Bonding to hypomineralized enamel – A systematic review

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Abstract

The aim of this paper was to systematically analyze the published literature on bonding adhesive resin to hypomineralized enamel, in order to answer the questions: “Does resin dental adhesives achieve inferior bonding to hypomineralized enamel when compared to normal enamel?” “Does self-etch dental adhesives bond better to hypomineralized enamel when compared with etch-and-rinse adhesives?” “Does deproteinization with 5% NaOCl before adhesive application procedure enhance bonding performance of resin dental adhesives to hypomineralized enamel?” Three electronic databases (Pubmed, Scopus and ISI web of Science) were searched to identify original studies that evaluated the bond achieved between resin adhesives and hypomineralized enamel. Only articles that met the specific inclusion criteria were included in the review. Among 6 studies included in this review, 4 studies that tested bond strength of resin composite to hypomineralized enamel showed significantly lower bond strength than that to sound enamel. Bonding was not compared between adhesives in 5 included studies as only one adhesive was used. Three out of four studies showed improved bonding performances when deproteinization was performed with 5% NaOCl to hypomineralized enamel before adhesive application. Resin dental adhesives achieve inferior bonding to hypomineralized enamel when compared to normal enamel. There are no sufficient evidences to prove that self-etch dental adhesives bond better to hypomineralized enamel when compared with etch-and-rinse adhesives. Enamel deproteinization with 5% NaOCl before adhesive application procedure may enhance bonding performance of resin dental adhesives to hypomineralized enamel.

Introduction

Enamel is the outermost layer of the crown of a tooth that protects underlying dentin and pulp tissue [1]. Enamel does not have the capacity to regenerate or repair. It is composed predominantly of inorganic structure, making up to 96% by weight and the remaining 4% by organic structure and plasma [2]. A defect in the enamel could either be qualitative, leading to hypomineralization or quantitative, leading to hypoplasia. The two most common conditions that affect enamel are Amelogenesis Imperfecta (AI) and Molar Incisor Hypomineralization (MIH).

Among the inherited enamel disorders, AI is a well-recognized condition that affects both primary and permanent dentitions. AI falls into two main groups: hypocalcified and hypoplastic types [3]. Hypocalcified AI (HAI) is a qualitative defect, in which enamel has less mineral content; whilst hypoplastic AI is a quantitative defect, in which enamel is reduced in thickness or in extreme cases even complete absent of it. Wright et al. [4] and El-Sayed et al. [5] from their studies on ultratructural analysis of sound teeth and teeth affected with HAI reported that there was a significant reduction in mineral content of enamel from teeth affected by HAI, when compared to teeth with sound enamel. Additionally, enamel of teeth with HAI may have 3-4% protein by weight compared with 0.5% for normal enamel [4,6].

Molar-Incisor Hypomineralization (MIH) is a condition of systemic origin that involves one to four first permanent molar teeth and often associated with affected incisors [7]. Etiology of MIH could be multifactorial, resulting from a variety of environmental

factors acting systemically, including prenatal, perinatal and childhood medical conditions that affect the developing enamel, while an underlying genetic predisposition could not be excluded [8]. The clinical appearance of the teeth affected by MIH shows distinguished areas of enamel opacities with a change in translucency. The colour of the affected enamel can vary from white to yellow or brown based on the extent of hypomineralization. In an affected person as a result of the variation in the extent of hypomineralization it is not uncommon to find one molar tooth with intact enamel opacity while the other molar tooth with enamel breakdown.

Enamel of teeth affected with MIH has altered inorganic and organic content. Accordingly, a mean 28% reduction in mineral content, 80% more carbonated apatite and 3- to 15- fold increase in protein content were found in enamel of teeth affected with MIH, when compared with enamel from sound teeth [9,10,11]. The hardness of MIH-affected enamel is also significantly lower than sound enamel [9]. The analysis of chemical profile of MIH-affected enamel has shown that Ca, P concentrations and mean Ca/P ratio are lower than normal; while C, Mg and K concentrations are higher [12,13].

Enamel bonding is performed in various clinical applications that include: (1) Sealing of occlusal pit and fissures, (2) restoration of shallow cavitated caries lesions that includes preventive resin restorations, (3) restoration of large cavitated caries where the margins of the cavity still lie within enamel and (4) bonding of orthodontic brackets for fixed appliance therapy. Unlike bonding to normal enamel from sound teeth, bonding to enamel from teeth affected with HAI or MIH is very challenging, due to it’s relatively

reduced mineral content and increased organic content. Therefore, research studies on bonding dental adhesives to hypomineralized enamel have been conducted in order to compare (i) bonding to hypomineralized enamel and normal enamel, (ii) bonding to hypomineralized enamel using etch-and-rinse and self-etch adhesives, and (iii) bonding to hypomineralized enamel following deproteinization with 5% NaOCl and no deproteinization. NaOCl is a proven protein denaturant [14,15]. As the hypominerlized enamel has increased protein content that could interfere with bonding from adhesives, researchers [6] have suggested the use of 5% NaOCl as a deproteinization agent to remove the excess protein and enhance the bond strength to hypominerlized enamel.

Until date, there is no published review on bonding to hypomineralized enamel substrate, though it is a clinically relevant topic. Therefore, this systematic review was performed in order to answer the following questions that had tremendous clinical importance:

1. Does resin dental adhesives achieve inferior bonding to hypomineralized enamel when compared to normal enamel?
2. Does self-etch dental adhesives bond better to hypomineralized enamel when compared with etch-and-rinse adhesives?
3. Does deproteinization with 5% NaOCl before adhesive application procedure enhance bonding performance of resin dental adhesives to hypomineralized enamel?

Methods

This systematic review was reported following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [16].

Search strategy

Clinical and laboratory studies that evaluated the bond achieved between resin adhesive and hypomineralized enamel were included. The electronic databases searched for identifying the relevant studies included PubMed, Scopus, and Web of Science. The key words and their sequence used for searching through electronic databases were:

#1 hypomineralization OR hypomineralized OR hypocalcified OR MIH OR amelogenesis imperfecta

#2 enamel OR tooth OR teeth

#3 Bonding OR bond OR adhesion

#4 (#1) AND (#2) AND (#3)

There was no limit set for the year of publication. The last search was performed on 10th July 2015. MeSH terms were not used. Only the specified keywords mentioned in this review were used for the search. Two authors (ME and CY) were involved in the search.

Study selection

Only studies with full text article were included. Further relevant articles quoted in the reference list of the retrieved studies were accessed through further electronic search and hand search. Sixty-six articles were identified as duplicates and were excluded. Two authors (ME and CY) screened the title and the abstract. Any disagreement was discussed with a third person (GL) and was decided.

Eligibility criteria

This review includes only studies that provided:

(1) A clear objective for conducting the study and/or a note of the hypothesis tested.

(2) Adequate information about the methodology, including the groups studied, sample size per group and the study design for testing the hypothesis.

(3) Adequate information on the materials used in the study and the equipment used for testing.

(4) For laboratory-based studies, test group(s) in which bonding was achieved to hypomineralized enamel substrate and a control group with bonding to sound enamel substrate.

(5) Teeth with natural enamel hypomineralization (including MIH and hypocalcified AI) only. Studies that used teeth with artificial enamel demineralization were excluded from this review.

(6) Adequate information on how hypomineralized enamel was differentiated from sound enamel.

(7) Laboratory-based studies that performed bond strength testing should have used composite resin for restoration/crown build-up, therefore studies in which teeth with restorations/crown build-up done exclusively with glass ionomer cements, resin-modified glass ionomer cements and compomers were not considered.

(8) Adequate information on the outcome measures. For laboratory-based studies, in particular the bond strength measurements with a standard testing protocol.

(9) For *in vivo* studies, the follow-up assessment should have been done in a blinded manner.

(10) An appropriate statistical test performed to analyze the data. Also any studies with inadequate information on the results obtained from the study (with the statistical inference) were not included in the review.

Data extraction

1 author (ME) independently completed the full text review. Inclusion was based on the consensus of 2 authors (ME and CY). In order to answer the specific questions raised in this review data were sought for the following variables: type of enamel substrate (sound Vs. hypomineralized), type of dental adhesive: (etch-and-rinse Vs. self-etch) and enamel treatment: (deproteinization Vs. no-deproteinization) based on objective of the included studies. Outcome measures for laboratory studies will be the mean bond strength between intervention and control groups. For in vivo studies, clinical performance of the bonded interfaces such as retention of restoration, presence/absence of marginal discoloration etc. will be considered as the outcome measures.

Data analysis

The extracted data from the included studies were assessed for risk of bias, summarized and conclusions were derived for answering the specific questions rose in this review.

Assessment of risk of bias

Each included study for the full text review was individually assessed for the risk of bias. For in vivo studies, proper randomization of study participants between intervention and control groups, blinding of the operator and/or observer during follow-up of the subjects

etc. will indicate reduced risk of bias. Similarly, for laboratory studies, randomization of the samples between the test and control groups, proper methodology including strict bonding protocols and use of standard test methods for bond strength evaluation will indicate reduced risk of bias.

Results

The progress through each stage of the review is shown in Fig. 1. The search using the electronic databases with the specified key words retrieved a total of 141 articles. Out of them, 130 articles were excluded after the initial screening, leaving 11 articles for full text evaluation. There were 2 articles that were retrieved from the reference lists and were added to these 11 articles and hence, a total of 13 articles were evaluated by full text. Nevertheless, 7 articles did not meet the inclusion criteria of this review and were excluded. Given this, a final total number of 6 studies that met the inclusion criteria were included for this review.

The descriptive statistics of the included studies are shown in Table 1 and 2. The list of excluded studies and the reasons for their exclusion are shown represented in Table 3. Bonding to teeth affected with HAI was studied by three included studies [17,18,19] of which 1 study [18] is an *in vivo* study and the other 2 studies [17,19] are laboratory studies. Bonding to first permanent molars affected with MIH was studied by three other included studies [20,21,22] of which 1 study [21] is an *in vivo* study and the other 2 studies [20,22] are laboratory studies.

Enamel treatment was performed in 4 studies [17,18,19,22] out of 6 included studies, in which enamel was treated with 5% NaOCl for 1 minute after acid etching and before adhesive application procedure. In one study [22], two additional groups in which resin infiltrant with ICON® (DMG, Hamburg, Germany) was performed as a pre-treatment before performing the bonding procedure.

Five studies [17,18,19,20,22] out of the 6 included studies have tested bonding composite resin restorations to the hypomineralized enamel and 1 study [21] compared retention of bonded sealant versus non-bonded sealant to occlusal surfaces of first permanent molars affected with MIH. Four laboratory studies [17,19,20,22] that compared bonding to hypomineralized enamel with sound enamel showed that the bond strength of resin composite bonded to hypomineralized enamel was significantly lower than that to sound enamel. The bonding performance of different adhesives to hypomineralized enamel was not extensively studied as among the included studies in this review, 5 studies [17,18,19,20,21] used only one type of 2-step etch-and-rinse adhesive, 2 studies [20,22] used only one type of 2-step self-etch adhesive and only 1 study [20] compared a 2-step etch-and-rinse adhesive with a 2-step self-etch adhesive. The study that compared the adhesives [20] concluded that, 2-step etch-and-rinse adhesive did not differ significantly from 2-step self-etch adhesive in their ability to bond to both normal and hypomineralized enamel.

Out of 4 studies [17,18,19,22] that tested deproteinization of hypomineralized enamel with 5% NaOCl before adhesive application, 3 studies [17,18,22] showed improved

bonding performances and one study [19] showed no difference in bonding performance to hypomineralized enamel with adhesives after deproteinization with 5% NaOCl when compared to no deproteinization.

The study [21] that compared the retention of bonded sealant versus non-bonded sealant to occlusal surfaces of first permanent molar teeth affected with MIH showed that improved sealant retention could be achieved when sealant placement was done after an adhesive application when compared to sealant placement without a prior adhesive application.

Discussion

Teeth affected with HAI (a hereditary enamel defect) and MIH (a developmental enamel defect of systemic origin) is very challenging to treat, as the affected teeth are hypersensitive and prone to caries and post-eruptive breakdown. Hypomineralized enamel from a first permanent molar tooth affected with MIH may show varying degree of hypomineralization which clinically appears as white to yellow or brown in colour based on the extent of hypomineralization. The chemical composition and mechanical properties also varies with the extent of hypominerlization, which influences the choice of restorative material and the bonding performances. Therefore, it requires systematic treatment planning for prevention of sensitivity and caries. In the affected teeth with post-eruptive breakdown, restorations with appropriate materials are required.

A reduction in mineral content [5,9,10,11] and an increase in protein content [23,24] pose great challenges to bonding to teeth with HAI and MIH using adhesive restorative materials. Therefore, a dentist planning for any preventive or restorative procedure that involves bonded materials should be aware of the alterations in this substrate that might have significant effect on bonding. The choice of appropriate restorative materials depends on several factors, such as overall stage of dental development, status of the affected teeth, such as extent of hypomineralization, post-eruptive breakdown, sensitivity, oral hygiene status and caries-risk of patient. Irrespective of the type of restorative material chosen for the restoration, bonding to the substrate is involved in all of them. An improved bonding to this affected tooth substrate at the early stage of dental development helps in preservation of this altered tooth substance, allowing multiple choice of definitive restorations at a later stage, when occlusion and final gingival level is well established. Additionally, improving durability of the bonded restorations can avoid unnecessary financial burden arising due to repeated restorations.

In general, there are a limited number of studies that have evaluated bonding to hypomineralized enamel. This could be due to difficulty in recruitment of study participants for an *in vivo* study and more so in collecting extracted teeth with hypominerlized enamel for a laboratory study. Two *in vivo* studies [18,21] included in this review used “split mouth study design” in order to test the bonding strategies to hypomineralized enamel. Split mouth design is a very good method to compare an intervention with a control in the same patient. Therefore, any results (success or failures) obtained would most likely be due to the tested intervention and not due to patient-related

confounding factors. Henceforth, this study design can significantly reduce bias in clinical oral research studies.

In this review, Sonmez et al. [18] have used only 4 patients in their *in vivo* study but have tested bonding on 32 teeth. It is important to note that conditions like HAI are not very common and therefore it is very challenging to conduct research studies involving more participants with such rare clinical conditions. Apart from considering the number of participants in the study by Sonmez et al. [18], other important factors like study design (split mouth), independent observer (blinded) evaluation of the bonded teeth have strictly been followed, which prove the validity of the study. Saroglu et al. [17] used exfoliated primary teeth affected with HAI in their laboratory study, as permanent teeth affected with HAI are not frequently extracted, unless otherwise the teeth are badly broken down.

Deproteinization with 5% NaOCl has been shown to improve bonding to hypomineralized enamel [17,18,22]. The studies included in this review that tested deproteinization on bonding [17,18,19,22] involved hypomineralized teeth from either of the conditions: HAI or MIH. The 5% NaOCl is commonly used in dental pulp therapy for dissolving organic part of necrotic pulp. Increased protein content in the hypomineralied enamel [23,24] compared to normal enamel could have interfered with achieving optimum bond. Therefore, deproteinization using 5% NaOCl helps in achieving better bond strength to this altered substrate. As only a few studies have been conducted in this area, it is difficult to draw definitive conclusions. Hence, more studies are needed in this area to confirm these findings.

Regarding the type of adhesives that could bond better to hypomineralized enamel, only one study [20] compared bonding to hypomineralized enamel (MIH molars) with normal enamel using a 2-step etch-and-rinse and a 2-step self-etch adhesives. The study results did not show any significant difference in bonding between the two tested adhesives to both normal and hypomineralized enamel. Therefore, there is no answer for the question on “type of adhesive” for superior bonding to hypomineralized enamel and again, more studies are needed to be performed in this area to draw any definitive conclusions.

Lygidakis et al. [21] showed that the retention of bonded sealant could be superior than retention of non-bonded sealant to occlusal surfaces of hypomineralized enamel. The authors explained that single-bottle adhesives have a great ability to flow deeply into capillary-like spaces of the etched enamel surface and promote an optimal resin tag penetration and enhanced adhesion. The hydrophilic monomers present in the contemporary bonding agents increase surface wetting and resin penetration [25].

From this systematic review, we conclude that:

(1) Resin dental adhesives achieve inferior bonding to hypomineralized enamel when compared to normal enamel.

(2) There are no sufficient evidences to prove that self-etch dental adhesives bond better to hypomineralized enamel when compared with etch-and-rinse adhesives.

(3) Enamel deproteinization with 5% NaOCl before adhesive application procedure may enhance bonding performance of resin dental adhesives to hypomineralized enamel.

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Figure 1. Flow chart of the articles selection process

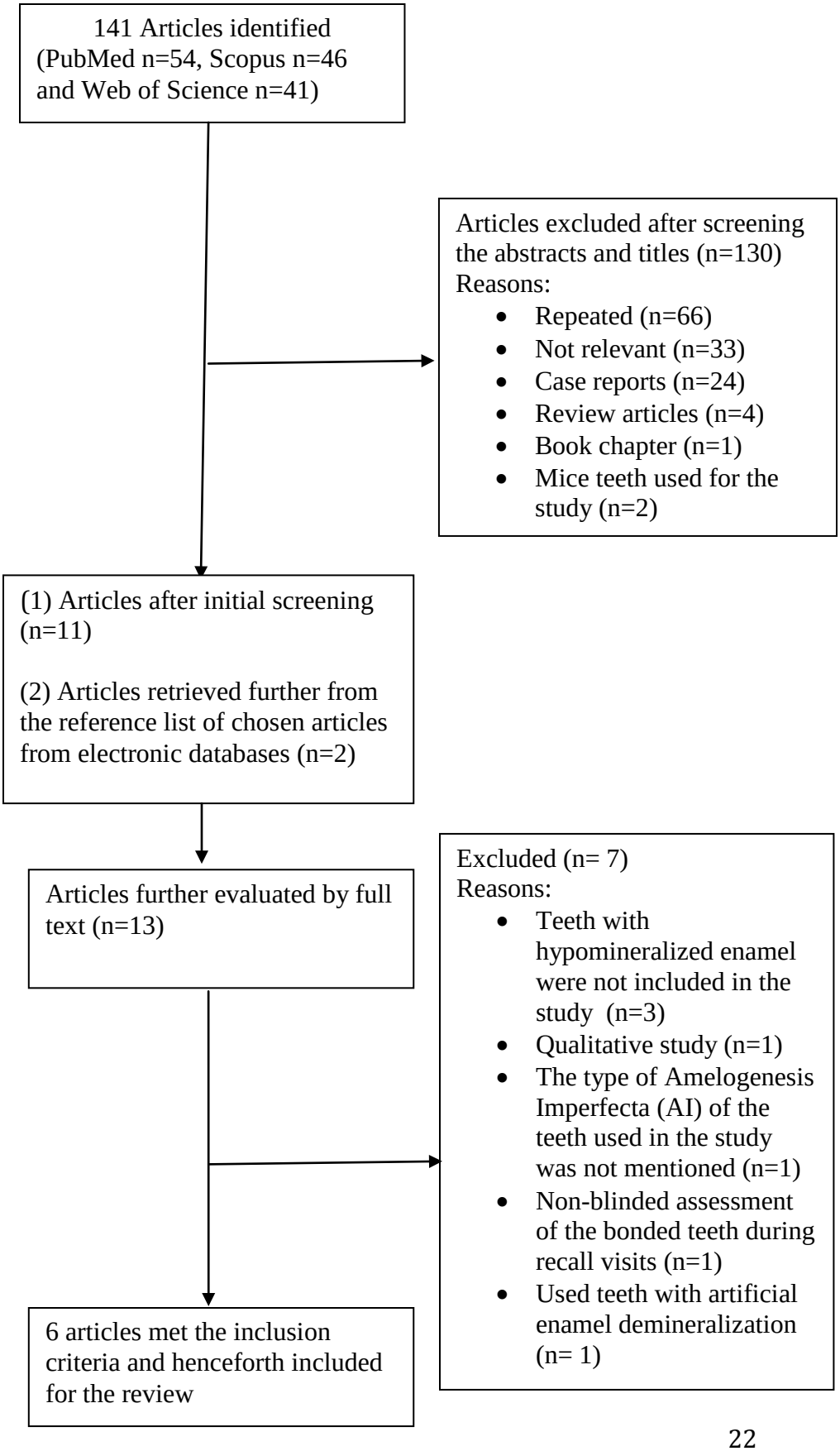

Table 1. Descriptive statistics of in vivo studies included in the review

Author & Year	Type of teeth	Sample size	Study groups	Resin sealant/Resin adhesive system(s) tested	Test method adopted for bond strength testing (*laboratory* studies only)	Finding(s)
Lygidakis et al 2009 [21]	Hypomineralized first permanent molars Split mouth design	Initial sample-54 children with two contra-lateral maxillary/mandibular hypomineralized first permanent molars, making a total of 108 molars. Final sample-After 48 months, 47 children with 94 teeth were available for assessment	Group A-etch+bond+seal Group B-etch+seal	Adhesive-One-step *(2-step E & R)* Resin sealant-Fissurit	-	After 48 months: Teeth in Group A: 70.2% were fully sealed, 29.7% were partly sealed and none were lost. Teeth in Group B: 25.5% were fully sealed, 44.6% were partly sealed and 29.7% were lost.
Sonmez et al 2009 [18]	Hypocalcified Amelogenesis imperfect Split mouth design	32 permanent teeth (30 incisors and 2 first premolars) from 4 children (aged 8 to 11 years of age).	Control group - no enamel deproteinization Test group – enamel deproteinization with 5% NaOCl for 1 minute after acid etching and before application of adhesive	Adhesive-Gluma One Bond *(2-step E & R)*	-	After 36 months of bonding: (1) Significantly less number of teeth from test group showed marginal discolouraton at the cervical area when compared with the control group. (2) No significant differences between the test and control groups for surface texture, maintenance of interproximal contact, and recurrent caries.

E & R- etch & rinse

Table 2. Descriptive statistics of laboratory studies included in the review

Author & Year	Type of teeth	Sample size	Study groups	Resin sealant/Resin adhesive system(s) tested	Test method adopted for bond strength testing (*laboratory* studies only)	Finding(s)
Chay et al 2014 [22]	Hypomineralized first permanent molars	152	Group 1- NE (No pre-treatment) Group 2- HE (No pre-treatment) Group 3-HE (pre-treated with a resin infiltrant, Icon ®) Group 4-HE pre-treated with 5.25% NaOCl then infiltrant Group 5-HE pre-treated with 5.25% NaOCl	Adhesive-Clearfil SE Bond *(2-step SE)*	Micro-shear test	Increased BS to HE was obtained by deproteinization with 5.25% NaOCl with or without subsequent resin infiltration
Faria-e-Silva et al 2011 [19]	Test group-Unerupted permanent molars with HAI Control group-Sound third molars	Test group -5 Control group -5	(a) Half the number of hemi-sections – no enamel deproteinization (b) The correspondent hemisection of the same tooth – soaked in 5% NaOCl for 1 minute after acid etching procedure	Adhesive-Single Bond 2 *(2-step E & R)*	Micro-shear test	(1) Hardness of NE was higher than hardness of enamel affected by HAI (2) Higher BS were obtained to NE (3) Deproteinization with NaOCl did not influence BS (4) A positive linear relationship between enamel hardness and BS was observed
Saroglu et al 2006 [17]	Test group-primary teeth with HAI Control group-comparable sound primary teeth	Test group -7 Control group -7	Group 1 (control group)- Half the number of hemi-sections – no enamel deproteinization (b) Group 2 (test group) The correspondent hemisection – enamel deproteinization with 5% NaOCl for 1 minute after acid	Adhesive-Gluma One Bond (*(2-step E & R)*	Shear test	(1) BS to enamel with HAI was significantly lower when compared with BS to sound enamel (2) Deproteinization with NaOCl to sound enamel did not significantly improve the BS

			etching procedure			when compared with the control group (3) Deproteinization with NaOCl to enamel with HAI significantly improved the BS when compared with the control group
William et al 2006 [20]	Hypomineralized first permanent molars	120 teeth were used in this study of which 55 teeth were used for BS testing	1. NE bonded with 2-step E & R adhesive 2. NE bonded with 2-step SE adhesive 3. HE bonded with 2-step E & R adhesive 4. HE bonded with 2-step SE adhesive	Adhesive- (1) Single Bond 2 *(2-step E & R)* (2) Clearfil SE Bond *(2-step SE)*	Microshear test	(1) The microshear bond strength of resin composite bonded to hypomineralized enamel was significantly lower than control enamel (2)The 2-step E & R adhesive and the 2-step SE adhesive did not differ significantly in their ability to bond to both NE and HE

NE-Normal enamel, HE-Hypomineralized enamel, HAI – Hypocalcified Amelogenesis imperfecta, NaOCl – sodium hypochlorite, E & R- etch & rinse, SE-Self-etch, BS- bond strength.

Table 3. Excluded studies from the review that did not fulfill the inclusion criteria.		
Author and Year	**Study design**	**Reasons for exclusion**
Alonso and Caserio 2012 [26]	Laboratory study	Teeth with hypomineralized enamel were not included in the study
Aras et al 2013 [27]	Laboratory study	Teeth with hypomineralized enamel were not included in the study
Gandhi et al 2012 [28]	Laboratory study	Qualitative study, bond strength was not measured
Harley and Ibbetson 1993 [29]	In vivo	(1) The type of Amelogenesis Imperfecta of the affected teeth included in the study was not mentioned. (2) No criteria for choosing material to bond to enamel (3) A part of the included teeth in the study was bonded with GIC
Lygidakis et al 2003 [30]	In vivo	No information about blinding of the observer who performed assessment of the bonded teeth during recall visits in the study
Newman et al 1995 [31]	Laboratory study	Teeth with hypomineralized enamel were not included in the study
Shahabi et al 2014 [32]	Laboratory study	Used teeth with artificial enamel demineralization