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ELISÂNGELA DE JESUS CAMPOS

AVALIAÇÃO ESTOMATOLÓGICA EM PACIENTES PEDIÁTRICOS TRANSPLANTADOS HEPÁTICOS ACOMPANHADOS NO SERVIÇO DE GASTROENTEROLOGIA PEDIÁTRICA DO COMPLEXO HUPES-CPPHO DA UNIVERSIDADE FEDERAL DA BAHIA

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Salvador- BA
2013

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Orientador: Prof[a.] Dr[a.] Luciana Rodrigues Silva
Co-Orientador: Prof. Dr. Marcel Lautenschlager Arriaga

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EPÍGRAFE

“Aprendi com as Primaveras a me deixar cortar para poder voltar sempre inteira.”

Cecília Meireles

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LISTAS DE ABREVIATURAS E SIGLAS

AGS	Alagille syndrome
BA	Biliary atresia
ceo-s	Superfícies cariadas, extraídas e obturadas
CsA	Ciclosporine A
dmfs	decayed, missing and filled primary surface
dmft	decayed, missing and filled primary teeth
DMFT	Decayed, Missing and Filled Permanente Teeth
DB	Direct bilirubin
EHBA	Exrahepatic biliary atresia
FSV	Fat-soluble vitamin
GBI	Gingival Bleeding Index
LT	Liver transplantation
NADPH	Nicotinamide adenine dinucleotide phosphate
OHI	Oral Hygiene Index
PSR	Periodontal Screening and Recording
SD	Standart deviation
TB	Total bilirubin
UFBA	Universidade Federal da Bahia
WHO	World Health Organization

RESUMO

OBJETIVO: O objetivo deste estudo foi avaliar as condições de saúde bucal de crianças com doença hepática terminal submetidas a transplante hepático.

MÉTODOS: Este estudo de série de casos foi realizado com uma amostra de 55 crianças e adolescentes (n=18 meninos e n=37 meninas) entre 1 e 17 anos, submetidos a transplante hepático (n=52) ou em lista de espera para o transplante (n=3) que faziam acompanhamento médico no Centro de Estudos de Gastroenterologia e Hepatologia Pediátricas do Complexo Hospitalar Professor Edgard Santos da Universidade Federal da Bahia. O estudo foi realizado através de um questionário, exame dos tecidos moles da boca, determinação da prevalência de cárie, hipoplasia, hipomineralização, descoloração dentária, condição periodontal e higiene oral. Os resultados foram determinados através de estatística descritiva.

RESULTADOS: A atresia biliar foi a principal indicação para o transplante hepático na amostra (n=36/65,45%). Foi observada presença de hipoplasia em 28 crianças (50,90%), hipomineralização em 44 (80%) e descoloração dentária em 31 (56,36%) delas. A hiperplasia gengival foi encontrada em apenas 3 (5,45%) crianças e a média de sextantes com sangramento gengival foi 4,07±1,76. A experiência de cárie entre as crianças foi de 3,59/ 2,06 (ceo/CPOD).

CONCLUSÕES: A ocorrência de hipoplasia, hipomineralização e descoloração dentária foi elevada entre as crianças com histórico de doença hepática, principalmente entre aquelas submetidas a transplante por atresia das vias biliares. A higiene oral deficiente, os hábitos alimentares e falta de acesso ao tratamento odontológico parecem ter influenciado a experiência de cárie e a condição periodontal observadas muito mais do que a doença hepática.

Palavras-chave: doença hepática, hiperbilirrubinemia, atresia biliar, transplante hepático, cárie dentária, hipoplasia

ABSTRACT

OBJECTIVE: The aim of this study was to assess the oral health status in children with end-stage liver disease undergoing liver transplantation.

METHOD: This is a case series study conducted in 55 children (18 boys and 37 girls / age range: 1 year to 17 years) who underwent LT (n=52) or were on waiting list (n=3) and were referred for medical follow-up at the Center for Pediatric Gastroenterology and Hepatology, University Hospital Complex Professor Edgard Santos, Federal University of Bahia, Brazil. Study procedures included the completion of a questionnaire, an oral soft tissues examination, assessment of caries, hypoplasia, hypomineralization, tooth discoloration, periodontal status, and oral hygiene index. Descriptive statistics were determined and the results are given as mean (SD or range).

RESULTS: Biliary atresia was the most common cause of liver transplantation in the sample (n= 36/ 65.45%). 28 children (50.90%) exhibited hypoplasia, enamel hypomineralization was observed in 44 children (80%), and tooth discoloration was present in 31 (56.36%) children. Gingival enlargement was observed only in 3 (5.45%) and the mean of gingival bleeding was 4.07±1.76. Caries experience among the children was 3.59/ 2.06 (dmft /DMFT).

CONCLUSION: The presence of hypoplasia, hypomineralization and tooth discoloration were high among children with history of liver disease, particularly among those undergoing transplantation for biliary atresia. The poor oral hygiene practices, dietary habits and access to dental care services appear to have influenced the experience of caries and periodontal status more than the liver disease.

Keywords: liver disease, hyperbilirubinemia, biliary atresia, liver transplantation, dental caries, hypoplasia.

SUMÁRIO

1 INTRODUÇÃO

A doença hepática na criança é causa significante de morbidade e mortalidade no mundo. Avanços no diagnóstico e tratamento, especialmente o transplante hepático, tem melhorado as taxas de sobrevivência em crianças com a doença hepática, que agora podem crescer e atingir a idade adulta.

Embora a icterícia fisiológica seja um achado comum em recém-nascidos, as crianças que desenvolvem icterícia grave ou persistente devem ser investigadas para excluir hemólise, sepse, ou doença hepática subjacente. Icterícia neonatal que persiste além de 14 ou 21 dias deve ser sempre investigada, sendo essencial determinar se a icterícia é devido a um aumento da bilirrubina conjugada ou não conjugada, uma vez que a doença hepática é associada à hiperbilirrubinemia conjugada.

As taxas elevadas da bilirrubina sérica provocam a sua deposição nas mucosas e na pele, contudo, quando estas taxas são normalizadas, a pigmentação desaparece em função da intensa renovação celular nestes tecidos. Na cavidade oral, a hiperbilirrubinemia se manifesta pela pigmentação da gengiva e dos tecidos moles, bem como dos dentes em desenvolvimento. Contudo, diferente do que ocorre nos tecidos moles, a pigmentação dos tecidos duros do dente em formação é permanente, conferindo-lhes uma coloração que varia do amarelo ao verde.

Outras manifestações orais que podem estar relacionadas à doença hepática são a hipoplasia e o retardo na erupção dentária. A ocorrência de lesões de cárie em crianças com história médica de doença hepática acompanhada de absorção intestinal deficiente de vitamina D, que é essencial para o processo de mineralização dos dentes, é creditada, muitas vezes, à presença de hipoplasias. Contudo, não há consenso sobre este aspecto na literatura, e a incidência de cáries parece estar mais relacionada aos cuidados deficientes com a higiene oral e ao uso prolongado da mamadeira do que à presença de defeitos na mineralização.

Nos últimos anos, o padrão das manifestações orais da doença hepática e do seu tratamento tem sido modificado, especialmente como uma consequência da realização do transplante de fígado precocemente e dos efeitos colaterais das drogas utilizadas na terapia imunossupressora pós-transplante. A incidência de hiperplasia gengival tem diminuído pelo

uso do tacrolimus em substituição à ciclosporina, assim como a ocorrência, gravidade e extensão da pigmentação dentária nas dentições decídua e/ou permanente. A realização precoce do transplante parece estar associada à diminuição da severidade da descoloração dentária.

O atendimento odontológico às crianças com doença hepática deve ser realizado antes e após o transplante de fígado de forma efetiva e segura. Para isso é necessário que o cirurgião-dentista conheça a doença hepática e as suas manifestações orais. Contudo, muitos profissionais se negam a atender estas crianças, especialmente após o transplante, por conta da terapia imunossupressora e do receio em relação ao uso de anestésicos e sua metabolização hepática.

O tratamento odontológico a que estas crianças tem acesso é, muitas vezes, limitado ao período pré-transplante, nas unidades hospitalares especializadas, não havendo o acompanhamento na fase de controle posterior ao transplante, o que pode contribuir para o surgimento de lesões cariosas e possibilitar o surgimento de focos infecciosos na cavidade oral. Além disso, o comprometimento estético causado pela deposição da bilirrubina na dentina, durante a formação dos dentes, pode influenciar negativamente o convívio social da criança e se prolongar até a fase adulta, exigindo uma avaliação criteriosa de cada caso para a indicação ou não de um tratamento estético de acordo com a idade do paciente.

Desse modo, esta tese teve como objetivo descrever as condições de saúde bucal de crianças submetidas a transplante de fígado no Hospital Antônio Cândido Camargo (A.C. Camargo Cancer Center) e acompanhadas no período pós-transplante no Centro de Estudos de Gastroenterologia e Hepatologia Pediátricas do Centro Pediátrico Prof. Hosanah de Oliveira (CPPHO) do Complexo Hospitalar Universitário Professor Edgard Santos (HUPES) da Universidade Federal da Bahia (UFBA) em relação às manifestações bucais da doença hepática e do tratamento imunossupressor, destacando a importância do conhecimento da história médica da criança como parte essencial para o sucesso do tratamento odontológico.

2 OBJETIVOS

- revisar a literatura sobre a as manifestações bucais da hiperbilirrubinemia associada à atresia das vias biliares em crianças (Artigo 1).

- identificar a relação entre a descoloração dentária e a atresia das vias biliares extra-hepática através de uma série de casos (Artigo 2).

- determinar a experiência de cárie dentária e descrever as condições de saúde bucal em crianças portadoras de doença hepática terminal submetidas a transplante de fígado (Artigo 3).

- descrever os achados clínicos odontológicos em crianças portadoras de doença hepática colestática através do relato de casos clínicos (Artigo 4 e 5).

3 RESULTADOS

Os resultados desta tese de doutorado foram traduzidos pela elaboração dos seguintes artigos:

3.1 Primeiro Artigo

- Manifestações bucais da hiperbilirrubinemia associada à atresia biliar em crianças: revisão da literatura

3.2 Segundo Artigo

- Tooth discoloration associated with extrahepatic biliary atresia in children: Case series

3.3 Terceiro Artigo

- Oral and dental aspects of children undergoing liver transplantation

3.4 Quarto Artigo

- Green teeth in children with biliary atresia: Case Reports

3.5 Quinto Artigo

- Oral Findings in Children with Alagille Syndrome: Case Reports

3.1 ARTIGO 1

Manifestações bucais da hiperbilirrubinemia associada à atresia biliar em crianças: revisão da literatura

Revista: Panamericana de Salud Pública

Situação: Submetido

Título: Manifestações bucais da hiperbilirrubinemia associada à atresia biliar em crianças: revisão da literatura

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RESUMO

Objetivo: Realizar uma revisão da literatura sobre a descoloração dentária associada à atresia das vias biliares em crianças.

Métodos: Foram pesquisadas as bases de dados Pubmed, Medline e Lilacs utilizando os termos “liver diseases”, “child”, “hyperbilirubinemia”,“tooth discoloration”, “green teeth”. A busca foi realizada sem delimitação de período de tempo . Para cada artigo foram registradas as informações concernentes ao título do estudo, ano de realização, autoria, doença hepática, presença de descoloração dentária, defeitos de esmalte, hiperplasia gengival e alteração dos tecidos moles da boca.

Resultados: Foram selecionados 15 artigos, sendo 12 relatos de casos clínicos e 3 estudos de corte transversal. Em todos os estudos selecionados a presença da descoloração dentária foi encontrada nos pacientes com atresia biliar, variando a coloração dos dentes desde o amarelo até o verde, enquanto outros parâmetros odontológicos (hiperplasia e descoloração gengival, hipoplasia, hipomineralização e retardo de erupção) variaram entre os estudos.

Conclusões: Esta revisão da literatura reforça as conclusões prévias de que atresia biliar causa a pigmentação dos dentes durante a sua formação pelo acúmulo da bilirrubina. Contudo, evidencia que não existem estudos longitudinais sobre as condições bucais na população pediátrica submetida a transplante hepático até fase adulta ou mesmo adolescência.

Palavras-chave: descoloração dentária, criança, doença hepática, atresia biliar

INTRODUÇÃO

Crianças portadoras de doença hepática e submetidas a transplante de fígado requerem cuidados odontológicos especiais a fim de reduzir o risco de infecções sistêmicas originadas na cavidade oral. A doença hepática apresenta vários aspectos a depender da gravidade: icterícia, anemia, déficit de crescimento, prurido, hepatoesplenomegalia, ascite, encefalopatia, hipertensão portal e varizes no esôfago, coagulopatia, metabolismo de medicamentos alterado e predisposição a infecções (Sheehy et al., 1999).

O transplante de fígado melhorou significativamente a taxa de sobrevida das crianças e adolescentes com doença hepática terminal. Na atualidade, as taxas de sobrevida são de aproximadamente de 90% no primeiro ano (Achar et al. 2011). As principais indicações para o transplante hepático em crianças são: atresia biliar (40-70%), desordens metabólicas, hepatite fulminante, desordens colestáticas, tumores malignos e doença hepática crônica (Sheehy et al., 1999). Contudo, tanto a doença hepática como a complexidade do tratamento imunossupressor prolongado, após o transplante de fígado, podem causar patologias orais e dentais.

As manifestações bucais mais encontradas em crianças submetidas a transplante de órgãos sólidos são: (a) pigmentação verde dos dentes e gengiva, devido à hiperbilirrubinemia antes do transplante; (b) hiperplasia gengival e gengivite, efeito adverso mais comum da terapia imunossupressora (principalmente com ciclosporina); (c) higiene oral deficiente, frequentemente devido à carência de cuidados odontológicos preventivos, característico de crianças com doenças crônicas; (d) hipoplasia dentária, devido a distúrbios sistêmicos durante a formação e mineralização do dente; e (e) aumento da incidência de cárie dentária (Davidovich et al., 2013).

Na literatura existem vários estudos que fazem a associação entre a presença de descoloração dentária e suas possíveis causas de acordo com a história médica. As causas mais comuns para a presença de dentes verdes em crianças incluem hipoplasia biliar (Sheehy et al., 1999; Chambers et al., 2012), colestase associada a sepse (Alto et al., 2004; Naudi et al., 2008; Conboy, Valentini, 2010), doença hemolítica (Barta et a., 1989), infecção por citomegalovírus (Tjon A Ten, Houwen, 2007) e, principalmente, atresia das vias biliares (Lin et al., 2003; Sommer et al., 2010; Carrillo et al., 2011; Rangé et al., 2012; Chambers et al., 2012).

A atresia biliar é a colangiopatia inflamatória obliterativa destrutiva mais significante nas crianças e afeta os ductos biliares intra- e extra-hepáticos e, se não for tratada, pode progredir para cirrose hepática e levar à morte até os 2 anos de vida (Hartley, Davenport, Kelly, 2009), representando a indicação mais comum de transplante hepático em crianças (Hartley Davenport, Kelly, 2009; Achar et al., 2011).

A descoloração dos dentes pode afetar as dentições decídua e permanente, levando à pigmentação de qualquer dente que esteja sendo formado durante o período de hiperbilirubinemia. Acredita-se que a extensão da descoloração e a sua intensidade estejam diretamente relacionadas com a duração e severidade da patologia, respectivamente (Alto et al., 2004; Chambers et al., 2012).

O objetivo deste trabalho foi realizar uma revisão narrativa da literatura sobre as manifestações bucais da atresia das vias biliares.

MATERIAIS E MÉTODOS

Para identificar os artigos acerca do tema proposto, realizou-se busca nas bases de dados Medline, Pubmed e Lilacs, no período de 1986 a 2013, mediante a utilização de termos em inglês com a seguinte estratégia de busca: *liver disease and children and tooth discoloration, hyperbilirubinemia and children and tooth discoloration, liver disease and children and green teeth, hyperbilirubinemia and children and green teeth*.

Após a consulta às bases de dados e a aplicação das estratégias de busca, foram encontrados estudos potencialmente elegíveis. Destes, após a identificação dos que apresentavam duplicidade entre as bases, foram selecionados os artigos para leitura dos resumos. Nos casos em que a leitura do resumo não era suficiente para estabelecer se o artigo deveria ser incluído, o artigo foi lido na íntegra para determinar sua elegibilidade. Desse modo, ao final, os artigos que não contemplavam os assuntos estudados foram excluídos.

Para a extração dos dados dos artigos, elaborou-se um instrumento contendo as seguintes informações: autores, ano de publicação, tipo de estudo, tamanho da amostra, diagnóstico,

presença/ausência de descoloração dentária, presença/ausência de alterações nos tecidos moles, índice de cárie ceo/CPOD, defeitos de formação do esmalte e atrasos na erupção dentária. A análise dos estudos identificados e selecionados foi feita de forma descritiva.

RESULTADOS

A busca eletrônica nas bases de dados resultou na identificação inicial de 139 artigos. Após o primeiro refinamento, para eliminação dos artigos em duplicidade (n =70) foram selecionados 69 artigos cujos títulos ou resumos tratavam da descoloração dentária associada à doença hepática ou da avaliação das condições bucais. Destes, 40 foram excluídos após a leitura dos títulos e resumos; 11 após a leitura integral do artigo; e 3 por não estarem disponíveis nas bases de dados, no portal CAPES ou para aquisição através do sistema SCAD da Bireme. Assim, após o segundo refinamento, foram selecionados 15 artigos para esta revisão (figura 1).

Dos 15 trabalhos selecionados, 12 eram relatos de casos clínicos e apenas 3 estudos de corte transversal (tabela 1). Em todos os estudos selecionados a presença da descoloração dentária foi encontrada nos pacientes com diagnóstico de atresia biliar, variando a coloração dos dentes desde o amarelo até o verde. E em função da grande variação da idade das crianças avaliadas, no momento dos exames clínicos dos respectivos estudos, a descoloração dentária foi identificada tanto em dentes decíduos como permanentes.

A avalição de cárie nos estudos, especialmente no relatos de casos clínicos, foi limitada à informação sobre a presença ou não de leões cariosas. A expressão desta avaliação na forma do índice ceo/CPOD foi descrita apenas em dois dos três estudos de corte transversal. A presença de defeitos na formação e/ou mineralização do esmalte não foi relatada na maioria dos estudos, assim como o retardo na erupção dos dentes.

A avaliação dos tecidos moles no estudos foi caracterizada, principalmente, pela referência à hiperplasia gengival causada pela terapia imunossupressora com ciclosporina.

DISCUSSÃO

A análise dos estudos selecionados na presente revisão da literatura aponta para a carência de estudos longitudinais e/ou transversais com amostras representativas da população infantil portadora da doença hepática ou submetida a transplante de fígado e as respectivas manifestações bucais. A maioria dos estudos são relatos de casos clínicos e os poucos estudos transversais contam com um número pequeno de participantes em suas amostras (tabela 1).

A icterícia fisiológica é um achado comum em recém-nascidos e está relacionada à fração não-conjugada da bilirrubina. A hiperbilirrubinemia conjugada, contudo, é definida pela concentração da bilirrubina conjugada maior do que 2mg/dL (34.2 mmol/L) ou maior do que 20% da bilirrubina total, e representa um marcador bioquímico da colestase, condição patológica que é definida como a redução na formação ou fluxo da bile (Brumbaugh, Mack, 2012).

A bilirrubina sérica é um produto da degradação da hemoglobina e pode ser depositada nos tecidos duros dentários durante a sua formação, resultando em descoloração e/ou hiploplasia nos períodos de hiperbilirrubinemia. Assim como, a sua deposição também ocorre em outros tecidos do corpo, contudo nos tecidos moles onde a renovação celular é intensa, após a remissão do quadro, a coloração desaparece (Wondimu et al., 1999).

Na maioria dos estudos selecionados (n=11/ 73,33%) a pigmentação dos tecidos moles na cavidade oral não foi relatada ou estava presente. O que pode ser explicado pelo fato de que após a realização do transplante os níveis de bilirrubina são controlados e retornam ao normal. No relato de caso descrito por Sommer et al. (2010) foi observada a pigmentação do lábio inferior, referida como um efeito da terapia imunossupressora.

No estudo de Lin et al. (2003) fotografias foram tiradas antes do transplante hepático para a avaliação da pigmentação dos dentes e gengiva. Os níveis de bilirrubina sérica estavam elevados no período pré-transplante e justificam os casos de pigmentação gengival observados. Concordam com este achado os resultados de Seow et al. (1991) que avaliaram a pigmentação da gengiva antes do transplante hepático e no período pós-transplante, que variou de 1 mês a 1 ano e 3 meses, apesar da redução dos níveis de bilirrubina. Morisaki et al. (1990) identificaram, por outro lado, a pigmentação da língua, mucosa bucal e assoalho da

boca, além da gengiva em um grupo de crianças com atresia biliar mas não submetidas a transplante hepático.

A distribuição das áreas pigmentadas nos dentes correspondem ao período no qual as taxas da bilirrubina estão elevadas por conta da atresia biliar no casos descritos, assim os autores afirmam que as regiões do dente que se desenvolvem após o tratamento cirúrgico, não são pigmentadas e apresentam aspecto de cor normal, podendo ser identificada uma linha dividindo as partes formadas antes e depois do tratamento da atresia biliar (Watanabe et al., 1999; Amaral et al., 2008; Carrillo et al., 2011).

A análise histológica de incisivos centrais superiores decíduos exfoliados, realizada e descrita por Carrillo et al. (2011), revelou que a pigmentação verde das unidades dentárias estava confinada à dentina, pois é nela e não no esmalte onde a bilirrubina se deposita. Concordam com este resultado Amaral et al. (2008) e Majewski et al.(1993) que também realizaram estudos histológicos em dentes com descoloração dentária provocada pela hiperbilirrubinemia associada à atresia das vias biliares.

Coras e facetas parecem ser uma boa alternativa para o tratamento estético nos casos de descoloração dentária causada pela hiperbilirrubinemia, pois uma vez que a dentina está pigmentada, a restauração com resinas pode não oferecer um resultado estético satisfatório (Carrilllo et al., 2011) e o clareamento dentário pode não ser efetivo (Amaral et al., 2008), como comprovado por Rangé et al. (2012) ao realizar a técnica clareadora sem sucesso em um paciente de 16 anos com dentes verdes e hiperplasia gengival. A opção de tratamento estético neste caso e no relato de Chambers et al. (2012) foi a colocação de coroas veneers. Contudo, para crianças pequenas este tratamento não tem indicação e o melhor a ser feito é orientar a família a não valorizar a cor dos dentes e aceitá-la apenas como uma consequência da doença.

O caso clínico relatado por Rangé et al. (2012) ilustra a combinação das consequências orais da terapia imunossupressora (hiperplasia gengival) e da hiperbilirrubinemia causada pela atresia biliar (dentes verdes). Este caso destaca a necessidade do conhecimento desta condição incomum pelos cirurgiões dentistas generalistas, a fim de melhorar o prognóstico para estes pacientes. O reconhecimento e a associação desta condição clínica com a história médica de atresia biliar podem evitar a realização de tratamentos odontológicos ineficazes, como o clareamento dentário, e auxiliar na escolha do tratamento estético mais adequado.

Os defeitos de formação do esmalte podem ocorrer nos pacientes com histórico de atresia biliar congênita em função do fato de que eles, muitas vezes, apresentam deficiência nutricional (Lin et al., 2003), especialmente das vitaminas lipossolúveis (A, D, E e K) (Brumbaugh, Mack, 2012), sendo a vitamina D essencial para a mineralização de ossos e dentes (Amaral et al., 2008). Além disso, a absorção deficiente da vitamina K pode favorecer a tendência ao sangramento nos pacientes com doença hepática crônica (Brumbaugh, Mack, 2012) e comprometer o tratamento odontológico.

Contudo, nos estudos selecionados verificou-se que apesar de a maioria não relatar o ceo/CPOD, eles fazem referência à presença de lesões cariosas e à necessidade de tratamento odontológico, destacando que a higiene oral deficiente (Zaia et al., 1993; Carrillo et al., 2011), o uso prolongado de mamadeira noturna (Rosenthal et al., 1986; Sheehy et al., 1999; Lin et al., 2003) e o uso de medicamentos contento açúcar (Rosenthal et al., 1986; Sheehy et al., 1999) parecem ser os responsáveis pelas leões cariosas observadas. Enquanto que os defeitos hiplopásicos parecem resultar dos efeitos da osteopenia e de distúrbios no metabolismo do cálcio e fósforo observados na doença hepática crônica. Do mesmo modo, o aumento da câmara pulpar , que é uma manifestação da hipoplasia da dentina, provavelmente resulta do raquitismo (Seow et al. 1991).

Wondimu et al. (2001) compararam os índices de cárie de crianças transplantadas, sendo a maioria delas por atresia das vias biliares, e verificaram não haver diferença significativa em relação a um grupo de crianças saudáveis. Contudo, observaram que os defeitos do esmalte, variando de opacidades a hipoplasia, e a pigmentação verde dos dentes era mais comum em crianças com atresia biliar antes do transplante.

Sheehy et al. (2000), compararam as condições de saúde bucal de um grupo controle com um grupo composto por 27 crianças submetidas a transplante hepático, sendo que 41% (n=11/27) delas tinha história médica prévia de atresia biliar. Os resultados mostraram não haver diferença significante na proporção de crianças livres de cárie nos dois grupos, bem como nas médias dos índices de placa bacteriana e gengivite. Contudo, verificaram que o componente “superfície perdida” do ceo-s no grupo de pacientes transplantados foi significante maior em relação ao grupo controle. Este resultado foi justificado como um reflexo da terapia cirúrgica radical de extração das unidades dentárias no período pré-transplante, pois a eliminação de focos infecciosos na cavidade oral é essencial para a realização do transplante. O caso

relatado por Majewski et al. (1993) relata a extração dos 20 dentes decíduos, sob anestesia geral, de uma criança de 3 anos de idade como parte do tratamento odontológico pré-transplante hepático.

Um dos principais problemas no tratamento da criança com doença hepática grave é a susceptibilidade para infecções e a tendência ao sangramento. Nos estudos selecionados, a hiperplasia gengival foi referida por alguns e associada ao uso da ciclosporina (Seow et al., 1991; Funakoshi et al, 1992; Rangé et al., 2012) ou ao seu uso em associação com a nifedipina, que pode causar hiperplasia gengival (Hosey et al., 1995). Contudo, Lin e Yang (2010) ao avaliar a hiperplasia gengival em crianças que receberam a ciclosporina após o transplante hepático, afirmaram que a hiperplasia gengival estava estatisticamente mais relacionada ao índice de placa bacteriana do que a outros fatores, como a idade, gênero, inflamação gengival e o nível sérico da ciclosporina.

Esta revisão da literatura reforça as conclusões prévias de que atresia biliar causa a pigmentação dos dentes durante a sua formação pelo acúmulo da bilirrubina, variando a cor da amarelo ao verde. Contudo, evidencia que não existem estudos longitudinais sobre as condições bucais na população pediátrica submetida a transplante hepático até fase adulta ou mesmo adolescência. A maioria dos trabalhos são relatos de casos clínicos de centros isolados.

É importante destacar que com a melhoria das técnicas cirúrgicas no transplante hepático e da terapia imunossupressora nos últimos anos, o número de crianças com atresia biliar que agora sobrevive tende a aumentar e, desse modo, o cirurgião-dentista deve estar preparado para reconhecer as consequências da doença e do seu tratamento para poder oferecer um atendimento odontológico adequado e de qualidade.

A erupção do primeiro dente de uma criança é sempre motivo de alegria e expectativa para os pais, assim a erupção de um dente pigmentado pode ser motivo de ansiedade e frustração. Em nenhum dos estudos analisados há referência a qualquer orientação ou informação aos pais sobre a possibilidade da criança portadora de atresia biliar e submetida a transplante hepático apresentar dentes pigmentados no futuro. A presença de dentes verdes, durante a fase infantil, apesar da estranheza que causa, é mais aceita do que na adolescência, fase do desenvolvimento humano permeada por tantos questionamentos e inseguranças.

Além do comprometimento estético, a pigmentação dos dentes traz implicações psicológicas que tendem a se agravar com a entrada da criança na adolescência e fase adulta. Desse modo, o cirurgião-dentista pode propor um tratamento odontológico que é ineficaz para este tipo de manchamento e gerar expectativas no paciente e seus pais que não serão satisfeitas. Conhecer a história médica do paciente com atresia biliar é essencial para o sucesso do tratamento odontológico, bem como a integração entre o cirurgião-dentista e o hepatologista a fim de diminuir o risco de infecções orais e dentais e de melhorar a qualidade de vida destes pacientes.

Conflito de interesses: os autores declaram não haver conflito de interesses.

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FIGURA 1. Fluxograma de identificação e seleção dos artigos para revisão da literatura sobre a associação entre descoloração dentária e doença hepática em crianças, Brasil, 1986 a 2012.

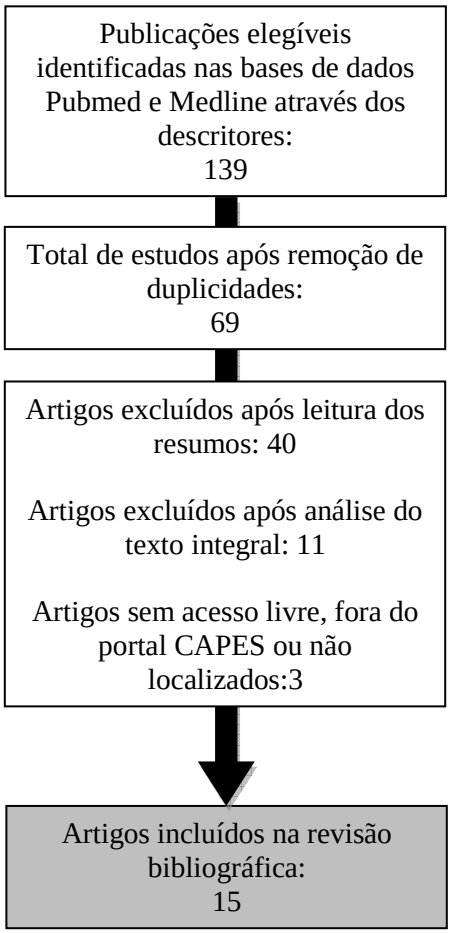

TABELA 1. Estudos sobre a associação entre descoloração dentária e atresia biliar em crianças.

Referência	Desenho do estudo	Diagnóstico	Grupo de estudo/ Sexo	Idade (anos)	ceo/ CPOD	Descolora-ção dos dentes	Descolora-ção dos tecidos moles	Hipoplasia dentária	Hipomine-ralização	Retardo de erupção	Hiperplasia gengival
Chambers et al., 2012 (United Kingdom)	Relato de caso	Atresia biliar	1(F)	7	NR	+(p)	-	NR	NR	NR	NR
Rangé et al., 2012 (França)	Relato de caso	Atresia biliar	1(M)	16	NR	+(p)	-	-	NR	NR	+
Carrillo et al., 2011 (Brasil)	Relato de caso	Atresia biliar	1(M)	7	NR	+(d)	-	NR	NR	-	-
Sommer et al., 2010 (Brasil)	Relato de caso	Atresia biliar	1(F)	11	NR	+(p)	+	+	NR	-	-
Amaral et al., 2008 (Brasil)	Relato de caso	Atresia biliar	1(F)	9	NR	+(d/p)	-	NR	NR	-	+
Lin et al., 2003 (Taiwan)	Corte transversal	Atresia biliar (n=31)	34 (22M/ 12F)	0-2 2-4 4-6	0±0 6,67±1,21 10,44±1,16	+ (d)	+	NR	NR	NR	NR
Wondimu et al., 2001 (Suécia)	Corte transversal	Atresia biliar (n=12)	30 (20M/10F)	2-19	2,0±2,8	+	NR	+	+	NR	+
Watanabe et al., 1999 (Japão)	Relato de caso	Atresia biliar (n=1)	2	11 7	NR	+ (d)	NR	NR	NR	NR	NR
Hosey et al., 1995 (United Kingdom)	Corte transversal	Atresia biliar (n=25)	55 (23M/32F)	4	NR	+(d/p)	NR	+	+	+	+
Zaia et al., 1993 (Brasil)	Relato de caso	Atresia biliar	1(M)	7	NR	+(d/p)	NR	+		_	+
Majewski et al., 1993 (EUA)	Relato de caso	Atresia biliar	1(M)	3	NR	+ (d)	NR	NR	NR	NR	NR
Funakoshi et al., 1992 (Japão)	Relato de caso	Atresia biliar (n=4)	5 (2M/3F)	4	NR	+ (d)	-	NR	NR	NR	+
Seow et al., 1991 (Australia)	Relato de caso	Atresia biliar (n=8)	9 (2M/7F)	3	NR	+ (d)	+	+	NR	+	+
Morisaki et al., 1990 (Japão)	Relato de caso	Atresia biliar (n=7)	7 (2M/5F)	3	NR	+ (d/p)	+	+	NR	+	NR
Rosenthal et al., 1986 (EUA)	Relato de caso	Atresia biliar (n=1)	2(M)	1	NR	+ (d/)	NR	NR	NR	NR	NR

Achados odontológidos: (-) ausente, (+) presente; NR, não relatado; NI, não investigado; (d) decíduo, (p) permanente
Sexo: (F) feminino, (M), masculino

3.2 ARTIGO 2

Tooth discoloration in children with extrahepatic biliary atresia: Case series

Revista: Clinical Oral Investigation

Situação: Submetido

TITLE PAGE

Title: Tooth discoloration in children with extrahepatic biliary atresia: Case series

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Abstract

Objectives The aim of this study was to assess tooth discoloration caused by hyperbilirubinemia associated with extrahepatic biliary atresia (EHBA) in children.

Material and methods Thirty children (20 girls and 10 boys) with history of EHBA were subdivided according to tooth discoloration into 4 groups: green, yellow–green, yellow, or normal aspect in color. Medical histories and previous serum bilirubin levels were obtained from patients' medical records using a questionnaire standardized data. The oral cavity was examined for the presence or absence of tooth discoloration, opacity, hypoplasia, and caries.

Results Twenty-one children (70%) exhibited hypoplasia, and enamel opacity was observed in 27 (90%). Five of the 30 children (16.66%) exhibited green tooth discoloration, and 14 of them (46.66%) a yellow pigmentation. Caries experience (dmft/DMFT) among the children was 3.33/1.42. The mean of serum bilirubin before liver transplantation was high in the groups of children with green and yellow–green tooth discoloration.

Conclusions The dental intrinsic staining by bilirubin in the sample resulted in discoloration vary from yellow to deep shades of green in both primary and permanent dentition. Teeth formed after the hyperbilirubinemia period and control of the disease was normal in color. In some cases the medical histories were incomplete and did not permit correlation between depth and duration of jaundice with the intensity of green staining.

Clinical Relevance The present case series supports the importance of patient's medical history and complete clinical examination in patients with EHBA for the presence of tooth discoloration.

Keywords: tooth discoloration, hyperbilirubinemia, extrahepatic biliary atresia, children

Introduction

Neonatal jaundice is a normal physiologic condition occurring during the transitional period after birth. It is not a rare disease in itself but rather a physical finding associated with multiple possible etiologies. Jaundice reflects the accumulation of the yellow–orange pigment bilirubin in the skin, sclera, and other tissues [1]. However, many pathological conditions also followed with cholestasis and jaundice. The largest diagnostic groups of pathological conditions related with increased of direct bilirubin are biliary atresia (BA), alpha-1-antitrypsin deficiency, and various forms of progressive familial intrahepatic cholestasis [2,3].

Prolonged jaundice is defined as jaundice lasting more than 14 days in term infants and 21 days in preterm infants [2,4,5]. Cholestatic jaundice is characteristic by direct bilirubin (DB) value greater than 1.0 mg/dL if the total bilirubin (TB) is less than 5 mg/dL, or a DB more than 20% of the TB if TB is greater than 5.0 mg/dL [5].

BA is the most life-threatening hepatobiliary disorder in children [4,6,7] resulting from a dynamic destructive inflammatory process of both intrahepatic and extrahepatic bile ducts [4,6,8]. BA is characterized by elevation of serum DB, and it presents shortly after birth with persistent jaundice, acholic stools, and dark urine [4,5].

There are few diseases where so much is known yet so little understood than the condition of BA [8]. The etiology of BA is largely unknown [4], and several mechanisms have been proposed to explain its progressive cholangiopathy [9]. Diagnosis of BA is difficult, and the golden standard for diagnosis is still operative cholangiography to visualize the biliary tract [4] and histologic examination of liver tissue.

BA is the most common indication of liver transplantation (LT) in pediatric patients [5,7,10], and extrahepatic biliary atresia (EHBA) is still the major cause [11]. There is a wide variation in incidence across the globe, from 1 in 5,000 in Taiwan to 1 in 20,000 live births in Northern Europe [8]. BA is reported in all racial groups [4], and there is usually a female preponderance [3,7–9].

Green staining of the teeth and gingiva appears to be associated with fetal or neonatal hyperbilirubinemia. Bilirubin is a breakdown product of red blood cells; at high levels, bilirubin can cause jaundice as it accumulates in several tissues, changing their coloration; in soft tissues (skin and mucosa), these changes are temporary as a result of cell renovation

[10,12,13].

However, in mineralized tissues, bilirubin is trapped permanently because, after maturation, those tissues lose their metabolic activity; this results in green pigmentation of the teeth [13,14]. Other oral manifestations of BA include various degrees of retardation in dental and bone development, higher susceptibility to dental caries [10,15,16] and enamel hypoplasia [10,15–17].

Bilirubin staining of dental hard tissues is an uncommon condition; therefore, the purpose of this article was to present a case series of tooth discoloration in children caused by hyperbilirubinemia associated with EHBA.

Materials and methods

The database of Pediatric Gastroenterology and Hepatology referral center of University Hospital, Federal University of Bahia, Salvador (UFBA), Brazil, was searched for EHBA reports between January 2011 and August 2012. Medical histories were reviewed along with all case notes, previous hyperbilirubinemia reports, and the presence or absence of tooth discoloration. Children diagnosed with other systemic diseases were excluded. Thirty children (n = 20 girls and n = 10 boys) with EHBA were added to the study and selected for clinical examinations. All clinical examinations were performed by one dentist at the Dentistry School, UFBA. The study was approved by the Ethics Committee of the Dentistry School UFBA. Informed consent was obtained from the parents or guardians of all the participants in the study.

Clinical examination

Oral cavity examinations were carried out on each child by the same examiner using a sterile dental mirror and World Health Organization’s (WHO) periodontal probe. The following information was recorded: dental caries, hypoplasia and hypomineralization/opacity defects, and staining of teeth. The oral soft tissues were examined for the absence or presence of yellow pigmentation or any abnormality and for gingival hyperplasia.

Enamel hypoplasia was diagnosed if there was a deficiency of enamel in the form of pits, grooves, or other quantitative surface loss. Enamel opacity was diagnosed if there was a qualitative change in the translucency of enamel without loss of enamel surface [18]. Dental caries was recorded using the World Health Organization's criteria. Indices were recorded as

decayed, missing and filled primary teeth/decayed, missing and filled permanent teeth (dmft/DMFT) [19]. All indices for the primary teeth were determined for children between 1 and 12 years of age and for the permanent teeth in age ≥ 5 years.

Review of patient characteristics

After collection of clinical data, the following information was obtained from patients' medical records using a questionnaire standardized data: age and gender of the patient; status: in waiting list or underwent liver transplantation; age at transplantation; diagnosis prior to transplantation; length of time since transplantation; drug history; and mean serum bilirubin samples before and after the LT. Clinical characteristics of the children (n=30) are listed in Table 2.

Patient Categorization

In these patients, the intrinsic stain showed different levels in green and yellow colors. To enable analysis of patient characteristics in relation to intrinsic staining of the teeth, the patients were divided according to the main teeth color into the following patient groups: I-Green, II-Yellow–Green, III-Yellow (yellow and little-yellow) and IV-Normal aspect (Table 1).

Data Analysis

This is an observational descriptive study based on a comprehensive retrospective medical records review and current health examinations from children with EHBA. The present case series provide a comprehensive description of oral findings and outcomes from liver disease. However, it is not possible to do statistical inferences from the data [20] because the sampling method was nonprobability. The results are given as mean (SD or range). Data were transferred in a custom-designed database interfaced within EpiData® Software version 3.1 [21] and statistical analysis were performed by R system.

Results

The age and sex distribution and tooth discoloration in 30 children with medical history of EHBA are summarized in Tables 1 and 2. Twenty-eight children had undergone LT, and two

were on the waiting list. In two others, there was no prior information about total bilirubin (TB) levels before LT, so this information was complete only in 26 patients. All of these children have been under a tacrolimus immunosuppressive regimen.

Twenty-one children (70%) exhibited hypoplasia, and enamel opacity was observed in 27 children (90%). Five of the 30 children (16.67%) exhibited a marked green discoloration in the teeth, and 14 of them (46.66%) a yellow pigmentation. Caries experience (dmft/DMFT) among the children was 3.33/1.42.

Seven (23.33%) children had undergone hepatic portoenterostomy (Kasai surgery) and 4 (57.14%) of those children exhibited teeth with normal aspect in color; the others (n = 3, 42.86%) exhibited a yellow discoloration.

Gingival overgrowth was observed only in 2 (6.66%) children under tacrolimus immunosuppressive regime, and jaundice in 2 (6.66%) children who were on the waiting list for LT.

The mean of serum total bilirubin before and after the LT from the patients groups is demonstrated in Table 1, and the difference of them is showed in Figure 1. The individual peak total bilirubin levels of each patient are demonstrated in Table 2 and Figure 2.

Discussion

Intrinsic pigmentation can affect primary or permanent dentition and has been frequently related to drug administration—particularly tetracycline—and systemic alterations present at birth, such as hemolytic disease, respiratory disorders in newborns [17,22]. BA, bile duct occlusion, absence of bile ducts, biliary hypoplasia, and cholestasis associated with sepsis [17,23,24].

The presence of green pigmentation in teeth is an indication of early hyperbilirubinemia during enamel and dentin formation [12,16,22] and is considered rare; the majority of reports are related to primary dentition [10,22,24,25] The intrinsic staining by bilirubin resulting in discoloration [16,22,24] that can vary from yellow to deep shades of green [24,26,27].

In agreement with previous studies that found tooth discoloration in children with EHBA

[16,28–30], green pigmentation was observed in 16.67% (n = 5) of the sample. However, some tooth discoloration was found in 73.33% (n = 22) of the children, ranging from green to yellow pigmentation, and it affected primary and permanent dentition.

The majority of the studies in the literature are case reports and present tooth discoloration associated with cholestasis caused by BA [10,15,16, 28–33] or sepsis [13,22–24,34,35]. It is the first survey of the oral status of children with EHBA who had undergone LT in Brazil.

If BA is diagnosed before 60 days of life, the resection of extrahepatic biliary remnants and a reconstruction portoenterostomy (Kasai surgery) can restore bile flow from the liver into the intestinal tract [5,6,8,9] in about 45% of patients who will reach adulthood with their own liver [7]. Despite successful surgery, progressive inflammation and fibrosis of intrahepatic bile ducts develops to varying degrees in all patients, leading to biliary cirrhosis in the majority of patients. Consequently, 70–80% of BA patients will eventually require LT, approximately half in the first 2 years of life [4,36].

Thus, BA is the most common indication for LT in children, responsible for almost 50% of all pediatric liver transplants [7,10,36]. In this study, LT was done to treat EHBA in 28 cases (93.33%); in 7 cases (23.33%), the hepatic portoenterostomy was done prior. This might be related to the finding that these children presented yellow tooth discoloration (42.86%) or normal aspect in color (57.14%).

Sommer et al. [10] reported a case of green teeth associated with neonatal hyperbilirubinemia caused by BA. The patient, an 11-year-old girl, developed cirrhosis—despite Kasai surgery—and a transplant was performed when the patient was 1 year old. All permanent anterior teeth and permanent first molars were green in varying levels of pigmentation, but the premolar teeth were not affected. The authors concluded that a possible explanation for the pattern observed was related to the period of exposure to the hepatic disease and odontogenesis. Dental changes mirror the period of hyperbilirubinemia, with the deepest discoloration affecting the earliest formed dental hard tissue [10].

Histological evaluation of green-stained deciduous teeth from patients with hyperbilirubinemia has shown bilirubin deposits [14]; perhaps because conjugated bilirubin is more water-soluble [7,34], it is able to be incorporated into developing dentition [34].

The color was attributed to biliverdin formed by autoxidation of bilirubin [29,30], but that

explanation is chemically unlikely [37]. Biliverdin is rapidly reduced in the cytosol by biliverdin reductase in the presence of NADPH to produce the yellow pigment, bilirubin. Bilirubin is a rather stable pigment, particularly when deposited in tissues. Because of bilirubin conjugates' reduced hydrogen bonding and greater conformational mobility, they are considerably more prone to free radical attack and autoxidation to the corresponding biliverdin conjugates [38].

In this study, there was no delay in the eruption of permanent teeth at the oral examination—commonly observed in pediatric patients with chronic liver disease—but hypoplasia and opacity were observed in most of the patients. Hypoplasia in green-stained teeth occurred in the majority of cases in patients with a medical history of BA [24]. In the present results, hypoplasia was observed in 100% (n = 5) of the children with green pigmentation and in 70% (n = 21) of the sample. The prevalence of opacity was high, affecting 90% (n = 27) of the children, and it was observed in 46.66% (n = 14) in both primary and permanent dentition. Investigators have suggested that defects in the formation of enamel and dentine in these patients might be related to change in the organic matrix [15,35], individual disturbances in the absorption of calcium, phosphate [15,35,39], and fat-soluble vitamins [15,16,35,39].

A review of literature found that hypoplasia of enamel was reported in 17 of 34 (50%) cases of BA. Permanent teeth were affected in 5 cases of hypoplasia, primary teeth were affected in 11 cases; in 1 case, both dentitions were affected [24]. In the present results, it was found that primary and permanent teeth were affected in 6 cases (20%), permanent dentition in 7 cases (23.33%) and primary teeth in 8 cases (26.67%).

The extent of discoloration and its intensity have been directly related to the duration and severity of the pathology, respectively, and may be proportional to the serum concentration of bilirubin [12,22]. Hypoplasia and hypomineralization were observed in Case 10 (5-year-old boy), as well as green pigmentation in all primary teeth as a result of high levels of bilirubin serum in the neonatal period (maximum serum TB of 29.75 mg/dl). The green pigmentation was also present in all permanent teeth in Case 5 (15-year-old girl), but bilirubin levels before the LT were not reported. Some cases' medical histories were incomplete and did not permit correlation between depth and duration of jaundice with the intensity of green staining [12,24].

Teeth formed after the hyperbilirubinemia period had complete resolution to normal color, with a sharp dividing line separating the green portions [10,16,22]. According to Amaral et al. [15], a line was detected by histological evaluation separating two portions of dentin of extracted deciduous canines—one formed before the hyperbilirubinemia phase and other formed after the control of the disease in a patient with history of BA. These findings suggest that dentin calcification was affected in these patients, not only the enamel [15]. Dentistry treatment of Case 5 required an extraction, and green pigmentation in the crown and the middle parts of the root was observed. The apical part of the root, calcificated after the LT, was normal in color.

Primary enamel supplies a unique opportunity of recording metabolic changes and stress experienced during development [40,41]. The primary central lower incisors start to mineralize between the 13th and 16th week of gestation and continue development and maturation during the first year of life. At birth, all primary teeth are in the process of mineralization [40,42].

The dental crown of the incisors is completely formed 1 month after birth and the canines and molars after 6 months [40,42]. In reported Case 10, the LT was performed at age 1 year 9 months, after the complete mineralization of primary teeth. Thus, in this patient, all primary teeth were green in color. The majority of mineralization of the permanent dentition is not complete until a child is 8 years of age (excluding third molars) [40]. Therefore, in Case 5, the LT occurred at the age 8, and the green pigmentation affected all permanent teeth.

Pigmentation of soft tissues was observed only in 6.66% (n = 2) and gingival overgrowth in 6.66% (n = 2) of the patients on the waiting list for LT. All of the children with LT were in immunosuppressive therapy with tacrolimus. There is evidence suggesting that this drug could be superior to cyclosporine (CsA), which is associated with gingival overgrowth [28,43,44]. However, in the present study, this side effect was observed in only 2 children under tacrolimus therapy associated with amlodipine; amlodipine is also known to cause gingival hyperplasia [45]. In contrast with CsA, tacrolimus is remarkably free of cosmetic adverse side-effects, including gingival hyperplasia, hirsutism and facial disfigurement [46].

The prevalence of dental caries in children with end-stage liver disease would seem to be no greater than in the normal population; however, rampant caries has been reported in children with BA, probably the result of frequent and prolonged bottle feeding and use of numerous

sugar-containing oral medications [16,44]. In this study, caries experience (dmft/DMFT) among the children was 3.33/1.42. The dmft/DMFT indices were determined for children between 1 and 12 years of age and for the permanent teeth in age ≥ 5 years. The DMFT score found was not in the global goals of the WHO for 12-year-olds for the year 2010 (DMFT< 1) [47]. Of the sample, five children < 7 years old presented dmft ≥ 8. In this study, 5 children were 5–6 years, and only 1 was caries free.

Green pigmentation is visible through the translucent enamel and can be difficult to mask with restorative materials. As the child grows older, cosmetic treatment of those teeth becomes a priority to improve their self-esteem and assist in their social integration [10,24].

Pediatric LT has become an accepted treatment for end-stage liver disease [2,4,5]. As the life expectancy of pediatric liver transplant recipients continues to rise with improving survival rates, the number of liver transplant children visiting dental clinics will increase [43]. It is possible that the frequency of green teeth will increase as a consequence [13]. Any aesthetic treatment needs to consider the medical history of the patient in regard to the status of his or her liver disease. Dental bleaching may not be effective since the pigmentation is confined in the dentin [15].

In summary**,** the present case series supports the importance of medical history and complete examination in patients with of EHBA in the presence of tooth discoloration in primary and permanent dentition. Physicians and dentists caring for children who have a history of hyperbilirubinemia should be careful of the risk of tooth pigmentation. It is important that pediatricians and dentists reassure parents and discuss the cosmetic treatments available.

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Tables

Table 1 Distribution of clinical and dental findings of the children groups (n=30) and bilirubin levels before and after liver transplantation (n=26). Mean (SD or range)

Groups	I Green	II Yellow/Green n(%)	III Yellow n(%)	IV Normal aspect n(%)	Total/ Mean n(%)
n. patients n(%)	5 (16.67)	3 (10)	14 (46.66)	8 (26.67)	30 (100)
Male n(%)	2 (6.67)	1 (3.33)	4 (13.33)	3 (10)	10 (33.33)
Female n(%)	3 (10)	2 (6.67)	10 (33.33)	5 (16.67)	20 (66.67)
Mean age (years) (range)	7 (4-15)	8.3 (5-12)	5.6 (1-9)	6.1 (1-16)	6.23(1-16)
Liver transplantation n(%)	5 (16.67)	3 (10)	14 (46.66)	6 (20)	28 (93.33)
TB before liver transplantation Mean (SD)	15.18(1.48)	13.07(2.23)	10.37(2.7)	8.13(3.86)	10,91(3,55)
TB after liver transplantation Mean (SD)	0.55 (0.26)	0.62 (0.24)	0.49(0.28)	0.41(0.14)	0,49(0,24)
dmft mean (SD)	5.75(4.79)	1.67(2.08)	3.07(3.27)	3.17(4.36)	3.33(3.64)
DMFT mean (SD)	1.25(2.5)	0	0.67(1.12)	5.33(7.51)	1.42(3.32)
Hypoplasia n(%)	5 (16.67)	3 (10)	11(36.66)	2 (6.67)	21 (70)
Opacity n(%)	5 (16.67)	3 (10)	12 (40)	7 (23.33)	27 (90)
Pigmentation of soft tissues n(%)	0	0	0	2 (6.67)	2 (6.67)
Hepatic portoenterostomy n(%)	0	0	3 (10)	4 (13.33)	7 (23.33)

TB (total bilirubin)
dmft/DMFT index (decayed, missing and filled primary teeth/decayed, missing and filled permanent teeth)

Table 2. Clinical characteristics of the children (n=30) with extrahepatic biliary atresia

Case	Sex, Age (Years)	Neonatal jaundice	Maximum serum total bilirubin (mg/dl)	Staining of teeth	Age at liver transplantation (year/month)	Hypoplasia	Hypomineralization
1	F,7	-	13,78	Yellow	9 m	+ (d/p)	+ (d/p)
2	F, 5	+	13,72	Little yellow	8 m	+ (d/p)	+ (d/p)
3	F, 4	+	14,05	Little yellow	10 m	-	+ (d)
4	F, 5	+	15,6	Green	1 y 9 m	+ (d)	+ (d)
5	F, 15	+	NR	Green	8 y	+ (p)	+ (p)
6	F, 9	+	18,64	Yellow	1y 7 m	+ (p)	+ (p)
7	F, 1	-	7,92	Normal	10 m	-	-
8	M, 9	-	18,3	Yellow	1 y 3m	+ (d/p)	+ (d/p)
9	F, 6	-	17,6	Green	1 y 11 m	+ (d)	+ (d/p)
10	M, 5	+	29,75	Green	1 y 9 m	+ (d/p)	+ (d/p)
11	F, 7	+	16,31	Yellow	1 y 5 m	+ (p)	+ (d/p)
12	F, 16	+	12	Normal	10 y	-	+ (p)
13	M, 4	-	12,9	Yellow	11 m	+ (d)	+ (d)
14	M, 8	+	7,6	Little yellow	1 y 10 m	+ (p	+ (d/p)
15	M, 3	+	5,9	Normal	1 y 6 m	-	+ (d)
16	M, 1	-	11,67	Normal	9 m	-	+ (d)
17	F, 12	+	13,7	Normal	-	-	+ (d/p)
18	F, 1	-	13,08	Little yellow	9 m	-	-
19	F, 2	-	16,04	Normal	8 m	+ (d)	+ (d)
20	F, 3	-	7,62	Little yellow	7 m	+ (d)	+ (d)
21	F, 3	+	9,97	Yellow	6m	-	+ (d)
22	M, 4	+	18,2	Green	1 y	+ (d)	+ (d/p)
23	M, 7	-	16,11	Yellow	1 y 3 m	+ (p)	+ (d/p)
24	F, 4	-	NR	Yellow	8 m	+ (d)	-
25	F, 10	+	8,8	Normal	5 a 6 m	+ (p)	+ (p)
26	F, 12	-	21,5	Yellow-green	4 y 11m	+ (p)	+ (d/p)
27	M, 4	-	2,9	Normal	-	-	+ (d)
28	F, 7	-	16,36	Yellow	1 y 2m	+ (d/p)	+ (d/p)
29	M, 8	+	17,1	Yellow-green	1 y 3 m	+ (d/p)	+ (d/p)
30	F, 5	-	17,2	Yellow-green	8 m	+ (d)	+ (d/p)

Medical history: extrahepatic biliary atresia, 30 cases.
Dental findings: (-) absent; (+) present; d, Deciduos; p, Permanent; NR, not reported.
Gender distribution: F, female, 20 cases; M, male, 10 cases.
Staining of teeth: green, 5 cases; yellow-green, 3 cases; yellow, 14 cases; normal aspect, 8 cases.

Figures

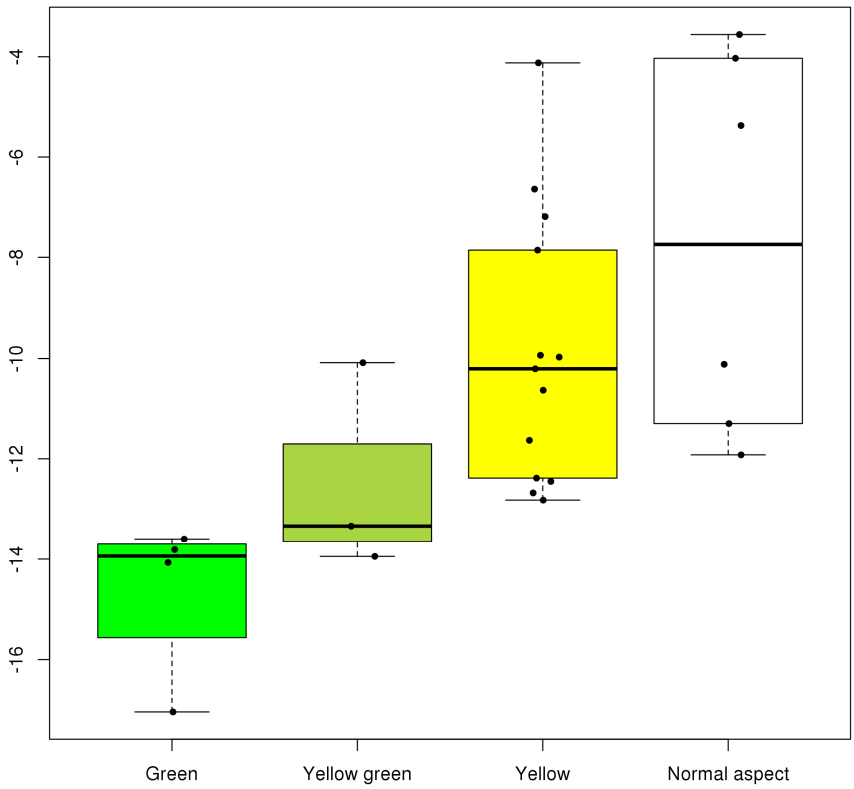

Fig. 1 Boxplot diagram illustrating the difference between the median of total bilirubin distribution before and after liver transplantation.The line through the middle of the box is the median while the top and bottom of the box are lower quartile and upper quartile

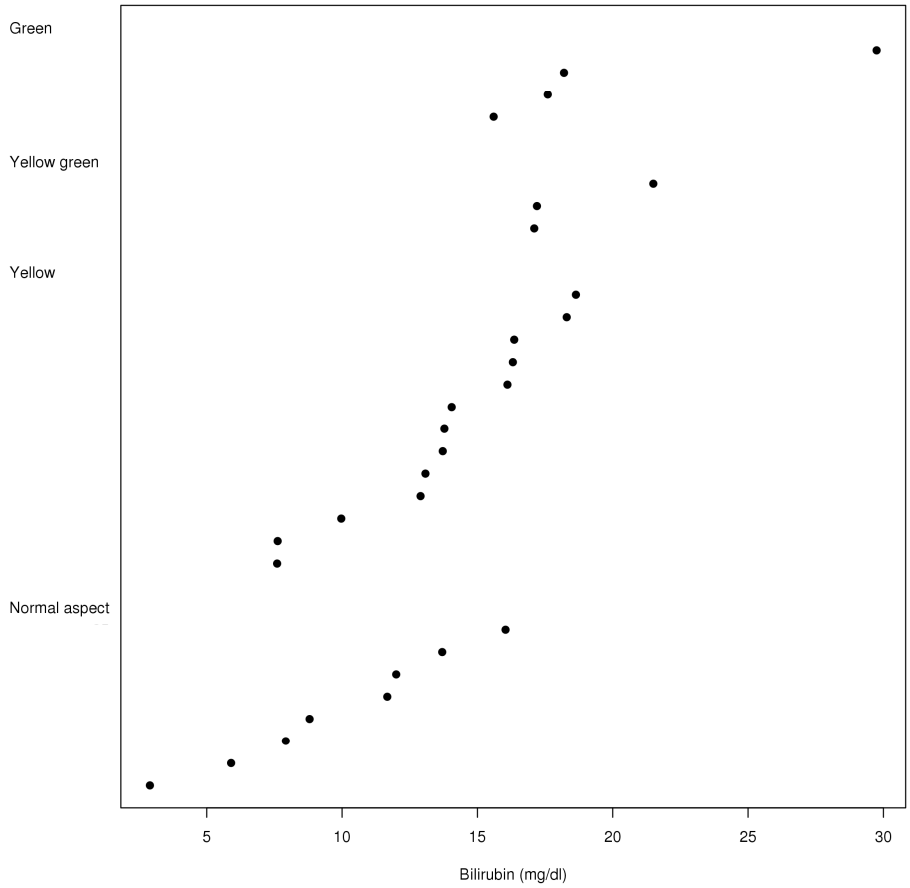

Fig. 2 Scatterplot diagram illustrating the individual peak of total bilirubin levels recorded for children with extrahepatic biliary atresia before liver transplantation

3.3 ARTIGO 3

Oral and dental aspects of children undergoing liver transplantation

Revista: Oral Diseases

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TITLE PAGE

TITLE: Oral and dental aspects of children undergoing liver transplantation

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ABSTRACT

OBJECTIVES: The aim of this study was to assess the prevalence of dental disease and oral health status in children with end-stage liver disease undergoing liver transplantation (LT).

PATIENTS AND METHOD: Fifty-five children (18 boys/37 girls) who underwent LT (n=52) or were on waiting list (n=3) were identified in this case series. Study procedures included the completion of a questionnaire, an oral mucosal examination, assessment of caries, hypoplasia, hypomineralization, tooth discoloration, periodontal status, and oral hygiene index. Descriptive statistics were determined and the results are given as mean (SD or range).

RESULTS: Biliary atresia was the most common cause of LT in the sample (n= 36/ 65.45%); 28 children (50.90%) exhibited hypoplasia, and enamel hypomineralization was observed in 44 children (80.5%). Tooth discoloration was present in 31 (56.36%) children and gingival enlargement in 3 (5.45%) of them. Caries experience among the children was 3.59/ 2.06 (dmft /DMFT).

CONCLUSION: The presence of hypoplasia, hypomineralization and tooth discoloration were high among children with history of liver disease, particularly among those undergoing transplantation for biliary atresia. The poor oral hygiene practices, dietary habits and access to dental care services appear to have influenced the experience of caries and periodontal status more than the liver disease.

Keywords: liver disease, liver transplantation, dental caries, developmental enamel defect.

Introduction

Pediatric liver transplantation (LT) has become an accepted treatment for end-stage liver diseases (Wondimu et al., 2001; Muiesan et al., 2007). These include decompensated chronic liver disease, acute liver failure, non-cirrhotic liver-based metabolic disorders, and liver tumors (Muiesan et al., 2007). The most common primary liver disease that manifests in childhood and causes end-stage liver disease is biliary atresia (BA). Children with biliary atresia (BA) comprise at least 50% of the pediatric liver transplant (LT) population (Tiao et al. 2006).

In recent years, the number of pediatric LT has increased, and patient survival has improved dramatically, primarily due to improvements in surgical techniques, management of complications, and immunosuppression. As the life expectancy of pediatric LT recipients continues to rise with improving survival rates, the number of LT children who visit dental clinics will increase (Wondimu et al., 2001).

Children with liver disease and LT require specialist dental care. Even simple dental treatment requires careful management because of the children's inadequate drug and protein metabolism and tendency toward pro- longed bleeding. Children with liver disease and liver grafts are more likely to have hypoplastic defects of the enamel of their teeth, delayed eruption of the primary dentition, intrinsic green staining of both primary and permanent teeth as well as of the oral soft tissues, and an increased susceptibility to dental caries or cyclosporine-induced gingival overgrowth (Hosey and Clark, 2008).

This study's aim was to assess the prevalence of dental disease and oral health status in children with end-stage liver disease who were undergoing LT.

Patients and methods

Patients

This is a case series study conducted in 55 patients (18 boys and 37 girls / age range: 1 year to

17 years) who underwent LT (n=52) or were on waiting list (n=3) and were referred for medical follow-up at the Center for Pediatric Gastroenterology and Hepatology, University Hospital Complex Professor Edgard Santos, Federal University of Bahia, Brazil. The sample was divided according to age group. The study was carried out from January 2011 to August 2012 and was approved by the Ethics Committee of the Dentistry School (n^{o}. 0046.0.368.000-11), Federal University of Bahia (UFBA). All parents/guardians provided written informed consent for the children to participate in the study before the interviews and examinations were conducted.

The sample was divided into age groups (<5 years, 5 years, 6 to <12 years, 12 years, 13 to <15 years, and ≥15 to <19 years) according to the epidemiologic national survey on oral health called the SBBrasil Project 2010, which divided the Brazilian population into 5 groups (5 years, 12 years, 15 years to 19 years, 34 years to 44 years, and 65 years to 74 years). The 2010 edition of SBBrasil is the principal oral health surveillance strategy for the production of primary data in Brazil (Ministério da Saúde 2010).

The medical histories were reviewed, and clinical oral examinations were performed on all of the children of the sample in the Dentistry School of UFBA by one of the authors (EJC). A structured questionnaire that included socio-demographic characteristics, liver disease, oral health, and dietary habits were used for data collection. Cases of dental caries or any treatment needs were referred to the Department of Pediatrics of Dentistry School of UFBA and Bahiana School of Medicine and Public Health for treatment.

Method

Clinical examinations of soft tissues and teeth were carried out with a conventional dental mirror and with the World Health Organization's (WHO) periodontal probe in an on-site dental chair under focused light, and photographs were taken. Oral examinations were conduced on 55 children for the presence of dental caries, dental plaque, calculus, hypoplasia and hypomineralization/opacity defect, and tooth discoloration. The mouth's soft tissues were examined for the absence or presence of yellow/green pigmentation or any abnormality, for gingival enlargement, and for periodontal bleeding. Diagnosis of oral lesions was based on

medical and dental history as well as clinical findings. The following parameters were assessed:

Dental caries

Dental caries was recorded using the WHO's criteria. Indices were recorded as decayed, missing, and filled primary teeth/Decayed, Missing and Filled permanent teeth (dmft/DMFT) index (Pereira, 2003). Caries were identified as cavitations evidenced by probing or directly visualized by the examiner.

Oral hygiene status

The oral hygiene was assessed using the Oral Hygiene Index (OHI). The OHI was developed by Greene and Vermillion (1960), has two components—dental plaque and calculus—and is an indication of oral cleanliness. Vestibular and lingual surfaces of molars and incisors were examined, and the presence of dental plaque and calculus was ranked from zero to three. Zero was attributed to the absence of dental plaque; 1 = less than 1/3 of tooth surface covered with dental plaque; 2 = more than 1/3 and less than 2/3 of tooth surface covered with dental plaque or the presence of intrinsic pigmentation and calculus; 3 = more than 2/3 of tooth surface covered with dental plaque and calculus. The OHI featured the average scores obtained from the number of surfaces examined. The oral hygiene of each child was classified as "good" when the OHI score was 0.0–1.2, "fair" when it was 1.3–3.0, and "poor" when it was 3.1 up to 6.0 (Neto et al., 2011).

Periodontal Status

The periodontal assessment index used in the study was the Periodontal Screening and Recording (PSR). Only the highest score was recorded for each sextant according to the following score: 0, colored area of probe completely visible, no calculus or defective margins, and no bleeding on probing; 1, colored area of probe completely visible, no calculus or defective margins, and bleeding on probing; 2, colored area of probe completely visible with supra- or subgingival calculus or defective margins; 3, colored area of probe remains partly visible; 4, colored area of probe is not visible (probing depth of more than 5.5mm); and code * for clinical abnormalities (Covington et al., 2003).

The Gingival Bleeding Index (GBI), introduced by Ainamo and Bay (1975), was performed by gently probing the gingival sulcus of the assigned anterior and posterior tooth surfaces in each sextant (Hebling, 2003). If bleeding occurred within 10 seconds, a positive finding was recorded. The gingival bleeding index scores of 0 or 1 described no bleeding (0) or bleeding gingiva (1). A subject was classified as having gingival bleeding when at least one area with a score of 1 was observed (Lin and Yang, 2010).

Tooth discoloration and enamel defects

Enamel hypoplasia is a quantitative defect of the enamel, resulting from a disturbance to the ameloblasts during matrix formation. Enamel hypomineralization/opacity is a qualitative defect of the enamel because of a disturbance during initial calcification and/or during maturation (Elfrink et al., 2012). Enamel hypoplasia was diagnosed if there was a deficiency of enamel in the form of pits, grooves, or other quantitative surface loss. Enamel opacity was diagnosed if there was a qualitative change in the translucency of enamel without the loss of enamel surface (Nyvad et al., 2008). The tooth discoloration was examined for the absence or presence of intrinsic yellow/green staining of the teeth.

Data Analysis

This is a case series study based on a comprehensive retrospective medical records review and current health examinations from children with liver disease underwent LT or were on a waiting list. The results are given as mean (SD or range). Data were transferred in a custom-designed database interfaced within EpiData® Software version 3.1 (EpiData computer program, 2011), and statistical analyses were performed by R system. The intra-examiner agreement for dmft/DMFT according Lin's concordance correlation coefficient was high (CCC > 0.99).

Results

Indications for pediatric LT in the sample presented obstructive cholestasis, such as BA (n=36/ 65.45%), choledochal cyst (n=5/ 9.09%) and Caroli disease (n=2/ 3.64%); metabolic disorders associated with cirrhosis, such as alpha-1 antitrypsin deficiency (n=5/ 9.09%), cystic fibrosis (n=1/ 1.82%), and Wilson's disease (n=1/ 1.82%); Alagille syndrome (n=2/ 3.64%);

Budd-Chiari syndrome (n=2/ 3.64%); and chronic liver disease leading to decompensated cirrhosis (n=1/ 1.82%) (Table 1).

The number and proportional distribution of enamel defects and gingival enlargement according to liver disease in the sample is presented in Table 1. Diffuse opacities were the defects that were most frequently found in the children (80%), followed by tooth discoloration (56.36%) and hypoplasia (50.90%). Gingival enlargement was present only in 5.45% (n=3) of the children.

Eleven children (20%) were caries-free. The dental caries dmft/DMFT index (mean values ± SD) by age group is shown in Table 2. The mean dmft/DMFT of the sample was 3.59/ 2.06.

The periodontal status was investigated in relation to the number of sextants (n= 317) affected by gingival bleeding and calculus. Gingival bleeding was found in 224 (70.66%) sextants, calculus was present only in 7 (2.21%) sextants, and 93 (29.34%) sextants were healthy. Oral hygiene was considered fair in the sample (2.21 ± 1.33) but poor in the older adolescent age groups (Table 3).

Means of 1.69 ± 1.46 healthy sextants, 4.07 ± 1.76 bleeding sextants, and 0.13 ± 0.47 calculus-accumulated sextants were calculated. Periodontal status was noted with age, with adolescents presenting predominately with bleeding sextants, calculus, and poor oral hygiene when compared with the children who presented more healthy sextants (Table 3).

Discussion

Few studies exist on the oral health status of children with liver disease who are undergoing LT (Belanger et al., 1982; Morisaki et al., 1990; Seow et al., 1991; Funakoshi et al., 1992; Hosey et al., 1995; Sheehy et al., 2000; Wondimu et al., 2001; Lin et al., 2003; Lin and Yang, 2010). The majority of the studies in this population are case reports of tooth discoloration associated with hyperbilirubinemia caused by BA (Zaia et al., 1993; Amaral et al., 2008; Sommer et al., 2010; Chambers et al., 2012) or neonatal sepsis (Guimarães et al., 2003).

The most common primary liver disease that manifests in childhood and causes end-stage liver disease is BA (Tiao et al., 2006). There are few diseases where so much is know yet so little understood than the condition of BA (Davenport, 2012). The first systematic review of the epidemiology and outcomes of BA that were conducted to assess population-based studies identified that the incidence of BA varies among countries (Jimenez-Rivera et al., 2013). A wide variation in incidence exists across the globe, from 1 in 5000 in Taiwan to 1 in 20,000 live births in Northern Europe, although the reasons for such a disparity remain obscure (Davenport, 2012). However, there is unanimous agreement in the published literature on the importance of early diagnosis and surgical intervention in infants with BA (Jimenez-Rivera et al. 2013).

BA accounted for 65.44% (n=36/55) of the pediatric LT in this center, compared with 41% (n=11/27) described for Sheehy et al. (2000). Lin et al. (2003) found 91, 2% (n=31/34) in Taiwan children. They divided the children into 3 groups, and the mean dmft scores were 0±0 (0–2 years), 6.67±1.21 (2–4 years), and 10.44±1.16 (4–6 years). In this study, the mean dmft of patients under 5 years old (3.65±4.56) and at 5 years old (7.17±4.07) were lower when compared with that of the Taiwanese children. They observed that children who were night-fed had significantly higher dmft scores than did children who were not. It could explain the high dmft score found in the 5-year-old group, where the “missing” component represented 34.87% as a result of the extractions of primary teeth for caries. This group had a history of night-fed children and had 4 children with a mean dmft ≥ 8. Sheehy et al. (2000) concluded that the high numbers of missing primary teeth in the LT group compared with in the controls probably reflected the aggressive extraction treatment approach in the management of dental caries to eliminate any foci of infection prior to LT.

Children with liver disease have been considered as having a high predisposition to dental caries. Nevertheless, Sheehy et al. (2000) found no significant difference between the percentage of caries-free children in the LT group (59.3%) and the control group (51.3%). According to Sheehy et al. (1999), the prevalence of dental caries in children with end-stage liver disease would seem to be no greater than it is in the normal population, but rampant caries has been reported in children with BA and was probably due to frequent and prolonged bottle feeding. The use of numerous sugar-containing oral medications is probably also a

contributing factor.

In this study, the dmft mean for the under-5 and 5-year-old groups were 3.65 (±4.56) and 7.17 (±4.07), respectively. They are high when compared with the national, regional, and local averages for dental caries—2.43, 2.89 and 1.70 dmft, respectively—at 5 years of age in Brazil. A prolonged night bottle-feeding habit was identified in these children and possibly contributed to this result. The component “decayed” represents 98.63% of the dmft score in this group (Table 2). The results highlight the importance of caries prevention advice from an early age in these high-risk patients.

The DMFT scores of the 12-year and 15–19-year-old groups were 0.5 (±0,71) and 7,38 (±4,14), respectively. The result of the first group was lower than the national, regional, and local averages for dental caries (2.07, 2.63 and 1.07, respectively), but this group was formed for only 2 children. Nevertheless, for the last group, the DMFT mean was elevated and was higher than the national, regional, and local averages for dental caries (4.25, 4.53, and 2.09, respectively). The most representative components of it were “filled” (47.43%) and “decayed” (33.87%) (Table 2). This result matches with the deficient oral hygiene (Table 3) and shows the history of dental caries in this group.

Nutritional deficiencies are frequent in children and adults with chronic liver disease, especially patients with cholestasis. An inadequate quantity of bile salts is delivered to the intestinal lumen and, consequently, results in fat and fat-soluble vitamin (FSV) malabsorption and deficiency. Deficiencies in FSVs induce multiple clinical complications (Shen et al., 2012). Vitamin D deficiency results in defective bone mineralization, and vitamin K deficiency induces abnormal coagulation function, as manifested by easy bruising (Shen et al., 2012) or bleeding (Davenport, 2012; Shen et al., 2012).

The overall rate of gingival bleeding in the sample (4.07±1.76) was high, and the results of the 12-year-old (5.0±1.41) and 15- to 19-year-old (4.75±2.05) age groups show that this sample was not comparable with the same age groups in the national (0.71) and regional (0.96) populations in Brazil. Nevertheless, the results for dental calculus in these groups were similar or lower than were the Brazilian results. In addition, OHI were significantly

overrepresented among the adolescents.

Andrade and Rapp (2002) carried out a study to assess the prevalence of periodontal disease in a very young population (3–6 years) in Bahia, Brazil. Stating that the PSR index took less time and was better accepted among the children, they examined a sample of 500 health children and found a high prevalence and low severity of parameters related to periodontal disease. Our findings showed this same feature. The prevalence of gingival bleeding was elevated in the age group < 5 years (58.33%), and it was caused by deficient oral hygiene (1.98±1.17). Nevertheless, the prevalence of dental calculus in all groups was low.

Sheehy et al. (2000) compared the oral status of children with end-stage liver disease before and after LT with that of the control group. They observed no significant differences between the LT patients and the controls for either mean plaque or gingivitis indices at each examination time.

This study's oral findings indicated a high prevalence of hypomineralization/opacity (80%), hypoplasia (50,90%), and tooth discoloration (56,36%). The last one was most prevalent in children with the diagnosis of BA. These results agree with Wondimu et al. (2001), who reported that enamel hypoplasia was present in 36% and that enamel opacities were observed in 76% of the children undergoing LT. They also reported that 50% of the children with hyperbilirubinemia associated with BA exhibited a marked greenish discoloration of the teeth. The same was observed by Hosey et al. (1995), who found intrinsic green staining in 47,27% (n=26/55) of the children, and all of the primary teeth of 25 of them were affected.

Hyperbilirubinemia is characterized by elevated serum levels bilirubin, a product of hemoglobin degradation (Amaral et al., 2008). Bilirubin is extensively distributed and deposited throughout the body during hyperbilirubinemia. However, in mineralized dental tissues, bilirubin is trapped permanently because, after maturation, those tissues lose their metabolic activity resulting in green pigmentation of the teeth (Sommer et al., 2010; Amaral et al., 2008).

The discoloration of teeth is common in children with chronic liver disease. The yellow-green

staining of primary and/or permanent teeth in children with chronic cholestasis is attributed to exposure of the developing dentin and enamel to elevated serum levels of conjugated bilirubin (Zaia et al., 1993; Amaral et al., 2008; Sommer et al., 2010; Chambers et al., 2012). Tooth discoloration was observed in 69.44% (n=25/36) of the children with BA and in 56.36% (n=31/55) of the sample. This result is in accordance with Wondimu et al. (2001), who found green teeth in 50% of the children with BA, and with Lin et al. (2003), who found green staining of the teeth and gingiva in 61.3% of the children with BA.

The cases of tooth pigmentation showed various degrees of mild yellow to a darker green shade in the primary and permanent dentition, suggesting a correlation between the degree, location, and extension of tooth pigmentation and the severity of disease (Morisaki et al., 1990; Lin et al. 2003; Chambers et al., 2012). The presence of yellow-green pigmentation is an indication of early hyperbilirubinemia (Lin et al. 2003). A possible explanation for the fact that not every child develops tooth pigmentation is the time, duration, and intensity of hyperbilirubinemia because it varies between them.

In agreement with previous findings (Seow et al., 1991; Li et al., 2003), a line was observed that separated two portions on the root of an extracted permanent molar from a 15-year-old girl with a medical history of BA and jaundice from her 2nd day of life until 8 years, when she underwent LT. One green portion formed during the hyperbilirubinemia phase, and the other formed after the control of the disease, which had a normal color. The extracted tooth showed that the deeply stained portion of the root that formed prior to LT was clearly demarcated from that which normally forms after transplantation.

Green discoloration may also affect intraoral soft tissues, including the gingiva, the tongue, the floor of the mouth, and the buccal mucosa. Nevertheless, cases of gingival pigmentation were not observed in this study, possibly as a result of the control of the liver disease by LT. The pigmentation disappears from the soft tissues due to high tissue turnover (Sommer et al., 2010). At the period of exams, the bilirubin levels were under control. The same was observed by Amaral et al. (2008).

Manifestations of developmental enamel defects were found in the sample. Developmental defects of dental enamel are common in both deciduous and permanent dentitions and are classified into hypomineralization and hypoplasia. Hypomineralized parts of teeth are weaker, and the enamel may chip off easily, resulting in the post-eruptive loss of enamel (Elfrink et al., 2012). Hypoplasia and hypomineralization were observed in both the primary and permanent dentition of the children as localized defects. However, the tooth pigmentation was present as being localized and affecting all of the dentition in some cases.

According to Guimarães and Silva (2003), hypoplasia in green teeth occurred in the majority of cases in patients with medical histories of BA. Enamel hypoplasia can stem from changes in the organic matrix of the developing enamel that resulted from metabolic disturbances (Amaral et al., 2008), but it is more likely to be related to the effects of osteopenia and other disturbances of calcium and phosphate metabolism encountered in chronic liver diseases (Amaral et al., 2008; Chambers et al., 2012). The poor absorption of calcium, phosphorus, and vitamin D due to chronic cholestasis may likewise lead to the decreased integrity of dental structures and increased susceptibility to the development of dental caries in children with liver disease (Sheehy et al., 1999).

In this study, no delay existed in the eruption of primary and permanent teeth. This result is according to Sommer et al. (2010), Amaral et al. (2008), and Zaia et al. (1993), who described case reports of children with green teeth associated with neonatal hyperbilirubinemia caused by BA. However, Hosey et al. (1995) found a delay in the eruption of the primary teeth in 41% (n=7/17) of children under 3 years of age with medical histories of BA, and Seow et al. (1991) observed it in 33,33% (n=3/9).

Morphologic changes in the teeth were evaluated via visual and radiographic examination in a sample of 11 children. Dental development was found to be delayed in 4 children, and 5 of them presented enlarged pulp chambers (Belanger et al. 1982). In this study, radiographic assess was not made.

During the past decade, pediatric LT has seen significant improvements in morbidity and

mortality. This improvement in patient and graft survival is attributed to advances in pre-transplant management, organ procurement, and preservation technology, donor liver options (whole or split cadaveric, living donor), surgical techniques, and immunosuppressive regimens (Turmelle et al., 2009).

It is important to observe that children who underwent LT require lifelong immunosuppressive therapy, and the side effects of these drugs include an increased susceptibility to infections and gingival enlargement. The calcineurin inhibitor tacrolimus has become the mainstay of most of these regimens (Tiao et al. 2006). In contrast with cyclosporine, tacrolimus is remarkably free of cosmetic adverse side-effects, including gingival hyperplasia, hirsutism, and facial disfigurement (Reding, 2002).

The lips, mucosa, gum, mouth floor, tongue, and soft and hard palates were inspected, and only 3 patients (5,45%) had some form of gingival enlargement. No abnormalities were detected in the other oral soft tissues. The same was reported previously by Funakoshi et al. (1992) and Sheehy et al. (2000).

The children under immunosuppression therapy in the sample were taking tacrolimus, and the ones who presented with the gingival enlargement (n=3) were taking concomitant nifedipine for hypertension control, which was implicated as a cause of gingival enlargement (Funakoshi et al., 1992; Lin and Yang, 2010). However, Sheehy et al. (2000) reported that the concurrent use of nifedipine with cyclosporine had no effect on the prevalence of gingival enlargement. They found gingival enlargement in 41% of liver recipients who received cyclosporine with or without nifedipine.

Wondimu et al. (2001) assessed the oral health of pediatric LT recipients who were administered cyclosporine or tacrolimus. The results showed no difference in enamel defects, discoloration, or caries experience between the groups. However, gingival enlargement was observed in 35% of the children who had been on cyclosporine therapy. In contrast, none of the children in the tacrolimus group exhibited gingival enlargement.

However, Lin and Yang (2010) investigated the effects of cyclosporine on the gingival tissues

of pediatric LT patients and concluded that gingival enlargement was statistically more related to plaque scores than others factors, such as the serum level of cyclosporine. Nevertheless, the prevalence of gingival enlargement after cyclosporine administration was found to be 40% to 88%, with an average of 63%. They suggested that this occurrence was possible due to the rapid onset of gingival growth after the initial use of cyclosporine, with a slowing of growth when a therapeutic level of the drug was reached.

It is accepted that a team approach is required for the dental management of children prior to LT, formed by the pediatric dentist, hepatologist, transplant surgeon, and other health professionals (Sheehy et al., 1999). Nevertheless, children with liver disease who have been considered for LT should be carefully examined for the presence of dental caries and periodontal disease not only before but after LT, too. The parents reported that many dentists are apprehensive about the liver function after LT and the compromised immune systems of the children. Dentists' refusal to care for children with liver disease or those who underwent LT along with the lower socioeconomic statuses of families contributed to the high frequency of oral disease. A dentistry service must become an integral part of the medical follow-up after the LT of children in order to improve oral hygiene practices. Good oral health is essential to reducing the risk of systemic infection that arises from the oral cavity.

In conclusion, the prevalence of dental caries and periodontal status observed can be explained via poor oral hygiene and deficient dental care. Tooth pigmentation is an uncommon condition but is not rare in children with histories of early severe hyperbilirubinemia. It is important to provide anticipatory information to families about the possibility of dental staining and its treatment. The dental management of children with end-stage liver disease can be effective and safe. Intensive dental care, especially prevention measurements, is necessary to improve the health quality of life in this population.

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Author contributions

EJ Campos and LR Silva have been involved in the conception, research design, data acquisition, interpretation of the results, and drafting and writing of the final version of the manuscript. IHA Bastos was involved in the data acquisition. CMC Mendes and ML Arriaga were involved in the data analysis. All authors were involved in the interpretation of the results and in the critical evaluation of the manuscript.

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Tables

Table 1 – Number and percentage distribution of children (n=55) according to liver disease and variables studied. Salvador, Bahia, Brazil, 2012.

	Sex		Hypoplasia		Hypomineralization/ Opacity		Tooth discoloration		Gingival enlargement	
Diagnosis	F	M	n	%	n	%	n	%	N	%
Biliary atresia	23	13	23	63.88	32	88.88	25	69.44	2	5.55
Alpha 1 antitrypsin deficiency	4	1	1	20	1	20	0	0	0	0
Choledocal cyst	4	1	2	40	2	40	4	80	0	0
Alagille syndrome	1	1	1	50	2	100	1	50	1	50
Wilson's disease	0	1	0	0	1	100	0	0	0	0
Budd-Chiari syndrome	1	1	0	0	2	100	1	50	0	0
Caroli disease	2	0	0	0	2	100	0	0	0	0
Cystic fibrosis	1	0	0	0	1	100	0	0	0	0
Liver cirrhosis	1	0	1	100	1	100	0	0	0	0
Total	37	18	28	50.90	44	80	31	56.36	3	5.45

Table 2–Dental caries experience (components of dmft/ DMFT) of children and adolescents (n=55) with liver disease by age. Mean values ± SD. Salvador, Bahia, Brazil, 2012.

	Group	Sound teeth	decayed		filled /decayed		filled		missing		dmft/ DMFT
Age group	n	Mean (±SD)	Mean (±SD)	%	Mean (±SD)	%	Mean (±SD)	%	Mean (±SD)	%	Mean (±SD)
<5 years	20	14.05 (4.93)	3.6 (4.48)	98.63	0	0	0	0	0.05 (0.22)	1.37	3.65 (4.56)
		0.15 (0.49)	-	-	-	-	-	-	-	-	-
5 years	6	10.5 (2.59)	3 (3.69)	41.84	0.67 (0.52)	9.34	1 (0.89)	13.95	2.5 (2.74)	34.87	7.17 (4.07)
		5.17 (3.71)	-	-	-	-	-	-	-	-	-
≥6 years <12 years	17	7.94 (5.62)	2.31 (2.6)	90.24	0.13 (0.33)	5.08	0.06 (0.24)	2.34	0.06 (0.24)	2.34	2.56 (2.63)
		12.47 (7.07)	0.56 (0.94)	90.32	0.06 (0.24)	9.68	0 (0)	0	0 (0)	0	0.62 (0.96)
12 years	2	2.5 (2.12)	0.5 (0.71)	100	0 (0)	0	0 (0)	0	0 (0)	0	0.5 (0.71)
		21.5 (3.54)	0.5 (0.71)	100	0 (0)	0	0 (0)	0	0 (0)	0	0.5 (0.71)
≥13 years<15years	2	-	-	-	-	-	-	-	-	-	-
		27 (0)	1.0 (0)	100	0 (0)	0	0 (0)	0	0 (0)	0	1.0 (0)
≥15 years<19years	8	-	-	-	-	-	-	-	-	-	-
		20.38 (3.96)	2.5 (1.6)	33.87	0.63 (0.74)	8.54	3.5 (4.47)	47.43	0.75 (1.16)	10.16	7.38 (4.14)

SD(standart deviation)
dmft/DMFT index (decayed, missing and filled primary teeth/Decayed, Missing and Filled permanent teeth)

Table 3 – Periodontal status in children and adolescents (n=55) with liver disease by age according to gingival bleeding, calculus and oral hygiene index (OHI) (Mean values ± SD). Salvador, Bahia, Brazil, 2012.

	Sample	Sextants	Healthy		Bleeding		Calculus		OHI
Age group	n	n	n (%)	Mean (SD)	n (%)	Mean (SD)	n (%)	Mean (SD)	Mean (SD)
<5 years	20	108	45 (41.67)	2.25 (1.68)	63 (58.33)	3.15 (2.16)	0 (0)	0 (0)	1.98 (1.17)
5 years	6	35	11 (31.43)	1.83 (0.75)	24 (68.57)	4.0 (0.63)	1 (2.86)	0.17 (0.41)	1.89 (0.75)
≥6 years <12 years	17	102	24 (23.53)	1.41 (0.94)	78 (76.47)	4.59 (0.94)	1 (0.98)	0.06 (0.24)	1.82 (0.89)
12 years	2	12	2 (16.67)	1.0 (1.41)	10 (83.33)	5.0 (1.41)	1 (8.33)	0.5 (0.71)	3.08 (1.53)
≥13 years<15years	2	12	1 (8.33)	0.5 (0.71)	11 (91.67)	5.5 (0.71)	1 (8.33)	0.5 (0.71)	3.66 (0.71)
≥15 years<19years	8	48	10 (20.83)	1.25 (2.05)	38 (79.17)	4.75 (2.05)	3 (6.25)	0.38 (1.06)	3.29 (2.14)
Total	55	317	93 (29.34)	1.69 (1.46)	224 (70.66)	4.07 (1.76)	7 (2.21)	0.13 (0.47)	2.21 (1.33)

3.4 ARTIGO 4

Green teeth in children with biliary atresia: Case Reports

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TITLE PAGE

Title: Green teeth in children with biliary atresia: Case Reports

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ABSTRACT

BACKGROUND: Children who have a history of hyperbilirubinemia associated with biliary atresia could be have the risk of tooth discoloration. Biliary atresia is an inflammatory process that results in hyperbilirubinemia. **CASE REPORTS**: The authors describe two cases of children who had a diagnosis of extrahepatic biliary atresia and displayed an uncommon form of tooth discoloration. They were treated successfully with liver transplantation (LT), but presented varying levels of pigmentation in primary and permanent dentition. The bilirubin levels remained elevated until LT in both cases, therefore primary and permanent teeth were compromised. In both cases the dental management involved improving oral hygiene, adjusting oral environment, fluoride therapy, and restorative treatment. **CONCLUSION:** Early diagnosis of liver disease facilitates the institution of medical treatment and reduces the potential risk of tooth discoloration. Knowing the medical history of the patient is essential for management of the oral and aesthetic complications of chronic liver disease.

Keywords: green teeth, hyperbilirubinemia, biliary atresia

Introduction

The liver has several functions, many of which depend on its ability to secrete bile. Jaundice is caused by elevated serum bilirubin and it refers to yellow discoloration of the skin, sclera, mucous membranes, and body fluids. Prolonged jaundice in an infant (lasting beyond 2 to 3 weeks after birth) is abnormal, yet it is a common problem that can be the presenting sign for many disorders. Impairment of bile flow or secretion from the liver can result in backup of its constituents within the liver canaliculi and hepatocytes, which ultimately creates cholestatic damage to the liver. [1]

Biliary atresia (BA) is a dynamic, inflammatory process that results in the obliteration and fibrosis of the extrahepatic biliary tract; it presents in the first few weeks of life in infants with jaundice. The progression of the disease, with involvement of the intrahepatic bile ducts, rapidly and predictably leads to cirrhosis and complications of end-stage liver disease before 2 years of age. [2] The bile duct can be normal and patent at the time of birth but become occluded secondarily. [3, 4]

BA is the most common cause of prolonged cholestatic jaundice in infants. [3,4] Although the cause of BA is largely unknown, [1,3] the factors that might contribute to its development include genetic, infective, inflammatory, and vascular causes, as well as toxic insult.[3] BA can be multifactorial in nature and has a common endpoint of obliterative cholangiopathy.[3] It remains the most common indication for liver transplantation (LT) in pediatric group. [3,4]

Chronic liver disease in children may have oral manifestations. During hyperbilirubinemia, bilirubin is distributed and deposited in different tissues of the body, which causes green staining of the teeth and gingiva. [5,6] In soft tissues, the pigmentation disappears, due to intense cell turnover. [7] However, in mineralized dental tissues, bilirubin is permanently trapped, because, after maturation, these tissues lose their metabolic activity. [7, 8] Therefore, the effects of end-stage liver disease are permanently recorded onto the teeth, even after successful LT. [6] Other oral manifestations include various degrees of delayed skeletal and dental development, enamel hypoplasia, and susceptibility to dental caries. [5]

This paper reports two cases of children with extrahepatic biliary atresia (EHBA) who underwent LT and were referred for medical follow-up at the Center for Pediatric Gastroenterology and Hepatology, University Hospital Complex Professor Edgard Santos,

Federal University of Bahia, Brazil. Their medical histories were reviewed and clinical examinations were performed. All patients/ guardians provided written informed consent to participated in the study.

Case Reports

Case 1

A 6-year-old girl showed good general health during her clinical evaluation. Her medical history revealed jaundice, pale stools, and dark urine from her 15th day of life until 1 year and 11 months, which evolved with ascites and posterior cirrhosis secondary to EHBA. She was born at term after an uncomplicated pregnancy. She had no medical history of sepsis or family history of jaundice and ABO incompatibility. The liver biopsy revealed an absence of portal spaces, degeneration of hepatocytes, biliary impregnation, and biliary capillary occluded by thrombus of bilirubin. The results of laboratory tests showed elevated levels of total bilirubin (TB) (ranging from 13.86 gm/dL to 17.6 gm/dL). At age 1 year and 11 months, she underwent LT and was placed on an immunosuppressive regime with tacrolimus.

Clinical examination revealed tooth discoloration (Figure 1), caries activity, enamel hypoplasia, and focal areas of opacity. The permanent maxillary right first premolar had erupted early; it was caused by the extraction of the primary predecessor tooth due caries and it presented normal color aspects. The primary mandibular right second molar with an extensive caries cavity on the occlusal surface showed a greenish dentin (Figure 2). The oral mucosa was normal. The treatment plan included oral hygiene instruction with fluoride therapy, restoration of teeth, and orthodontic appliances to maintain space.

Case 2

A 15-year-old girl with neuro-psychic deficit revealed a medical history of jaundice from her 2nd day of life until 8 years. She was born at term after an uncomplicated pregnancy. She had no medical history of sepsis or family history of jaundice and ABO incompatibility. The levels of liver enzymes and TB were high before the LT, according to the mother’s report, but there is no prior information on the medical record. At age 8, she underwent LT, and she was treated with tacrolimus.

An oral examination revealed that all permanent teeth showed an intrinsic greenish discoloration (Figure 3). Her mother reported that all primary teeth presented the same discoloration. Enamel hypoplasia, focal areas of opacity, and one rudimentary supernumerary tooth that was conically shaped were identified. There was high caries activity, with carious lesions on permanent maxillary and mandibular right molars and the upper supernumerary tooth. The maxillary supernumerary tooth and the permanent maxillary right first molar were indicated for extraction due caries (Figure 4).The permanent mandibular left first molar had been extracted, due to caries too. The permanent maxillary left central incisor was avulsed, due to trauma at age 7 (Figure 3). The panoramic radiography revealed four supernumerary teeth with eruptive potential, impacted tooth, and anodontia of two teeth. These findings affected her dental development. Poor oral hygiene was observed, with abundant dental biofilm and supragingival calculus, and her gingiva showed evidence of inflammation. Her dental management involved improving her oral hygiene, adjusting her oral environment, fluoride therapy, surgical extraction, and restorative treatment.

Discussion

Normal calcification chronology of deciduous teeth can provide a starting point for the evaluation of dental defects caused by certain systemic and local conditions. [9] Permanent green pigmentation of the primary dentition can result from neonatal hyperbilirubinemia, as a result of BA, [10-13] hemolytic disease, [10] or cholestasis caused by severe neonatal sepsis. [10, 14-16] Clinical [5,6,11] and experimental [7,8,12] studies have shown that bilirubin may be deposited when forming hard dental tissues, which may cause discoloration and/or enamel hypoplasia. [7]

Tooth development begins in the fetus, at about 28 days in utero. Indeed, all the primary teeth [17] and small parts of the permanent molars begin to develop in utero.[10] Mineralization of the primary dentition begins at about 14 weeks in utero, and all primary teeth are mineralizing by birth. [9,17] The permanent incisors and first molars begin to mineralize at or close to the time of birth, while the other permanent teeth start to mineralize later. [17]

Green intrinsic staining of the teeth due to elevated total bilirubin from liver disease is well-documented. [11-13,18] However, this is considered to be rare, and the majority of reports are related to the primary dentition. [11] Green teeth, hypoplasia, and opacities were observed in all cases reported. The pigmentation of soft tissues was not observed at the oral examination, because the disease had been controlled by LT. There was no delay in the eruption of permanent teeth in case 1, and abundant dental biofilm and caries lesions were found in all

cases, as a consequence of poor oral hygiene.

The presence of green pigmentation in teeth is an indication of early hyperbilirubinemia, and it can also determine when in life this disorder occurred. [19] Hyperbilirubinemia was present during the neonatal period until LT in all cases; consequently, both sets of dentitions were compromised.

In these case reports, the patients presented varying levels of pigmentation in their primary and permanent teeth. In case 1, the pigmentation was located on the cervical third of all primary teeth, and the permanent mandibular central incisors were completely pigmented. In this case, there were also caries lesions on the lower arch and evidence of hypoplasia. These findings are in accordance with Amaral et al. [12]

In case 1, all premolars are expected to have normal color aspects, because the LT was performed at 1 year and 11 months. However in Case 2, the LT was late — at age 8 — and all permanent teeth were affected (Figure 3). The greenish discoloration of the permanent teeth is compatible with the medical history in case 2. The mother reported that her daughter's total bilirubin levels remained elevated until LT at age 8, when all crowns of her permanent teeth were mineralized.

Early tooth loss was found in all cases because of extraction, as a result of dental caries. Interestingly, in case 1, the premature loss of primary maxillary right first molar caused the eruption of permanent maxillary right first premolar at 6 years old, and this tooth was not discolored (Figure 1). Also, in this case, the permanent mandibular central incisors and first molars were pigmented, and evident greenish dentin was detected on primary mandibular right second molar, with an extensive caries lesion (Figure 2). A clinical and histological study reports that this alteration in color is in the dentin and the cosmetic treatment dental bleaching may not be effective, since the pigmentation is confined in the dentin. [12] Nevertheless, Zaia et al. [13] affirm that bilirubin seems to be incorporated into the enamel and dentin during matrix formation.

A line was observed that separated two portions on the root of the extracted molar in case 2; one formed during the hyperbilirubinemia phase, and the other formed after the control of the disease (Figure 4). This finding is agreement with previous studies that reported extracted teeth with deeply stained portions of the roots formed prior to LT, which were clearly demarcated from the portion formed after LT that were normal in color. [5-7,12]

Tooth enamel can become discolored during amelogenesis from a number of causes, and it can often be difficult for dentists to determine the exact cause of tooth discoloration when it appears after tooth eruption. [20] Thus, if there is no prior information about the medical history of the patient, then it is more difficult to determine the adjusted treatment.

Systemic disturbance during early life can affect tooth mineralization as described in these case reports, through an uncommon form of tooth discoloration caused by hyperbilirubinemia associated with BA. It is appropriate that pediatric physicians refer any child who has conjugated hyperbilirubinemia or evidence of chronic liver disease to both a pediatric gastroenterologist center for evaluation and to dental examination.

In conclusion, early diagnosis of liver disease facilitates the institution of medical treatment and reduces the potential risk of tooth discoloration. Knowing the medical history of the patient is essential for management of the oral and aesthetic complications of chronic liver disease. Cosmetic treatments of the affected teeth should be a priority to improve the self-esteem and social integration of these children.

Conflict of interest and funding sources

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Authorship

All authors have made substantive contribution to this study and manuscript, and all have reviewed the final paper prior to its submission.

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FIGURES

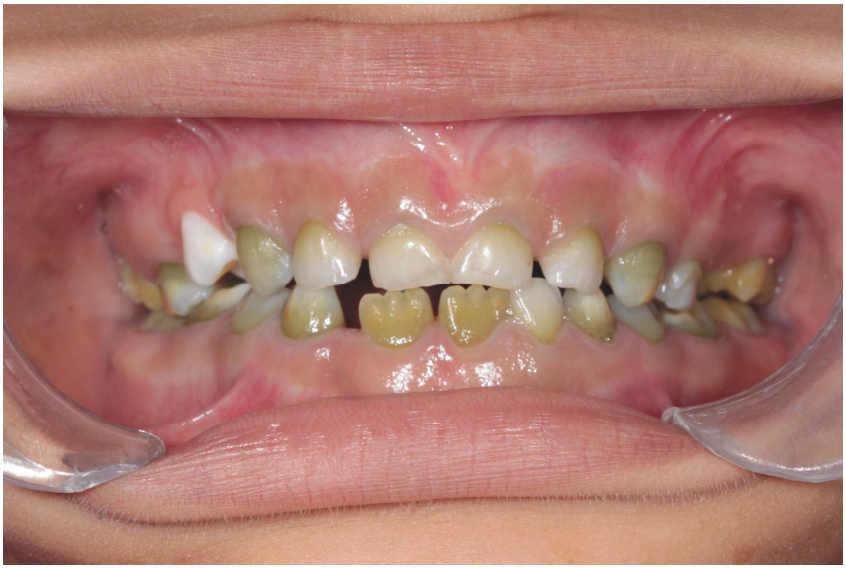

Figure 1. Photograph of a 6-year-old girl with a medical history of hiperbilirubinemia shows the primary and permanent teeth pigmented by bilirubin and early erupted unit 14 without discoloration.

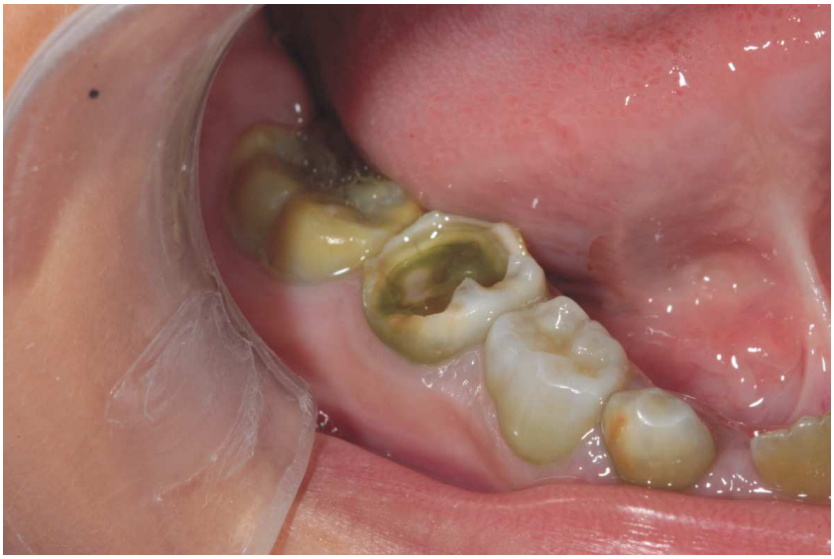

Figure 2. Note the occlusal caries lesion on the primary mandibular right second molar, with green pigmentation in the dentin.

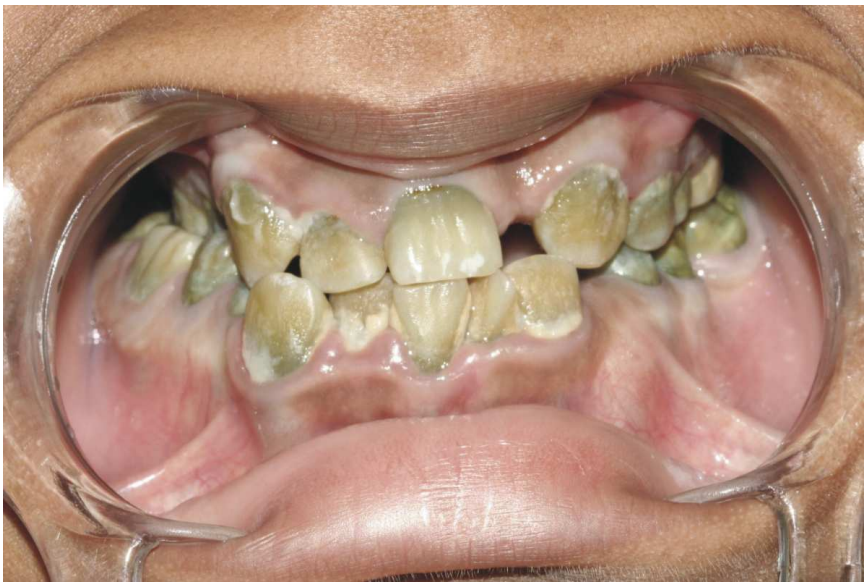

Figure 3. Photograph of a 15-year-old girl with a medical history of hiperbilirubinemia and late liver transplantation. The anterior view shows all teeth pigmented by bilirubin, as well as poor oral hygiene, with abundant dental biofilm and supragingival calculus.

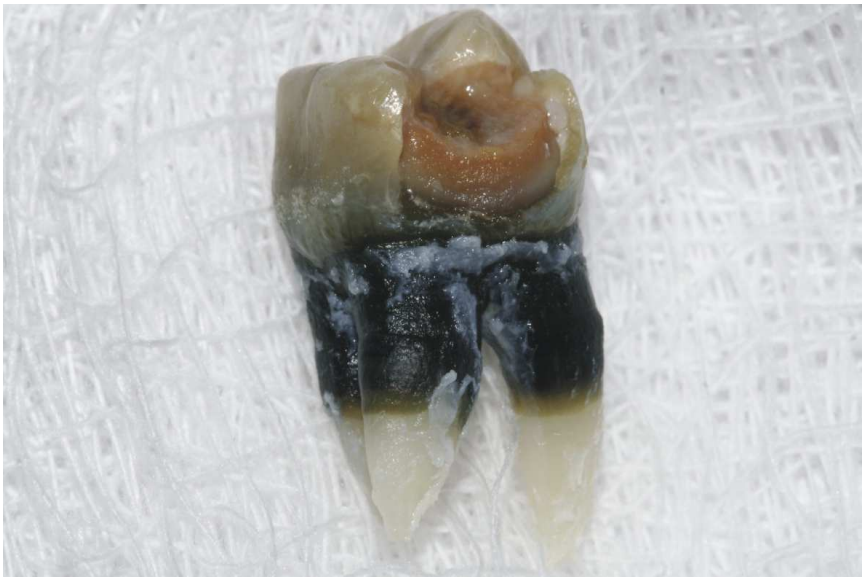

Figure 4. The extracted permanent molar shows a demarcated line separating the stained portion of the root, which was formed before liver transplantation (LT), from the normally-colored portion, which was formed after LT.

3.5 ARTIGO 5

Oral Findings in Children with Alagille Syndrome: Case Reports

Revista: Oral Health & Preventive Dentistry
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TITLE PAGE

TITLE: Oral Findings in Children with Alagille Syndrome: Case Reports

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ABSTRACT

Background: Alagille syndrome (AGS) is an autosomal dominant disorder that affects liver, heart, eyes, and skeleton. AGS is also associated with short stature and anomalies of the teeth. There is significant variability in the extent to which each of these systems is affected in an individual, if at all. **Case description**: This paper reports two cases of children (11-year-old boy and 9-year-old girl) with AGS underwent liver transplantation showing different oral findings. Medical history and oral exam pointed an uncommon form of tooth pigmentation caused by bilirubin deposition during dental formation, variance of normality, morphological defects in teeth and tooth erosion. After providing oral hygiene instructions and improving their tooth-brushing skills, it was decided that the cosmetic treatment for the tooth pigmentation will placed when the permanent dentition is complete. **Clinical implications**: The reported cases confirm the relevance of past medical history in regular and aesthetic dental care in pediatric dentistry.

Keywords: Alagille syndrome, liver disease, tooth discoloration, dental erosion

INTRODUCTION

Alagille syndrome (AGS) is an autosomal dominant disorder (Kamath et al, 2010a; Turnpenny and Ellard, 2012; Vajro et al, 2012) with reduced penetrance and variable expression (Turnpenny and Ellard, 2012). AGS is caused by mutations in the *Jagged1 (JAG1)* gene (Al-Mutawa et al, 2002; Huang et al, 2007; Kamath et al, 2010a); and mutations in the *NOTCH2* gene have also been demonstrated in a few patients (Kamath et al, 2010a).

AGS affects the liver, heart, eyes, and skeleton with recognizable facial dysmorphic features including triangular facies, prominent quadrangular forehead, pointed chin, and hypertelorism (Kamath et al, 2010a; Vajro et al, 2012). Less common clinical features include renal abnormalities, growth and mental retardation, intracranial bleeding, and pancreatic insufficiency (Huang et al, 2007). AGS is also associated with short stature (Emerick et al, 1999; Turnpenny and Ellard, 2012) and anomalies of the teeth (Chatterjee and Manson, 2007; Kamath et al, 2010a;). There is a significant variability in the extent to which each of these systems is affected in an individual, if at all (Kamath et al, 2010a).

The estimated prevalence of AGS is reported from 1:70,000 (Kamath et al, 2010a; Turnpenny and Ellard, 2012) to1:100,000 (Vajro et al, 2012). Hepatic disease in patients with AGS ranges from asymptomatic elevation of hepatic transaminases to end stage liver disease, which occurs in approximately 20-30% of cases (Kamath et al, 2010b). Liver transplantation (LT) is required in 20% to 50% of cases (Kamath et al, 2012) in AGS and it is a therapeutic option that requires careful consideration because of the multisystem nature of the condition. The best candidates for the operation are children with unremitting cholestasis and resistant pruritus, who have a simple cardiac defect, subclinical renal involvement, and relatively good nutritional state (Kamath et al, 2010a).

The present paper reports two cases of children with AGS who underwent liver transplantation exhibiting different oral findings.

CASE REPORTS

These case reports included two children with AGS who underwent LT and were referred for medical follow-up at the Center for Pediatric Gastroenterology and Hepatology, University

Hospital Complex Professor Edgard Santos, Federal University of Bahia, Salvador, Brazil. Their medical histories were reviewed and clinical examinations were performed. All patients/ guardians provided written informed consent to participated in the study.

Case 1

An 11-year-old boy was diagnosed with AGS and revealed cholestasis syndrome and jaundice from the 3rd day of life until 4 years and 6 months. He was born at term after an uncomplicated pregnancy and there was no family history of hepatopathies or jaundice. The levels of total bilirubin (TB) were high before LT, and intense pruritus was present. Clinical tests found a grade III/IV systolic murmur of pulmonary artery stenosis, but normal from the cardiac viewpoint. The arteriography identified accentuated stenosis of the celiac trunk; the upper gastrointestinal endoscopy revealed hypertrophy of the mesenteric artery; and the chest x-ray revealed butterfly vertebrae. Physically, he had characteristic facies. At age 3 years and 5 months, he underwent LT and was placed on an immunosuppressive regimen with tacrolimus and antihypertensive therapy. An oral examination revealed that the permanent maxillary lateral incisors were conically shaped; all teeth showed a greenish yellow intrinsic discoloration and were identified as having enamel hypoplasia and focal areas of opacity with pronounced horizontal developmental lines (Fig. 1 and Fig. 2). There was no carious lesion and his dental development was normal. The oral mucosa had no evidence of discoloration, but gingival overgrowth was found. His dental management so far has involved improvement of oral hygiene. Aesthetics treatment was recommended for the conically shaped incisors and composite veneers for the anterior pigmented teeth. Dental bleaching for pigmentation caused by bilirubin was not recommended, since the pigmentation is confined to dentin and it is unlikely to be effective (Amaral et al, 2008). The patient and her mother decided wait for the complete eruption of permanent teeth to do the cosmetic treatment. It will be necessary to improve self-esteem of the patient and assist in your social integration.

Case 2

A 9-year-old girl with AGS showed at a clinical evaluation good general health. Her medical history revealed that she was jaundiced from the 20th day of life until 2 years old; intense pruritus, xanthomas on fingers and elbows, and food allergies. She was born at term after an uncomplicated pregnancy. There was no family history of hepatopathies or jaundice. The results of the biopsy and the bile ducts scintigraphy revealed neonatal hepatitis. A cholangiography also showed the presence of biliary stenosis. The results of laboratory tests

showed elevated levels of total bilirubin (maximum level equal 7.93 mg/dL). A physical examination showed that she had deep-set eyes, prominent ears, a straight nose with a bulbous tip, a prominent forehead, and pointed chin, giving the face a triangular appearance characteristic facies. There were no cardiac abnormalities. At age 2, she underwent LT and was treated with tacrolimus. Her dental development was normal and all teeth showed normal aspect in color, but opacities and hypoplasia, and tooth erosion on primary and permanent molars (Fig. 3) were observed. Tooth pigmentation was not present in this case, which is possibly due the fact that bilirubin levels were not high enough to disturb the primary and permanent tooth formation. Poor oral hygiene was observed with abundant and pigmented dental biofilm. All the teeth had normal morphological characteristics, but it was noted that the permanent maxillary first molars had the cusp of Carabelli, a tooth abnormality (Fig. 4). The oral mucosa was normal with no evidence of discoloration or overgrowth. Her dental treatment plan included improvement of oral hygiene, dietary counseling to reduce consumption of acidic beverages and, replacement of an amalgam filling. However, no treatment was undertaken in this patient because she was lost to follow-up.

DISCUSSION

Chronic liver diseases in children who require LT may include congenital biliary atresia, biliary hypoplasia (AGS) syndromatic and non-syndromatic, metabolic disorders (α-1 antitrypsin deficiency, cystic fibrosis, Wilson's diseases) and acute liver failure (Sheehy et al, 1999).

Conventional indications for LT in chronic liver diseases of childhood, such as decompensation of synthetic function, uncontrolled portal hypertension or chronic encephalopathy are rare in AGS. However, in patients with AGS associated with cholestasis and severe pruritus, LT is a well-established therapy. It is estimated to be required in 21% to 31% of patients with AGS (Kamath et al, 2010a).

Cholestasis is defined as the impairment of bile flow (NASPGHAN, 2004; Shen et al, 2012;) or bile formation (NASPGHAN, 2004) either from hepatocellular dysfunction or from biliary obstruction (Shen et al, 2012) resulting in the retention of substances normally excreted into bile (NASPGHAN, 2004; Shen et al, 2012). Cholestatic jaundice is characterized by elevation

of serum conjugated bilirubin (NASPGHAN, 2004) and was related in both cases.

In Case 1, persistent cholestasis was found and LT was the treatment for the liver disease. Intractable pruritus was observed in both cases; however, xanthomas were observed only in Case 2. In this case, severe pruritus started at age 10 months until 2 years and affected the quality of life prior to the LT.

Nutritional deficiencies in children are commonly observed in pediatric patients with AGS (Shen et al, 2012). Diarrheal episodes occurred frequently in Case 1, but not in Case 2. In patients with AGS, malabsorption may occur because bile is necessary to absorb fat and fat-soluble vitamins (FSV). Deficiencies of FSV were associated with the severity of cholestasis in children and higher bilirubin levels were positively associated with vitamin D deficiency (Shen et al, 2012).

As stated by Olsen et al (2005) malabsorption is likely involved in the development of nutritional and bone deficits. Specific nutrient deficits such as vitamins A, D, E and K (Shen et al, 2012), calcium and magnesium also play a role in the development of children with cholestatic liver disease (Olsen et al, 2005).

AGS is essentially related to a defect of vasculogenesis, thus congenital heart disease and noncardiac vascular anomalies are frequently observed in AGS patients. Cardiac abnormalities are observed in 85 to 97% of patients with AGS (Vajro et al, 2012). In the cases reported, heart murmur of pulmonary artery stenosis was observed only in Case 1 and it did not cause clinical problems.

During hyperbilirubinemia, bilirubin is distributed and deposited in different tissues of the body. In soft tissues, the pigmentation immediately disappears due to the intense cell turnover. However, in mineralized dental tissues, bilirubin is permanently trapped (Amaral et al, 2008). Intrinsic green discoloration of the teeth caused by hyperbilirubinemia is considered to be rare. When it occurs biliary atresia is the most common cause of green discoloration (Sheehy et al, 1999; Guimarães and Silva, 2003; Sommer et al, 2010). Studies on oral manifestations associated with AGS are limited and reports of green tooth discoloration in AGS are uncommon.

In this study, green pigmentation was observed in all teeth of the Case 1 and enamel hypoplasia. The oral findings of Case 1 can be associated with the hyperbilirubinemia. Tooth discoloration was also observed by Victoria et al (2010), who described a case of a patient with AGS who presented complete green pigmentation of the roots of the primary teeth due to bilirubin. In Case 2 the teeth presented normal aspects in color, but opacity was present. In both cases morphological abnormalities were observed. Conically shaped teeth were found in Case 1 and cusp of Carabelli in Case 2.

Al-Mutawa et al (2002) report a case of a 13-year-old girl with medical history of AGS with grayish/yellow intrinsic discoloration and enamel hypoplasia, but normal morphological characteristics. Enamel hypoplasia can be caused by changes in the organic matrix of the developing enamel resulting from metabolic disturbances of calcium and phosphate metabolism encountered in chronic liver diseases (Amaral et al, 2008).
Nevertheless, Chatterjee and Mason (2007) described a case of a 9-year-old girl with AGS who presented lateral incisors with a talon cusp, a rare dental anomaly that manifests as an accessory cusp. However, tooth pigmentation were not related. They did not find evidence of discoloration in oral mucosa or gingival overgrowth, in accordance with Al-Mutawa et al (2002).

In Case 1, there was no evidence of discoloration on soft tissue but gingival overgrowth was present. This patient was placed on an immunosuppressive and antihypertensive therapy after LT; gingival overgrowth was probably caused by antihypertensive drugs, such as amlodipine and nifedipine, which were used by the patient. These drugs may not only impair oral aesthetics but may also lead to gingival inflammation and periodontal tissue damage (Marshal and Bartold, 1999). There is evidence suggesting that tacrolimus could not be associated with gingival overgrowth (Sheehy et al, 2000; Wondimu et al, 2001). In contrast with cyclosporin, tacrolimus is remarkably free of cosmetic adverse side effects, including gingival hyperplasia, hirsutism, and facial disfigurement (Reding, 2002).

CONCLUSION

The authors present an uncommon form of tooth pigmentation caused by bilirubin deposition during dental formation, variance of normality, and morphological defects on teeth in children

with AGS. Despite being a rare condition, the clinical and pathologic features of AGS are well documented, but there are no conclusive studies that make evident the association between oral findings with AGS, or with the multiple organ systems affected by AGS. The reported cases confirm the relevance of past medical history in regular and aesthetic dental care in pediatric dentistry.

Acknowledgments

The authors wish to thank all staff at the Center for Pediatric Gastroenterology and Hepatology, University Hospital Complex Professor Edgard Santos, Federal University of Bahia, Salvador, Bahia, Brazil for their help.

Conflict of interest and funding sources

The authors have no conflicts of interest, and there was no external funding support for this manuscript. Informed consent to use the clinical information and photographs was obtained from the parents of each patient described in this study.

Authorship

All authors have made substantive contribution to this study and manuscript, and all have reviewed the final paper prior to its submission.

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FIGURES

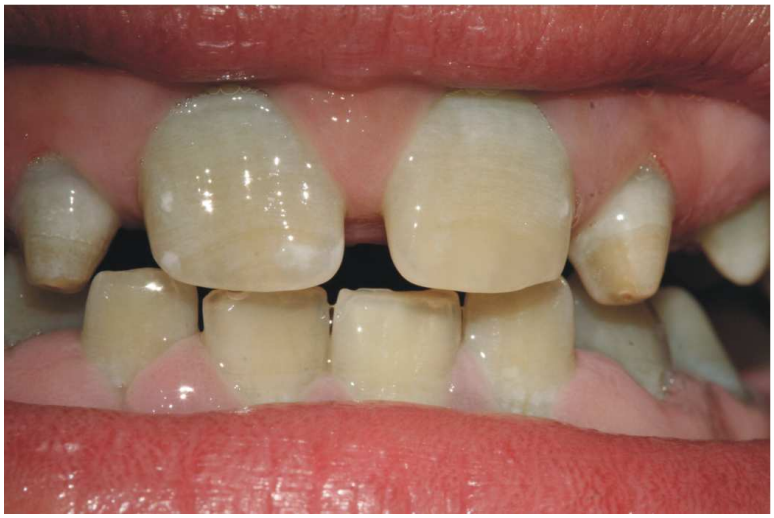


Fig. 1. Aspect of anterior teeth of case 1. Tooth pigmentation, opacities and gingival overgrowth were observed.

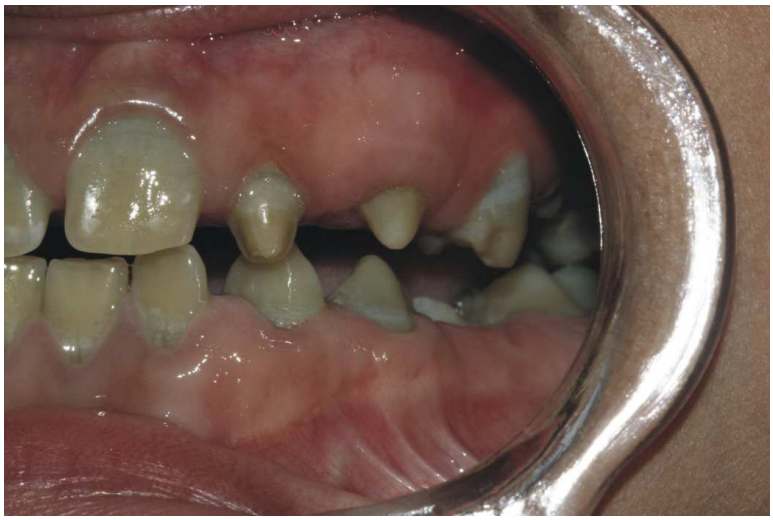


Fig. 2. Lateral view of case 1 showing all permanent teeth greenish yellow pigmented and upper lateral incisor conically shaped.

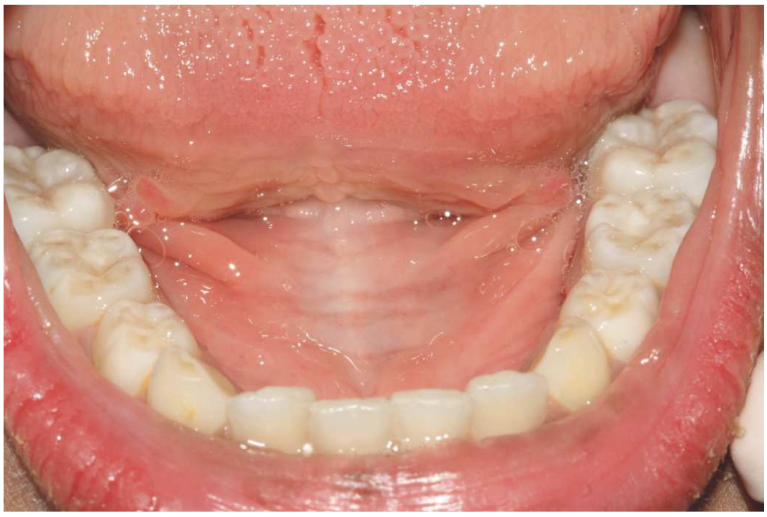


Fig. 3. Occlusal erosive tooth wear of case 2. Note rounding of the cusps and grooves on molars.

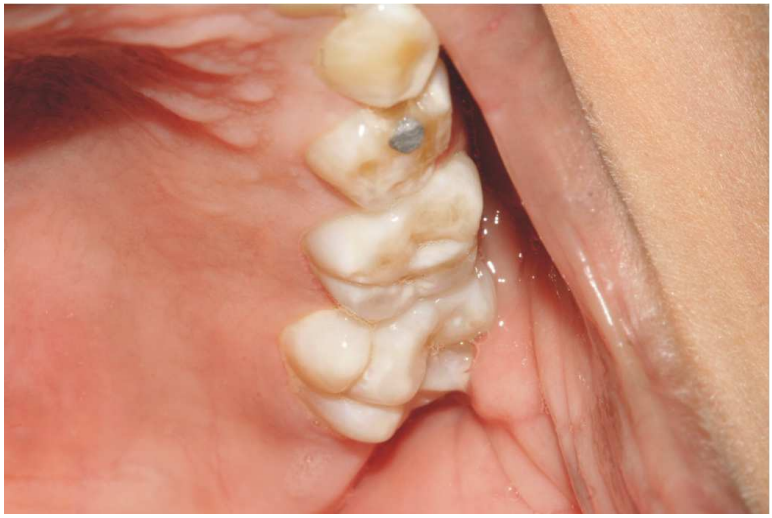


Fig. 4. Carabelli cusp on upper left permanent first molar of case 2.

4 CONCLUSÃO

- A experiência de cárie observada neste estudo encontra-se acima das médias nacional e regional para o ceo/CPOD, na maioria dos grupos etários, e parece estar relacionada diretamente com a higiene oral deficiente das crianças com história médica de doença hepática submetidas ao transplante hepático ou em lista de espera.

- O componente cariado representou o maior percentual dos índices ceo/CPOD em todos os grupos etários, evidenciando a falta de acesso ao tratamento odontológico por este grupo de crianças.

- A descoloração dentária, a hipoplasia e hipomineralização foram mais prevalentes nas crianças com história médica de atresia das vias biliares.

- A extensão e severidade da descoloração dentária causada pela hiperbilirrubinemia conjugada parece estar diretamente relacionada com o período de realização do transplante hepático.

- A condição de saúde bucal do grupo estudado parece ter sido mais influenciada pelos hábitos alimentares e a higiene oral deficientes do que pela doença hepática.

5 CONSIDERAÇÕES FINAIS

5.1 IMPACTO DA TESE

Os resultados deste estudo evidenciam a atual extensão da doença hepática e do seu tratamento como uma causa importante de manifestações bucais em crianças, apontando para a necessidade de mudanças no atendimento odontológico prestado a elas, especialmente no período pós-transplante, quando apenas o controle e seguimento médico são realizados como parte do tratamento.

Existe uma grande dificuldade de acesso aos serviços públicos e privados de Odontologia por esta população. No entanto, mesmo quando ele é conseguido, o atendimento odontológico é negado, pois os cirurgiões-dentistas, na sua grande maioria, desconhecem as manifestações da doença hepática na cavidade oral e demonstram apreensão e insegurança para tratar a criança submetida ao transplante hepático e sob terapia imunossupressora.

Desse modo, espera-se que, com a divulgação dos resultados deste estudo através dos meios científicos de comunicação, a integração entre os médicos pediatras, hepatologistas e gastroenterologistas com os cirurgiões-dentistas possa ultrapassar os limites das unidades hospitalares de transplante a fim de melhorar a qualidade de vida e promover saúde bucal nesta população.

5.2. LIMITAÇÕES DO ESTUDO

O número de pacientes que estão cadastrados e que fazem o acompanhamento médico pós-transplante no Centro de Estudos de Gastroenterologia e Hepatologia Pediátricas do CPPHO-HUPES é limitado às crianças residentes no estado da Bahia e, desse modo, representa uma população reduzida. Associado a isso, a disponibilidade para fazer parte do estudo dificultou a obtenção de uma amostra representativa, resultando em um estudo de série de casos.

As crianças estudadas e que residiam no interior do estado dependiam do poder público local para viajarem até Salvador. Desse modo, retornavam para a cidade de origem logo após a consulta médica e o agendamento da consulta odontológica muitas vezes ficava

comprometido, com remarcações sucessivas. A falta de um centro odontológico no CPPOH-HUPES para o atendimento exclusivo de crianças representou a maior dificuldade deste estudo, pois as crianças eram referidas para a Faculdade de Odontologia da UFBA e da FBDC e nem sempre conseguiam os recursos financeiros para o deslocamento até Salvador.

6 PERSPECTIVAS DE ESTUDOS

A realização deste estudo significou a solidificação de uma linha de pesquisa que integra a Odontologia e a Gastro-Hepatologia no Centro de Estudos em Gastroenterologia e Hepatologia Pediátricas do CPPHO/HUPES da UFBA. Desse modo, as possibilidades de estudos são amplas e promissoras.

A finalização desta tese representa o fim de uma etapa da linha de pesquisa com as crianças submetidas ao transplante hepático, mas que continua visando ampliar e aprofundar os estudos sobre as repercussões bucais da doença hepática. Além disso, significa também o início do desenvolvimento de novos projetos de pesquisa:

1. Avaliação da prevalência da hipomineralização molar-incisivo em crianças portadoras de doença inflamatória intestinal.

2. Avaliação das condições de saúde bucal em crianças portadoras de doenças hepáticas crônicas.

7 ANEXOS

7.1 ANEXO A Parecer do Comitê de Ética

UNIVERSIDADE FEDERAL DA BAHIA
FACULDADE DE ODONTOLOGIA
COMITÊ DE ÉTICA EM PESQUISA

APROVAÇÃO

Os membros do Comitê de Ética em Pesquisa da Faculdade de Odontologia da UFBA, em sessão ordinária no dia 30 de novembro de 2011, resolveu através do Parecer Consubstanciado nº 15/11, aprovar o projeto "Avaliação estomatológica em pacientes pediátricos submetidos a transplante hepático, acompanhados no Serviço de Gastroenterologia Pediátrica do Complexo HUPES-CPPIO da UFBA", da pesquisadora Elisângela de Jesus Campos, área temática Grupo III, registro no SISNEP FR: 484686, CAAE: 0046.0.368.000-11.

Salvador, 14 de março de 2012.

Prof. Dr. André Carlos de Freitas
Coordenador do CEP FOUFBA

7.2 ANEXO B - Termo de Consentimento Livre e Esclarecido

Universidade Federal da Bahia
Faculdade de Odontologia – Faculdade de Medicina
Curso de Pós-graduação em Medicina e Saúde
Projeto : Avaliação estomatológica em pacientes pediátricos submetidos a transplante hepático acompanhados no Serviço de Gastroenterologia Pediátrica do Complexo HUPES-CPPHO da Universidade Federal da Bahia

Termo de Consentimento Livre e Esclarecido

Por este instrumento particular declaro, para fins éticos e legais, que eu (nome)....., portador do RG: ....., CPF: ....., residente e domiciliado à Rua: ...., cidade:....., estado:.....tel. ..... concordo, em absoluta consciência, em participar deste estudo através da realização de exame clínico odontológico e da aplicação de um questionário, sem nenhum prejuízo para mim, e cujos resultados serão utilizados na pesquisa intitulada: "Avaliação estomatológica em pacientes pediátricos submetidos a transplante hepático acompanhados no Serviço de Gastroenterologia Pediátrica do Complexo HUPES-CPPHO da Universidade Federal da Bahia", realizada pela Profª. Elisângela de Jesus Campos, tendo como orientadora a Profª. Drª. Luciana Silva, nos termos abaixo relacionados:

1. Esclareço que recebi todas as informações sobre minha participação nesta pesquisa, possuindo plena liberdade em retirar meu consentimento de participar da referida pesquisa a qualquer momento, sem prejuízo financeiro, hierárquico ou de qualquer natureza;
2. Todas essas normas estão de acordo com o Código de Ética Odontológica, segundo a resolução do Conselho Federal de Odontologia 179/91, com Declaração de Helsinque II e com a resolução n º 196 de 10 de Outubro de 1996 do Conselho Nacional de Saúde do Ministério da Saúde.

Por estar de pleno acordo com o teor do presente termo, assino abaixo o mesmo.

....., ..., de ..... de .....

.....
Assinatura do Voluntário/ Responsável

Comitê de Ética em Pesquisa da FOUFBA
Av. Araújo Pinho, 62 – Canela - CEP: 40110-912 Salvador- BA
Tels. Gerais: 3283-8980 / 8982

Universidade Federal da Bahia
Faculdade de Odontologia – Faculdade de Medicina
Curso de Pós-graduação em Medicina e Saúde
Projeto : Avaliação estomatológica em pacientes pediátricos submetidos a transplante hepático acompanhados no Serviço de Gastroenterologia Pediátrica do Complexo HUPES-CPPHO da Universidade Federal da Bahia

Termo de Consentimento Livre e Esclarecido

Introdução
Você está sendo convidado (a) a participar de uma pesquisa. Antes de decidir, é importante que você entenda o porquê da realização desta pesquisa e o que ela envolve. Por favor, dedique um tempo para ler cuidadosamente as informações seguintes e, se preferir, discutir com seus familiares, amigos ou com seu médico. Se você desejar, pode levar este material para casa para pensar melhor. Pergunte-nos se houver qualquer coisa que não esteja clara ou se precisar de mais informações.

Para ser lido para ou por todos os participantes do estudo
As informações a seguir descrevem o estudo e seus direitos como participante. Além do que foi aqui esclarecido, o entrevistador poderá responder qualquer questão que você tenha referente ao estudo. Por favor, leia ou ouça com atenção e sempre que achar necessário interrompa para perguntar.

Justificativa
Vários autores têm sugerido que os indivíduos submetidos a transplante hepático podem apresentar, além dos sintomas clássicos, manifestações bucais e dentais. Considerando a importância da adoção de cuidados com a saúde bucal na infância com vistas à promoção de saúde tanto na dentição decídua como permanente, a avaliação das condições se saúde bucal, a identificação precoce de alterações dentais, suas causas e a escolha do tratamento adequado podem evitar a sua progressão na dentição permanente.

Objetivo do estudo
Avaliar a presença de complicações orais e dentais em pacientes pediátricos que foram submetidos a transplante hepático.

Procedimentos
Será realizado o exame clínico da cavidade oral do paciente, por um cirurgião-dentista e o preenchimento, pelo paciente ou responsável, de um questionário composto por questões relacionadas à sua dieta.

Benefícios que se pode ter
Participando desta pesquisa você **não** receberá nenhum tipo de benefício direto como dinheiro, mas estará contribuindo para a elaboração de um trabalho científico que poderá proporcionar benefícios futuros à sociedade. Independente da sua decisão de participar ou não desta pesquisa, nada será alterado com relação ao seu tratamento, que seguirá conforme estabelecido e de acordo com o protocolo definido pelo serviço de Gastroenterologia Pediátrica do Complexo Universitário Professor Edgard Santos (HUPES)- Centro Pediátrico Prof. Hosanah de Oliveira (CPPHO) da Universidade Federal da Bahia. Os benefícios esperados, contudo, serão traduzidos na obtenção de informações que possam contribuir para uma melhoria na qualidade do atendimento aos pacientes pediátricos que foram submetidos a transplante hepático.

Garantia de resposta a qualquer pergunta
A qualquer momento, você poderá fazer perguntas sobre esta pesquisa com a garantia de que estas serão respondidas.

Liberdade de abandonar a pesquisa sem prejuízo para si
A qualquer momento você poderá entrar em contato com os pesquisadores responsáveis por este estudo e pedir que os seus dados sejam retirados do mesmo. A concordância ou não em participar deste estudo, não irá alterar de nenhuma maneira o seu tratamento.

Garantia de privacidade
Os dados obtidos neste estudo serão apresentados em congressos e eventos da comunidade científica e poderão ser publicados em revistas especializadas. No entanto, **a sua identidade nunca será revelada**.

Contato: As dúvidas não esclarecidas ou o não cumprimento do que foi acordado podem ser informados ao responsável pela pesquisa, Prof[a.] Elisângela Campos, no Instituto de Ciências da Saúde da UFBA - 4[0]. Andar - sala 400.Tels. 3283-8891/ 9962-1130

7.3 ANEXO C - Questionário

Universidade Federal da Bahia
Faculdade de Odontologia – Faculdade de Medicina
Curso de Pós-graduação em Medicina e Saúde
Projeto : Avaliação estomatológica em pacientes pediátricos submetidos a transplante hepático acompanhados no Serviço de Gastroenterologia Pediátrica do Complexo HUPES-CPPHO da Universidade Federal da Bahia

QUESTIONÁRIO E FICHA CLÍNICA - EXAME ANAMNÉSICO

Questionário respondido por: _____ Nome do responsável:_____
Prontuário/CPPHO- HUPES: _____ Data:___/___/____ N°.:_____
Nome: _____
Endereço:_____
Bairro: _____ Cidade: _____ Estado: _____ CEP: _____
Tel.: _____ Cel.: _____ Naturalidade: _____
Data de nascimento: ____/____/____ Idade: _____ anos _____ meses Sexo: ( ) M ( ) F
Escolaridade.: _____ €Escola pública €Escola particular €Não estuda
Profissão dos pais: ( ) Pai Ocupação: _____ Grau de instrução: _____ ( ) Mãe Ocupação: _____ Grau de instrução: _____

IDENTIFICAÇÃO

1. Você acha que tem algum problema de saúde?	€ Não	€ Sim € Doença cardíaca € Doença respiratória € Diabetes € Doença celíaca € Doença hepática € DRGE € outra: _____ Quando você soube?_____	
2.Você fez transplante de fígado? 2.1. Diagnóstico: _____ _____ _____ _____ Retransplante:___/___/___ Motivo:_____ _____ _____	€ Não	€ Sim Data do transplante: ___/___/____ Local do transplante: _____ Idade ao fazer o transplante: _____anos_____meses Medicamentos em uso: € Aciclovir /Dose: _____ Período: de _____ até _____ € Predisona/Dose: _____ Período: de _____ até _____ € Micofenolato de Mofertil/Dose: ____ Período: de _____ até _____ €Tacrolimus/ Dose: _____ Período: de _____ até _____ €Ciclosporina/ Dose: _____Período: de _____ até _____ €Azatioprina/ Dose: _____Período: de _____ até _____ €A.A.S. / Dose: _____Período: de _____ até _____ €Persentin/ Dose: _____Período: de _____ até _____ €Outras: _____	
3. Faz uso de algum medicamento?	€ Não	€ Sim Atual /Qual?_____ Anterior / Qual? _____	
4.Tem alergia?	€ Alimento: Qual?_____	€ Medicamento: Qual? _____	€ Não sabe
5. Pratica atividade física?	€ Não	€ Sim Tipo:_____ Há quanto tempo?_____ N°. de vezes/semana:_____	
6. Consome bebida alcoólica?	€ Não	€ Sim Tipo:_____ Há quanto tempo? _____ N°. de vezes/semana:_____	
7. É fumante?	€ Não	€ Sim Tipo:_____ Há quanto tempo? _____	

		Nº. de vezes/semana:_____
8. Usa outro tipo de droga?	€ Não	€ Sim Tipo:_____ Há quanto tempo?_____ Nº. de vezes/semana:_____

HISTÓRIA MÉDICA

AVALIAÇÃO DA HIGIENE BUCAL

9. Última visita ao cirurgião-dentista?	( ) Nunca foi ao CD	( ) menos de 1ano	( ) de 1 a 2 anos	( ) de 2 a 3 anos	( ) há mais de 3 anos
10. Freqüência de visita(s) ao dentista	( ) Não frequenta	( ) 1x/ano	( ) 2x/ano	( ) 3x/ano	( ) mais de 3x/ano
	Motivo:_____				
11.Freqüência diária de escovação	( ) Não escova	( ) 1x/dia	( ) 2x/dia	( ) 3x/dia	( ) mais de 3x/dia
12.Intervalo de troca da escova	( ) a cada mês	( ) a cada 3 meses	( ) a cada ano	( ) Outro: _____	( ) Não sabe
13. Orientação da escovação	( ) Nunca recebeu	( ) Pediatra	( ) Dentista	( ) Pai/Mãe	( ) Outro: _____
14. Técnica de escovação	( ) Horizontal	( ) Circular	( ) Vertical	( ) Vibratório	( ) Não sabe
15.Freqüência diária de utilização do fio dental	( ) Não usa	( ) 1x/dia	( ) 2x/dia	( ) 3x/dia	( ) mais de 3x/dia
16. Freqüência diária de utilização de enxaguatório bucal	( ) Não usa	( ) 1x/dia	( ) 2x/dia	( ) 3x/dia	( ) mais de 3x/dia
17.Você usa aparelho ortodôntico?				( ) Sim	( ) Não
18.O creme dental que você usa foi indicado pelo seu dentista?				( ) Sim	( ) Não
19. A TV/mídia influencia na escolha do creme dental que você usa?				( ) Sim	( ) Não
20. A escova dental que você usa foi indicada pelo seu dentista?				( ) Sim	( ) Não
21. A TV/mídia influencia na escolha da escova dental que você usa?				( ) Sim	( ) Não
22. A) Você sabe o nome do creme dental que você está usando?				( ) Sim Qual:	( ) Não
22. B)O creme dental que você usa é fluoretado?				( ) Sim	( ) Não
23.Você sabe qual a concentração de flúor do creme dental que você está usando?				( ) Sim Qual:_____	( ) Não
24.Você sabe qual o tipo de flúor do creme dental que você está usando?				( ) Sim Qual:_____	( ) Não

AVALIAÇÃO SOBRE RISCO DE EROSÃO DENTAL

25. Freqüência diária de lanches	( ) Não realiza	( ) 1x/dia	( ) 2x/dia	( ) 3x/dia	( ) mais de 3x/dia
26.Você ingere muitos alimentos ácidos, incluindo frutas, molhos para salada e iogurte?				( ) Sim	( ) Não
27.Você ingere bebidas ácidas usualmente (suco de frutas e refrigerantes)?				( ) Sim	( ) Não
28. Você ingere bebidas esportivas usualmente (ex.: Gatorade)?				( ) Sim	( ) Não
29. Você bochecha/ deixa na boca os sucos ou refrigerantes antes de engolir?				( ) Sim	( ) Não
30. Você ingere sucos ou refrigerantes usualmente com canudo?				( ) Sim	( ) Não
31. Você pratica natação/ frequenta piscina regularmente?				( ) Sim	( ) Não
32.Você tem problemas de refluxo, indigestão ou vômitos freqüentes?				( ) Sim	( ) Não
33.Você é portador da doença do refluxo gastro-esofágico?				( ) Sim	( ) Não
34.Você escova seus dentes imediatamente após se alimentar?				( ) Sim	( ) Não
35.Você utiliza uma escova dental de cerdas duras?				( ) Sim	( ) Não
36.Você escova os dentes por um período muito longo?				( ) Sim	( ) Não
37.Você utiliza creme dental arenoso demais?				( ) Sim	( ) Não
38.Você visita o seu dentista pelo menos uma vez ao ano?				( ) Sim	( ) Não
39.Seus dentes doem quando você ingere comidas ou bebidas quentes/ geladas/ doces ou quando você escova ou passa o fio dental ou quando passa algum tempo em um ambiente frio?				( ) Sim	( ) Não
40.Os seus dentes têm uma aparência semelhante a vidro ou são transparentes, amarelados, arredondados, lisos ou brilhantes com pequenas trincas?				( ) Sim	( ) Não

AVALIAÇÃO DE HÁBITOS ASSOCIADOS

41. Aleitamento materno	( ) Não foi amamentada	( ) até 3 meses	( ) >6meses	( ) >1 ano	( ) em amamentação
42.Faz uso de mamadeira?	( ) Nunca usou	( ) Usou até_____anos	( ) Sim ( ) Diurno n°. de vezes_____ ( ) Noturno n°. de vezes: _____		
43. Faz uso de chupeta?	( ) Nunca usou	( ) Não/ usou até_____anos	( ) Sim ( ) Diurno € M € V ( ) Noturno (dorme com a chupeta)		
44.Chupa o dedo?	( ) Nunca	( ) Não até_____anos	( ) Sim ( ) Diurno € M € V ( ) Noturno		
45. Roer as unhas	( ) Nunca	( ) Não/ Roeu até_____anos	( ) Sim		
46.Bruxismo/Ranger dos dentes	( ) Nunca	( ) Não/ Rangeu até_____anos	( ) Sim ( ) Diurno € M € V ( ) Noturno		

AVALIAÇÃO DOS HÁBITOS ALIMENTARES

47.Você acha que sua ingestão de alimentos por refeição é:	( ) pequena	( ) moderada	( ) alta	( ) muito alta	( ) não sabe
48.Como você classifica sua dieta?	( ) balanceada	( ) rica em gordura	( ) rica em açúcar	( ) rica em proteínas	( ) não sabe
49.Local das refeições	( ) na mesa de casa com a família	( ) no quarto	( ) na frente da televisão	( ) na frente do computador	( ) na rua
50. O seu consumo de açúcar é:	( ) Não consome	( ) pequeno	( ) moderado	( ) alto	( ) muito alto
51.Como você classifica a tempo da sua mastigação?	( ) devagar	( ) moderado	( ) rápido	( ) muito rápido	( ) não sabe
52.Durante as refeições como você mastiga os alimentos?	( ) mastiga bastante	( )engole pedaços mal mastigados			( ) não sabe
53.Ingestão de líquidos durante as refeições	( ) Não consome	( ) pouco	( ) moderado	( ) alto	( ) não sabe
54.Você adoça as bebidas/ alimentos que consome com maior freqüência com o açúcar comum (sacarose)?				( ) Sim	( ) Não
55.Você consome adoçantes?				( ) Sim	( ) Não
56.Você prefere o açúcar em relação aos adoçantes?				( ) Sim	( ) Não
57.Você tem preferência por alimentos:	( ) líquidos	( ) pastosos		( ) sólidos	( ) fibrosos

INVESTIGAÇÃO DA DRGE – HISTÓRIA CLÍNICA

58. Você acha que tem refluxo/ sente o retorno do alimento para a boca?	( ) Sim Idade de início dos sintomas:__ dias__ meses ___anos		( ) Não	( ) Não sabe
59. Sinais/ Sintomas	( ) regurgitações pós-alimentares	( ) vômitos persistentes	( ) vômitos não persistentes	( ) náuseas
	( ) anorexia	( ) sialorréia	( ) distensão abdominal	( ) apnéia
	( ) engasgos	( ) tosse	( ) soluços	( ) dispnéia
	( ) hematêmese	( ) melena	( ) cianose	( ) choro
	( ) irritabilidade noturna	( ) perda de peso	( ) dor no estômago	( ) azia
60. Investigação diagnóstica já realizada	( ) nenhum exame		( ) ultra-sonografia para estudo de RGE	
	( ) EREED		( ) endoscopia digestiva alta	
	( ) pHmetria		( ) outro	
61. Medicações ou medidas anti-refluxo que já tenha feito uso	( ) nenhum tratamento		( ) fracionamento da dieta	
	( ) elevação da cabeceira		( ) espessamento da dieta	
	( ) suspensão do leite materno devido ao refluxo		( ) substituição da fórmula láctea por outra fórmula ou “comida de prato”	
	( ) substituição da fórmula láctea por alimento		( ) antiácidos	
	( ) pró-cinéticos	( ) domperidona	( ) bromoprida	( ) metoclorpramida

	( ) outro: _____			
62. Patologias associadas	( ) pneumopatia	( ) cardiopatia	( ) diabetes	( ) hepatopatia
	( ) neuropatia	( ) anemia falciforme	( ) síndrome genética	( ) nenhuma
	( ) outra:			
63. DIAGNÓSTICO:				

AVALIAÇÃO DO PERFIL ALIMENTAR

Frequência **Alimento**	Não	Sim/ às vezes	Sim/ 1x/dia	Sim/ 2x/dia	Sim/ 3x/dia	Sim/ +3x/dia
Leite						
Café						
Chá						
Achocolatado						
Mingaus						
Iogurte/derivados						
Pão						
Legumes						
Raízes						
Verduras						
Massas						
Arroz						
Feijão						
Farinha						
Carnes						
Molhos (Catch up)						
Laranja						
Tangerina						
Limão						
Maracujá						
Abacaxi						
Acerola						
Goiaba						
Cajú						
Morango						
Cajá						
Tamarindo						
Uva						
Kiwi						
Melão						

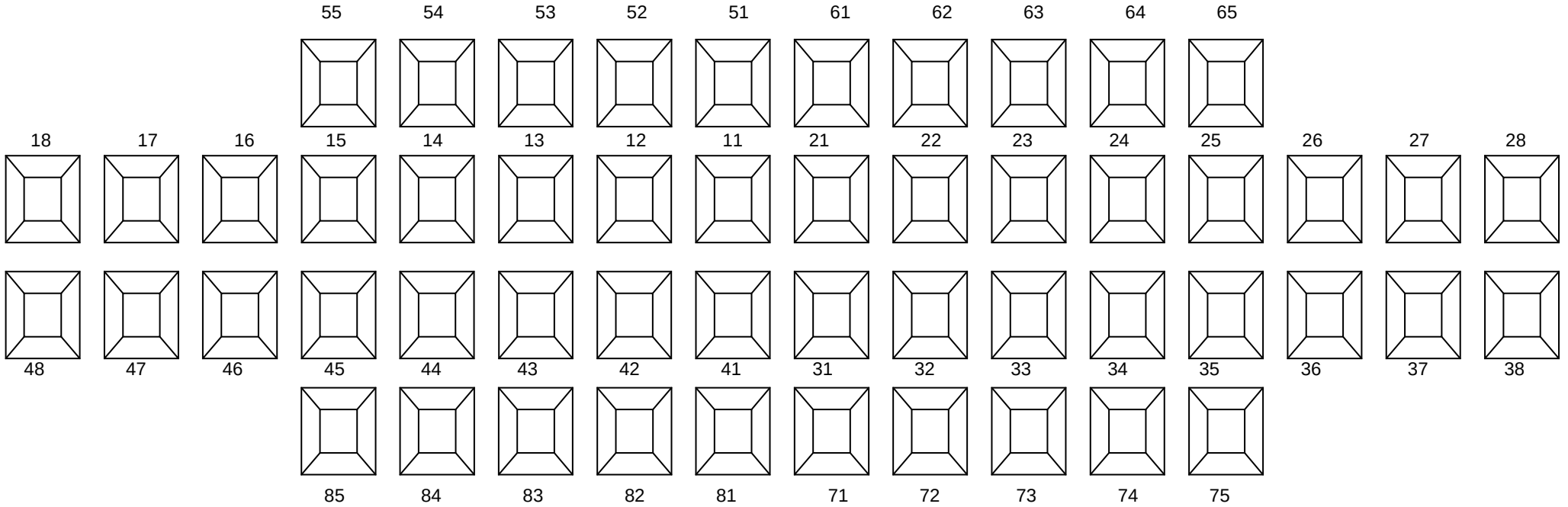
Manga						
Maçã						
Mamão						
Umbu						
Outra fruta:						
Frituras						
Sanduíche						
Chocolate						
Bala						
Chiclete						
Bolos						
Biscoitos doce/recheado						
Biscoitos salgado						
Salgadinhos						
Refrigerantes						
Bebida gaseificada						
Sucos naturais						
Sucos industrializado						
Sorvete/Picolé						

EXAME CLÍNICO

1.Avaliação geral	
2. Avaliação loco-regional	Cabeça
	Pescoço
3. Exame intrabucal (exame das partes moles)	Lábios
	Língua
	Bochecha
	Mucosa jugal
	Gengiva
	Assoalho de boca
	Palato duro
	Palato mole
	Orofaringe
	Freios
4. Exame salivar	Horário da última refeição:
	Fluxo salivar estimulado ml/min:
	Capacidade de tamponamento:

Exame clínico - Cárie

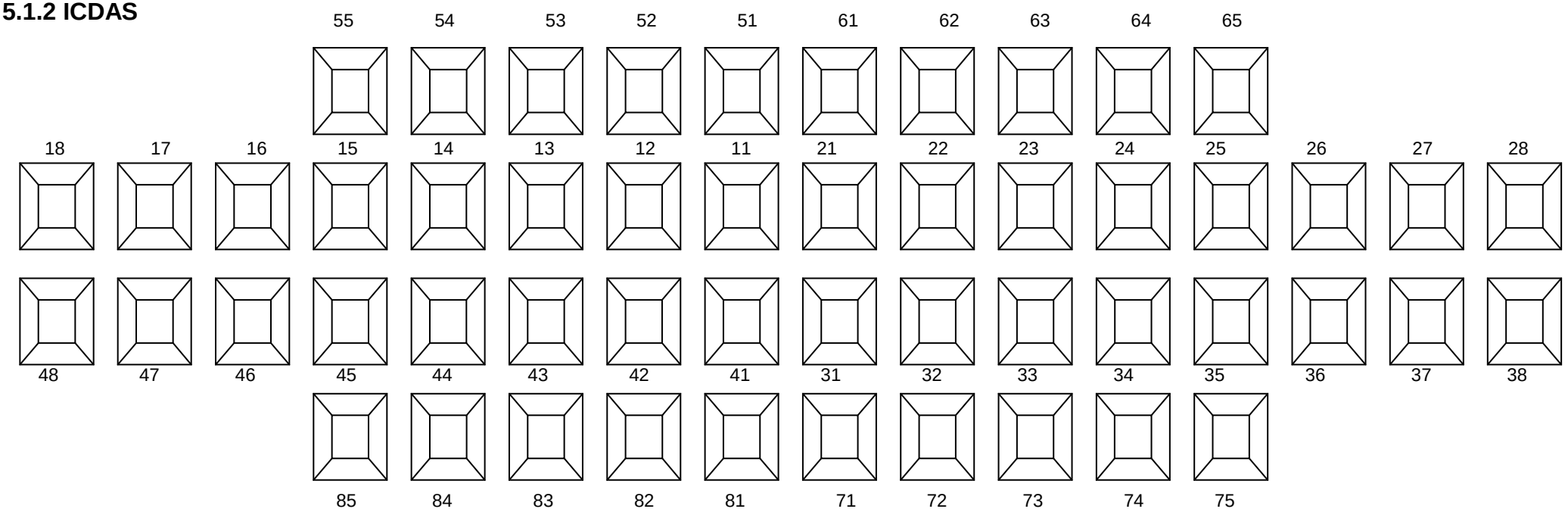
5.1.1 CPO-D/ ceo



CÓDIGOS

CPO-D =		ceo =	
Código 0	Hígido	Código A	Hígido
Código 1	Cariado	Código B	Cariado
Código 2	Restaurado com cárie	Código C	Restaurado com cárie
Código 3	Restaurado sem cárie	Código D	Restaurado sem cárie
Código 4	Perdido por cárie	Código E	Perdido por cárie
Código 5	Perdido por outras razões	Código -	Perdido por outras razões
Código 6	Selante	Código -	Selante
Código 7	Apóio de prótese	Código G	Apóio de prótese
Código 8	Não erupcionado	Código -	Não erupcionado
Código 9	Excluído	Código -	Excluído
Código T	Trauma/ Fratura	Código T	Trauma/ Fratura

5.1.2 ICDAS

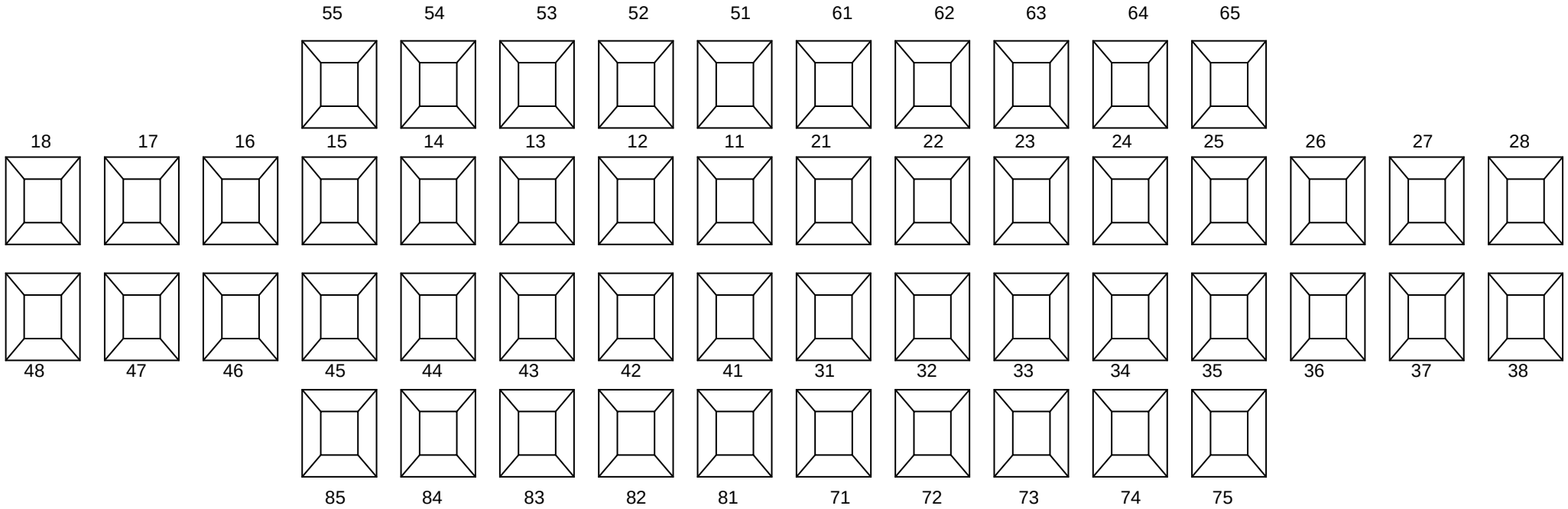


ICDAS

Código para dentes restaurados e selados		Código de lesões de cárie		Código de dentes ausentes	
Código 0	Não restaurado ou não selado	**ESMALTE**		Código 97	Extraído devido à cárie
Código 1	Selante parcial	Código 0	Superfície dentária integra	Código 98	Ausente por outro motivo
Código 2	Selante integral	Código 1	Mudança inicial visível no esmalte	Código 99	Não erupcionado
Código 3	Restauração na cor do dente	Código 2	Mudança nítida visível no esmalte		
Código 4	Restauração de amálgama	Código 3	Descontinuidade do esmalte, sem dentina visível		
Código 5	Coroa de aço inoxidável	**DENTINA**			
Código 6	Porcelana ou ouro ou coroa RMF ou veneer	Código 4	Sombreamento da dentina subjacente (sem cavitação em dentina)		
Código 7	Restauração perdida ou deficiente	Código 5	Cavidade nítida com dentina visível		
Código 8	Restauração temporária	Código 6	Cavidade extensa nítida com dentina visível		

5.2 Exame clínico – Erosão Dental

5.2.1 Índice BEWE (Basic Erosive Wear Examination)



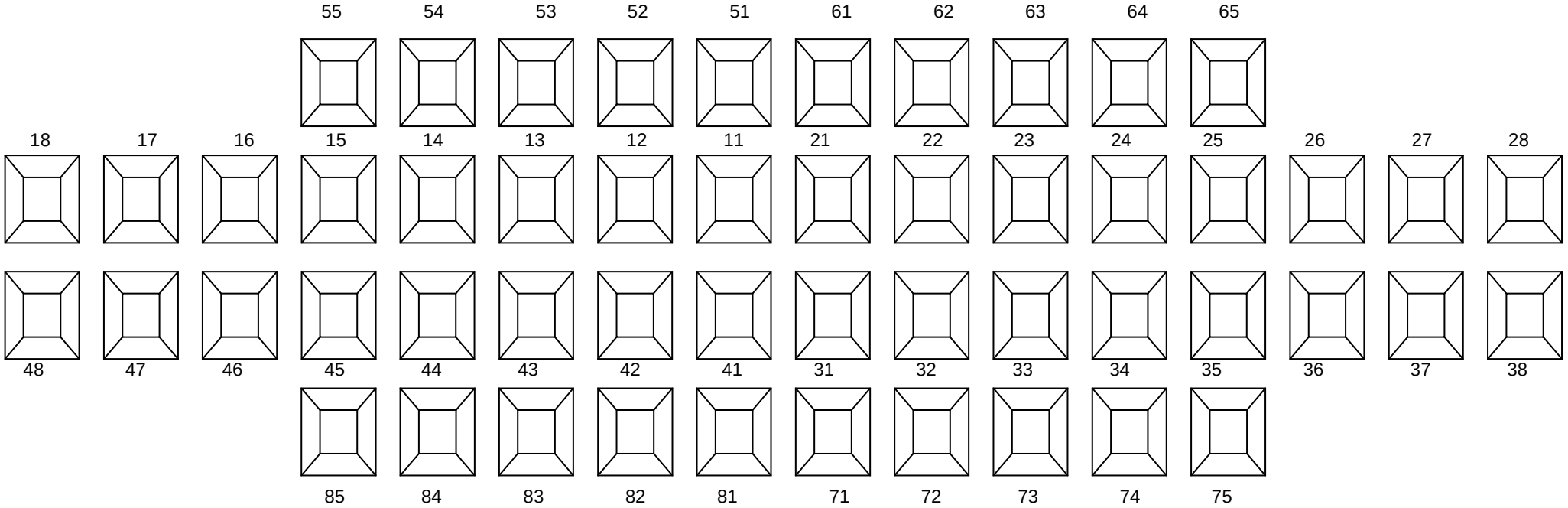
ESCORE / CÓDIGOS

0	Sem desgaste dental por erosão
1	Perda inicial da textura da superfície
2*	Defeito distinto, perda do tecido duro em < 50% da área da superfície
3*	Perda do tecido duro em ≥ 50% da área da superfície

*nos escores 2 e 3 a dentina está frequentemente afetada

Escore mais alto 1º. sextante (17-14): _____	Escore mais alto 2º. sextante (13-23):_____	Escore mais alto 3º. sextante (24-27):_____	Soma dos escores: _____
Escore mais alto 6º. sextante (44-47): _____	Escore mais alto 5º. sextante (33-43):_____	Escore mais alto 4º. sextante (37-34):_____	Média: _____

5.2.2 Índice de O’Sullivan (2000)

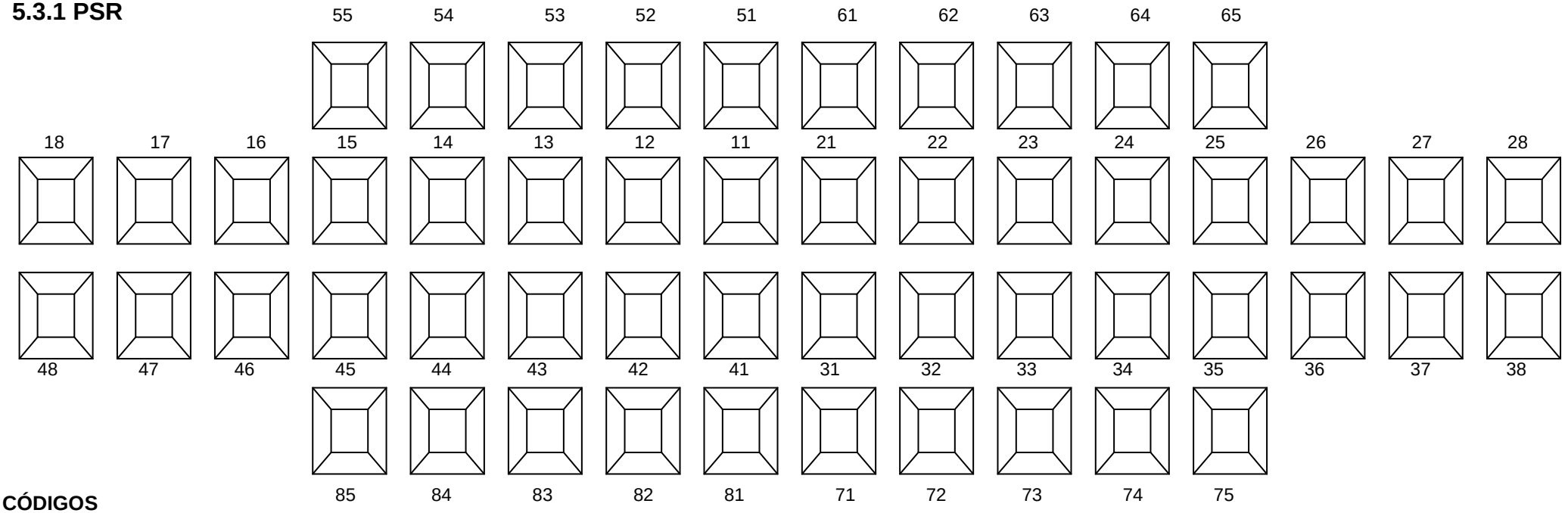


ESCORES /CÓDIGOS

LO CALIZAÇÃO DA EROSÃO EM CADA DENTE		GRAU DA SEVERIDADE (pior escore para cada dente examinado)	
Código A	Apenas superfície vestibular	Código 0	Esmalte normal
Código B	Apenas superfície palatina	Código 1	Esmalte alterado, mas sem perda do contorno
Código C	Apenas superfície incisal ou oclusal	Código 2	Esmalte alterado com perda de contorno
Código D	Superfície vestibular e incisal/ oclusal	Código 3	Perda de esmalte com exposição de dentina (visível limite amelodentinário)
Código E	Superfície palatina e incisal/ oclusal	Código 4	Perda de esmalte e dentina além do limite amelodentinário
Código F	Mais de duas superfícies	Código 5	Perda de esmalte e dentina com exposição pulpar
		Código 9	Não analisado (restauração extensa ou outra condição)
ÁREA DA SUPERFÍCIE AFETADA PELA EROSÃO			
Código -	Menos da metade da área afetada	Código +	Mais da metade da área afetada

5. 3. Exame Periodontal

5.3.1 PSR

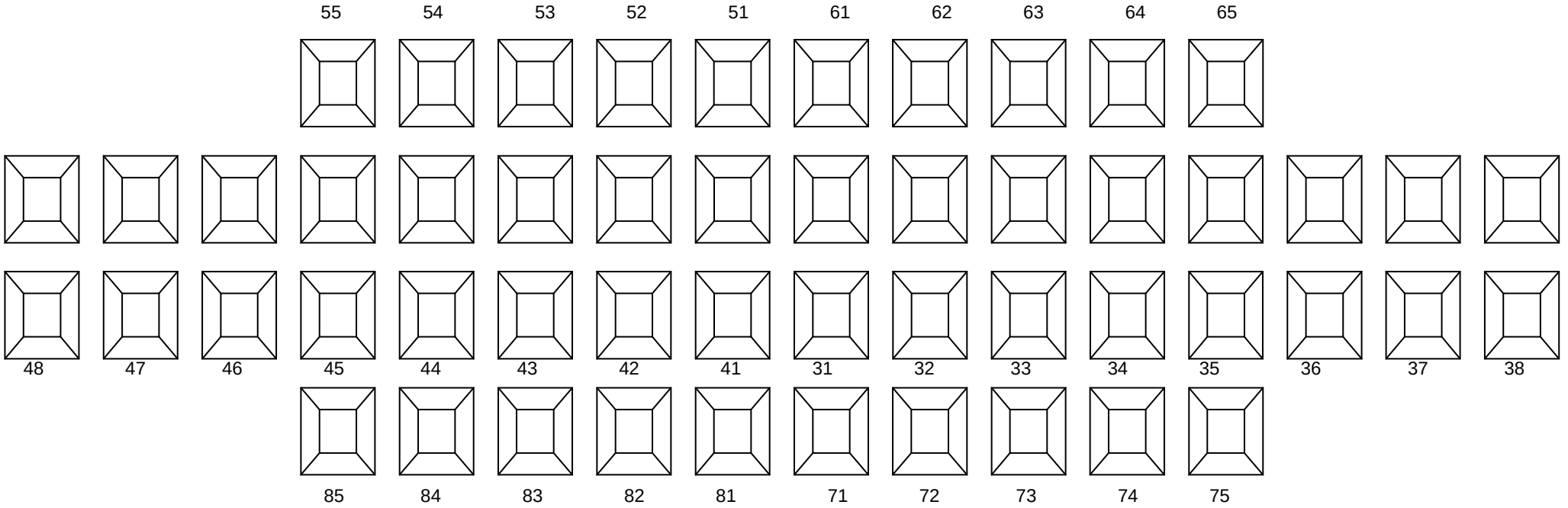


CÓDIGOS

Código 0	Faixa colorida totalmente visível, sem sangramento a sondagem, ausência de cálculo e excessos de margens restauradoras.
Código 1	Faixa colorida totalmente visível, com sangramento a sondagem, ausência de cálculo e excessos de margens restauradoras.
Código 2	Faixa colorida totalmente visível, com sangramento a sondagem, presença de cálculo supra e/ou subgengival e/ou excessos de margens restauradoras.
Código 3	Faixa colorida parcialmente visível, presença de bolsa de 3,5 a 5,5 mm.
Código 4	Faixa colorida não visível, presença de bolsa periodontal acima de 5,5 mm.
Código *	A inserção deste código significa a presença de outros problemas como envolvimento de furcas, mobilidade, perda de gengiva inserida e recessão gengival acima de 3,5 mm.

Escore mais alto 1º. sextante (17-14): _____	Escore mais alto 2º. sextante (13-23):_____	Escore mais alto 3º. sextante (24-27):_____	Soma dos escores: _____
Escore mais alto 6º. sextante (44-47): _____	Escore mais alto 5º. sextante (33-43):_____	Escore mais alto 4º. sextante (37-34):_____	Média: _____

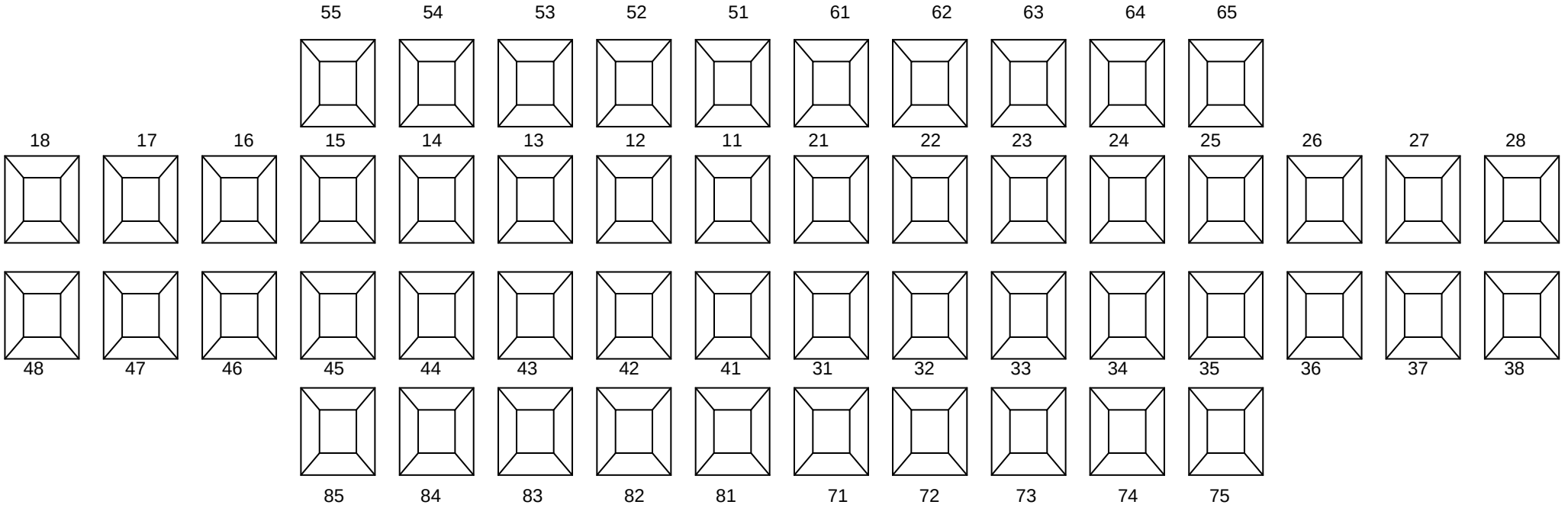
5.3.2 Índice de Placa de Turesky, Gilmore e Glickman (1970) – Superfície Vestibular e Lingual



ESCORES

Escore 0	Nenhuma placa
Escore 1	Porções separadas ou faixa descontínua de placa na margem cervical da superfície dentária
Escore 2	Faixa fina contínua de até 1mm de placa na margem cervical da superfície
Escore 3	Faixa de placa mais larga que 1mm, mas menor que 1/3 da superfície
Escore 4	Placa cobrindo entre 1/3 e 2/3 da superfície
Escore 5	Placa cobrindo 2/3 ou mais da superfície

5.3.2 Índice de Higiene Oral (IHO) - Greene e Vermilion (1960) – Superfície Vestibular e Lingual



ESCORES

ÍNDICE DE RESÍDUOS

Escore 0	Nenhum resíduo ou mancha presentes
Escore 1	Resíduos cobrindo não mais do que 1/3 da superfície do dente ou presença de pigmentação
Escore 2	Resíduos cobrindo mais do que 1/3, mas não mais do que 2/3 da superfície do dente
Escore 3	Resíduos cobrindo mais do que 2/3 da superfície do dente

ÍNDICE DE CÁLCULO

Escore 0	Nenhuma cálculo presente
Escore 1	Cálculo supragengival cobrindo não mais do que 1/3 da superfície do dente
Escore 2	Cálculo supragengival cobrindo mais do que 1/3, mas não mais do que 2/3 da superfície do dente ou presença de pontos de partículas de cálculo subgengival na porção cervical do dente ou ambos
Escore 3	Cálculo supragengival cobrindo mais do que 2/3 da superfície do dente ou presença de uma faixa estreita e contínua de cálculo subgengival na porção cervical do dente ou ambos

7.4 ANEXO D – Resumos Publicados em Anais de Congressos