) patients, the odds ratio (OR) is 2.57 (-0.47 – 1.56) signifying that American population with denture stomatitis on an average had 2.57 times higher odds of having candida species prevalence (*p*<0.05). The risk ratio (RR) is 1.62 (1.01 – 2.61) signifying that American population with denture stomatitis on an average had 1.62 times risk of having candida species prevalence (*p*=0.05). [Figure 2]

Three studies[29,31,32] containing data on 390 denture stomatitis had OR of 2.35 (0.89 – 6.24) signifying that Asian population with denture stomatitis on an average had 2.35 times higher odds of having candida species prevalence (*p*>0.05). A RR of 1.53 (0.94 – 2.49) signifies that Asian population with denture stomatitis on an average had 1.53 times risk of having candida species prevalence (*p*>0.05). [Figure 3]

Assessment of three studies[33-35] containing data on 2720 patients suffering from DS showed anOR of 1.24 (0.29 – 5.30) signifying that European population with DS on an average had 1.24 times higher odds of having candida species prevalence (*p*>0.05). A RR of 1.11 (0.54 – 2.29) signified that European population with

DS on an average had 1.11 times risk of having candida species prevalence (*p*>0.05).

## DISCUSSION

Denture wear alters the oral cavity's microenvironment, causing mechanical irritation, inflammation and increased susceptibility to Candida albicans fungal infection.[1] Denture provides an agreeable conditions for retention and multiplication of microorganisms.[14] Thus, denture pose a risk of increased Candida colonization, leading to development of Candida infection resulting in denture stomatitis.

Arslanov et al[42]., carried out a systematic review of existing literature to analyze and assess the changes in oral microbiota in patients with complete dentures. Databases were searched yielding 12 studies been included in review. From the results of the studies, it was found that there has been a significant increase in fungal colonization especially candida species and changes in the levels of bacterial species. It was concluded that complete denture wearing is frequently associated with changes in oral microbiota which has an adverse effect on oral health. However, due to small sample size and presence of considerable amount of data heterogeneity, it was not possible to conduct a meta-analysis so as to validate the study findings.

Singh et al.[43] systematic reviewed and conducted meta-analysis to estimate DS prevalence and its association between candida albicans in India. Databases searched yielded four studies with data from 415 participants. Results from meta-analysis showed a significant association between DS and candida albicans through the OR of 0.75 (95% CI 0.56 – 0.99) and RR of 0.83(95% CI 0.70 – 1.00). Many other factors like denture wearing for longer time, poor denture hygiene, high sugar intake might lead to development of DS.

Peric et al[44]., updated the global literature on the epidemiology, aetiology, and distribution of candida species associated with denture stomatitis using a systematic review. Searches of databases spanning the last two decades turned up twenty-eight papers. Seven studies looked at candida colonisation in people with dentures, and twenty-one looked at DS. Additionally, it brought attention to the primary causes of DS, such as poor oral hygiene leading to the development of a candida biofilm and long-term use of dentures.

There have been few systematic reviews and meta-analysis[42-44] published in past but due to presence of data heterogeneity, none of them actually could provide a comprehensive qualitative and quantitative analysis on providing a comparative analysis to provide updated evidence on Candida species diversity among denture-wearing patients. We believe this to be the first global systematic study and meta-analysis to examine the diversity of Candida species among patients with dentures.

Databases were searched from January 2000 till December 2023 yielding 15 studies[21-35] being included in review. Among 15 studies, seven studies[21-27] were from American continent, five studies[28-32] from Asian continent and three studies[33-35] from European continent. A wide range of candida diversity was found in these population. Meta-analysis revealed that American, Asian and European population with denture stomatitis (DS) had a strong association and risk of acquiring candida colonisation and infection (p<0.05). Funnel plot did not reveal presence of any publication bias in meta-analysis.

A thorough literature search and rigorous methodology, including the Newcastle Ottawa scaleROB assessment, were utilised in the systematic review, which was conducted in accordance with PRISMA criteria. A strong evidence base for treatment recommendations on optimising dentin bonding techniques was produced by high-quality studies with low bias.

Transparency and reproducibility in answering certain research issues are offered by systematic reviews and meta-analyses, which are regarded as the highest level of evidence. The strength of the evidence is, however, affected by the quality of the included research. Included in this meta-analysis were adequate studies with short follow-up times and an established potential for bias.

## CONCLUSION

The findings provide sufficient evidence to inform therapeutic recommendations addressing the focus question. Notably, this study focused solely on denture-related factors contributing to Candida Associated Denture Stomatitis (CADS). Future research should investigate additional local and systemic etiological factors contributing to CADS, as denture wear is just one causative factor.

**Table 1:** Search Strategy according to PECOS

|  | **Strategy** |
|---|---|
| **Population** | ((("denture"[MeSH Terms] OR "stomatitis" OR "adult" OR ("adult"[MeSHTerms] OR "adult" OR ("adult, edentualism dentition"[MeSH Terms] OR "adult" AND "complete anodontia" |
| **Exposure** | (((("candida albicans"[MeSH Terms] OR ("prosthetic stomatitis" AND "infection" AND "therapy" OR "immunocompromised" OR "candida species" OR ("yeast species"[MeSH Terms] OR ("candida infection" AND "therapy" OR "microbial composition" OR ("microbial diversity"[MeSH Terms] |
| **Comparison** | (("Denture infection" OR "candida colonization"[MeSH Terms] OR ("risk factors" AND "dietary counselling" OR "oral infection" OR ("inflammation"AND "denture hygiene" OR "high sugar intake" AND ("fungal species" OR "candida species"[MeSH Terms] |
| **Outcome** | ((("prevalence"[MeSH Terms] OR "rate" OR ("epidemiology"[MeSH Terms] OR ("Denture stomatitis" AND "candida species diversity" OR "worldwide population" OR ("comparative study" AND "cross-sectional study" AND "clinical study" OR "prospective study" |

**Table 2:** Descriptive study details of included studies for candida species diversity inAmerican, Asian and European population

| Author,year of study | Country | Sample size | Candida species identified |
|---|---|---|---|
| Barbeau et al.,2003[21] | Canada | 48/68 | C. albicans, C. glabrata, C. tropicalis |
| Motta-Silva et al.,2010[22] | Brazil | 247 | C. albicans, C. glabrata, C. tropicalis. C. Krusei, C. famata |
| Sanita et al.,2011[23] | Brazil | 210 | C.albicans, C. glabrata, C. tropicalis |
| Altarawneh et al.,2013[34] | Brazil | 15/32 | C. albicans 71.4% Non-albicans 28.6% |
| Pereira et al.,2013[25] | Brazil | 100 | C. albicans, C. glabrata, C. tropicalis, C.dubliniensis, C. guilliermondii, C. krusei, C. Lusitaniae |
| Gauch et al.,2018[26] | Brazil | 36 | C. albicans, C. famata, C. tropicalis, C. Parapsilosis |
| Qiu et al.,2023[27] | Brazil | 30 | C. albicans, C. glabrata, C. tropicalis, C. parapsilosis, C. dubliniensis |

| Author,year of study | Country | Sample size | Candida species identified |
|---|---|---|---|
| Abaci et al.,2010[28] | Turkey | 110 | C. albicans, C.glabrata, C.Krusei, C.Kefyr, C.famata, C. sphaerica |
| Dagistan et al.,2009[29] | Turkey | 70 | C. albicans, C. Krusei, C. Pseudotropicalis, C. guilliermondii, C. lipolytica, C. boidini |
| Kilic et al.,2014[30] | Turkey | 37 | C. albicans, C. glabrata, C. kefyr, C. norvegensis |
| Navabi et al.,2013[31] | Yemen | 288 | C. albicans, C. glabrata |
| Bhat et al.,2013[32] | India | 55 | C. albicans, C. tropicalis, C. glabrata |
| Calcaterra et al.,2013[33] | Italy | 190 | C. albicans, C. glabrata, C. dubliniensis, C. tropicalis, C. Kruse |
| Loster et al.,2016[34] | Poland | 920 | C. albicans, C. glabrata, C. tropicalis |
| Peric et al.,2018[35] | Serbia | 250 | C. albicans, C. glabrata, C., C. tropicalis, C. krusei |

| Author, Year | Selection(Max=4) | Comparability(Max=2) | Exposure(Max=3) | Overall quality score(Max=9) |
|---|---|---|---|---|
| Barbeau et al.,2003[21] | ** | ** | ** | 6 |
| Motta-Silva etal.,2010[22] | *** | * | ** | 6 |
| Sanita et al.,2011 | ** | ** | *** | 7 |
| Altarawneh etal.,2013[34] | **** | ** | *** | 9 |
| Pereira et al.,2013[25] | ** | * | ** | 5 |
| Gauch et al.,2018[26] | ** | ** | ** | 6 |
| Qiu et al.,2023[27] | *** | ** | ** | 7 |
| Abaci et al.,2010[28] | **** | ** | *** | 9 |

| Author, Year | Selection(Max=4) | Comparability(Max=2) | Exposure(Max=3) | Overall quality score(Max=9) |
|---|---|---|---|---|
| Dagistan et al.,2009[29] | ** | ** | * | 5 |
| Kilic et al.,2014[30] | ** | ** | ** | 6 |
| Navabi et al.,2013[31] | *** | ** | ** | 7 |
| Bhat et al.,2013[32] | **** | ** | *** | 9 |
| Calcaterra etal.,2013[33] | **** | ** | *** | 9 |
| Loster et al.,2016[34] | ** | * | ** | 5 |
| Peric et al.,2018[35] | ** | ** | ** | 6 |
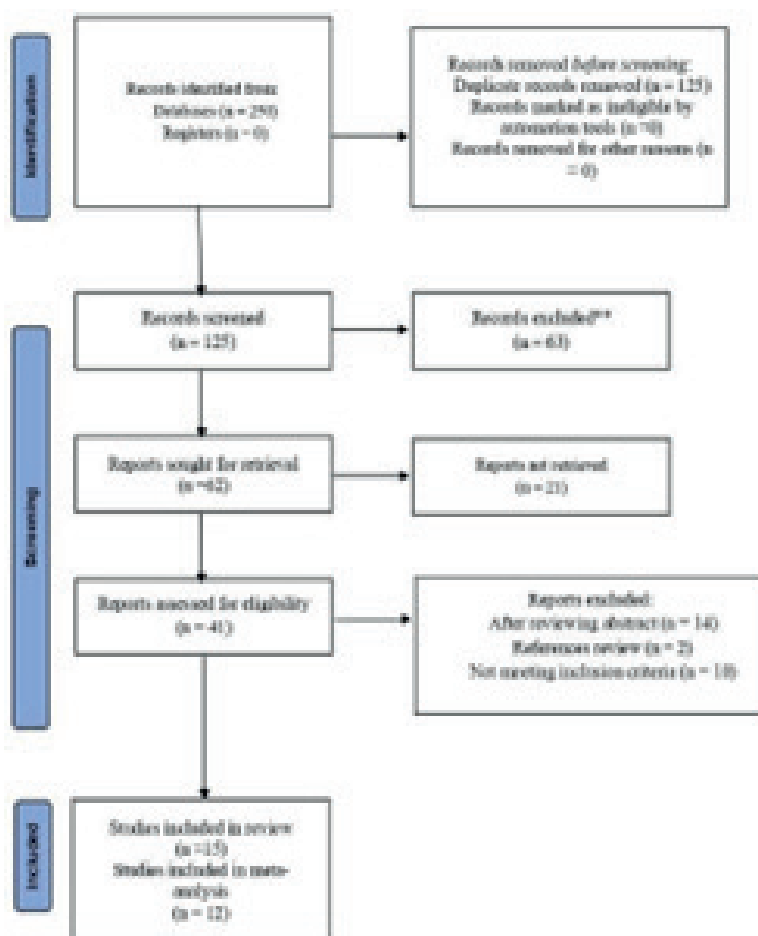


**Figure 1:** PRISMA 2020 Flow Diagram
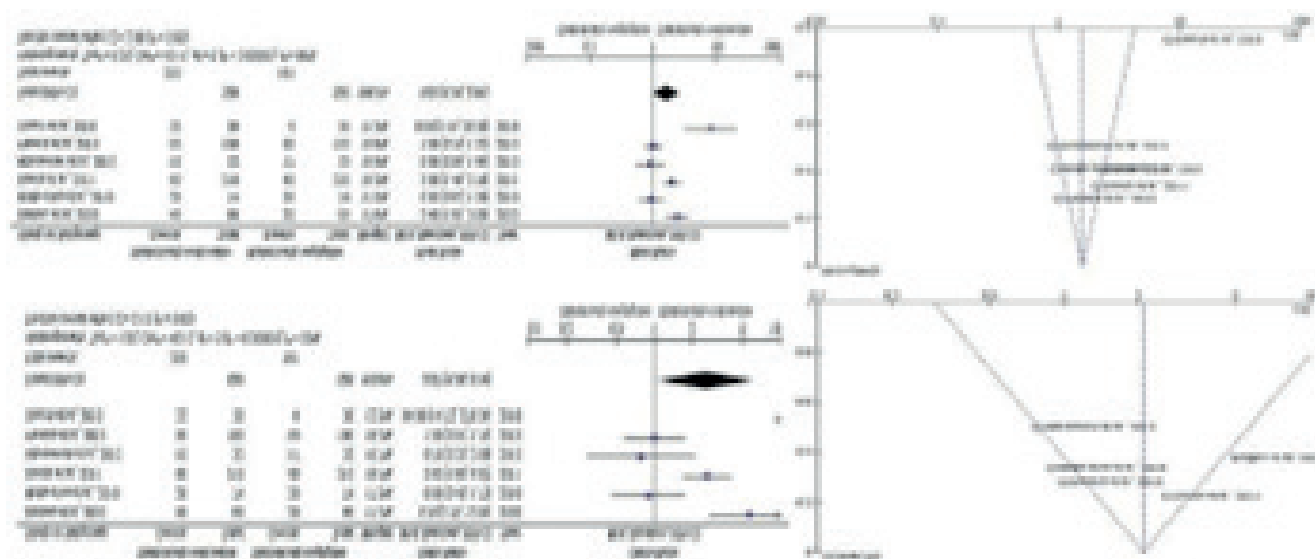
**Figure 2:** Odds ratio and risk ratio along with Funnel plot demonstrating absence of publication bias depicting prevalence of candida species in American patients with denturestomatitis
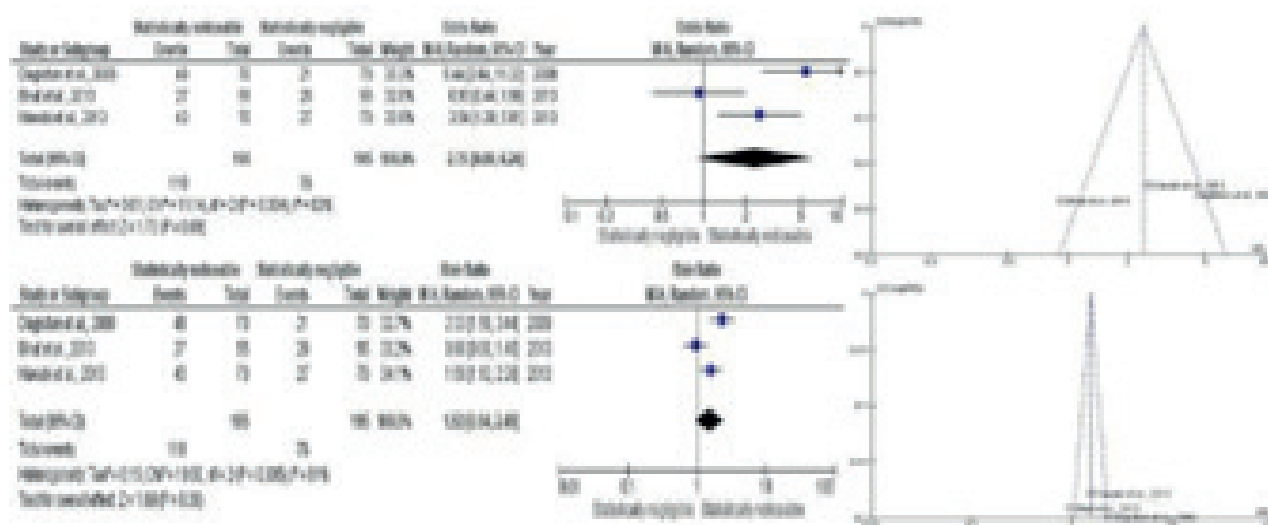


**Figure 3:** Odds ratio and risk ratio along with Funnel plot demonstrating absence of publication bias depicting prevalence of candida species in Asian patients with denturestomatitis.
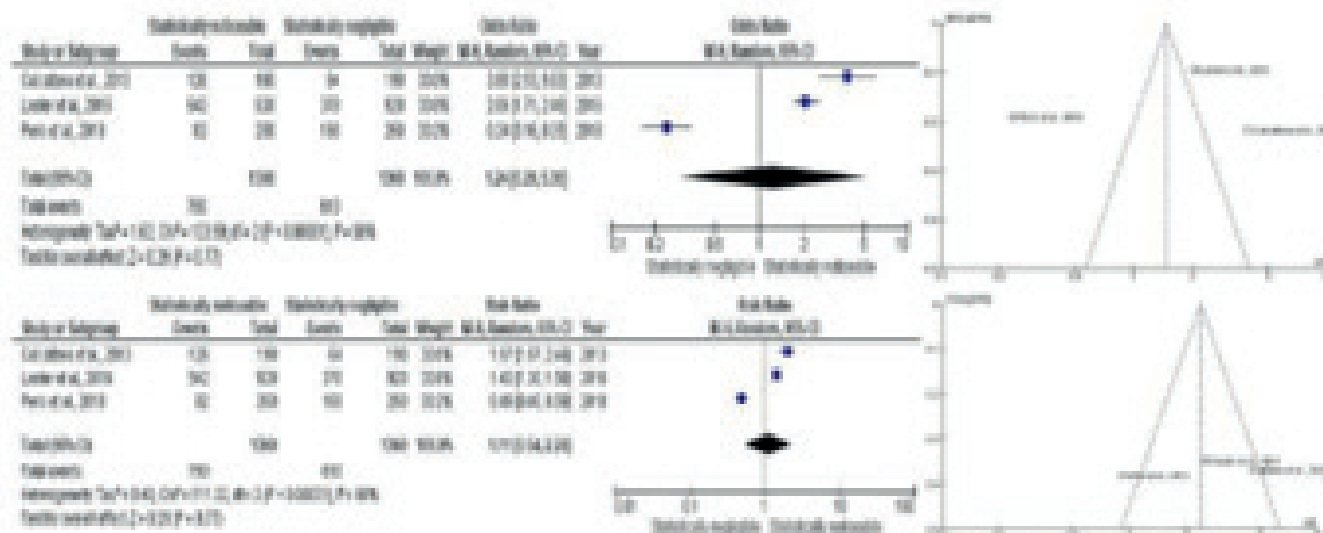
**Figure 4:** Odds ratio and risk ratio along with Funnel plot demonstrating absence of publication bias depicting prevalence of candida species in European patients with denturestomatitis

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