A Meta-Analysis of Oral Health Status of Children with Autism

Xiaoqin Pi */Chang Liu **/Zhen Li ***/Haiying Guo ****/Han Jiang *****Minquan Du ******

Purpose: *To present a meta-analysis whether the risks of caries and periodontal problems in autistic children are higher than those in healthy children.* ***Study design:*** *A literature search that included PubMed, Embase, Web of Science, Cochrane, China National Knowledge Infrastructure (CNKI), Wan fang, and Chinese Scientific and Technological Journal (VIP) databases was conducted. The primary outcomes of interest included the DMFT index, Plaque index (PI), Gingival index (GI), and Salivary pH. Quality assessment was performed in accordance with the Newcastle-Ottawa Scale (NOS). Dichotomous variables are presented as relative risk (RR), and continuous variables are presented as weighted mean difference (WMD).* ***Results:*** *Eight studies were included in this meta-analysis. Among these 8 studies, six studies compared the DMFT index, three studies compared PI, three studies compared GI, and three studies compared salivary pH. Meta-analysis showed that the mean DMFT index in autistic children was higher than that in healthy children, and the difference was statistically significant {MD = 0.50, 95% CI [0.04–0.96], P<0.00001}. Similarly, PI and GI in autistic children were higher than those in healthy children, and the difference between PI was statistically significant {MD = 0.59, 95%CI [0.36–0.82], P=0.02}, while the difference between GI was not statistically significant {MD = 0.52, 95%CI [0.30–0.75], P=0.08}. But the salivary pH in autistic children was lower than that in healthy children {MD = -0.28, 95%CI [-0.54–-0.02], P = 0.02}, and the difference was statistically significant.* ***Conclusion:*** *The present analysis suggests that children with autism have poorer oral hygiene, higher risk of caries, and a lower salivary pH than healthy children.*

Keywords: *Autism, oral hygiene, oral health, meta-analysis*

INTRODUCTION

Autism is a neural developmental disorder characterized by varying degrees of speech development and interpersonal communication disorder, narrow interests, and stereotyped behavior patterns. It is a complex, behaviorally defined, static disorder of the immature brain, and it is a syndrome with multiple non-genetic and genetic causes [1-3]. Diagnostic techniques for autism have improved, and awareness of the prevalence of autism has increased in the last few decades. The prevalence of ASDs in developed countries is now considered to be at least 60 per 10000, and the male to female ratio is about 4.3:1 [4,5]. Over the past 30 years, the number of cases diagnosed has increased and the current prevalence of autistic spectrum disorders (ASD) is about 1/100 [6]. A recent report stated that one out of every 68 children at the age of eight have autism [7]. Various eating problems such as being choosy about food, keeping food in the mouth, and rejecting food are frequently seen in children with ASD. Changes in the amount of saliva in autistic children, poor eating habits, abnormal behaviors, bruxism, and inadequate oral and self-care remain the major problems that can result in poor oral health and can increase the risks of caries and periodontal diseases [8,9]. Studies have indicated that in autistic children who do not express their needs for oral health care, the risk of dental caries is two times higher than that in healthy children [9-11]. Although there is a growing interest in clinical research on children

From the State Key Laboratory Breeding Base of Basic Science of Stomatology & Key Laboratory of Oral Biomedicine, Ministry of Education, School & Hospital of Stomatology, Wuhan University, Wuhan, China

Send all correspondence to:
Minquan Du.
Hubei-Most KLOS&KLOBM, School & Hospital of Stomatology, Wuhan University, Luoyu Road 237, Wuhan City, Hubei, China.
Phone: +8627 87686227
E-mail: duminquan@whu.edu.cn

with autism and oral health, there are some inconsistencies and complete and relevant evidence-based data are not available.

This suggests that the possibility of dentists encountering children with autism during their careers is rather high. Therefore, to develop dental approaches more suitable for individuals with ASD, more light should be shed upon this matter and awareness should be raised.

There is inadequate information about the prevalence of dental disease and access to dental care among children with autism, The aims of this meta-analysis were to fill this knowledge gap by assessing oral health status of children with ASD in comparison with that of children without ASD and to determine the oral status of a group of patients with autism. provide baseline data for further study and serve as treatment guideline for dental conditions in autistic children

MATERIALS AND METHOD

Information sources and search strategy

We searched English and non-English language publications in the PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), Wan fang, and Chinese Scientific and Technological Journal (VIP) databases up to September 2018. The following key words were used: child, children, autism, periodontal health status, dental caries, and periodontal disease. For example, the search strategy in PubMed was as follows: #1: children; #2: autism; #3: child; #4: periodontal health status; #5: dental caries; #6: periodontal disease; #7: #1AND#2AND#3; #8:4OR#5OR#6; and #9: #7AND#8.

Eligibility criteria

Study design: A case-control study

Diagnostic criteria for children with autism were as follows [12]: (1) There are signs of qualitative damage in social interactions, no emotional connection with people around them, and extreme loneliness; (2) barriers to speech and non-verbal communication, lack of imaginative activities, inability to understand instructions, and lack of expression of one's needs and pain, asking questions rarely, lack of response to other words, abnormal tone, accent, speed, and rhythm of the speech, and rigidity of words; (3) stereotypes and repeated actions, and the activity of interest is severely limited.

Study population: Autistic children and healthy children

Outcome measures: DMFT, Plaque index (PI), Gingival index (GI), and salivary pH.

The exclusion criteria were as follows: Abstracts, case reports, animal experiments, and non-clinical trials; studies with a small sample size (less than 10 cases); and studies with inadequate research data.

Inclusion of studies

Two authors extracted the data independently, and discrepancies were resolved by mutual discussion. A standardized data extraction form was used to extract the data. The extracted information included the following: the first author, the year in which the study was performed, country, type, sample size of the included studies, mean, and standard deviation. If the articles provided inadequate information, we contacted the authors to obtain the missing details.

Quality assessment

According to the Newcastle-Ottawa Scale (NOS) [13], the included studies were evaluated for population selection, inter-group comparability, and outcome measurement. The highest quality score was nine points. Studies with scores greater than or equal to six points were categorized as high-quality studies and were included in this study, while studies with scores lower than six points were considered as low-quality studies and were excluded from this study.

Statistical analysis

Meta-analysis was performed using Review Manager 5.3. Dichotomous variables are presented as relative risk (RR) and 95% confidence interval (CI). Continuous variables are presented as weighted mean difference (WMD) (statistics were unit-consistent) or standardized mean difference (SMD) (statistics were unit-inconsistent) with 95% CI. The I^2 measure was used to quantify the extent of heterogeneity, and statistical significance was defined as $P < 0.05$. A random-effect model was used to pool the study data if $I^2 \geq 50\%$ or $P < 0.1$, which indicated significant heterogeneity; otherwise, a fixed-effect model was used. Heterogeneity was detected using sensitivity analysis, subgroup analysis, and meta-regression analysis.

Publication bias and sensitivity analysis

Sensitivity analysis: For data without any obvious heterogeneity, the random effect model was compared with the fixed effect model to combine the MD values, and the stability of the results was analyzed. For heterogeneous data, large samples were eliminated one by one or the results were different. The MD value was calculated after a literature search to determine the stability of the results, and the funnel plot test was used to determine whether there was any publication bias. The test level was considered as $\alpha = 0.05$.

RESULTS

Figure 1 shows a flow diagram of the study selection process. A total of 258 studies were identified after removing the duplicates. Full texts were obtained for articles where the title and abstract alone were inadequate for determining their eligibility for inclusion in this meta-analysis. Eventually, eight studies were eligible for inclusion in this study. Table 1 summarizes the characteristics of the included studies.

Table 2 presents the results of the study quality assessment. All the eight studies scored more than seven points and were categorized as high-quality studies on the NOS [4,13-19].

DMFT A total of six studies [4,14-16,18,19]. compared the mean DMFT between autistic children and healthy children. There were 391 cases of autistic children and 481 cases of healthy children. Due to significant heterogeneity ($I^2 = 88\%$), the random effect model was used to analyze the data. The combined results showed the following: MD = 0.50 and 95% CI [0.04–0.96]; thus, suggesting that children with autism had a higher DMFT than healthy children ($P < 0.00001$).

Sensitivity analysis: There was no significant change in the overall results before and after sensitivity analysis, thus suggesting a relatively stable and reliable combined result. See Figure 2

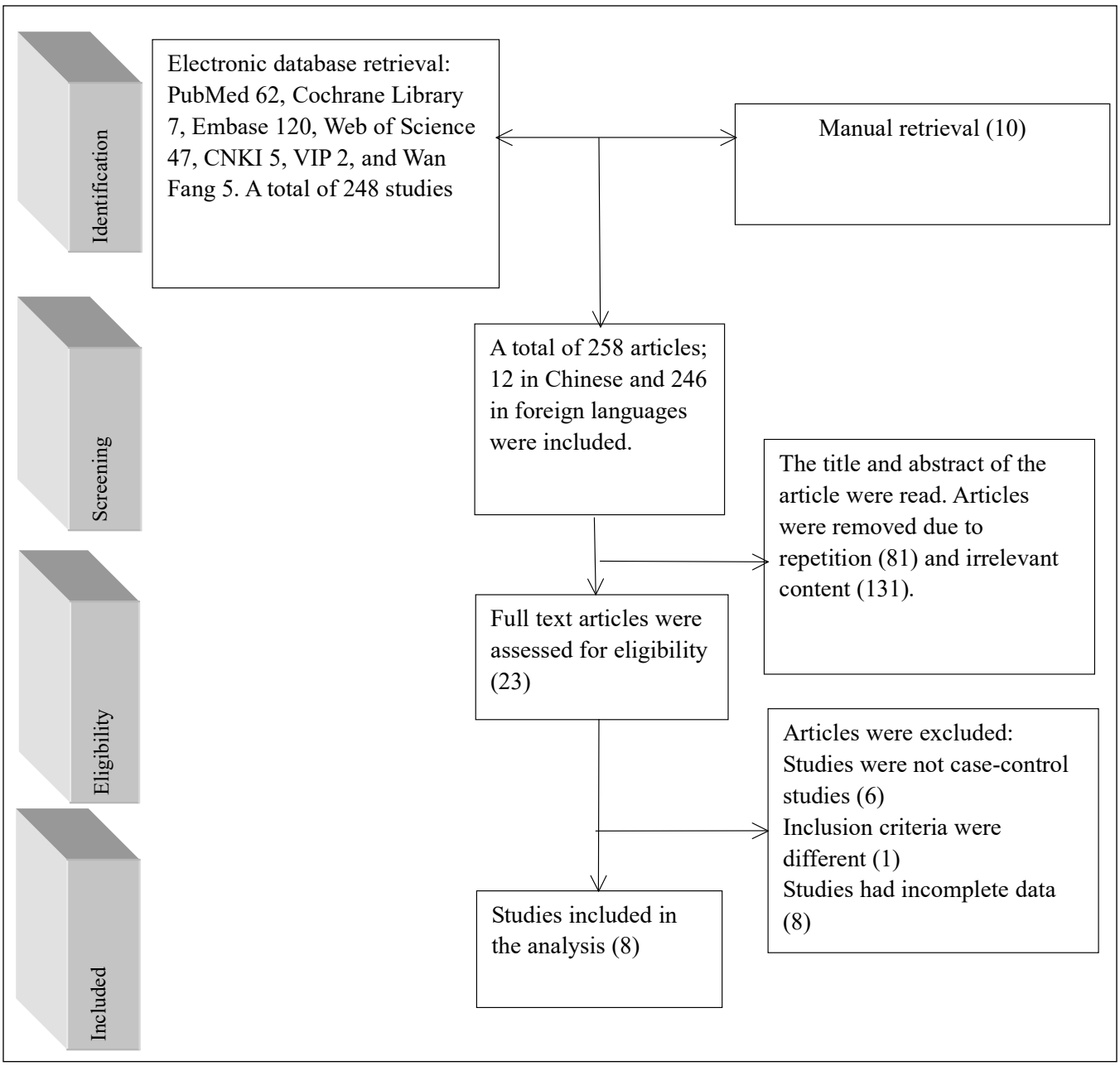

Figure 1 Flow diagram of the study selection process

Table 1 The Characteristics Of The Included Studies

First author	Year	Country	Study type	Sample	Group	Age	n	mean DMFT		PI		GI		Salivary pH	
								mean	SD	mean	SD	mean	SD	mean	SD
Al-Maweri, S. A.	2014	Yemen	Case-control Study	126	Autism Group	5-16 years	42	2	2.2	1.5	0.8	1.36	0.8	-	-
					Healthy Group		84	1.27	1.8	1.05	0.5	1.02	0.5	-	-
Bhandary. s.	2017	India	Case-control Study	60	Autism Group	6-12 years	30	0.37	0.6	-	-	-	-	6.49	0.58
					Healthy Group		30	0.37	0.6	-	-	-	-	7.08	0.62
Diab, H. M.	2016	Riyadh	Case-control Study	100	Autism Group	Average 8.5 years	50	-	-	1.93	0.4	1.83	0.7	6.85	0.55
					Healthy Group		50	-	-	1.44	0.4	1.36	0.9	7.09	0.44
Jaber. M.A.	2011	Dubai and Sharjah	Case-control Study	122	Autism Group	6-16 years	61	2	2.3	-	-	-	-	-	-
					Healthy Group		61	2.22	1.8	-	-	-	-	-	-
Kalyoncu.l.o	2017	Turkey	Case-control Study	120	Autism Group	6-14years	60	3.59	3.6	2.06	0.7	1.91	0.6	-	-
					Healthy Group		60	2.37	1.9	1.24	0.5	1.22	0.5	-	-
Morales-Chavez M.C.	2018	Caracas	Case-control Study	68	Autism Group	4-13 years	34	0.86	1.2	-	-	-	-	-	-
					Healthy Group		34	0.46	1.1	-	-	-	-	-	-
Onol. S.	2018	Turkey	Case-control Study	174	Autism Group	6-14 years	63	-	-	-	-	-	-	7.2	0.48
					Healthy Group		111	-	-	-	-	-	-	7.27	0.34
Richa	2014	India	Case-control Study	270	Autism Group	4-15 years	135	1.6	0.6	-	-	-	-	-	-
					Healthy Group		135	0.6	0.3	-	-	-	-	-	-

Table 2 The Results Of The Study Quality Assessment

Studies	Selection				Comparability	Outcome			Total score
	I	II	III	IV	V	VI	VII	VIII	
Al-Maweri S A	1	1	1	1	1	1	1	0	7
Bhandary S	1	1	1	1	1	1	1	0	7
Diab, H M	1	1	1	1	1	1	1	0	7
Onol S	1	1	1	1	1	1	1	1	8
Richa	1	1	1	1	1	1	1	0	7
Morales-Chavez MC	1	1	1	1	1	1	1	0	7
Jaber MA	1	1	1	1	1	1	1	0	7
Kalyoncu.l.o	1	1	1	1	1	1	1	0	7

I: Represents adequate case definition; II: Represents activeness of the cases; III: Selection of Controls; IV: Definition of Controls; V: Comparability of cases and controls on the basis of the design or analysis; VI: Ascertainment of exposure; VII: Same method of ascertainment for cases and controls; VIII: Non-Response rate.

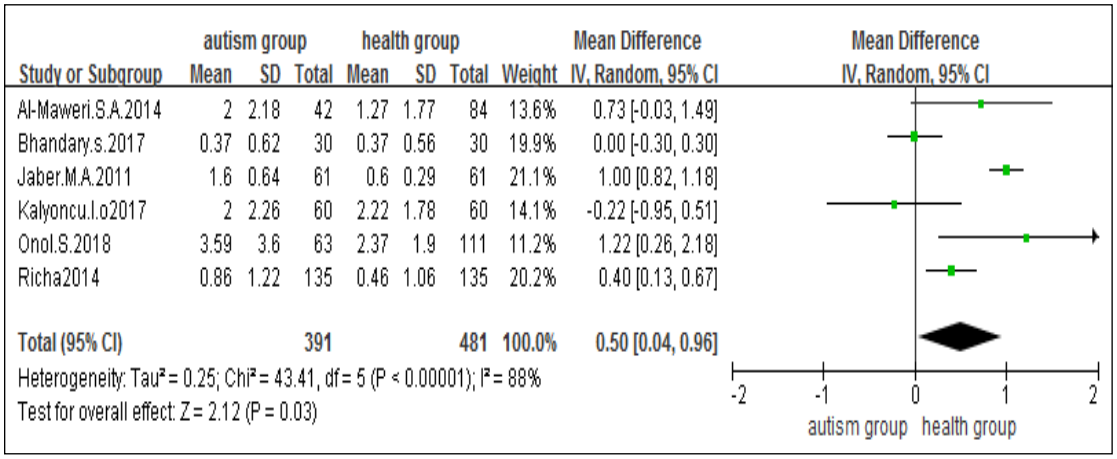

Figure 2.

PI A total of three studies [15,17,18] including 155 autistic children and 245 healthy children compared the two groups. The random effect model was used due to high heterogeneity (I^2 = 73%). The combined results showed the following: MD = 0.59 and 95% CI [0.36–0.82], thus suggesting that children with autism had a higher PI than healthy children (P = 0.02).

Sensitivity analysis: We found that when the study by Onol S. was removed, the heterogeneity became zero. This may be due to the relatively large sample size, but it could not be explained clearly. Therefore, the study was retained in our analysis. See Figure 3.

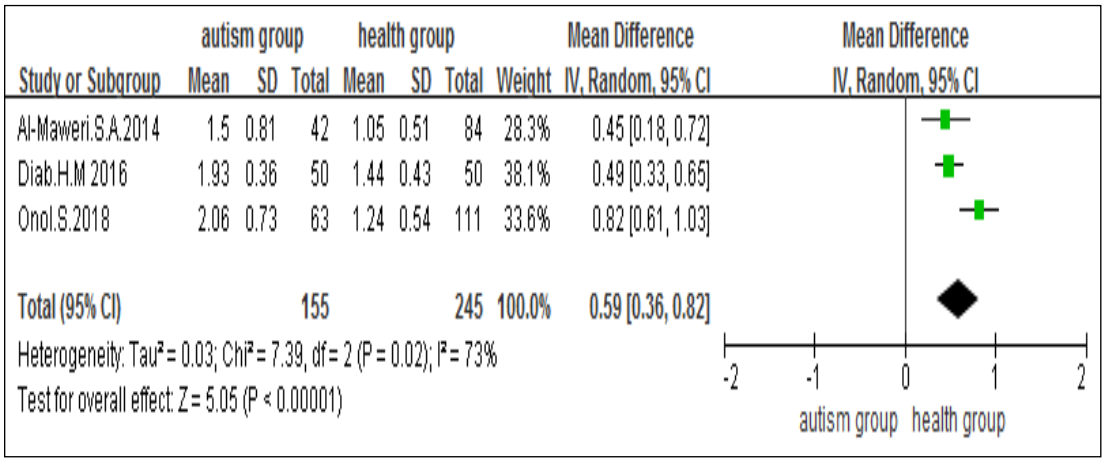

Figure 3.

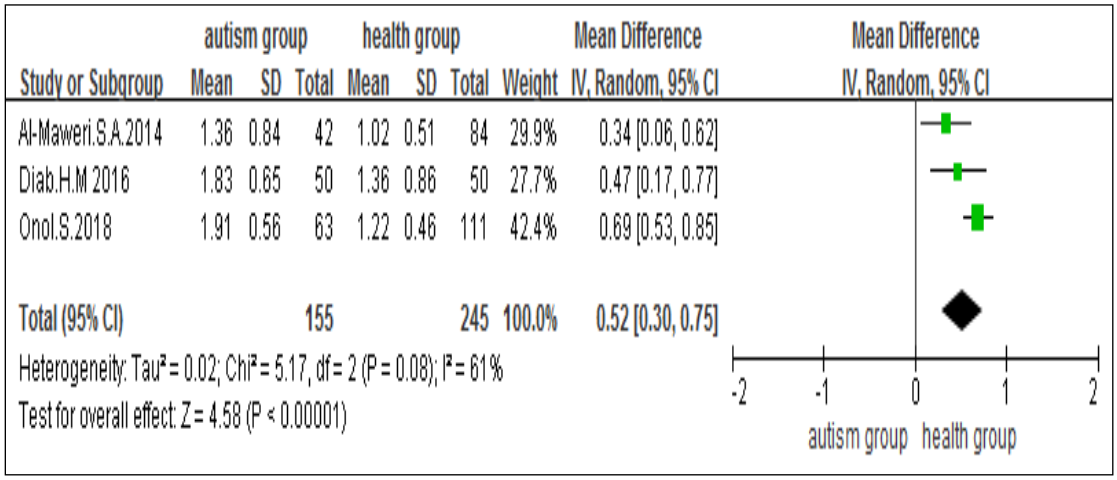

Figure 4.

GI A total of three studies [15,17,18] including 155 autistic and 245 healthy children compared the GI between the two groups. The I^2 statistic showed significant heterogeneity(I^2=61%); therefore, the random effect model was used and the combined results showed the following: MD=0.52 and 95% CI [0.30-0.75]. Thus, these differences were not statistically significant (P=0.08).

Sensitivity analysis: We found that when the study by Onol S. was removed, the heterogeneity became zero. This may be due to the relatively large sample size, but it could not be explained clearly. Therefore, the study was retained in our analysis. See Figure 4

Salivary pH A total of three studies [14,15,20] compared the salivary pH of autistic children and healthy children. There were 114 cases of autistic children and 114 cases of healthy children. Significant heterogeneity (I^2 = 75%) was observed; thus, the random effect model was used to analyze the data. The combined results showed the following: MD = -0.28 and 95% CI [-0.54—0.02], thus suggesting that children with autism had a lower salivary pH than healthy children (P = 0.02).

Sensitivity analysis: No significant change was observed in the overall results before and after sensitivity analysis, thus suggesting a relatively stable and reliable combined result. See Figure 5.

DISCUSSION

Our analysis showed that compared with healthy children, the average DMFT and PI were high, but the salivary pH value was low in the autism group [4,14-20]. But, there is a lack of adequate data on the oral health examination of autistic children, and their brushing habits are poor compared with healthy children [10]. Most of these children have gingivitis.

While the previous studies showed higher amounts of caries in children with ASD ,which is consistent with the World Health Organization classification ,some Studies have shown different results [4,21,22.] which is reported lower caries prevalence. But, it can be observed that the conclusions are not very reliable. For example, in a study conducted in Turkey, the oral status of 62 children with ASD was evaluated and it was found that these children had lower DMFT values, but they had a greater number of missing permanent teeth. Therefore, the similarities in DMFT values suggest that there may be this factor involved, this conclusion is not consistent. Studies conducted in the western countries that have been reported in the literature have found no or little difference in the caries status of children with ASD when compared to normal healthy children, thereby justifying the protective role of saliva [23-25]. Regarding salivary factors, Bassoukou *et al* and Rai *et al* [26,27] conducted similar studies and they did not find any statistically significant differences. Nevertheless, it is always considered in the studies because the saliva buffering capacity works by counteracting the decrease in pH and is an important protective factor against caries. Some salivary factors might provide protection against caries, even under unfavorable oral conditions in autistic patients, Due to limited research in this area, salivary factors remain to be confirmed. Therefore, further investigations are needed to draw a conclusion from this kind of research. As far as the evidence is concerned, the conclusion that the risk of caries in autistic children is higher than that in healthy children is worthy of further investigation. Therefore, Autistic children, their parents and oral health providers should be made more aware of the importance of oral hygiene, Four types of oral soft tissue lesions were identified among this study subjects , children with autism revealed higher proportion of fistulae, ulcerative lesions, gingival hyperplasia, and cheilitis; The prevalence of oral soft tissue lesions was also higher among children with autism as compared to the controls, which is consistent with many previous studies [28-30] , however, our meta-analysis shows that these differences were not statistically significant(P>0.05).

Also, we cannot ignore the fact that patients with autism usually have some factors that increase the risk of developing caries, these changes could be related to irregular brushing habits because of the difficulties the trainers and the parents encountered when they brushed the children's teeth. The possible explanation for the presence of generalized gingivitis might be the side effects of medications that are used to control the manifestations of autism, such as psychoactive drugs or anticonvulsants, with the most common drug classes being antidepressants, stimulants, and antipsychotics [4,31.] We should analyze this possibility on a case-by-case basis.

A number of studies have been conducted to illustrate the significance of oral health in autistic children, but the findings are not suggestive mainly due to the relatively small number of participants. Thus, paucity of relevant cases remains a major hurdle in further research in this field. The limited number of special schools for children with autism makes it difficult to obtain the typical samples,

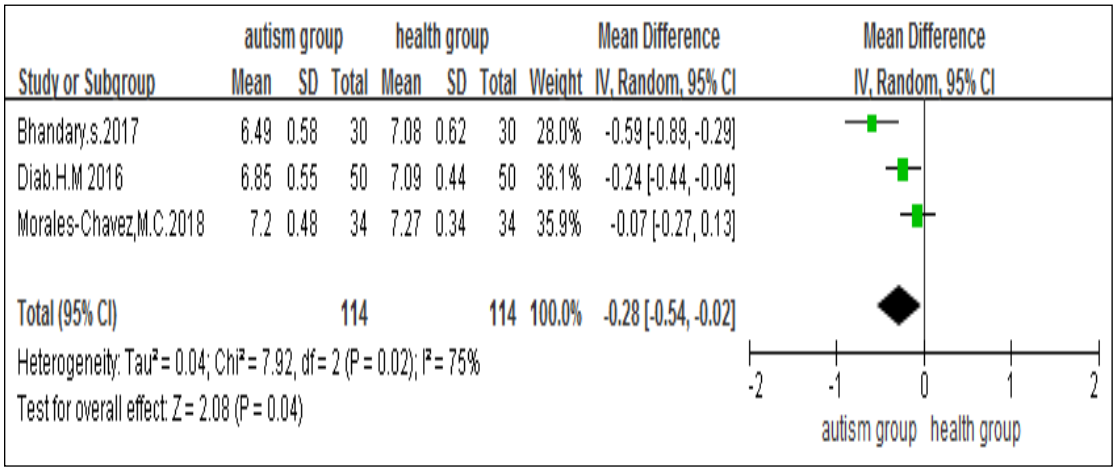

Figure 5

which results in the inability to be very rigorous in many aspects such as age. This in turn affects the quality of the study performed. We believe that by pooling all the available relevant data, this meta-analysis provides valuable information on the status of oral health in autistic children [6]. One study suggested that children with autism do not have good daily life skills and have bad eating habits, which result in decreased chewing ability. These children are picky about food, prefer soft and sweet food, and retain food in their mouth for a longer period [18]. All of these factors increase the risk of caries [6].

Only eight studies related to oral health of autistic children were found eligible for the final analysis, and heterogeneity was significant. This may be due to the limited number of studies included. To determine the cause of heterogeneity, sensitivity analysis was performed by using the elimination method. But no significant change was observed in the overall results before and after the sensitivity analysis, thus suggesting relatively stable and reliable combined results.

Several limitations of our analysis should be considered. The studies do not include the functional level data of autism children limiting our analysis to logical reasoning. All the included studies were case-control trials, which may reduce the reliability of the conclusions. High heterogeneity was noted, which may be due to the small sample size in some studies, research performed in different geographical locations, and larger age range. Due to the limited number of included studies (< 10 articles), funnel plot analysis could not be performed. Thus, the outcomes need to be verified further by including more high-quality, randomized, controlled trials.

CONCLUSION

Children with autism have higher risk of caries prevalence and poor oral hygiene, and a lower salivary pH, they seem to need much more effort for providing oral care than healthy children, In this special needs group, it is very important to help them achieve the dental care.

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