UNIVERSIDADE FEDERAL DA BAHIA
FACULDADE DE MEDICINA DA BAHIA
PROGRAMA DE PÓS-GRADUAÇÃO
EM CIÊNCIAS DA SAÚDE

DURAÇÃO DE VÔMITO MAIOR OU IGUAL A 2,5 DIAS: FATOR INDEPENDENTEMENTE ASSOCIADO COM PIOR EVOLUÇÃO EM CRIANÇAS COM BRONQUIOLITE

Vivian Botelho Lorenzo

Dissertação de Mestrado

Salvador (Bahia), 2017

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Duração de vômito maior ou igual a 2,5 dias: Fator independentemente associado com pior evolução em crianças com bronquiolite

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Dissertação apresentada ao Colegiado do PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE, da Faculdade de Medicina da Universidade Federal da Bahia, como pré-requisito obrigatório para a obtenção do grau de Mestre em Ciências da Saúde.

Salvador (Bahia), 2017

Universidade Federal da Bahia
Faculdade de Medicina da Bahia
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Lorenzo, Vivian Botelho.
L869 Duração de vômito maior ou igual a 2,5 dias: fator independentemente associado com pior evolução em crianças com bronquiolite / Vivian Botelho Lorenzo. – 2017.

144 f.: il.

Inclui anexos.
Orientadora: Profª. Drª. Cristiana M. Nascimento-Carvalho.

Dissertação (Mestrado) – Universidade Federal da Bahia, Faculdade de Medicina da Bahia, Programa de Pós-Graduação em Ciências da Saúde, Salvador, 2017.

1. Bronquiolite - Complicações. 2. Recém-Nascido. 3. Fatores de Risco. I. Nascimento-Carvalho, Cristiana M. II. Universidade Federal da Bahia. Faculdade de Medicina da Bahia. III. Título.

CDU: 616.233-002

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"*A tarefa não é tanto ver aquilo que ninguém viu, mas pensar o que ninguém ainda pensou sobre aquilo que todo mundo vê. "*

(Arthur Schopenhauer)

DEDICATÓRIA

Dedico este trabalho à professora Dra. Célia Maria Stolze Silvany que através da sua história e exemplo cotidiano ensina-me que o verdadeiro sábio é um eterno aprendiz e deve seguir sempre se surpreendendo com o novo.

AGRADECIMENTOS

À minha orientadora Cristiana Maria Nascimento Carvalho por fazer despertar em mim o interesse investigativo, pela disponibilidade e atenção dispensada. Obrigada ainda pela paciência, palavras de incentivo e importantes ensinamentos ao longo de todo este trabalho.

Aos professores e colegas do Programa de Pós-Graduação em Ciências da Saúde da Universidade Federal da Bahia pelas críticas, comentários e sugestões úteis para o aprimoramento do meu trabalho.

À equipe multidisciplinar do Hospital da Criança das Obras Sociais Irmã Dulce pelas condições de trabalho que tornaram possíveis a realização deste estudo, em especial aos Residentes de Pediatria pelo entusiasmo com a pesquisa e pelo auxílio na coleta de dados dos prontuários médicos dos pacientes hospitalizados.

Às equipes das Unidades de Terapia Intensiva Pediátrica do Hospital Santo Antônio e Hospital do Subúrbio que promoveram condições na minha carga horária para que eu me dedicasse a este trabalho.

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I. RESUMO

DURAÇÃO DE VÔMITO MAIOR OU IGUAL A 2,5 DIAS: FATOR INDEPENDENTEMENTE ASSOCIADO COM PIOR EVOLUÇÃO EM CRIANÇAS COM BRONQUIOLITE: Introdução: Bronquiolite é a principal causa de internamento em lactentes. É uma doença de curso variado. O grupo de crianças que evolui com deterioração clínica encontra-se mal definido na literatura. Objetivo: Identificar fatores presentes na admissão que são associados com pior evolução em crianças hospitalizadas com bronquiolite. Metodologia do Estudo: Estudo de coorte prospectivo conduzido em enfermaria pediátrica nas Obras Sociais Irmã Dulce, Salvador, Brasil, realizado de maio de 2015 a julho de 2016. Critérios de inclusão: Idade <2 anos, diagnóstico de bronquiolite na admissão hospitalar e assinatura do termo de consentimento livre e esclarecido (TCLE). Dados clínicos, exame físico na admissão e desfechos foram registrados. Um modelo de regressão logística multivariada ajustado para idade foi utilizado para avaliar associação entre necessidade de tratamento em Unidade de Terapia Intensiva (UTI) e duração de internamento hospitalar (DIH) ≥5 dias (variáveis de desfecho) e fatores detectados durante admissão (variáveis preditoras). Resultados: O grupo de estudo compreendeu 172 pacientes. Destes, 5 (2.9%;IC 95%:1.1%-6.3%) foram transferidos para UTI e 69 (40.1%;IC 95%:33.0%-47.6%) tiveram DIH ≥5 dias. A mediana da idade foi 5.2 meses (IQR:3.6-8.2) e a mediana da duração de vômitos foi de 1 dia (IQR:1-3); prematuridade <30 semanas (3.5%), <37 semanas (14.5%) foram reportados, além de desnutrição grave (4.7%) e presença de estertores crepitantes na ausculta pulmonar (27.9%). Desnutrição grave (OR 21.53;IC95% 1.43–323.66), prematuridade <30 semanas (OR 13.85;IC95% 1.23–155.89) e duração de vômitos (OR 1.92;95%CI1.16–3.17) foram independentemente associados com transferência para UTI. Prematuridade <37 semanas (OR 3.89; IC95% 1.55–9.79) e presença de estertores

crepitantes na ausculta pulmonar durante admissão (OR 3.11;95%CI 1.45–6.70) foram independentemente associados com DIH ≥5 dias. A area abaixo da curva ROC entre duração de vômito como fator preditor de transferência para UTI foi 0.92(IC95% 0.81–1.04) com ponto de corte na melhor performance 2.5 dias (sensibilidade 100%; especificidade 79%). Conclusão: Crianças admitidas com bronquiolite e relatando vômitos por ≥2.5 dias devem receber atenção máxima.

Palavras-chaves: 1. Bronquiolite; 2. Fatores de risco; 3. Desfecho; 4. UTI

II. OBJETIVOS

II.1. GERAL

Identificar fatores presentes na admissão hospitalar que são associados com pior evolução em crianças hospitalizadas com bronquiolite.

II.2. ESPECÍFICOS

II.1.1. Descrever as características clínicas de crianças hospitalizadas com bronquiolite.

II.1.2. Descrever as características radiológicas de crianças hospitalizadas com bronquiolite.

II.1.3. Descrever tratamento utilizado em crianças hospitalizadas com bronquiolite.

II.1.4. Estimar frequência de pacientes com bronquiolite que evoluem com desfecho desfavorável.

III. INTRODUÇÃO

A bronquiolite é a principal causa de internamento em lactentes (Nair et al., 2010). Estima-se que 1 a cada 3 crianças irão desenvolver bronquiolite no primeiro ano de vida e que destes, 2 a 3% necessitarão de hospitalização (NICE, 2015). Nos Estados Unidos, aproximadamente 120 mil admissões devido à bronquiolite ocorrem anualmente, representando 16,2% de todas as hospitalizações durante os primeiros 24 meses de vida e gerando um gasto anual de 1,73 bilhões de dólares em cuidados com a saúde (Hasegawa et al., 2013). No Brasil, embora não haja vigilância epidemiológica oficial, estudos em diversas regiões do país e os dados de hospitalização por bronquiolite indicam que a carga da doença entre nós assemelha-se aos relatos mundiais (SBP, 2011; Viera et al., 2001).

O curso variável da doença e a dificuldade para determinar o nível apropriado de suporte em crianças atendidas com bronquiolite resultam com freqüência em admissões hospitalares, ainda que o paciente não apresente sinais e sintomas de gravidade (Mansbach et al., 2012; Meissner et al., 2016). Por outro lado, os escores de gravidade disponíveis para esta patologia até o momento têm baixos poderes para predizer a progressão para complicações graves e quais pacientes podem necessitar de cuidados intensivos (Meissner et al., 2016; Ralston et al., 2014).

Diversos fatores demográficos, ambiententais e história médica pregressa têm sido associados com evolução grave da doença (AAP, 2014; Mansbach et al., 2012; DiFranza et al., 2012; Marlais et al., 2012). No entanto, a disponibilidade de evidências relacionando achados preditores específicos para desfechos clínicos de gravidade na avaliação da bronquiolite é limitada (Ralston et al., 2014). O grupo de crianças que cursa com deterioração clínica subsequente permanece mal definido na literatura (Hasegawa et al., 2015).

Neste contexto, é importante identificar fatores presentes na admissão hospitalar de crianças com bronquiolite que estejam associados com uma pior evolução.

IV. REVISÃO DA LITERATURA

IV. 1. Definição e diagnóstico de bronquiolite

Bronquiolite é uma infecção viral de vias aéreas inferiores caracterizada por inflamação aguda, edema, necrose das células epiteliais das pequenas vias aéreas e aumento da produção de muco (Ralston et al., 2014).

Uma definição frequentemente utilizada é a descrição de McConnochie (1983) que propôs que o diagnóstico de bronquiolite deveria seguir os seguintes critérios clínicos: 1) Paciente com idade menor que 24 meses; 2) Relato de primeiro episódio de dispneia; 3) Apresentar sinais de doença respiratória viral como coriza, otite média ou febre; 4) Presença de sibilos expiratórios de início agudo ao exame físico e 5) Podendo apresentar ou não sinais de desconforto respiratório, pneumonia ou atopia.

Várias outras definições têm sido propostas, sendo definido segundo a Academia Americana de Pediatria como um conjunto de sinais e sintomas respiratórios que ocorrem em crianças abaixo de 2 anos e que inclui um período prévio de pródromos de infecção de vias aéreas superiores seguido por desconforto respiratório e sibilância (Ralston et al., 2014). Outra definição também aplicada tem sido o primeiro episódio de desconforto respiratório em crianças abaixo de 12 meses de idade (Friedman et al., 2014; Meissner et al., 2016).

IV. 2. Evolução clínica da bronquiolite

A doença apresenta um curso clínico variável e dinâmico, podendo iniciar-se por uma fase de 2 a 4 dias de coriza, com ou sem febre baixa, congestão nasal e rinorréia,

progredindo nos dias seguintes para sintomas de acometimento do trato respiratório inferior incluindo tosse, taquipnéia, uso de musculatura acessória e aleteo nasal. Estertores crepitantes e sibilância são achados importantes na ausculta pulmonar (Ralston et al., 2014; Meissner et al., 2016).

Apnéia, especialmente em crianças abaixo de 6 semanas de vida pode estar presente, sem outros sinais clínicos (NICE, 2015). Sinais de desidratação podem ser observados em caso de dificuldade respiratória suficiente para interferir na ingestão oral (Friedman et al., 2014). Frequentemente pode-se observar redução nos níveis de saturação de oxigênio (Friedman et al., 2014). O estado respiratório é descrito como um importante determinante da gravidade da bronquiolite (Fernandes et al., 2015). Trata-se geralmente de uma doença de curso limitado com uma duração média dos sintomas de 8 a 15 dias, com resolução dos sintomas em 90% dos casos em até 21 dias (Thompson et al., 2013).

Resultados de estudos epidemiológicos para bronquiolite sugerem que a doença apresenta um alto grau de morbidade, apesar do baixo grau de mortalidade (Zorc et al., 2010; Hasegawa et al., 2013). Muitas crianças com diagnóstico de bronquiolite apresentam uma evolução sem intercorrências, no entanto uma em cada dez crianças necessita de internamento hospitalar colocando esta patologia como a principal causa de hospitalização em crianças menores (Shay et al., 1999). A variabilidade no curso clínico da bronquiolite associado à impossibilidade dos profissionais em prever no início do quadro quais pacientes evoluem com deterioração clínica, resulta muitas vezes em admissão hospitalar mesmo quando a criança não apresenta sinais de gravidade (Hasegawa et al., 2015; Meissner et al., 2016).

A evidência relacionando a presença de achados específicos na avaliação de bronquiolite para desfechos clínicos é limitada (Ralston et al., 2014). Diversos sistemas de

escores foram desenvolvidos para quantificar objetivamente o desconforto respiratório, embora nenhum tenha alcançado aceitação generalizada e poucos tenham demonstrado alguma validade preditiva, provavelmente devido à substancial variabilidade temporal nos achados físicos em lactentes com bronquiolite (Ralston et al., 2014; Fernandes et al., 2015; Justicia-Grande et al., 2016).

Um dos escores frequentemente utilizado é o Respiratory Distress Assessment Instrument (RDAI) descrito primeiramente por Lowell et al. em um ensaio clínico avaliando uso de epinefrina em crianças com bronquiolite. Este instrumento consiste em uma escala de 17 pontos baseada na presença de sibilos e retrações torácicas (Lowell et al., 1987).

IV. 3. Aspectos microbiológicos e fisiopatologia da bronquiolite

Trata-se de uma doença reconhecidamente de causa viral. (Meissner et al., 2016). A maior disponibilidade de técnicas de detecção molecular tornou possível identificar diversos grupos de vírus implicados na patogênese da doença (Henrikson et al., 2004). Embora os relatos de hospitalizações atribuíveis a cada tipo de vírus sejam variados quanto à área geográfica e o ano do estudo, o vírus sincicial respiratório (VSR) é o mais importante agente etiológico, respondendo por 50 – 80% dos casos (Vieira et al., 2001; Stempel et al., 2009; Mação et al., 2011; Bueno et al., 2009).

Outros agentes relevantes são: Rinovírus, metapneumovírus humano, parainfluenza, influenza, adenovírus, coronavírus e bocavírus humano, sendo a proporção relativa de cada agente específico variável conforme o ano e a estação. (Stempel et al., 2009; Mação et al., 2011). A co-infecção por mais de um desses agentes não é rara e pode ocorrer em cerca de um terço das bronquiolites (Mansbach et al.,

2008).

Zorc et al. (2010) descreveram o processo histopatológico da bronquiolite. A infecção viral ocorre através das vias aéreas superiores e progride para o trato respiratório baixo em poucos dias, resultando em uma inflamação do epitélio bronquiolar com infiltração de mononucleares e edema das camadas submucosa e adventícia. A deposição de células descamativas, necrose epitelial e fibrina nas vias aéreas causa obstrução parcial ou total do fluxo aéreo. O grau de obstrução pode variar, resultando em rápida mudança dos sinais clínicos o que prejudica a acurácia na avaliação da gravidade da doença. Um mecanismo de válvula pode resultar em aprisionamento na parte distal das áreas obstruídas, com subsequente absorção, ocorrendo atelectasias e alteração entre a perfusão e ventilação pulmonar que pode resultar em hipoxemia. A falta de canais colaterais na árvore respiratória de crianças jovens e a administração de altas concentrações de oxigênio propiciam a formação de atelectasias. A constricção da musculatura lisa tem um pequeno papel neste processo patológico, o que pode explicar o benefício limitado dos broncodilatadores observado nos estudos clínicos.

IV. 4. Uso de exames complementares na bronquiolite

O diagnóstico é baseado somente na história clínica e nos achados do exame físico, sendo contra-indicados exames complementares para diagnóstico em pacientes com apresentação clássica de bronquiolite (Friedman et al., 2014; Ralston et al., 2014; Meissner et al., 2016). Exames complementares só estão indicados em situações específicas. A pesquisa de vírus respiratório não altera o manejo individual e a solicitação de radiografia de tórax está indicada somente para os casos em que haja uma

apresentação clínica grave, pacientes que necessitem de hospitalização (Schuh et al., 2007; Ralston et al., 2014).

A radiografia de pacientes com bronquiolite frequentemente apresenta somente achados inespecíficos que não têm impacto na decisão terapêutica como sinais de hiperinsuflação, infiltrado peribronquiolar e atelectasia**s** (Ecochard-Dugelay et al., 2014). Alguns achados podem ser interpretados equivocadamente como consolidação, o que poderia aumentar o uso inapropriado de antibióticos (Swingler et al., 1998). Um estudo de coorte prospectivo envolvendo 265 crianças com apresentação típica de bronquiolite observou que aqueles pacientes submetidos ao exame radiológico foram mais propensos a receber antibioticoterapia, sem diferenças nos desfechos mensurados (Schuh et al., 2007). A solicitação de radiografia deve ser reservada para casos de desconforto respiratório grave com necessidade de admissão em UTI ou quando outros sinais de complicações em vias aéreas como pneumotórax estiverem presentes (Ralston et al., 2014; NICE, 2015).

A pesquisa de vírus respiratórios através de swab de nasofaringe geralmente não auxilia no diagnóstico e não altera o tratamento, não estando recomendada a solicitação de rotina (Ralston et al., 2014).

Apesar da saturação de oxigênio ser um fraco preditor de desconforto respiratório, sua medida é constantemente associada à decisão sobre a necessidade de hospitalização na bronquiolite (Corneli et al., 2012). O uso da monitorização contínua de oximetria de pulso em crianças hospitalizadas com bronquiolite é apropriado para pacientes com fatores de risco associados, enquanto que a monitorização intermitente é mais apropriada para pacientes de baixo risco, que necessitem de oxigênio suplementar ou demonstrem aumento do trabalho respiratório (Friedman et al., 2014).

IV. 5. Fatores de risco

A maioria das crianças que são hospitalizadas com bronquiolite é nascida a termo sem nenhuma comorbidade ou fator de risco predisponente identificado, porém o risco de admissão hospitalar é maior em determinados grupos de riscos conhecidos (Hall et al., 2009; Murray et al., 2014).

Trata-se de uma doença muito grave em lactentes pequenos, prematuros e em crianças com doenças subjacentes como displasia broncopulmonar, imunodeficiências, cardiopatia congênita e Síndrome de Down (Garcia et al., 2010; Sommer et al., 2011; Alvarez et al., 2013).

Alguns estudos tem tentado explorar os fatores preditores de admissão hospitalar em crianças com bronquiolite (Walsh et al., 2004; Mansbach et al., 2008; Marlais et al., 2011, Aziz et al., 2015; Green et al., 2015), porém poucos avaliaram os fatores preditivos de deterioração clínica nos pacientes hospitalizados e dentre os estudos que o fizeram, uma lista limitada de fatores foi avaliada ou somente grupos específicos de pacientes foram envolvidos (Damore et al., 2008; Mansbach et al., 2012; Hasegawa et al., 2015; McCallum et al., 2016).

IV. 6. Tratamento

Ainda em 1965, os autores Wright & Beem publicaram uma orientação sobre bronquiolite, alertando que se tratava de uma doença autolimitada e de bom prognóstico, devendo o tratamento ser baseado no princípio de *primum non nocere*, evitando-se medicamentos desnecessários ou procedimentos fúteis. Os autores

recomendavam o repouso como medida terapêutica. Há mais de 50 anos depois, nos dias atuais, observa-se que poucas mudanças ocorreram na condução da bronquiolite. A terapêutica da doença permanece sem medidas curativas e consiste ainda em manter somente medidas de suporte sintomáticas (Ralston et al., 2014; Friedman et al., 2014; NICE, 2015).

Pacientes com bronquiolite cursam com quadro de sibilância clinicamente semelhante ao observado na asma. No entanto, a fisiopatologia da bronquiolite é mais de obstrução do que de constricção bronquiolar (Zorc et al., 2010). Os estudos clínicos que avaliam o uso de broncodilatadores na bronquiolite têm demonstrado pouca melhora nos escores de gravidade, não aumentando SO2, sem redução nas taxas de admissões ou da duração de internamento hospitalar (Gadomski et al., 2014). Quando o diagnóstico de bronquiolite é bem definido, o uso de broncodilatadores mesmo como teste terapêutico não se encontra atualmente recomendado (Ralston et al., 2014).

A adrenalina é um agente adrenérgico com atividade agonista sobre os receptores α e β e é frequentemente utilizada para o tratamento de doenças respiratórias através de soluções de nebulização (Ralston et al., 2014). Uma revisão sistemática concluiu que o uso da adrenalina em pacientes com bronquiolite reduziu as hospitalizações em comparação com placebo quando utilizados na unidade de emergência, porém sem efeitos no tempo de internamento hospitalar (Hartling et al., 2011). Outros estudos avaliando o uso de adrenalina em pacientes com bronquiolite não demonstraram evidências da sua utilidade em pacientes com bronquiolite (Walsh et al., 2008; Skjerven et al., 2013). A evidência atual é insuficiente para recomendar o uso de rotina da adrenalina para pacientes com bronquiolite, mesmo nas unidades de emergência (Friedman et al., 2014; Ralston et al., 2014).

Corticosteróides como a dexametasona, prednisona e prednisona ou

glicocorticóides inalatórios não estão associados com melhoria clínica significativa na doença, assim como não apresenta redução dos escores de gravidade, nas taxas de hospitalização ou da duração de internamento hospitalar (Fernandes et al., 2013; Cornelli et al., 2007). Embora haja uma boa evidência de benefício com o uso de corticóides em outras doenças respiratórias como asma e crupe, na bronquiolite este uso não está recomendado (Ralston et al., 2014).

Solução salina hipertônica é uma solução salina que possui uma pressão osmótica maior que a solução salina isotônica (NaCl 0.9%) (NICE, 2015). O uso de nebulização com solução hipertônica (SH) é uma terapia cada vez mais estudada para o tratamento da bronquiolite (Ralston et al., 2014). Algumas evidências apontam que a SH 3% é um tratamento seguro e efetivo para melhorar sintomas de bronquiolite leve a moderada após 24 horas de uso, além de reduzir o tempo de internamento hospitalar para aqueles pacientes com mais de 3 dias de hospitalização (Ralston et al., 2014). Por outro lado, outras publicações não observaram evidências suficientes para considerar o uso da SH no manejo da bronquiolite (Cornfield et al., 2014; NICE, 2015).

Não se deve administrar antibióticos em pacientes com diagnóstico de bronquiolite, a menos que haja uma infecção bacteriana concomitante ou forte suspeição de co-infecção (Ralston et al., 2014).

Em crianças com bronquiolite não existem dados suficientes para sugerir que o uso de oxigênio com SO2 acima de 90% resulta em melhora clínica com diferença significativa na função fisiológica, nos sintomas apresentados ou modificação de desfechos clínicos (Ralston et al., 2014). O uso de oxigênio suplementar só está recomendado quando houver persistência de uma SO2 abaixo de 90% (Ralston et al. 2014, Friedman et al., 2014).

Crianças com bronquiolite frequentemente cursam com dificuldades de

alimentação e este é um problema que pode ser manejado associando o fracionamento com aumento do número de refeições (NICE, 2015). O grau de desconforto respiratório atribuído à bronquiolite guia a indicação de reposição de fluidos (Ralston et al., 2014). O aumento do trabalho respiratório pode inabilitar temporariamente a criança para manter uma alimentação por via oral. Nestes momentos, a oferta de fluidos pode ser realizada tanto através de sondas gástricas quanto por fluidos intravenosos (Oakley et al., 2013; NICE, 2015; Ralston et al., 2014).

Alguns estudos têm trabalhado com a hipótese de que a oferta de oxigênio de alto fluxo através de cânula nasal poderia melhorar os escores respiratórios por manter uma pressão positiva de baixo grau constante nas vias aéreas (Beggs, 2014; Mikalsen et al., 2016; Turnham et al., 2017). A evidência para o seu uso é baseada em estudos observacionais que encontraram escores respiratórios melhorados e taxas reduzidas de intubação traqueal (Ralston et al., 2014; Mikalsen 2016). A despeito das descrições promissoras destes estudos, a ausência de ensaios clínicos demonstrando a eficácia desta terapia restringe a recomendação do seu uso rotineiro (Ralston et al, 2014). Recentemente foram publicados os resultados de um ensaio clínico randomizado avaliando crianças com bronquiolite, conduzido na Austrália por Kepreotes et al. (2017) onde não foi observado redução do uso de oxigenoterapia no grupo que utilizou terapia com cânula nasal de alto fluxo, quando comparado com o grupo controle.

V. METODOLOGIA DO ESTUDO

V.1. CASUÍSTICA

V.1.1. População de referência

Pacientes com idade inferior a 2 anos admitidos com diagnóstico de bronquiolite na enfermaria pediátrica do Hospital da Criança localizado nas Obras Sociais Irmã Dulce em Salvador-Bahia, no período de 21 de maio de 2015 a 21 de julho de 2016.

V.1.2. Características da população de estudo

Pacientes lactentes (idade inferior a 24 meses) admitidos com diagnóstico de bronquiolite dado pelo médico plantonista na enfermaria pediátrica do Hospital da Criança localizado nas Obras Sociais Irmã Dulce em Salvador-Bahia.

V.1.3. Critérios de inclusão

Idade abaixo de 2 anos, diagnóstico de bronquiolite na admissão e assinatura do Termo de Consentimento Livre e Esclarecido (ANEXO 1).

V.1.4. Critérios de exclusão

Episódio prévio de dispnéia ou sibilância.

V.1.5. Período de inclusão

O período de inclusão dos pacientes no estudo foi de 21 de maio de 2015 a 21 de julho de 2016.

V.1.6. Técnica de amostragem

Revisão diária dos livros de registro da enfermagem da enfermaria de pediatria, os quais contêm todos os internamentos com os respectivos diagnósticos, leito e número de prontuário do arquivo médico. Identificação de pacientes com diagnóstico de bronquiolite. Revisão dos prontuários com coleta de dados realizada por meio de ficha padronizada e entrevista com responsável pela criança utilizando questionários pré-definidos (ANEXO 2). A partir da revisão, a amostra foi constituída de forma não aleatória ao serem selecionados os casos que apresentavam os critérios de inclusão e não apresentavam os critérios de exclusão.

V.2. MATERIAL E MÉTODO

V.2.1. Desenho do estudo

Estudo de coorte prospectiva.

V.2.2. Classificação das variáveis

2.2.1. Variáveis-dependentes para o objetivo geral e objetivo específico 4: 1)

Necessidade de internamento em Unidade de Terapia Intensiva; 2) Duração de internamento hospitalar ≥ 5 dias.

2.2.2. Para os objetivos específicos 1, 2 e 3 foi feita análise exploratória de dados, não havendo uma variável-dependente definidora de um evento resposta.

2.2.3. Principais variáveis de predição para o objetivo geral: Idade, sexo, raça, peso, altura, temperatura, estado geral e sensorial, escore RDAI, presença de alterações na ausculta pulmonar, tempo de início de sinais e sintomas, motivo que levou a procura de cuidados médicos, duração da doença, presença de dermatite atópica, uso de profilaxia com Palivizumab, uso prévio de ventilação mecânica, comorbidades (Síndrome de Down, cardiopatia congênita, doença pulmonar crônica, imunodeficiência), prematuridade, tipo de parto, fumo materno ou história de asma durante a gravidez, estação de nascimento, uso de aleitamento materno exclusivo ou misto, história materna de atopia (asma, rinite, bronquite, eczema), fumantes no domicílio, presença de mofo, quantidade de cômodos na casa, número de habitantes, número de crianças na residência e renda familiar.

V.2.3. Variáveis de confusão

A presença de broncodisplasia ou outras doenças respiratórias de base podem interferir no diagnóstico.

V.2.4. Coleta de dados

Os dados coletados a partir da revisão dos prontuários selecionados e de entrevista com os responsáveis foram sistematizados em um formulário padronizado (ANEXO 2), que inclui as seguintes variáveis independentes:

a) Dados demográficos: idade, sexo e raça.

b) Dados antropométricos: peso e altura.

c) Dados clínicos na admissão: estado geral, freqüência cardíaca, freqüência respiratória, temperatura, estado geral e sensorial, presença de tiragens torácicas, ausculta respiratória e cardíaca, hepatomegalia, esplenomegalia, distensão abdominal e presença de cianose.

d) Dados sobre história da doença atual: presença e tempo de início de sinais e sintomas, motivo que levou a procura de cuidados médicos, duração da doença, tratamento utilizado em domicílio e tratamento na unidade de emergência.

e) Dados sobre antecedentes patológicos: presença de comorbidades - Síndrome de Down, cardiopatia congênita, doença pulmonar crônica, imunodeficiência. Presença de dermatite atópica, uso de profilaxia com Palivizumab e uso prévio de ventilação mecânica.

f) Dados sobre antecedentes obstétricos e neonatais: prematuridade, tipo de parto, fumo materno ou história de asma durante a gravidez, estação de nascimento, uso de aleitamento materno exclusivo ou misto, história materna de atopia (asma, rinite, bronquite, eczema).

g) Fatores ambientais, sociais e econômicos: fumantes no domicílio, presença de mofo, tipo de moradia, presença de água encanada, presença de esgotamento sanitário, presença de energia elétrica, regularidade de coleta de lixo, modo de preparo da comida (tipo de fogão), quantidade de cômodos na casa, número de habitantes, número de crianças na residência, nível de instrução materna e paterna, trabalho principal da mãe e do pai, bens e renda familiar.

h) Tratamento durante hospitalização: uso de broncodilatadores, corticóides, solução salina hipertônica, adrenalina inalatória, antibióticos, uso de oxigênio, hidratação

parenteral e ventilação mecânica.

i) Dados clínicos sobre o curso da hospitalização: duração do internamento, transferência para UTI, data da alta hospitalar e óbito.

As radiografias de tórax foram solicitadas a critério dos médicos assistentes. Pacientes que tinham exame radiológico no momento da admissão tiveram os exames avaliados por radiologista pediátrico blindado para os dados clínicos usando formulário padronizado (ANEXO 3) (Cherian et al., 2005).

V.2.5. Operacionalização das variáveis

Os dados coletados e sistematizados nos formulários foram organizados em um banco de dados construído no programa de computador SPSS para "Windows" versão 17.0 para a realização das análises epidemiológicas e estatísticas. As variáveis contínuas foram transformadas em variáveis dicotômicas de acordo com os parâmetros que seguem:

A avaliação nutricional dos pacientes foi realizada utilizando-se o programa de computador Anthro, versão 3.22, e AnthroPlus de acordo com as indicações da Organização Mundial de Saúde (WHO, 2008). Desnutrição e desnutrição grave foram definidas como o índice Z-escore menores que -2 e -3 para o parâmetro peso-para-idade respectivamente.

Definição dos valores de referência por faixa etária para os dados de exame físico: febre, como temperatura axilar > 37,5°C (El-Radhi et al., 2005), taquicardia como frequência cardíaca > 200 bpm e taquipnéia como frequência respiratória > 70 ipm (Ralston et al, 2014; NICE, 2015). Desconforto respiratório na admissão foi quantificado de acordo com o Respiratory Distress Assessment Instrument (RDAI), uma escala categórica de 17 pontos baseada na presença de sibilância e retrações,

estabelecida para avaliação de crianças abaixo de 24 meses com bronquiolite (Lowell et al, 1987). Um RDAI escore ≤5 foi considerado como forma leve a moderada da doença, enquanto uma classificação RDAI escore ≥6 foi considerado como bronquiolite grave.

As estações do ano foram definidas de acordo com as indicações do Instituto Nacional de Meteorologia seguindo os critérios do Observatório Nacional (Instituto Nacional de Meteorologia, 2015): Verão (22 de dezembro de 2015 a 19 de março de 2016), Primavera (23 de setembro 2015 a 21 de dezembro de 2015), Outono (20 de março de 2015 a 20 de junho de 2015 e 20 de março de 2016 a 19 de junho de 2016) e Inverno (21 de junho de 2015 a 22 de setembro de 2015 e de 20 de junho de 2016 a 21 de setembro de 2016).

As radiografias de tórax obtidas na admissão foram encaminhadas e analisadas por radiologista pediátrico blindado para os dados clínicos. Foi utilizado formulário padronizado (Cherian et al., 2005). Os exames foram classificados como “normal” ou “anormal”. Anormalidades incluíram: consolidação, infiltrado intersticial ou alveolar, hiperinsuflação, espessamento peribronquiolar, atelectasia, derrame pleural, pneumatocele e pneumotórax.

V.3. ANÁLISE ESTATÍSTICA

V.3.1. Análise exploratória dos dados

O procedimento estatístico utilizado para descrição da amostra foi a Estatística Descritiva, com as técnicas de cálculos de frequências, de medidas de tendência central e dispersão.

V.3.2. Estatística Inferencial

As variáveis categóricas foram comparadas utilizando-se os testes qui-quadrado ou teste exato de Fisher, quando adequados. As variáveis contínuas foram avaliadas, usando o teste de Mann-Whiteney U, de acordo com a distribuição das variáveis. Análise de regressão logística foi utilizada para avaliar a relação independente entre necessidade de internamento em UTI e fatores de risco que foram significativamente diferenciados na análise bivariada. Também foi utilizado análise de regressão logística para avaliar a relação independente entre duração de internamento hospitalar (DIH) ≥5 dias e fatores de risco que foram significativamente diferenciados na análise bivariada. A análise multivariada foi realizada em um modelo ajustado para idade. Os testes estatísticos foram bicaudais, com nível de significância de 5%.

Uma curva ROC (receiver operating characteristic) foi utilizada para avaliar a predição da duração de vômitos para identificar crianças mais propensas a serem transferidas para UTI.

V.3.3. Cálculo do tamanho amostral

Análise exploratória dos dados.

V.3.4. Possibilidade de perda de seguimento

Devido à rotina de trabalho estabelecida, com visita diária à enfermaria e acompanhamento de todas as crianças internadas dentro da faixa etária estudada, a possibilidade de perda de seguimento foi mínima.

V.3.5. Controle para variáveis de confusão

Análise estratificada, considerando doença de base, associada aos critérios de exclusão.

V.4. QUESTÕES ÉTICAS

O projeto foi aprovado pelo comitê de ética das Obras Sociais Irmã Dulce. Parecer/Resolução de número 1.068.915/2015 (ANEXO 4). Foi aplicado o Termo de Consentimento Livre e Esclarecido segundo a Resolução CONEP n° 196 de 1996 (ANEXO 1).

VI. ARTIGO

"Vomiting for more than 2.5 days is independently associated with poor evolution in bronchiolitis". ***Pediatrics*** [submetido, *vide* Normas de Publicação no ANEXO 5 e comprovante de envio nos ANEXOS 6 e 7], Fator de Impacto (2016) 5,800.

Vomiting for More than 2.5 Days Is Independently Associated With Poor Evolution in Bronchiolitis

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Short title: Longer vomiting and poor evolution in bronchiolitis

Funding Source: There was no specific funding for this research. Cristiana M. Nascimento-Carvalho is a senior investigator at the Brazilian Council for Scientific and Technological Development (CNPq), Brazil.

Financial Disclosure: The authors have no financial relationships relevant to this article to disclose.

Conflict of Interest: The authors have no conflicts of interest relevant to this article to disclose.

Abbreviations:

95% CI - 95% confidence interval

CXR - Chest radiographs

ICU - Intensive Care Unit

IQR - Interquartile range

LOS - Length of hospital stay

OR – Odds ratio

RDAI - Respiratory Distress Assessment Instrument

ROC - Receiver operating characteristic

Table of Contents Summary: This article identifies a simple clinical complaint that predicts worse evolution in young children with bronchiolitis included in a prospective cohort.

What´s Known on This Subject: The variable course of bronchiolitis results in an uncertainty to predict which patients will progress to severe complications. Currently, the group of children with subsequent clinical deterioration after hospitalization is poorly defined in published literature.

What This Study Adds: Prolonged duration of vomiting is an independent predictor of ICU admission in children hospitalized with bronchiolitis. Vomiting for ≥2.5 days may be used in clinical practice as an alert sign in children hospitalized with bronchiolitis.

Contributors' Statement:

Dr Lorenzo collected the data, drafted the initial manuscript, carried out the analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Dr Araújo-Neto read the chest radiographs, took part in the results interpretation, and approved the final manuscript as submitted.

Dr Nascimento-Carvalho conceptualized and designed the study, carried out the analyses, reviewed and revised the manuscript and approved the final manuscript as submitted.

Abstract

Objective: To identify factors present upon admission that are associated with worsening evolution among children hospitalized with bronchiolitis**.**
Methods: This prospective cohort was conducted at the pediatric ward of the Children's Hospital, Salvador, Brazil, from May 2015 to July 2016. Inclusion criteria comprised age <2 years, admission to hospital due to bronchiolitis, and written informed consent. Clinical data, physical findings upon admission and outcome were registered. Multivariable logistic regression analysis in a model adjusted for age was used to assess association between Intensive Care Unit (ICU) treatment/length of hospital stay (LOS)≥5 days (outcome variables) and factors detected upon admission (predictor variables).
Results: The study group comprised 172 patients, out of which 5 (2.9%;95%CI:1.1%-6.3%) were transferred to ICU and 69 (40.1%;95%CI:33.0%-47.6%) whose LOS≥5 days. Overall, the median age was 5.2 months (IQR:3.6-8.2) and the median duration of vomiting was 1 day (IQR:1-3); prematurity <30 weeks (3.5%), <37 weeks (14.5%) were reported and severe malnutrition (4.7%) and crackles (27.9%) were found. Severe malnutrition (OR 21.53;95%CI 1.43–323.66), prematurity <30 weeks (OR 13.85;95%CI 1.23–155.89) and duration of vomiting (OR 1.92;95%CI1.16–3.17) were independently associated with ICU transfer. Prematurity <37 weeks (OR 3.89;95%CI 1.55–9.79) and crackles (OR 3.11;95%CI 1.45–6.70) were independently associated with LOS ≥5 days. The area under the ROC curve for duration of vomiting to predict transfer to the ICU was 0.92(95%CI 0.81–1.04) the cutoff for best performance being 2.5 days (sensitivity 100%; specificity 79%).
Conclusion: Children admitted with bronchiolitis reporting vomiting ≥2.5 days should receive maximal attention.

Introduction

Bronchiolitis is a leading cause of acute illness and hospitalization among young children.[1] Approximately 120 000 bronchiolitis admissions occur annually, accounting for 16.2% of all hospitalizations during the first 24 months of life, and equating to $1.73 billion in total inpatient costs, in the United States.[2]

The variable course of disease and the uncertainty of determining the appropriate level of supportive care for children with bronchiolitis often result in hospital admission even when symptoms are not severe.[3,4] In contrast, current scoring systems have limited effectiveness in predicting whether illness will progress to severe complications that would necessitate intensive care.[4,5] Several demographic, environmental, and medical history factors have been associated with severe bronchiolitis.[6] However, the available evidence relating the presence of specific findings in the assessment of bronchiolitis to predict clinical outcomes is scarce.[5] The group of children with subsequent clinical deterioration after hospitalization remains poorly defined in published literature.[7] In this context, we aimed to identify factors present upon admission that are associated with a worsening evolution among children hospitalized with bronchiolitis.

Material and methods

This was a prospective cohort study. All patients younger than 24 months admitted at the pediatric ward of the Children's Hospital in the Charitable Works Foundation of Sister Dulce, in Salvador, Northeastern Brazil, from May 21, 2015 to July 21, 2016 were evaluated after admission. Bronchiolitis was diagnosed by the attending pediatrician and patients were enrolled after obtaining informed consent from the legal guardian of each child. Therefore, the inclusion criteria comprised age under 24 months, admission to hospital due to bronchiolitis, and written informed consent.

Children with any previous episode(s) of difficulty breathing or wheezing were excluded, in order to ensure that clinical findings were not abnormal due to other respiratory diseases.

Clinical data, findings on physical examination performed upon admission, treatment, and outcome were recorded in standardized forms. Each child's caregiver was interviewed by using structured questionnaires. Collected data included age, gender, race, co-morbidities, prematurity, environmental factors, obstetrical history, breastfeeding, tobacco smoke exposure, mother's history of atopy, and socioeconomic aspects. Report of difficulty breathing, cough, fever, wheezing, and vomiting, along with the respective duration during this illness, was registered. Treatment and outcome were collected from their medical records during their evolution in the hospital.

Fever was defined as axillary temperature ≥37.4°C.[8] Tachypnea was defined as respiratory rate ≥70 breaths/min and tachycardia as cardiac rate ≥200 beats/min.[5] Respiratory distress at admission was quantified by using the Respiratory Distress Assessment Instrument (RDAI), a 17 point categorical score.[9] RDAI score ≤5 classified the patient as mild or moderate bronchiolitis whereas RDAI score ≥6 classified the patient as severe bronchiolitis. The seasons were defined as: Fall (from March 20, 2015 to June 20, 2015, and from March 20, 2016 to June 19, 2016), Winter (from June 21, 2015 to September 22, 2015, and from June 20, 2016 to September 21, 2016), Spring (from September 23, 2015 to December 21, 2015), and Summer (from December 22, 2015 to March 19, 2016). [10]

The software Anthro, version 3.22 released by the World Health Organization, was used to perform the nutritional status evaluation in accordance with the National Centre for Health Statistics, United States standard. Z score under -2.00 or -3.00 for the weight-for-age index defined malnutrition and severe malnutrition, respectively.

Overweight and obesity were defined as Z score higher than 2 and higher than 3 for the weight-for-age, respectively.[11]

Chest radiographs (CXR) were taken at admission at the discretion of the attending pediatrician and read by a pediatric radiologist blinded to clinical data using a standardized form.[12] CXR was read as either normal or abnormal. Abnormalities included consolidation, interstitial-alveolar or interstitial infiltrate, hyperinflation, peribronchial thickening, atelectasis, pleural effusion, pneumatocele, and pneumothorax.

Analyses were performed using SPSS version 17.0. The primary outcome was Intensive Care Unit (ICU) treatment and the secondary outcome was length of hospital stay (LOS) ≥5 days. Descriptive statistics were used to summarize demographic and all clinical characteristics. The 95% confidence interval (95% CI) of the outcome variables were calculated. Categorical variables were expressed as absolute and relative frequency. Continuous variables were presented as median, along with interquartile range (IQR). Categorical variables were compared using chi-square or Fischer's exact test as appropriate; continuous variables were assessed by using Mann-Whitney *U* test. Multi-variable logistic regression analysis by enter method was used to assess independent association between ICU treatment or LOS ≥5 days and factors which significantly differed in the bivariate analysis. The multi-variable analysis was performed in a model adjusted for age. The statistical tests were two-tailed, with a significance level of 0.05. Covariates were chosen based on clinical plausibility and *a priori* knowledge. [4,5,13-16] The receiver operating characteristic (ROC) curve was used to evaluate the prediction of the duration of vomiting to identify children more prone to being transferred to ICU.

The study was approved by the Ethics Committee from the Charitable Works Foundation of Sister Dulce (approval n° - 1.068.915/2015).

Results

Of 225 children evaluated, 1 (0.4%) was excluded due to refusal to give informed consent and 52 (23.1%) due to report of previous episode of wheezing / difficulty breathing. Therefore, the study group comprised 172 patients. Five (2.9%; 95% CI: 1.1%-6.3%) were transferred to ICU and 69 (40.1%; 95% CI: 33.0%-47.6%) patients had a LOS equal to or longer than 5 days. One (0.6%) child died.

The baseline characteristics of the study group are described in Table 1. The median age was 5.2 months (IQR: 3.6 – 8.2). The most frequent complaints were difficulty breathing (95.3%), cough (93.6%), and fever (56.7%). Others complaints included wheezing (40.9%), and vomiting (20.5%). The most common findings were chest retraction (48.8%), ronchi (44.8%), expiratory wheezing (40.4%), and crackles (27.9%). According to RDAI score classification, 18.8% of the patients were severe upon admission. Patients living conditions were registered: all homes were made of bricks and had electricity supply; running water supply (98.3%), sewage systems (89.5%), and regular trash collection (85.5%). Gas stoves were used for food preparation in almost all houses (98.8%).

One hundred and forty-seven patients had CXR taken at admission, out of which 17 (9.9%) were excluded due to their poor-quality technique. Among 130 CXR read by the pediatric radiologist, 108 (83.1%) were normal, 12 (9.2%) found pneumonia and other findings were registered for 10 (7.7%): hyperinflation (n = 9); peribronchial thickening (n = 2), and atelectasis (n = 1). Among the 12 CXR diagnosed with pneumonia, consolidation (n = 8), interstitial-alveolar (n = 3), and interstitial (n = 1) infiltrates were described.

Treatment comprised inhaled hypertonic saline (77.3%), inhaled beta 2 agonists (69.8%), corticosteroids (47.1%), intravenous hydration (44.2%), antibiotics (30.2%), oxygen (12.8%), mechanical ventilator (1.2%), and inhaled adrenaline (0.6%). Patients with crackles received antibiotics more frequently than those without (43.8% *vs.* 25.0%, p=0.02).

Table 2 shows the comparison of baseline characteristics between patients who were or were not transferred to ICU and between patients who did or did not stay ≥5 days in the hospital. In this bivariate analysis, severe malnutrition and gestational age <30 weeks were associated with ICU transfer, as well as patients with longer periods of vomiting. On the other hand, severe malnutrition, gestational age < 37 weeks, and crackles were directly associated with LOS ≥5 days, whereas currently non-exclusive breastfeeding presented an inverse association.

In the multivariable logistic regression model to predict intensive care admission (Table 3), the significant predictors were severe malnutrition (OR, 21.53; 95% CI 1.43 – 323.66; P<0.03), prematurity under 30 weeks of gestational age (OR, 13.85; 95% CI 1.23 – 155.89; P<0.03) and duration of vomiting (OR, 1.92; 95%CI 1.16 – 3.17; P<0.01). In the multivariable logistic regression model to predict LOS ≥5 days (Table 4), the significant predictors were prematurity under 37 weeks of gestational age (OR, 3.89; 95% CI 1.55 – 9.79; P<0.004) and crackles (OR, 3.11; 95%CI 1.45 – 6.70; P<0.004).

Out of 35 (20.5%) children whose caregiver reported vomiting, 2 were transferred to ICU. The area under the ROC curve for duration of vomiting to predict transfer to ICU was 0.92 (95%CI 0.81 – 1.04) and the cutoff for best performance was 2.5 days (sensitivity 100%; specificity 79%) (Figure 1).

Discussion

In this bronchiolitis cohort study, transfer to ICU was uncommon (2.9%;95%CI:1.1%-6.3%) whereas 40.1% of the patients were hospitalized for at least 5 days. Host factors such as severe malnutrition and prematurity were independently associated with ICU transfer (both factors) or LOS ≥5 days (only prematurity <37 weeks). Notably, duration of vomiting ≥2.5 days was a good predictor (sensitivity 100%; specificity 79%) for ICU transfer. Additionally, crackles upon admission predicted LOS ≥5 days.

The report of vomiting has been previously assessed as a risk factor for worsening evolution in a Spanish study. Therein, the authors included 53 healthy children and 8 children with severe neonatal malformations, all of them admitted to hospital due to bronchiolitis. The authors reported OR 4.22 (95% CI:1.21-14.70) for those with report of vomiting (65.51% *vs.* 21.87%) and deterioration (respiratory rate >80 breaths/minute, audible wheezing without stethoscope, persistent cyanosis with FiO2 >0.4, PaO2 <50, PaCO2 >70, mixed or respiratory acidosis) at any time during hospital stay.[17] Herein, vomiting was reported for 20.5% of the included patients. Therefore, it was not as frequent as in the Spanish cohort study. This difference may explain why we did not identify vomiting as a risk factor for ICU transfer. However, to the best of our knowledge, the duration of vomiting was identified as an independent factor associated with ICU transfer for the first time in this study (Table 3). These findings are probably due to dehydration which was found to be a predictor of the need for admission in other studies conducted among children with bronchiolitis.[18-19] It is possible to assume that the longer the vomiting duration, the higher the probability of dehydration. Therefore, vomiting for ≥2.5 days may be used in clinical practice as an alert sign to provide maximal attention among children hospitalized with bronchiolitis.

This prospective cohort also identifies some host factors, such as prematurity and severe malnutrition, as independently associated factors with ICU transfer or LOS ≥5 days (only prematurity in the latter outcome). Notably, the great majority of our patients were born at term and well-nourished. Our data are in line with the results of previous studies that identified preterm infants as a high-risk group for ICU admission due to lower respiratory tract infection.[14,20-22] In the UK, Murray and cols conducted a population-based birth cohort study and reported that only 15% of the children hospitalized due to bronchiolitis were born preterm; additionally preterm infants were found to have higher relative risk for hospital admission in comparison with infants born at term. In the US, Garcia and cols also found that prematurity and low weight were associated with severe bronchiolitis in a retrospective cohort among children hospitalized for bronchiolitis. The OR of an ICU admission was inversely exponentially related to the weight of the patients; given that the other risk factors were constant, for every increase (decrease) in weight by 1 kg, the OR of an ICU admission decreases (increases) by 9.2% (10.2%).[14]

In our study, crackles detected upon admission were independently associated with LOS ≥5 days. Curiously, we found higher frequency of antibiotics administration among patients with crackles in comparison to patients without them. In spite of the different bronchiolitis guidelines, which suggest that antibacterial agents should not be routinely used,[5,23,24] many clinicians persistently prescribe antibiotics for children with bronchiolitis. For instance, in Naples, Italy, 50% of the cases admitted because of bronchiolitis received antibiotics.[25] It is possible to infer that children with crackles stayed longer in the hospital because they were receiving antibiotics.

Our study has some limitations. Firstly, our sample size was not sufficient to assess risk factor for death as our case fatality rate was very low (0.6%). Hopefully, this

finding is in agreement with other investigations which report death as an uncommon outcome among children with bronchiolitis. Secondly, we did not investigate the etiology of our cases. Therefore, our results can be generalized to patients under 24 months of age admitted with bronchiolitis, and should not be used among patients with an established specific etiology.

Vomiting for ≥2.5 days is an independent predictor of ICU admission in children hospitalized with bronchiolitis. Therefore, these children should be closely monitored, and prolonged duration of vomiting may be used in clinical practice as an alert sign in children hospitalized with bronchiolitis. Further studies are necessary to consolidate our findings and determine intervention points that can reduce the severity of bronchiolitis in infants.

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Figure 1. ROC curve for duration of vomiting to predict transfer to ICU.

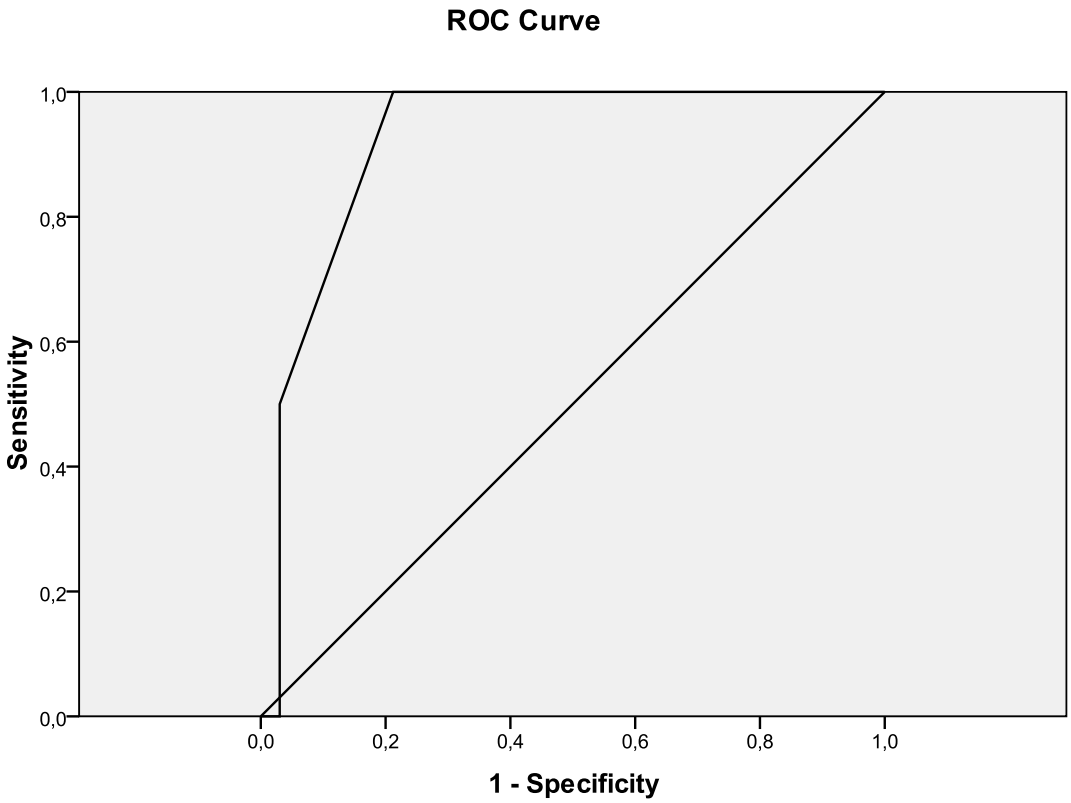


Table 1. Baseline characteristics of 172 children hospitalized with bronchiolitis

Characteristics	n (%)	Median (p25-p75)
Age (months)		5.2 (3.6 – 8.2)
< 2 month	15 (8.7)	
2 – 11 month	138 (80.2)	
≥ 12 months	19 (11.1)	
Male gender	109 (63.4)	
Race		
Mixed	87 (50.6)	
Black	57 (33.1)	
White	28 (16.3)	
History		
Duration of disease ≤ 7 days	133/171 (77.8) [a]	
Duration of disease ≤ 5 days	89/171 (52.0) [a]	
Difficulty breathing	163/171 (95.3) [a]	2.0 (1 – 4) [c]
Cough	160/171 (93.6) [a]	5.0 (3 - 7) [c]
Fever	97/171 (56.7) [a]	2.0 (1 – 3) [c]
Wheezing	70/171 (40.9) [a]	2.0 (1 – 4) [c]
Vomiting	35/171 (20.5) [a]	1.0 (1 – 3) [c]
Co-morbidities	10 (5.8)	
Congenital heart disease	4 (2.3) [b]	
Chronic lung disease	2 (1.2) [b]	
Down's syndrome	1 (0.6)	
Diabetes mellitus type 1	1 (0.6)	
Chronic liver disease	1 (0.6)	
Sickle cell disease	1 (0.6)	
HIV – infected mother	1 (0.6)	
Hydronephrosis	1 (0.6) [b]	
Obstetric history		
Prematurity < 30 weeks	6 (3.5)	
Prematurity 30 – 36 weeks	19 (11.0)	
Delivery		
Vaginal	109/171 (63.8) [a]	
C - section	62/171 (36.2) [a]	
Smoking mother during pregnancy	20 (11.6)	
Mother with asthma during pregnancy	7 (4.1)	
Mechanical ventilator	8 (4.7)	
Season of birth		
Summer	59 (34.3)	
Spring	38 (22.1)	
Fall	38 (22.1)	
Winter	37 (21.5)	

Infant history	
Atopic dermatitis	2 (1.2)
Previous bronchiolitis	2 (1.2)
Palivizumab use	1 (0.6)
Environmental factor	
Smokers at home	42 (24.4)
Mold at home	65 (37.8)
Breastfeeding	
Currently exclusive	43 (25)
Currently non-exclusive	73/167 (43.7) [a]
Mother's history of atopy	47 (27.3)
Asthma	22 (12.8)
Rhinitis	20 (11.6)
Bronchitis	4 (2.3)
Eczema	1 (0.6)
Physical examination	
Fever ($\geq$ 37.4°C)	7/145 (4.8) [a]
Tachypnea $\geq$ 70 breaths/min	7/168 (4.2) [a]
Tachycardia $\geq$ 200 beats/min	0
RDAI score [d]	
0 – 5 points	138/170 (81.2) [a]
6 – 10 points	32/170 (18.8) [a]
Nutritional status	
Well-nourished	142 (82.6)
Malnutrition	13 (7.6)
Severe malnutrition	8 (4.7)
Overweight	7 (4.1)
Obesity	2 (1.2)
Sensorial status	
Normal	168 (97.7)
Irritable	3 (1.7)
Lethargic	1 (0.6)
Chest retraction	84 (48.8)
Prolonged expiratory phase	26/170 (15.3) [a]
Hypersonant chest	2/167 (1.2) [a]
Stridor	4/171 (2.3) [a]
Reduced vesicular murmur	5 (2.9)
Rhonchi	77 (44.8)
Expiratory wheezing	69/171 (40.4) [a]
Inspiratory wheezing	15/170 (8.8) [a]
Crackles	48 (27.9)
Regular cardiac rhythm	172 (100)

Normal heart sounds	172 (100)
Cardiac murmurs	2 (1.2)
Enlarged liver	4 (2.3)
Enlarged spleen	1 (2.3)
Abdominal bloating	4 (2.3)
Cyanosis	0

[a] The denominator was not 172 because there was missing information.
[b] One patient presented cardiac disease and chronic lung disease concomitantly and another patient presented chronic lung disease and hydronephrosis concomitantly.
[c] Duration in days
[d] Respiratory Distress Assessment Instrument score

Table 2. Comparison of baseline characteristics between patients who were or were not transferred to ICU and between patients who did or did not stay ≥5 days in the hospital

Characteristics	Intensive Care Unit treatment			Length of hospital stay ≥ 5 days		
	Yes n = 5	No n = 167	*p*	Yes n = 69	No n = 103	*p*
Age (months)[a]	7.1 (4.1 – 6.8)	5.1 (1 – 23)	0.5	5.0 (1.1 – 23.0)	5.3 (1.0 – 22.2)	0.3
Male gender	4 (80.0)	105 (62.9)	0.7	44 (63.8)	65 (63.1)	0.9
Mixed or Black race	5 (100)	139 (83.2)	1.0	57 (82.6)	87 (84.5)	0.7
History						
Duration of disease ≤ 7 days	4 (80.0)	129/166 (77.7)[b]	1.0	49/68 (72.1)[b]	84 (81.6)	0.1
Duration of disease ≤ 5 days	2 (40.0)	87/166 (52.4)[b]	0.7	34/68 (50)[b]	55 (53.4)	0.7
Difficulty breathing	5 (100)	158/166 (95.2)[b]	1.0	65/68 (95.6)[b]	98 (96.1)	0.1
Duration of difficulty breathing (days) [a]	1 (1-8.5)	2 (1-4)	0.4	2 (1-4)	2 (1-4)	0.9
Cough	5 (100)	155/166 (93.4)[b]	1.0	61/68 (89.7)[b]	99 (96.1)	0.1
Duration of cough (days) [a]	3 (2 – 6.5)	5 (3 - 7)	0.3	5 (3-7)	5 (3-7)	0.8
Fever	2 (40.0)	95/166 (57.2)[b]	0.7	37/68 (54.4)[b]	60 (58.3)	0.6
Duration of fever (days) [a]	2 (1 – 3)	2 (1 – 3)	0.9	2 (1-3)	2 (1-3)	0.9
Wheezing	1 (20.0)	69/166 (41.6)[b]	0.7	33/68 (48.5)[b]	37 (35.9)	0.1
Duration of wheezing (days) [a]	4 (4-4)	2 (1 – 3.5)	0.3	2 (1,5 – 4)	2 (1 – 3)	0.1
Vomiting	2 (40.0)	33/166 (19.9)[b]	0.3	15/68 (22.1)[b]	20 (19.4)	0.7
Duration of vomiting (days) [a]	4 (3 – 5)↑	1 (1 – 2)	0.026	1 (1-3)	1 (1-2)	0.8
Co-morbidities						
Congenital heart disease	0	4 (2.4)	1.0	3 (4.3)	1 (1.0)	0.3
Chronic lung disease	0	2 (1.2)	1.0	2 (2.9)	0	0.2
Down’s syndrome	0	1 (0.6)	1.0	1 (1.4)	0	0.4

Obstetric history						
Prematurity < 30 weeks	2 (40.0)↑	4 (2.4)	0.01	6 (8.7)↑	0	0.004
Prematurity 30 – 36 weeks	0/3 (0)[c]	19 / 163 (11.7)[c]	1.0	11/63 (17.5)[c]	8 (7.8)[c]	0.06
C - section delivery	1 (20)	61/166 (36.7)[b]	0.7	24 (34.9)	38 (37.3)	0.7
Smoking mother during pregnancy	0	20 (12.0)	1.0	7 (10.1)	13 (12.6)	0.6
Mother with asthma during pregnancy	0	7 (4.2)	1.0	1 (1.4)	6 (5.8)	0.2
Neonatal mechanical ventilator	0	8 (4.8)	1.0	5 (7.2)	3 (2.9)	0.3
Season of birth						
Spring	0	38 (22.8)	0.6	12 (17.4)	26 (25.2)	0.2
Summer	1 (20.0)	58 (34.7)	0.7	26 (37.7)	33 (32.0)	0.4
Fall	2 (40.0)	36 (21.6)	0.3	13 (18.8)	25 (24.3)	0.4
Winter	2 (40.0)	35 (21.0)	0.3	18 (26.1)	19 (18.4)	0.2
Infant history						
Atopic dermatitis	0	2 (1.2)	1.0	1 (1.4)	1 (1.0)	1.0
Environmental factor						
Smokers at home	0	42 (25.1)	0.3	14 (20.3)	28 (27.2)	0.3
Breastfeeding						
Currently exclusive	1 (20)	42 (25.1)	1.0	14 (20.3)	29 (28.2)	0.2
Currently non-exclusive	1 (20)	72/162 (44.4)[b]	0.4	22 /68 (32.4)[b]	51/99 (51.5)[b] ↑	0.01
Mother's history of atopy	1 (20)	46 (27.5)	1.0	18 (26.1)	29 (28.2)	0.8
Physical examination						
Malnutrition	0	13/161 (8.1)[b]	1.0	7/61 (11.5)[b]	6 (5.8)	0.2
Severe malnutrition	2 (40.0)↑	6 (3.6)	0.02	8 (11.6)↑	0	0.001
Fever (≥ 37.4°C)	0	7/140 (5.0)[b]	1.0	4/58 (6.9)[b]	3/87 (3.4)[b]	0.4
Tachypnea ≥ 70 breaths/min	0	5/163 (3.1)[b]	1.0	1/67 (1.5)[b]	4/101 (4.0)[b]	0.6

RDAI [d] score 6 – 10 points	1 (20.0)	31/165 (18.8)[b]	1.0	16/68 (23.5)[b]	16/102 (15.7)[b]	0.2
Chest retraction	3 (60.0)	8 (48.5)	0.7	40 (58.0)	44 (42.7)	0.05
Prolonged expiratory phase	4 (80.0)	140/165 (84.8)[b]	0.6	9/68 (13.2)[b]	17/102 (16.7)[b]	0.5
Rhonchi	4 (80.0)	91 (54.5)	0.4	27 (39.1)	50 (48.5)	0.2
Expiratory wheezing	1 (20.0)	68/166 (41.0)[b]	0.6	30.0 (44.1)	39 (37.9)	0.4
Inspiratory wheezing	1 (20.0)	14/165 (8.5)[b]	0.4	8/68 (11.8)[b]	7/102 (6.2)[b]	0.3
Crackles	2 (40.0)	46 (27.5)	0.6	26 (37.7)↑	22 (21.4)	0.02

Results as n (%) otherwise when not informed.
[a] Results as median (interquartile range).
[b] Different denominator due to missing information.
[c] Excluded premature < 30 weeks.
[d] Respiratory Distress Assessment Instrument score.

Table 3. Multivariable logistic regression analysis of risk factors for Intensive Care Unit treatment in children hospitalized with bronchiolitis.

Factors	ICU		OR	95%CI	*P*
	Yes n = 5	**No** n = 167			
Age (months)[a]	7.1 (4.1 – 6.8)	5.1 (1 – 23)	1.05	0.79 – 1.39	0.7
Severe malnutrition	2 (40%)	6 (3.6%)	**21.53**	**1.43 – 323.66**	**0.03**
Prematurity < 30 weeks	2 (40%)	4 (2.4%)	**13.85**	**1.23 – 155.89**	**0.03**
Duration of vomiting (days) [a]	4 (3-5)	1 (1-2)	**1.92**	**1.16 – 3.17**	**0.01**

[a] Median (IQR)

ICU, Intensive Care Unit; OR, odds ratio; CI, confidence interval

Table 4. Multivariable logistic regression analysis of risk factors for length of hospital stay ≥5 days in children hospitalized with bronchiolitis.

Factors	**LOS ≥5 days**		**OR**	**95%CI**	***P***
	Yes n = 69	**No** n = 103			
Age (months) [a]	5.0 (1.1 – 23.0)	5.3 (1.0 – 22.2)	0.92	0.85 – 1.01	0.07
Severe malnutrition	8 (11.6%)	0 (0%)	3030.55	0.0 – 2.227E+20	0.7
Prematurity (< 37 weeks) [b]	17 (24.6%)	8 (7.8%)	**3.89**	**1.55 – 9.79**	**0.004**
Ongoing non-exclusive breastfeeding	22/68 (32.3%)[c]	51/99 (51.5%)[c]	0.56	0.28 – 1.15	0.1
Crackles	26 (37.7%)	22 (21.4%)	**3.11**	**1.45 – 6.70**	**0.004**

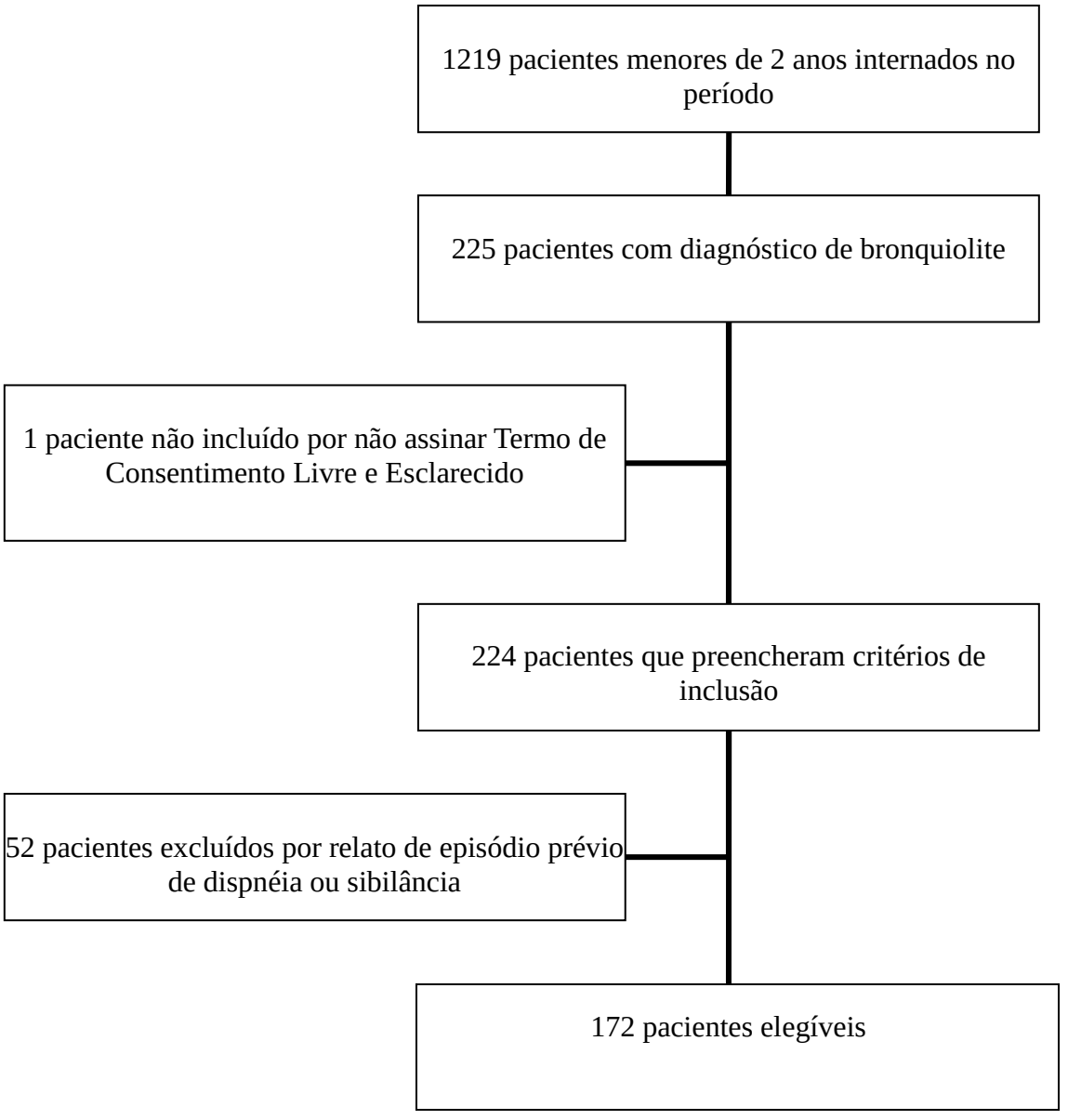
[a] Median (IQR); LOS, length of hospital stay; OR, odds ratio; CI, confidence interval
[b] Prematurity was included as 2 levels: < 30 weeks and 30 – 36 weeks of gestational age.
[c] The total denominator was not 172 because there was missing information.

VI. RESULTADOS

VII. 1. Constituição da amostra

Durante o período do estudo, 1219 pacientes com idade inferior a 24 meses foram admitidos. Destes, 225 tiveram diagnóstico de bronquiolite na admissão hospitalar. O representante legal de 1 paciente (0,4%) não concordou em assinar o TCLE, sendo o mesmo excluído. Adicionalmente, 52 (23,1%) preencheram critério de exclusão por reportarem episódio prévio de desconforto respiratório ou sibilância. Portanto, o grupo de estudo compreendeu 172 pacientes (Figura I). Cinco pacientes (2,9%; IC95%: 1,1%-6,3%) foram transferidos para UTI e 69 pacientes (40,1%; IC95%: 33,0%-47,6%) tiveram DIH maior ou igual a 5 dias. Um paciente veio a óbito (0,6%).

Figura I. Processo de construção da amostra de estudo de coorte prospectivo realizado em Salvador-BA, na enfermaria do Hospital da Criança das Obras Sociais de Irmã Dulce.



VII. 2. Características dos pacientes no momento da admissão

As características de base do grupo de estudo estão descritas na Tabela 1. A mediana de idade foi 5,2 meses (IQR: 3,6 – 8,2). As queixas mais frequentes foram dificuldade para respirar (95,3%), tosse (93,6%) e febre (56,7%). Outras queixas foram sibilância (40,9%) e vômitos (20,5%). Os achados mais comuns ao exame físico foram tiragens torácicas (48,8%), roncos (44,8%), sibilos expiratórios (40,4%) e estertores crepitantes (27,9%). De acordo com o escore RDAI, 18.8% dos pacientes apresentavam dispnéia grave na admissão.

Tabela 1. Características de 172 crianças hospitalizadas com bronquiolite no momento da admissão na enfermaria.

Características	n (%)	Mediana (p25-p75)
Idade (meses)		5,2 (3,6 – 8,2)
< 2 meses	15 (8,7)	
2 – 11 meses	138 (80,2)	
≥ 12 meses	19 (11,1)	
Gênero masculino	109 (63,4)	
Raça		
Pardo	87 (50,6)	
Negro	57 (33,1)	
Branco	28 (16,3)	
História		
Duração da doença ≤ 7 dias	133/171 (77,8) [a]	
Duração da doença ≤ 5 dias	89/171 (52,0) [a]	
Dispnéia	163/171 (95,3) [a]	2,0 (1 – 4) [c]
Tosse	160/171 (93,6) [a]	5,0 (3 - 7) [c]
Febre	97/171 (56,7) [a]	2,0 (1 – 3) [c]
Sibilância	70/171 (40,9) [a]	2,0 (1 – 4) [c]
Vômito	35/171 (20,5) [a]	1,0 (1 – 3) [c]
Comorbidades	10 (5,8)	
Cardiopatia congênita	4 (2,3) [b]	
Doença pulmonar crônica	2 (1,2) [b]	
Síndrome de Down	1 (0,6)	
Diabetes mellitus tipo 1	1 (0,6)	
Doença hepática crônica	1 (0,6)	

Anemia falciforme	1 (0,6)
HIV – infecção materna	1 (0,6)
Hidronefrose	1 (0,6) [b]
História obstétrica	
Prematuridade < 30 semanas	6 (3,5)
Prematuridade 30 – 36 semanas	19 (11,0)
Tipo de parto	
Vaginal	109/171 (63,8) [a]
Cesariana	62/171 (36,2) [a]
Fumo materno durante a gestação	20 (11,6)
História materna de asma durante a gestação	7 (4,1)
Uso de ventilação mecânica	8 (4,7)
Estação de nascimento	
Verão	59 (34,3)
Primavera	38 (22,1)
Outono	38 (22,1)
Inverno	37 (21,5)
Antecedentes patológicos	
Dermatite atópica	2 (1,2)
Bronquiolite prévia	2 (1,2)
Uso de Palivizumab	1 (0,6)
Fatores ambientais	
Presença de fumantes em domicílio	42 (24,4)
Mofo em casa	65 (37,8)
Aleitamento materno	
Exclusivo atualmente	43 (25,0)
Misto atualmente	73/167 (43,7) [a]
História materna de atopia	47 (27,3)
Asma	22 (12,8)
Rinite	20 (11,6)
Bronquite	4 (2,3)
Eczema	1 (0,6)
Exame físico	
Febre ($\geq$ 37,4°C)	7/145 (4,8) [a]
Taquipneia $\geq$ 70 incursões/min	7/168 (4,2) [a]
Taquicardia $\geq$ 200 bpm	0
RDAI escore [d]	
0 – 5 pontos	138/170 (81,2) [a]
6 – 10 pontos	32/170 (18,8) [a]
Estado nutricional	
Eutrofia	142 (82,6)

Desnutrição	13 (7,6)
Desnutrição grave	8 (4,7)
Sobrepeso	7 (4,1)
Obesidade	2 (1,2)
Estado sensorial	
Normal	168 (97,7)
Irritado	3 (1,7)
Letargia	1 (0,6)
Tiragem torácica	84 (48.8)
Tempo expiratório prolongado	26/170 (15,3) [a]
Tórax hipertimpânico	2/167 (1.2) [a]
Estridor	4/171 (2,3) [a]
Murmúrio vesicular reduzido	5 (2,9)
Roncos	77 (44,8)
Sibilos expiratórios	69/171 (40,4) [a]
Sibilos inspiratórios	15/170 (8,8) [a]
Estertores crepitantes	48 (27,9)
Ritmo cardíaco regular	172 (100)
Bulhas normofonéticas	172 (100)
Sopro cardíaco	2 (1,2)
Hepatomegalia	4 (2,3)
Esplenomegalia	1 (2,3)
Distensão abdominal	4 (2,3)
Cianose	0

a O denominador não foi 172 devido a falta da informação.
b Um paciente tinha cardiopatia e doença pulmonar crônica concomitantemente e outro paciente tinha doença pulmonar crônica e hidronefrose concomitantemente.
c Duração em dias
d Respiratory Distress Assessment Instrument escore

VII. 3. Características radiológicas

Cento e quarenta e sete pacientes tinham exame radiológico na admissão. Destes, 17 (9,9%) foram excluídos devido à má qualidade técnica. Foram avaliados 130 exames por radiologista pediátrico: 108 (83,1%) normais, 12 (9,2%) compatíveis com pneumonia e outros achados em 10 (7,7%) - hiperinsuflação (n = 9); espessamento peribrônquico (n = 2) e atelectasia (n = 1). Dentre os 12 exames compatíveis com pneumonia, consolidação (n = 8), infiltrado intersticial-alveolar (n = 3) e infiltrado intersticial (n = 1) foram descritos.

VII. 4. Características socioeconômicas

Presença de água encanada (97%), esgotamento sanitário (89,5%), rede elétrica (100%), coleta regular de lixo (85,5%) foram registrados. A Tabela 2 descreve os aspectos socioeconômicos encontrados.

Tabela 2. Aspectos socioeconômicos de 172 crianças com bronquiolite no recrutamento.

Características	n (%)	Mediana (p25-p75)
Casa de alvenaria	172 (100)	
Fornecimento de água		
Rede pública interna	146 (84)	
Rede pública externa	23 (13,4)	
Poço	2 (1,2)	
Outros (fora de casa)	1 (0,6)	
Esgotamento sanitário		
Rede pública de esgotos	154 (89,5)	
Esgoto a céu aberto	23 (13,4)	
Fossa seca	2 (1,2)	
Fossa negra	1 (0,6)	

Energia elétrica	172 (100)	
Banheiro		
Dentro de casa	169 (98,3)	
Fora de casa	1 (0,6)	
Não possui	2 (1,2)	
Coleta de lixo		
Regular	147 (85,5)	
Irregular	16 (9,3)	
Não possui	9 (5,2)	
Preparo da alimentação		
Fogão a gás	170 (98,8)	
Fogão a lenha	1 (0,6)	
Outro (álcool)	1 (0,6)	
Grau de escolaridade materna		
Não alfabetizadas	1/170 (0,6)	
2° grau completo	76/170 (44,7)	
Nível superior (em curso ou completo)	5/170 (2,9)	
Grau de escolaridade paterno		
Não alfabetizados	7/153 (4,6)	
2° grau completo	70/153 (45,8)	
Nível superior (em curso ou completo)	2/153 (1,3)	
Trabalho da mãe		
Trabalha em casa	78 (45,4)	
Não trabalha	41 (23,8)	
Estudante	1 (0,6)	
Trabalha fora de casa	52 (30,2)	
Trabalho do pai		
Trabalha em casa	2/165 (1,2)	
Não trabalha	21/165 (12,7)	
Trabalha fora de casa	142/165 (86,1)	
Casa		
Própria	91 (52,9)	
Alugada	44 (25,6)	
Emprestada	31 (18,0)	
Invadida	6 (3,5)	
TV	170 (98,8)	
Som	118 (68,6)	
Geladeira	166 (96,5)	
Carro	23 (13,4)	
Renda familiar (R$)		900 (800-1600)

VII. 5. Fatores de risco

A Tabela 3 demonstra a comparação das características entre pacientes transferidos para UTI com aqueles não transferidos, além de também comparar os pacientes que tiveram ou não tiveram uma DIH ≥5 dias.

Tabela 3. Comparação de características entre pacientes transferidos ou não transferidos para Unidade de Terapia Intensiva e entre pacientes que tiveram ou não tiveram duração de internamento hospitalar ≥ 5 dias.

Características	Unidade de Terapia Intensiva			Duração de internamento ≥ 5 dias		
	Sim n = 5	Não n = 167	*p*	Yes n = 69	No n = 103	*p*
Idade (meses)[a]	7,1 (4,1 – 6,8)	5,1 (1 – 23)	0,5	5,0 (1,1 – 23,0)	5,3 (1,0 – 22,2)	0,3
Gênero masculino	4 (80,0)	105 (62,9)	0,7	44 (63,8)	65 (63,1)	0,9
Pardo ou negro	5 (100)	139 (83,2)	1,0	57 (82,6)	87 (84,5)	0,7
História da doença						
Duração da doença ≤ 7 dias	4 (80,0)	129/166 (77,7)[b]	1,0	49/68 (72,1)[b]	84 (81,6)	0,1
Duração da doença ≤ 5 dias	2 (40,0)	87/166 (52,4)[b]	0,7	34/68 (50)[b]	55 (53,4)	0,7
Dispnéia	5 (100)	158/166 (95,2)[b]	1,0	65/68 (95,6)[b]	98 (96,1)	0,1
Duração da dispnéia (dias) [a]	1 (1-8,5)	2 (1-4)	0,4	2 (1-4)	2 (1-4)	0,9
Tosse	5 (100)	155/166 (93,4)[b]	1,0	61/68 (89,7)[b]	99 (96,1)	0,1
Duração da tosse (dias) [a]	3 (2 – 6,5)	5 (3 - 7)	0,3	5 (3-7)	5 (3-7)	0,8
Febre	2 (40,0)	95/166 (57,2)[b]	0,7	37/68 (54,4)[b]	60 (58,3)	0,6
Duração da febre (dias) [a]	2 (1 – 3)	2 (1 – 3)	0,9	2 (1-3)	2 (1-3)	0,9
Sibilância	1 (20,0)	69/166 (41,6)[b]	0,7	33/68 (48,5)[b]	37 (35,9)	0,1
Duração da sibilância (dias) [a]	4 (4-4)	2 (1 – 3,5)	0,3	2 (1,5 – 4)	2 (1 – 3)	0,1
Vômito	2 (40,0)	33/166 (19,9)[b]	0,3	15/68 (22,1)[b]	20 (19,4)	0,7
Duração do vômito (dias) [a]	4 (3 – 5)↑	1 (1 – 2)	0,026	1 (1-3)	1 (1-2)	0,8

Comorbidades						
Cardiopatia congênita	0	4 (2,4)	1,0	3 (4,3)	1 (1,0)	0,3
Doença pulmonar crônica	0	2 (1,2)	1,0	2 (2,9)	0	0,2
Síndrome de Down	0	1 (0,6)	1,0	1 (1,4)	0	0,4
História obstétrica						
Prematuridade < 30 semanas	2 (40,0)↑	4 (2,4)	0,01	6 (8,7)↑	0	0,004
Prematuridade 30 – 36 semanas	0/3 (0)[c]	19 / 163 (11,7)[c]	1,0	11/63 (17,5)[c]	8 (7,8)[c]	0,06
Parto cesáreo	1 (20)	61/166 (36,7)[b]	0,7	24 (34,9)	38 (37,3)	0,7
Fumo materno durante gestação	0	20 (12,0)	1,0	7 (10,1)	13 (12,6)	0,6
História materna de asma durante a gestação	0	7 (4,2)	1,0	1 (1,4)	6 (5,8)	0,2
Ventilação mecânica neonatal	0	8 (4,8)	1,0	5 (7,2)	3 (2,9)	0,3
Estação de nascimento						
Primavera	0	38 (22,8)	0,6	12 (17,4)	26 (25,2)	0,2
Verão	1 (20,0)	58 (34,7)	0,7	26 (37,7)	33 (32,0)	0,4
Outono	2 (40,0)	36 (21,6)	0,3	13 (18,8)	25 (24,3)	0,4
Inverno	2 (40,0)	35 (21,0)	0,3	18 (26,1)	19 (18,4)	0,2
Antecedentes médicos						
Dermatite atópica	0	2 (1,2)	1,0	1 (1,4)	1 (1,0)	1,0
Fatores ambientais						
Presença de fumantes em domicílio	0	42 (25,1)	0,3	14 (20,3)	28 (27,2)	0,3
Aleitamento materno						

Exclusivo atualmente	1 (20,0)	42 (25,1)	1,0	14 (20,3)	29 (28,2)	0,2
Misto atualmente	1 (20)	72/162 (44,4)[b]	0,4	22 /68 (32,4)[b]	51/99 (51,5) [b] ↑	0,01
História materna de atopia	1 (20)	46 (27,5)	1,0	18 (26,1)	29 (28,2)	0,8
Exame físico						
Desnutrição	0	13/161 (8,1)[b]	1,0	7/61 (11,5)[b]	6 (5,8)	0,2
Desnutrição grave	2 (40,0)↑	6 (3,6)	0,02	8 (11,6)↑	0	0,001
Febre (≥ 37.4°C)	0	7/140 (5,0)[b]	1,0	4/58 (6,9)[b]	3/87 (3,4)[b]	0,4
Taquipnéia ≥ 70 incursões/min	0	5/163 (3,1)[b]	1,0	1/67 (1,5)[b]	4/101 (4,0)[b]	0,6
RDAI [d] escore 6 – 10 pontos	1 (20,0)	31/165 (18,8)[b]	1,0	16/68 (23,5)[b]	16/102 (15,7)[b]	0,2
Tiragens torácicas	3 (60,0)	8 (48,5)	0,7	40 (58,0)	44 (42,7)	0,05
Tempo expiratório prolongado	4 (80,0)	140/165 (84,8)[b]	0,6	9/68 (13,2)[b]	17/102 (16,7)[b]	0,5
Roncos	4 (80,0)	91 (54,5)	0,4	27 (39,1)	50 (48,5)	0,2
Sibilos expiratórios	1 (20,0)	68/166 (41,0)[b]	0,6	30.0 (44,1)	39 (37,9)	0,4
Sibilos inspiratórios	1 (20,0)	14/165 (8,5)[b]	0,4	8/68 (11,8)[b]	7/102 (6,2)[b]	0,3
Estertores crepitantes	2 (40,0)	46 (27,5)	0,6	26 (37,7)↑	22 (21,4)	0,02

Resultados em n (%) quando não informado.
a Resultados em mediana (intervalo interquartil).
b Denominador diferente devido a falta da informação.
c Prematuros < 30 semanas excluídos.
d Respiratory Distress Assessment Instrument escore.

Na análise bivariada, desnutrição grave e prematuridade <30 semanas foram associados com transferência para UTI, assim como pacientes que apresentaram maior tempo de duração de vômitos. Desnutrição grave, prematuridade < 37 semanas, presença de estertores crepitantes na admissão foram diretamente associados com DIH ≥5 dias. Uso de aleitamento misto no momento da admissão foi inversamente associado com DIH ≥ 5 dias.

Foi utilizado um modelo de regressão logística para predizer uso de cuidados intensivos (Tabela 4). Os preditores significativos foram desnutrição grave (OR 21,53; IC 95% 1,43 – 323,66; P<0,03), prematuridade abaixo de 30 semanas de idade gestacional (OR 13,85; IC 95% 1,23 – 155,89; P<0,03) e duração de vômitos (OR 1,92; IC 95% 1,16 – 3,17; P<0,01).

Tabela 4. Análise de regressão logística multivariada entre fatores de risco e necessidade de tratamento em Unidade de Terapia Intensiva em crianças hospitalizadas com bronquiolite.

Fatores	**UTI**		**OR**	**IC 95%**	***p***
	Sim n = 5	**Não** n = 167			
Idade (meses)*	7,1 (4,1 – 6,8)	5,1 (1 – 23)	1,05	0,79 – 1,39	0,7
Desnutrição grave	2 (40%)	6 (3,6%)	**21,53**	**1,43 – 323,66**	**0,03**
Prematuridade < 30 semanas	2 (40%)	4 (2,4%)	**13,85**	**1,23 – 155,89**	**0,03**
Duração de vômitos (dias)*	4 (3-5)	1 (1-2)	**1,92**	**1,16 – 3,17**	**0,01**

* Mediana (IQR); UTI, Unidade de Terapia Intensiva Pediátrica; OR, odds ratio; IC, intervalo de confiança.

No modelo de regressão logística multivariada para DIH ≥5 dias (Tabela 5), os preditores significativos foram prematuridade abaixo de 37 semanas de idade gestacional (OR 3,89; IC 95% 1,55 – 9,79; P<0,004) e presença de estertores crepitantes (OR 3,11; 95%CI 1,45 – 6,70; P<0,004).

Tabela 5. Análise de regressão logística multivariada entre fatores de risco e duração de internamento hospitalar ≥5 dias em crianças hospitalizadas com bronquiolite.

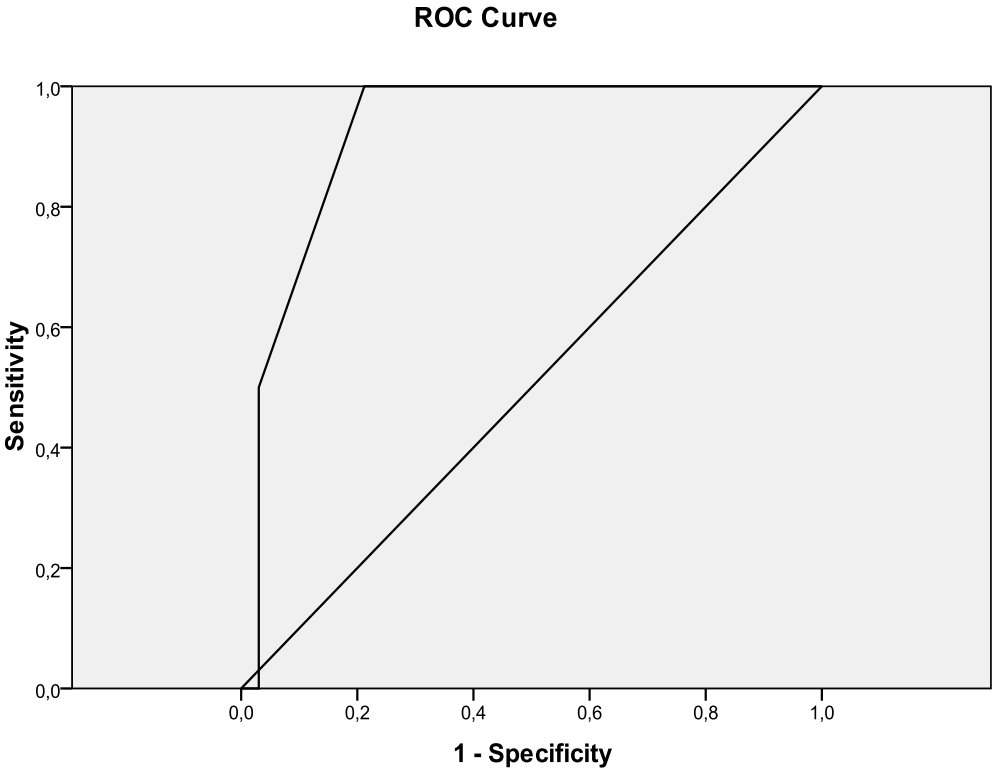
Fatores	**DIH ≥5 dias**		**OR**	**IC 95%**	***p***
	Sim n = 69	**Não** n = 103			
Idade (meses)*	5,0 (1,1 – 23,0)	5,3 (1,0 – 22,2)	0,92	0,85 – 1,01	0,07
Desnutrição grave	8 (11,6%)	0 (0%)	3030,55	0,0 – 2,227E+20	0,7
Prematuridade (< 37 semanas)[a]	17 (24.6%)	8 (7.8%)	**3,89**	**1,55 – 9,79**	**0,004**
Uso atual de aleitamento misto	22/68 (32,3%) [b]	51/99 (51,5%) [b]	0,56	0,28 – 1,15	0,1
Estertores crepitantes	26 (37,7%)	22 (21,4%)	**3,11**	**1,45 – 6,70**	**0,004**

* Mediana (IQR); DIH, duração de internamento hospitalar; OR, odds ratio; IC, intervalo de confiança.
a Prematuridade foi incluída em 2 níveis: < 30 semanas e 30 – 36 semanas de idade gestacional.
b O denominador total não foi 172 devido a falta da informação.

Dentre as 35 (20,5%) crianças que reportaram na admissão história de vômitos, 2 foram transferidas para UTI. A Figura II representa a curva ROC para duração de vômito como preditor de transferência para UTI. A área abaixo da curva ROC foi 0,92 (95%CI 0,81 – 1,04) e o ponto de corte na melhor performance foi 2,5 dias (sensibilidade 100%;

especificidade 79%).

Figura II. ROC curve: Duração de vômitos x internamento UTI



VII. 6. Tratamento para o quadro de bronquiolite

As opções terapêuticas utilizadas na enfermaria e voltadas para o tratamento da bronquiolite foram: Solução salina 3% inalatória (77,3%), beta-2-agonista inalatório (69,8%), corticóides (47,1%), hidratação venosa (44,2%), antibióticos (30,2%), oxigênio

(12,8%), ventilação mecânica (1,2%) e adrenalina inalatória (0,6%). Pacientes que apresentaram estertores crepitantes na ausculta pulmonar receberam antibióticos mais frequentemente que aqueles que não apresentaram tal achado (43,8% *vs.* 25,0%, p=0,02).

As principais opções terapêuticas utilizadas pelos cuidadores em domicílio antes de procurar serviço médico de emergência foram: Sintomáticos (41,3%), broncodilatadores (22,0%), xaropes fitoterápicos (18%), corticóide (14,0%), antibióticos (10,7%) e anti-histamínicos (6,7%).

VIII. DISCUSSÃO

VIII.1. Fatores de risco associados com desfecho desfavorável em crianças hospitalizadas com bronquiolite

Neste estudo de coorte, transferência para UTI foi um evento incomum (2,9%;IC95%:1,1%-6,3%), enquanto 40,1% dos pacientes permaneceram internados por pelo menos 5 dias no hospital. Fatores intrínsecos ao hospedeiro como desnutrição grave e prematuridade foram independentemente associados com transferência para UTI (ambos os fatores) ou DIH ≥5 dias (somente prematuridade <37 semanas). Notavelmente, duração de vômitos ≥2,5 dias foi um bom preditor (sensibilidade 100%; especificidade 79%) de transferência para UTI. Presença de estertores crepitantes na ausculta pulmonar durante a admissão foi um preditor para DIH ≥5 dias.

A presença de vômitos foi previamente descrita como fator de risco para pior evolução em crianças com bronquiolite. Em um estudo de coorte espanhol, os autores incluíram 53 crianças previamente hígidas e 8 crianças com má formação neonatal grave, sendo todos admitidos devido a bronquiolite. Os autores reportaram OR 4,22 (IC95%:1,21-14,70) para aqueles que relataram episódios de vômitos na história clínica (65,51% vs. 21,87%) com pior evolução (frequência respiratória >80 batimentos/minuto, sibilos audíveis sem estetoscópio, cianose persistente com FiO2 >0,4, PaO2 <50, PaCO2 >70, acidose respiratória ou mista) em qualquer momento durante o internamento hospitalar (Garcia et al., 2000).

No nosso estudo, história de vômitos foi reportada em 20,5% dos pacientes incluídos, não sendo portanto um achado tão freqüente quanto no estudo realizado na Espanha. Esta diferença pode explicar porque não identificamos presença de vômitos como fator de risco para transferência para UTI. Contudo, observamos que duração de vômitos foi um fator independentemente associado com transferência para UTI (tabela 4). Estes achados podem ser devido a desidratação que foi um fator relatado em estudos prévios como preditor de necessidade de hospitalização em pacientes com bronquiolite (Walsh et al., 2004; Aziz et al., 2015). É possível presumir que quanto maior o tempo de duração de vômitos, maior a probabilidade de desidratação. Assim sendo, duração de vômitos por ≥2,5 dias pode ser utilizado na prática clínica como um sinal de alerta em crianças hospitalizadas com bronquiolite.

Esta coorte prospectiva também identificou que alguns fatores intrínsecos ao hospedeiro como desnutrição grave e prematuridade são independentemente associados com necessidade de transferência para UTI (ambos) ou DIH ≥5 dias (somente prematuridade). Notavelmente, a maioria dos pacientes internados foram eutróficos e nascido a termo. Nossos dados estão em concordância com resultados de estudos prévios que identificaram que lactentes prematuros são um grupo de alto risco para admissão em UTI devido a infecção de vias aéreas inferiores, não devendo ser considerados com risco similar àqueles lactentes nascidos a termo (Garcia et al., 2010; Garcia-Garcia et al., 2015; Gunville et al., 2010; Murray et al., 2014).

No Reino Unido, Murray et al. (2014) conduziram um estudo de coorte de base populacional e reportaram que somente 15% dos pacientes internados com bronquiolite

foram prematuros. Por outro lado, o risco relativo para uma admissão por bronquiolite foi maior em crianças prematuras (RR=1,9, IC95% 1,8–2,0) quando comparado com crianças nascidas a termo. Nos Estados Unidos, Garcia et al. (2010) em um estudo de coorte retrospectivo também encontraram que prematuridade e baixo peso são associados com bronquiolite grave. A chance para admissão em UTI foi inversamente e exponencialmente relacionada com o peso dos pacientes: Uma vez que outros fatores de risco se mantiveram constantes, para cada aumento (ou decréscimo) de 1 kg de peso, a chance para admissão em UTI diminui (aumenta) em 9,2% (10,2%).

No presente estudo, nós encontramos curiosamente uma maior frequência de administração de antibióticos em pacientes que apresentavam estertores crepitantes na admissão quando comparados àqueles que não apresentavam. A despeito da recomendação de diversas diretrizes que sugerem que o uso de agentes antimicrobianos não deve ser utilizado na rotina (Ralston et al., 2014; Friedman et al., 2014; NICE, 2015), muitos médicos prescrevem persistentemente antibióticos para crianças com bronquiolite. Em um estudo de coorte prospectivo realizado na cidade de Nápoles, Itália, De Brasi et al. (2010) observaram que antibióticos foram prescritos em 50% dos casos de pacientes com bronquiolite. Diante do exposto, é possível inferir que crianças que apresentavam estertores crepitantes na ausculta pulmonar permaneceram mais tempo internados no hospital, pois estavam recebendo antibióticos.

VIII.2. Características radiológicas de crianças hospitalizadas com bronquiolite

Dentre as radiografias analisadas neste estudo, observou-se que a quantidade predominante dos exames não apresentou alterações radiográficas (83,1%) ou apresentavam somente achados inespecíficos (7,7%). Achados semelhantes foram relatados previamente na literatura (Schuh et al., 2007; Ecochard-Dugelay et al.,2014).

No Canadá, Schuh et al. (2007) em um estudo de coorte prospectivo envolvendo pacientes admitidos com bronquiolite de um departamento de emergência encontraram que 92,8% das radiografias solicitadas não tinham alterações ou apresentavam somente achados inespecíficos (infiltrado peribronquiolar, hiperinsuflação ou atelectasia). Em outro estudo de coorte também envolvendo crianças admitidas com bronquiolite em um departamento de emergência realizado por Ecochard-Dugelay et al. (2014) na França, os exames com achados inespecíficos e sem alterações compreendeu 90,3% das radiografias analisadas.

Estes achados suportam as orientações para bronquiolite das diretrizes mais atuais da Academia Americana de Pediatria (2014) e do Instituto Nacional de Saúde e Cuidados de Excelência do Reino Unido (2015) que recomendam que solicitação de radiografia deve ser reservada para casos de desconforto respiratório grave com necessidade de admissão em UTI ou quando outros sinais de complicações em vias aéreas como pneumotórax estiverem presentes.

VIII.3. Tratamento utilizado em crianças hospitalizadas com bronquiolite

No Reino Unido, Carande et al. (2016) conduziram um estudo junto a médicos de especialidades variadas ao redor do mundo para avaliar de forma comparativa entre o ano de 1995 e 2015 como estes tratavam os pacientes com bronquiolite. Neste estudo foi observado uma redução no uso de broncodilatadores (95% *vs.* 82%, $p = 0{,}0024$) e de corticóides (81% *vs*. 45%, $p < 0.0001$). Apesar da redução observada neste intervalo de 20 anos, verifica-se ainda uma elevada frequência na prescrição de terapias não recomendadas pelas diretrizes mais atuais (Ralston et al., 2014; Friedman et al., 2014; NICE, 2015). No nosso estudo também foi observado uma alta frequência de terapias não recomendadas, o que evidencia uma dificuldade de adesão dos profissionais às recomendações. Na literatura, outros autores também descreveram achados semelhantes apontando uma alta variabilidade no manejo da bronquiolite (Christakis et al., 2005; Dios et al., 2010; De Brasi et al., 2010).

De Brasi et al. (2010) em estudo conduzido na Itália envolvendo médicos pediatras nos dois principais hospitais de Nápoles, avaliaram as principais razões para o largo uso de medicamentos não recomendados em crianças hospitalizadas com diagnóstico de bronquiolite. Os autores observaram que as principais razões reportadas para o uso de broncodilatadores (91,6% dos casos) foram detecção de melhora após o uso (37%), a gravidade clínica (23%) ou por causa de achados do exame físico respiratório (21%). Para o uso de corticóides (85,7% dos casos) as principais razões apresentadas foram a gravidade clínica (36%), achados do exame físico respiratório

(20%) e detecção de melhora após o uso (15,5%). Foi também observado uso de antibióticos (50% dos casos) devido à gravidade clínica (43%), resultados de exames radiológicos ou sorológicos (15%) e para prevenir superinfecção bacteriana (10%). Outra razão reportada, porém com menor frequência foi "somente para fazer algo e/ou somente por segurança profissional" indicada em 1,5 a 3,0% dos casos. Este comportamento expõe o quanto a bronquiolite é considerada como uma afecção grave por parte dos médicos assistentes, que por vezes se veem impelidos a utilizar qualquer terapêutica na condução clínica destas crianças sob justificativa da segurança profissional ou mesmo por pressão dos pais dos pacientes envolvidos.

Nosso estudo tem algumas limitações. Primeiro, nossa amostra não teve tamanho suficiente para avaliar fatores de risco para óbito devido à taxa de mortalidade encontrada no nosso estudo ter sido muito baixa (0,6%). Este achado está de acordo com outros estudos que reportam óbito como um desfecho incomum para bronquiolite (Zorc et al., 2010; Hasegawa et al., 2013). Segundo, nós não investigamos o agente etiológico dos nossos casos de bronquiolite. Assim sendo, nossos resultados podem ser generalizados para pacientes abaixo de 24 meses de vida e admitidos devido a bronquiolite, não sendo extrapolado para grupos restritos de pacientes com etiologia específica estabelecida.

IX. PERSPECTIVAS DE ESTUDO

Realização de outros estudos envolvendo um número maior e mais diversificado de pacientes com identificação do fator etiológico da bronquiolite.

Realização de estudos avaliando as medidas terapêuticas ainda não bem estabelecidas na literatura como utilização de adrenalina inalatória, solução hipertônica ou oxigenação por cânula nasal de alto fluxo.

X. CONCLUSÕES

1. Vômitos por ≥2.5 dias é um preditor independente de admissão em UTI para crianças hospitalizadas com bronquiolite. Assim sendo, estas crianças devem ser monitoradas de perto e a duração prolongada de vômitos pode ser utilizada na prática clínica como um sinal de alerta em crianças hospitalizadas com bronquiolite.

2. A maior parte das crianças hospitalizadas devido a bronquiolite constitui-se de pacientes previamente hígidos, sem comorbidades associadas. Por outro lado, existe um reconhecido grupo de risco com fatores intrínsecos ao hospedeiro de crianças mais propensas a evoluir desfavoravelmente nos quadros de bronquiolite - a exemplo de prematuros e desnutridos graves.

3. Os exames radiológicos em pacientes hospitalizados com bronquiolite geralmente não apresentam alterações ou apresentam achados inespecíficos compatíveis com a doença.

4. A identificação e a correção de anormalidades fisiológicas enraizadas na cultura médica tem sido dominante no manejo da bronquiolite o que leva aos profissionais ao amplo uso de medidas terapêuticas consideradas fúteis no enfrentamento da doença. A implementação de diretrizes que restrinjam essa tendência fundamental é desafiadora, exigindo determinação e afirmação consistente sobre a terapêutica adequada.

5. A frequência do número de pacientes hospitalizados devido a bronquiolite que evoluem para óbito ou com necessidade de internamento em UTI é baixa, porém observa-se um maior número de pacientes que necessita de internamento hospitalar ≥5 dias.

XI. SUMMARY

DURATION OF VOMITING: INDEPENDENT FACTOR ASSOCIATED WITH POOR EVOLUTION IN BRONCHIOLITIS. Background: Bronchiolitis is a leading cause of acute illness and hospitalization among young children. This disease has a variable course. The group of children with subsequent clinical deterioration after hospitalization remains poorly defined in the literature. Objective: To identify factors present upon admission that are associated with worse evolution among children hospitalized with bronchiolitis. Methods: This prospective cohort was conducted at the pediatric ward of the Children's Hospital, Salvador, Brazil, from May 2015 to July 2016. Inclusion criteria comprised age <2 years, admission to hospital due to bronchiolitis, and written informed consent. Clinical data, physical findings upon admission and outcome were registered. Multi-variable logistic regression analysis in a model adjusted for age was used to assess association between Intensive Care Unit (ICU) treatment/length of hospital stay (LOS)⩾5 days (outcome variables) and factors detected upon admission (predictor variables). Results: The study group comprised 172 patients, out of which 5 (2.9%;95%CI:1.1%-6.3%) were transferred to ICU and 69 (40.1%;95%CI:33.0%-47.6%) had LOS⩾5 days. Overall, the median age was 5.2 months (IQR:3.6-8.2) and the median duration of vomiting was 1 day (IQR:1-3); prematurity <30 weeks (3.5%), <37 weeks (14.5%) were reported and severe malnutrition (4.7%) and crackles (27.9%) were found. Severe malnutrition (OR 21.53;95%CI 1.43–323.66), prematurity <30 weeks (OR 13.85;95%CI 1.23–155.89) and duration of vomiting (OR

1.92;95%CI1.16 – 3.17) were independently associated with ICU transfer. Prematurity <37 weeks (OR 3.89;95%CI 1.55 – 9.79) and crackles (OR 3.11;95%CI 1.45 – 6.70) were independently associated with LOS ⩾5 days. The area under the ROC curve for duration of vomiting to predict transfer to the ICU was 0.92(95%CI 0.81–1.04) being the cutoff with best performance 2.5 days (sensitivity 100%; specificity 79%). Conclusion: Children admitted with bronchiolitis reporting vomiting ⩾2.5 days should receive maximal attention.

Key-words: 1. Bronchiolitis; 2. Risk factors; 3. Outcome; 4. ICU

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XIII. ANEXOS

ANEXO 1

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Termo de Consentimento Livre e Esclarecido

Projeto De Pesquisa: **Características clínico-radiológicas de crianças hospitalizadas com bronquiolite**

A recusa à presente autorização em nada repercutirá sobre a assistência à saúde a ser prestada ao paciente. ID: {ID} ____ ____ ____

A qualquer momento poderei interromper para perguntar sobre qualquer dúvida que surgir durante a apresentação das informações abaixo descritas.

Eu, ..., fui procurado(a) pela Dra. Vivian Botelho Lorenzo da Faculdade de Medicina da Universidade Federal da Bahia, CRM 17915 sobre o projeto de pesquisa com o título acima citado.

O menor.....sob a minha inteira responsabilidade, foi convidado a participar deste projeto.

Bronquiolite é uma das principais causas de hospitalização em crianças menores que 2 anos nos países em desenvolvimento. Não há estudos que tenham investigado bem a apresentação clínica e evolução de pacientes com bronquiolite em países tropicais como o Brasil. Este estudo busca realizar esta investigação através da análise de dados do prontuário e entrevista com o responsável para coleta de dados clínicos e sociais.

Se eu concordar, minha criança poderá participar deste estudo, e as informações clínicas, radiológicas e laboratoriais registradas do caso serão utilizadas de forma anônima para esta investigação. Independente da participação no estudo a criança receberá o tratamento completo e os procedimentos padronizados clinicamente para diagnóstico e acompanhamento, bem como a qualquer momento poderei manifestar o desejo de abandono do estudo ou questionar dúvidas pelo telefone (71) 3310-1152.

CONSENTIMENTO

Autorizo a inclusão do menor _____ sob a minha responsabilidade no estudo acima referido.

Assinatura de um dos pais / guardiões: _____

Assinatura do médico: _____

Assinatura da testemunha: _____

Local: _____ Data: ____/_____/___

Uma via para ser entregue a pessoa responsável do paciente que vai participar da pesquisa e uma para ser guardada.

ANEXO 2

MODELOS DE FORMULÁRIOS PADRONIZADOS

Formulário de Avaliação Clínica Inicial

Projeto De Pesquisa: **Características clínico-radiológicas de crianças hospitalizadas com bronquiolite**

ID: ___ ___ ___ ___

Iniciais do nome{CINICIAL}_____ Prontuário{CPRONT}_____

Médico{CMEDICO}_____

Data Admissão{CFECHAC}____/____/____ Horário chegada hospital(h/min.): {CLLEGADA}_____

Data Entrevista:{CFENTREV}____/____/____ Horário Entrevista(h/min.): {CENTREV} _____

Unidade de origem: {CORIGEM}: _____

HISTÓRIA DA MOLÉSTIA ATUAL

1. Doença: (Razão para procurar cuidados médicos, máximo de 3)

{CPADEC1}

_____

{CPADEC2}

_____

{CPADEC3}

_____

2. Duração de doença (em dias): {CDURA} _____ (99) NS/NR

3. A criança está tomando algum medicamento? {CMEDIC}

   (0) Não (1) Sim, Qual: {CQUALM} _____ (9) NS/NR

4. Antes da hospitalização a criança teve ? Durante quanto tempo (dias)?

   4.1. Tosse {CTOS} (0) Não _____ (99) NS/NR

   4.2. Febre {CFIEBRE} (0) Não _____ (99) NS/NR

   4.3. Dificuldade para respirar {CDIFRESP} (0) Não _____ (99) NS/NR

4.4. Sibilos {CSILBI} (0) Não _____ (99) NS/NR

4.5 Vômitos {CVOMIT} (0) Não _____ (99) NS/NR

4.6. Outros {COUTROS} (0) Não _____ (99) NS/NR

Qual {CQUAL} _____

HISTÓRIA PATOLÓGICA

5. Quantas vezes a criança teve sibilos ou dificuldade respiratória nos últimos doze meses?

{CSIBL12} (00) Nenhuma ____ ____ (99) NS/NR

EXAME FÍSICO (na admissão hospitalar)

6. Peso (g): {CPESO} ____ ____ ____ ____ ____ (99999) NS/NR

7. Altura (cm): {CALT} ____ ____ ____ (999) NS/NR

8. Temperatura axilar (ºC): {CTEMP} ____ ____ . ____ (999) NS/NR

9. Freq Respiratória(Quieto)/min (contar 60seg.){CFREQRE1} 1a.vez ____ ____ (99) NS/NR

{CFREQRE2} .. 2a. vez ____ ____ (99) NS/NR

10. Freqüência cardíaca/min (contar 60 seg): {CFREQCAR} ____ ____ ____ (999) NS/NR

11. Estado Geral: {CESTGEN} (0) Bom (1) Regular (2) Ruim (9) NS/NR

12. Estado Sensorial: {CESTSEN} (0) Normal (1) Irritado (2) Sonolento (9) NS/NR

13. Tórax:

13.1. Tiragens: {CTIRAG} (0) Não (1) Subcostal (2) Intercostal (3) Subclavicular

13.2. Expiração prolongada: {CEXPIRA} (0) Não (1) Sim (9) NS/NR

13.3. Hipersonoridade a percussão: {CHIPER} (0) Não (1) Sim (9) NS/NR

13.4. Estridor {CSTRIDOR} (0) Não (1) Sim (9) NS/NR

14. Ausculta:

14.1. Murmúrio vesicular diminuído: {CMURM}

(0) Não (9) NS/NR

(1) Sim, Onde: {CLUGAR} _____

14.2. Roncos: {CRONCOS} (0) Não (1) Sim (9) NS/NR

14.3. Sibilos expiratórios: {CSIBILOEXP}
(0) Não (1) No final da expiração (2) ½ expiração
(3) ¾ expiração (4) Durante toda expiração (9) NS/NR

14.4. Sibilos inspiratórios: {CSIBILAINSP}
(0) Não (1) Em parte da inspiração (2)Total da inspiração

14.5. Respiratory Distress Assessment Instrument {CRDAI}:___ _____ (99) NS/NR

14.6. Crépitos: {CCREPITA}
(0) Não (9) NS/NR
(1)Sim, onde: {CLOCALC} _____

14.7. Ritmo cardíaco: {CRITMO} (0) Regular (1) Irregular (9) NS/NR

14.8. Bulhas cadíacas: {CBULHAS}
(0) Normais (9) NS/NR
(1) Anormais, onde: {CLOCALBUL}
_____

14.9. Sopro: {CSOPROC}
(0) Não (9) NS/NR (1) Sim, onde: {CLOCALSC}
_____

15. Abdomen:
15.1. Hepatomegalia: {CFIGADO} (0) Não (1) Sim (9) NS/NR

15.2. Esplenomegalia: {CBACO} (0) Não (1) Sim (9) NS/NR

15.3. Distensão Abdominal: {CDISTABD}
(0) Não
(1) Sim, descrição: {CDESCRI} _____

16. Extremidades
16.1.Cianose: {CCIANOSE} (0) Não (1) Sim central (2)Sim periférica (9) NS/NR

Formulário de Avaliação Clínica Inicial

Projeto De Pesquisa: **Características clínico-radiológicas de crianças hospitalizadas com bronquiolite**

ID ____

Iniciais criança{FINICIAL}_____Informante{FINFORM}: (1) Mãe (2) Pai (3) Avó (4) Outro

Iniciais nome informante_____ Data da Entrevista: {FDATAE} _____

Raça {FCOR}: (1) branca (2) negra (3) parda (4) indígena Data nascimento: _____

Unidade de Saúde de origem {FORIG}_____

Data de entrada na unidade de origem {FDATAORIG}_____ (dia/mês/ano)

ANTECEDENTES PESSOAIS E FAMILIARES

1.Aleitamento materno exclusivo até quantos meses de vida? {FLMEXCLUSIV}	___ ___ meses (99) NS/NR
2. Aleitamento materno misto até quantos meses de vida? {FLMMISTO}	___ ___ meses (99) NS/NR
3. Mãe biológica fumou durante a gestação? {FFUMOMAE}	(1) Não (2) Sim (99) NS/NR
4. Alguém fuma dentro de casa? Em caso afirmativo, quantos cigarros são fumados na casa diariamente? {FFUMOPAS}	___ ___ cigarros/dia (00) Nenhum (99) NS/NR
5. Mãe biológica tem ou teve história de atopia? {FATOPIAMAE}	(1) Não (2) Bronquite (3) Asma (4) Rinite (5) Eczema (99) NS/NR
6. Mãe biológica teve asma na gestação? {FASMAGEST}	(1) Não (2) Sim (99) NS/NR
7. O paciente tem dermatite atópica? {FATOPIAP}	(1) Não (2) Sim (99) NS/NR
8. A criança já teve diagnóstico de bronquiolite alguma vez? {FBRONQ}	(1) Não (2) Sim (99) NS/NR
9. Paciente possui as seguintes comorbidades? {FCOMORB}	(1) Não (2) Síndrome de Down (3) Doença pulmonar crônica------(4) Cardiopatia congênita (99) NS / NR
10. Paciente fez uso de Palivizumab? {FPALIVIZUMAB}	(1) Não (2) Sim (9) NS/NR
11. Paciente fez uso de ventilação mecânica nos primeiros 30 dias de vida? {FVMNEO}	(1) Não (2) Sim Tempo: __ __ (dias)
12. Estação do nascimento da criança {FESTACAO}	(1) Primavera (2) Verão (3) Outono (4) Inverno
13. Paciente nasceu de parto prematuro? {FPREMAT}	(1) Não (2) Abaixo de 30 sem (3) 30 – 36 sem (9) NS/NR
14. Tipo de parto {FPARTO}	(1) Cesárea (2) Normal (9) NS/NR

Formulário Socioeconômico

Projeto De Pesquisa: **Características clínico-radiológicas de crianças hospitalizadas com bronquiolite**

CASA

15. Tipo de casa: {FTIPODOM}	(1) alvenaria (2)barro (3)madeira (4)outro_____
16. De onde vem a água a ser utilizada na casa? {FAGUA}	(1) Rede pública interna (2) Rede pública externa (3) Poço interno (4) Poço ou fonte (fora da casa) (6) Outro (fora de casa) (9) NS/NR
17. Qual o destino do esgoto da casa? {FELIMINA}	(1) Rede pública de esgotos (fechada) (2) Esgoto a céu aberto (3) Fossa séptica e seca (4) Fossa negra (5) Outro (9) NS/NR
18.Qual tipo de luz da casa? {FLUZ}	(1) Elétrica (2) Querosene (3) Gás (4) Outro (9) NS/NR
19.Tem banheiro? {FBANH}	(1)Não (2)Sim, dentro de casa (3)Sim, fora de casa
20. Coleta de lixo? {FLIXO}	(1)Não (2)Sim, regularmente (3)Sim, irregularmente
21. Como e onde se prepara a comida? {FCOMIDA}	(1)Fogão a gás dentro de casa (2)Fogão a gás fora da casa (5) Outro (3)Fogão à lenha dentro da casa (4) Fogão à lenha fora da casa (9)NS/NR

22. Se forma com freqüência mofo nas paredes ou no teto da casa? {FMOHO}	(1) Não (2) Sim (9) NS/NR
23. Quantos cômodos tem a casa, incluindo a cozinha e o Banheiro sem incluir varandas ou terraços abertos? {FHABIT}	___ ___ (99) NS/NR
24. Quantas pessoas vivem no domicílio da criança? {FPERSON}	___ ___ (99) NS/NR
25. Quantas são menores de 5 anos (incluindo a criança)? {FMENORES}	___ ___ (99) NS/NR
26. Quantas pessoas dormem no mesmo quarto que a criança dorme (incluindo a criança)? {FDUERMEN}	___ ___ (99) NS/NR
27. Quem toma conta da criança? {FCONTA}	_____

Formulário Socioeconômico

Projeto De Pesquisa:**Características clínico-radiológicas de crianças hospitalizadas com bronquiolite**

28. Qual o nível de instrução da mãe (ou do guardião legal)? {FEDUCM} [consulte o código abaixo]	____		
29. Qual o nível de instrução do pai (ou do guardião legal)? {FEDUCP} [consulte o código abaixo]	____		
30. Qual é o trabalho principal da mãe (ou do guardião legal)? {FOCUPM} [consulte o código abaixo]	___ ___		
31. Qual é o trabalho principal do pai (ou guardião legal)? {FOCUPP} [consulte o código abaixo]	___ ___		
32. A casa pertence à família da criança? {FPERTEN}	(1)Não, é alugada (2)Não, é emprestada (3) Não, é invadida (4)Sim (9)NS/NR		
33. A família tem:	Não	Sim	NS/NR
TV? {FTELE}	(1)	(2)	(9)
Aparelho de som? {FSONIDO}	(1)	(2)	(9)
Geladeira? {FNEVERA}	(1)	(2)	(9)
Carro (carro)? {FCOCHE}	(1)	(2)	(9)
34.¿Qual foi a renda dos habitantes da casa no último mês (incluindo todas a formas de rendas como pensão, benefícios, ajudas, donativos, aluguéis, aposentadoria)? {FINGRESO}	R$ _____ (99999,99) NS/NR		

CÓDIGO INSTRUÇÃO

(0) Não sabe ler nem escrever (1) Primário incompleto, sabe ler ou escrever ou ambos
(2) Primário completo (3) Ginásio incompleto (4) Ginásio completo
(5) Segundo grau incompleto (6) Segundo grau completo (7) Universitário (9) NS/NR

CÓDIGO OCUPAÇÃO PRINCIPAL

(1)Dona de casa (afazeres domésticos) (2)Trabalha em casa p/ alguém de fora na sua própria casa
(3)Empregada doméstica (4) Trabalho manual não qualificado (além dos afazeres domésticos)
(5)Trabalho manual semiqualificado (6) Trabalho manual qualificado (7) Trabalho de escritório
(8)Administrador/gerente/diretor (9)Profissional de nível universitário (não administrador,gerente /diretor)
(10) Artista (11) Dono de negócio (12)Trabalhos esporádicos (trabalhador ocasional)
(13)Estudante (14)Aposentado ou pensionista (15)Outro (16)Desempregado (sem trabalho remunerado)……. (99) Não sabe/não refere

Formulário de Seguimento Hospitalar

Projeto De Pesquisa: **Características clínico-radiológicas de crianças hospitalizadas com bronquiolite**

Iniciais do nome: {Sinicial} _____ ID: {ID}_____

Registro Tratamento / Data		
Data	Início	Término
1. BRONCODILATADOR {SBRONCODIL}		
2. CORTICÓIDES {SCORTIC}		
3. SOLUÇÃO SALINA HIPERTÔNICA {SHIPERT}		
4. ADRENALINA {SADRENA}		
5. OXIGÊNIO {SOXIGEN}		
6. ANTIBIÓTICO {SATB}		
7. HIDRATAÇÃO PARENTERAL{SHIDRAT}		

RESULTADO DA HOSPITALIZAÇÃO (realizar ao final da hospitalização).

8. Resultado da hospitalização: {SRESHOSP}	(1) alta (2) alta voluntária (3) UTI (4) óbito
9. Para quem vai para UTI, desfecho na UTI {SUTI}:	(1) alta (2) óbito (99) Não de aplica
10. Data de admissão na UTI {SADMUTI}:	____/____/____
11. Data de alta da UTI {SALTAUTI}:	____/____/____
19. Data último dia de hospitalização: {SDATAUH}	____/____/____

ANEXO 3

FORMULÁRIO DE INVESTIGAÇÃO RADIOLÓGICA

Formulário Radiológico

Projeto De Pesquisa: **Características clínico-radiológicas de crianças hospitalizadas com bronquiolite**

Iniciais da criança: {RINICIAL}_____ **ID** {ID}: ___ ___

Radiologista:_____

Data da Radiografia: {RDATA} _____/_____/_____
Observações:{ROBS}_____

1. QUALIDADE {RQUALID} (1) Boa (2) Ruim

Se ruim por que?_____

2. ALTERAÇÕES PARENQUIMATOSAS **SEG (1 a 6)**

2.1. Intersticial: linear / reticular {RINTER} (1) Não (2) SD (3) ID (4) SE (5) IE ____
2.2. Alveolar {RALVEOL} (1) Não (2) SD (3) ID (4) SE (5) IE ____
2.3. Misto (intersticial/ alveolar) {RMISTO}(1) Não (2) SD (3) ID (4) SE (5) IE ____
2.4. Colapso / atelectasia {RCOLAPSO} (1) Não (2) D (3) E ____
2.5. Cavitação: abscesso {RABSCES} (1) Não (2) Apenas um (3) Muitos ____
2.6. Cavitação: pneumatocele {RNEUMAT} (1) Não (2) Apenas um (3) Muitos ____
2.7. Espessamento peri-brônquico {RESSPESA} (1) Não (2) D (3) I ____
2.8. Outro: {ROUTROAP} (1) Não (2) Sim, qual: {RQUALAP} _____
2.9 Condensação {RCONDENSA}: (1) Não (2) Sim, diâmetro {RDIAMETRO}: _____ (cm)

3. OUTRAS ALTERAÇÕES

3.1. Derrame Pleural {RDERRAME} (1) Não (2) D (3) E
3.2. Pneumotórax {RNEUMOT} (1) Não (2) D (3) E
3.3. Hiperinsuflação {RHIPERINSUF} (1) Não (2) D (3) E
3.4. Cardíaco/vascular {RCARDIO} (1) Não (2) Sim
3.5. Outro: {ROUTROA} (1) Não (2) Sim, qual: {RQUALOA} _____

4. AVALIAÇÃO RADIOLÓGICA

4.1. DIAGNÓSTCOS: {RDIAG} (1) Normal (2) Pneumonia
(3) Outro, qual: {ROTROD} _____

4.2. *Se há pneumonia*, causa provável: {RCAUSA} (1) Bacteriana (2) Não bacteriana
(3) Indeterminada

SD=*superioir direito;* ID=*inferior direito;* SE=*superior esquerdo;* IE=*inferior esquerdo*

ANEXO 4

OFÍCIO DO COMITÊ DE ÉTICA EM PESQUISA (CEP) DAS OBRAS SOCIAIS IRMÃ DULCE, APROVANDO A INVESTIGAÇÃO

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: "Características clínico-radiológicas de crianças hospitalizadas com bronquiolite"

Pesquisador: Vivian Botelho Lorenzo
Área Temática:

Versão: 2
CAAE: 41540814.3.0000.0047
Instituição Proponente: Hospital Santo Antônio/ Obras Sociais Irmã Dulce
Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.068.915
Data da Relatoria: 13/05/2015

Apresentação do Projeto:

O Projeto, foi reapresentado ao CEP, contendo todas as correções solicitadas, na formatação correta e com todos o s termos obrigatórios

Objetivo da Pesquisa:

A pesquisa tem como objetivo principal descrever as características clinicas e radiológicas de lactentes hospitalizados com bronquiolite.

Avaliação dos Riscos e Benefícios:

Foi identificado um risco em relação ao manejo dos exames radiológicos dos pacientes, risco esse que foi bem sinalizado na correção do trabalho, deixando bem definidas todas as condutas que serão

tomadas para evitar esses riscos. Os benefícios são as descrições das características clinicas uma vez que existe uma alta ocorrência de lactantes com bronquiolites, auxiliando dessa forma as condutas clínicas bem como a avaliação.

Comentários e Considerações sobre a Pesquisa:

Pesquisa de grande relevância clínica.

Considerações sobre os Termos de apresentação obrigatória:

Os termos de consentimento livre e esclarecido foi colocado no trabalho, bem como todos os documentos que são de presença obrigatória.

Recomendações:

Conclusões ou Pendências e Lista de Inadequações:

Trabalho segue sem pendências.

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

Considerações Finais a critério do CEP:

Diante do exposto, o Comitê de Ética em Pesquisa - CEP, de acordo com as atribuições definidas na Resolução CNS 466/2012 e na Norma Operacional Nº 001/2013 do CNS, manifesta-se por aprovar este projeto.

SALVADOR, 19 de Maio de 2015

Assinado por: Leila Santos de Souza (Coordenador)

ANEXO 5

NORMAS DE PUBLICAÇÃO NO PERIÓDICO “PEDIATRICS”

Pediatrics Author Guidelines

Pediatrics is the official peer-reviewed journal of the American Academy of Pediatrics.*Pediatrics* publishes original research, clinical observations, and special feature articles in the field of pediatrics, as broadly defined. Contributions pertinent to pediatrics also include related fields such as nutrition, surgery, dentistry, public health, child health services, human genetics, basic sciences, psychology, psychiatry, education, sociology, and nursing.
Pediatrics considers unsolicited manuscripts in the following categories: reports of original research, particularly clinical research; review articles; special articles; and case reports. When preparing a manuscript for *Pediatrics*, authors must first determine the manuscript type and then prepare the manuscript according to the specific instructions below.
The electronic edition of *Pediatrics* is the journal of record. Some accepted articles may also be presented in full in the print version. The editors reserve the right to determine whether an accepted manuscript will be published in the print edition in addition to the electronic edition of *Pediatrics*.

Acceptance Criteria

Relevance to readers is of primary importance in manuscript selection. The readership includes general and specialist pediatricians, pediatric researchers and educators, and child health policy-makers. *Pediatrics* receives many more high quality manuscripts than can be accommodated based on our available space. The current acceptance rate is approximately 10%. An article that is thought by the editors to be not relevant to readers, outside of scope or very unlikely to be accepted may be rejected without review. All manuscripts considered for publication are peer reviewed. Peer reviewers are selected by the editors based on their expertise in the topic of the manuscript; generally at least 2 reviews are required before a decision is rendered. Authors may suggest appropriate reviewers and may also suggest reviewers who should not review the manuscript.
Authors should carefully follow instructions for manuscript preparation, and ensure that the manuscript is proofread before submission. Manuscripts that do not adhere to the author instructions will not be considered for review. Careless preparation of a manuscript suggests careless execution of the research and therefore makes acceptance unlikely. Manuscripts are scanned for plagiarism using the latest software; if potential plagiarism is detected, the editors will contact the authors for clarification, and may also contact the authors' institution.

Submissions of original research are judged on the importance and originality of the research, scientific strength, clinical relevance, the clarity of the manuscript, and the number of submissions on the same topic. *Pediatrics* does not publish manuscripts that involve animal research.

Pediatrics accepts review articles, with preference given to systematic reviews, which may include meta-analyses. State-of-the-Art Review Articles and Perspectives are generally solicited by the editors or the associate editors for their respective sections. Special Articles reflect topics or issues of relevance to pediatric health care that do not conform to a traditional study format. Case Reports must challenge an existing clinical or pathophysiologic paradigm; provide a starting point for novel hypothesis-testing clinical research; and/or focus on topics pertinent to the pediatric generalist. Quality Reports provide a venue for manuscripts that describe the implementation and outcome of quality-improvement projects. Authors should review and follow the comprehensive reporting guidelines for a wide variety of study designs that are available at http://www.equator-network.org/home/.
Authors submitting manuscripts involving adverse drug or medical device events or product problems should also report these to the appropriate governmental agency.

Unsolicited commentaries will be considered for publication; however, most commentaries are solicited by the editors. Responses to a published article should be submitted as online comments; selected comments may be considered for publication in the journal as Letters to the Editor.

Incorrect grammar, language use, or syntax may distract readers from the science being communicated and may lead to less favorable reviews. To help reduce this possibility, we strongly encourage authors to have their manuscripts reviewed for clarity by colleagues. If the authors' native language is not English, we strongly encourage review and editing by a colleague whose native language is English or the use of an English language editing service.

Peer reviewers are asked to assess each manuscript for originality; for interest to scientists, practitioners and policy makers; for quality of the analysis; and for quality of the presentation, and are asked to assess the priority of the paper for publication. After the reviews are received, the editors may take one of the following actions: *Accept*; *Accept with Revisions*; *Reject with option to Resubmit*; or *Reject*. A rejected manuscript may not be resubmitted. A manuscript may be rejected with an option to resubmit when additional data or analyses are requested by reviewers, or when extensive revision of the text is needed. The resubmitted manuscript receives an additional round of peer review (which may include new reviewers), and the manuscript may or may not be accepted. A decision of*Accept with Revision* indicates that the editors intend to accept the manuscript contingent on adequate response to reviewers. A decision of *Accept* (which is exceedingly rare on first submission) indicates that the manuscript is ready to place into production without further modification. Decisions by the editors are final.
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Publication Ethics

Authorship. An "author" is someone who has made substantive intellectual contributions to a published study. Each author is required to meet ALL FOUR of the following criteria:

1. Substantial contribution(s) to conception and design, acquisition of data, or analysis and interpretation of data; **and**
2. Drafting the article or revising it critically for important intellectual content; **and**
3. Final approval of the version to be published, **and**
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

NOTE: Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute a sufficient basis for authorship.

All persons listed as authors must meet these criteria, and all persons who meet these criteria must be listed as authors. Although *Pediatrics* does not specifically limit the number of authors (except for Case Reports), articles submitted with an unusual number of authors invite scrutiny by editors and reviewers for clear justification for the presence of each person on the authorship list. *Pediatrics* does not permit more than one author to claim any particular position in the author list (*e.g.*, two first authors, or two senior authors).

Decide authorship issues, including the order, before submission. Except in instances where the editorial office has determined that a person does not qualify for authorship,*Pediatrics* does not allow changes to the author order, including adding or removing authors from a paper or any subsequent revisions.

Conflict of Interest and Disclosure. After a paper is accepted by *Pediatrics* for publication, all authors must submit conflict of interest and disclosure forms. *Pediatrics*adheres to the policy and uses the standardized disclosure form of the International Committee of Medical Journal Editors (ICMJE). The collection of the forms is automated within the online system.

IRB Approval. All studies that involve human subjects must be approved or deemed exempt by an official institutional review board; this should be noted in the Methods section of the manuscript.

Industry Sponsorship. *Pediatrics* generally does not accept reports of studies in which all authors are employed by a commercial entity with a financial interest in the results of the study.

Registration of Clinical Trials. All clinical trials must be registered in a World Health organization-approved Clinical Trial registry prior to enrollment of the first subject. The registry name and registration number should be included on the title page. Reports of unregistered trials will be returned to authors without review. Publication of the results of a trial that was initiated prior to the ICMJE requirement for trial registration will be considered by the editors on a case-by-case basis.

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Journal Style

All aspects of the manuscript, including the formatting of tables, illustrations, and references and grammar, punctuation, usage, and scientific writing style, should be prepared according to the most current *AMA Manual of Style*(http://www.amamanualofstyle.com).[1]

Author Listing. All authors' names should be listed in their entirety, and should include institutional/professional affiliations and degrees held.

Authoring Groups. If you choose to include an organization, committee, team, or any other group as part of your author list, you must include the names of the individuals as part of the Acknowledgments section of your manuscript. This section should appear after the main text prior to your References section. The terms "for" or "on behalf of" must also be used when referencing the authoring group in the by-line.

Titles. *Pediatrics* generally follows the guidelines of the *AMA Manual of Style* for titles. Titles should be concise and informative, containing the key topics of the work. Declarative sentences are discouraged as they tend to overemphasize a conclusion, as are questions, which are more appropriate for editorials and commentaries. Subtitles, if used, should expand on the title; however, the title should be able to stand on its own. It is appropriate to include the study design ("Randomized Controlled Trial"; "Prospective Cohort Study", etc.) in subtitles. The location of a study should be included only when the results are unique to that location and not generalizable. Abbreviations and acronyms should be avoided. The full title will appear on the article, the inside table of contents, and in MEDLINE. Full titles are limited to 97 characters, including spaces. Short titles must be provided as well and are limited to 55 characters, including spaces. Short titles may appear on the cover of the journal as space permits in any given issue.

Abbreviations. List and define abbreviations on the Title Page. Unusual abbreviations should be avoided. All terms to be abbreviated in the text should also be spelled out at first mention, followed by the abbreviation in parentheses. The abbreviation may appear in the text thereafter. Abbreviations may be used in the abstract if they occur 3 or more times in the abstract. Abbreviations should be avoided in tables and figures; if used they should be redefined in footnotes.

Units of Measure. Like many US-based journals, *Pediatrics* uses a combination of Système International (SI)[2,3] and conventional units. Please see the *AMA Manual of Style* for details.

Proprietary Products. Authors should use nonproprietary names of drugs or devices unless mention of a trade name is pertinent to the discussion. If a proprietary product is cited, the name and location of the manufacturer must also be included.

References. Authors are responsible for the accuracy of references. Citations should be numbered in the order in which they appear in the text. Reference style should follow that of the *AMA Manual of Style*, current edition. Abbreviated journal names should reflect the style of Index Medicus.

Visit: http://www.nlm.nih.gov/tsd/serials/lji.html

References

1. Iverson C, Christiansen S, Flanagin A, et al. *AMA Manual of Style*. 10th ed. New York, NY: Oxford University Press; 2007.

2. Lundberg GD. SI unit implementation: the next step. *JAMA*. 1988;260:73-76.
3. Système International conversion factors for frequently used laboratory components.*JAMA*. 1991;266:45-47.

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Clinical Trials

A study is considered a clinical trial if it prospectively assigns human subjects (whether randomized or not) to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like.

If authors report the results of a clinical trial, they must affirm that the study has been registered at www.clinicaltrials.gov or another WHO-approved national or international registry prior to the enrollment of the first subject. Information on requirements and appropriate registries is available at www.icmje.org. The trial registration number must be listed on the title page, and at the end of the abstract.
Authors are required to complete both pages of a CONSORT Form (flowchart and checklist) and submit these with their manuscript. In our submission system, these files appear under “Instructions and Forms”. For observational epidemiological studies, follow the appropriateSTROBE checklist.

- *Download a CONSORT form checklist (PDF) here*.
- *Download a CONSORT form flowchart (PDF) here*.

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Reuse of Data Sets

If a manuscript uses the same or similar data contained in previously published articles, the authors must state this in the cover letter (and provide citations to the related or possibly duplicative materials).

If a separate manuscript by the same authors using the same data set is under review or accepted but not yet published in another journal, the authors must state this in the cover letter and provide enough information to assure that the manuscript submitted to*Pediatrics* is not duplicative.

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Formatting Requirements

All submissions must adhere to the following format:

- Times New Roman font, size 12, black
- Title Page, Contributors' Statement Page, Abstract, Acknowledgments, and References should be **single-spaced**
- Only the Main Body Text should be **double-spaced**
- Main Submission Document as Microsoft Word or RTF file (no PDFs)
- Do **not** include page headers, footers, or line numbers in new submissions.
- Do **not** include footnotes within the manuscript body. Footnotes are allowed only in tables/figures.

Refer to the "Article Types" section for specific guidelines on preparing a manuscript in each category. Note in particular the requirements regarding abstracts for different categories of article.

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Title Page

The "title page" should appear first in your manuscript document, and depending on the individual needs of a paper may encompass more than one page.

Title pages for all submissions **must** include the following items (as shown in the sample Title Page):

1. **Title** (97 characters [including spaces] or fewer)
2. **Author listing.** Full names for all authors, including degrees, and institutional/professional affiliations.
3. **Corresponding Author.** Contact information for the Corresponding Author (including: name, address, telephone, and e-mail).
4. **Short title** (55 characters [including spaces] or fewer). Please note: the short title may be used on the cover of the print edition.
5. **Financial Disclosure Statement** for all authors. Disclose any financial relationships that could be broadly relevant to the work. If none, say "Financial Disclosure: The authors have no financial relationships relevant to this article to disclose."
6. **Funding source**. Research or project support, including internal funding, should be listed here; if the project was done with no specific support, please note that here. Technical and other assistance should be identified in

Acknowledgments. If your funding body has open access requirements, please contact the Editorial Office prior to submission. Pediatrics has a 12 month embargo on articles (followed by a 4 year open access period) and does not allow articles to be opened for Creative Commons or similar licenses.

7. **Conflict of Interest Statement** for all authors. If none, say “Potential Conflicts of Interest: The authors have no conflicts of interest relevant to this article to disclose.”
8. **If applicable, Clinical Trial registry name and registration number**. We adhere to ICMJE guidelines, which require that all trials must be registered with ClinicalTrials.gov or any other WHO Primary registry.
9. **Abbreviations**. List and define abbreviations used in the text. If none, say "Abbreviations: none".
10. **Table of Contents Summary.** This is required for all articles with abstracts. This brief summary is limited to 25 words. For accepted manuscripts, this will appear under the author names in the table of contents to give the reader a brief insight into what the article is about. It should entice the reader to read the full article. For example: *"Through linkage of state Medicaid and Child Protective Services databases, this study captures similarities and differences in health care expenditures based on a history of child maltreatment."*
11. For Regular Article submissions, include the **“What’s Known on This Subject; What This Study Adds”** (see below under article type for description). This is not needed for any other article type.

If a title page does not include all of the above items, the submission may be returned to the authors for completion.

- **Download and view a sample Title Page (PDF)** here.

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Contributors' Statement Page

All submissions must contain a Contributors’ Statement Page, directly following the Title Page. Manuscripts lacking this page will be returned to the authors for correction.

All persons designated as authors should qualify for authorship (see "Publication Ethics" above), and all those who qualify should be listed. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. The Contributors' Statement Page should list the authors and specify the contribution(s) made by each individual. If multiple individuals have identical contributions they may be listed together; do not list an author more than once.

You must follow the required format shown in this example when creating your Contributors’ Statement Page or your manuscript will be returned for correction. Each author should only appear once. Use names, not initials. If multiple authors have identical contributions, you can list them on the same line; otherwise, list each author separately.

Contributors' Statement:

Dr Smith conceptualized and designed the study, drafted the initial manuscript, and approved the final manuscript as submitted.

Drs Jones, Lee, and Weber carried out the initial analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Ms Green designed the data collection instruments, and coordinated and supervised data collection at two of the four sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Note: Contributors who do not meet the criteria for authorship (such as persons who helped recruit patients for the study, or professional editors) should be listed in an Acknowledgments section placed after the manuscript's conclusion and before the References section. Because readers may infer their endorsement of the data and conclusions, these persons must give written permission to be acknowledged. These permissions do not need to be submitted with the manuscript unless requested by the editors.

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Word Count

To determine article length, count the body of the manuscript (from the start of the Introduction to the end of the Conclusion). The title page, contributors' statement page, abstract, acknowledgments, references, figures, tables, and multimedia are not included.

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Figures, Tables, and Supplementary Material

Figures

Authors should number figures in the order in which they appear in the text. Figures include graphs, charts, photographs, and illustrations. Each figure must include a legend (placed on the figure itself or as a list appearing after the References) that does not exceed 50 words. Abbreviations previously expanded in the text are acceptable. If a figure is reproduced from another source, authors are required to obtain permission from the copyright holder, and proof of permission must be uploaded at the time of submission.

Figure arrays should be clearly labeled, preassembled, and submitted to scale. Figure parts of an array (A, B, C, etc.) should be clearly marked in capital letters in the upper left-hand corner of each figure part.

Technical requirements for figures: The following file types are acceptable: TIFF, PDF, EPS, and PNG. Color files must be in CMYK (cyan, magenta, yellow, black) mode.
Style for figures: Readers should be able to understand figures without referring to the text. Avoid pie charts, 3-dimensional graphs, and excess ink in general. Make sure that the axes on graphs are labeled, including units of measurement, and that the font is large enough to read. Generally delete legends or other material from the graph if it makes the picture smaller. Color graphs should be interpretable if photocopied in black and white.
Pediatrics cannot accept Excel or PowerPoint files for any part of your submission.

Tables

Tables should be numbered in the order in which they are cited in the text and include appropriate headers. Tables should not reiterate information presented in the Results section, but rather should provide clear and concise data that further illustrate the main point. Tabular data should directly relate to the hypothesis. Table formatting should follow the current edition of the *AMA Manual of Style*.
Style for tables: Tables should be self-explanatory. Avoid abbreviations; define any abbreviations in footnotes to the table. Avoid excess digits and excess ink in general. Where possible, rows should be in a meaningful order (e.g., descending order of frequency). Provide units of measurement for all numbers. In general, only one type of data should be in each column of the table.
Presentation of Numbers and Statistics

- Results in the abstract and the paper generally should include estimates of effect size and 95% confidence intervals, not just P- values or statements that a difference was statistically significant.
- Statistical methods for obtaining all P-values should be provided
- Units of independent variables must be provided in tables and results sections if regression coefficients are provided
- Authors should avoid expressing effect sizes in the form of highly derived statistics.

Equations should be typed exactly as they are to appear in the final manuscript. The following table, adapted from the guidelines for authors for the *Annals of Internal Medicine*by editors of *Medical Decision Making*, shows how to present certain percentages and some statistical measures:

Reporting:	Details:
Percentages	Report percentages to one decimal place (i.e., xx.x%) when sample size is greater than or equal to 200. To avoid the appearance of a level of precision that is not present with small samples, do not

	use decimal places (i.e., xx%, not xx.x%) when sample size is less than 200.
Error Measures	Report confidence intervals, rather than standard errors, when possible. Use "mean (error measures)" rather than "mean ± error measure" notation.
P values	Except when one-sided tests are required by study design, such as in noninferiority trials, all reported P values should be two-sided. In general, P values larger than 0.01 should be reported to two decimal places, those between 0.01 and 0.001 to three decimal places; P values smaller than 0.001 should be reported as P [is less than sign]0.001. Notable exceptions to this policy include P values arising in the application of stopping rules to the analysis of clinical trials and genetic-screening studies.
"Trend"	Use the word trend when describing a test for trend or dose-response. Avoid the term "trend" when referring to p-values near but not below 0.05. In such instances, simply report a difference and the confidence interval of the difference (if appropriate) with or without the p-value.

Supplemental Information

Authors may wish to include additional information as part of their article for inclusion in the online edition of *Pediatrics*. References to any online supplemental information must appear in the main article. Such supplemental information can include but are not limited to additional tables, figures, videos, audio files, slide shows, data sets (including qualitative data), and online appendices. If your study is based on a survey, consider submitting your survey instrument or the key questions as a data supplement. Authors are responsible for clearly labeling supplemental information and are accountable for its accuracy. Supplemental information will be peer reviewed, but not professionally copyedited.

Videos

Pediatrics encourages the submission of videos to accompany articles where relevant. Links can be placed in the article for use when it is accessed electronically. All videos must adhere to the same general permission rules that apply to figures (i.e.: parental consent when a patient is identifiable).

All videos should be submitted at the desired reproduction size and length. To avoid excessive delays in downloading the files, videos should be no more than 6MB in size, and run between 30 and 60 seconds in length. In addition, cropping frames and image sizes can significantly reduce file sizes. Files submitted can be looped to play more than once, provided file size does not become excessive. Video format must be either .mov or .mp4.

Authors will be notified if problems exist with videos as submitted, and will be asked to modify them if needed. No editing will be done to the videos at the editorial office—all changes are the responsibility of the author.

Video files should be named clearly to correspond with the figure they represent (i.e., figure1.mov, figure2.mp4, etc.). Be sure all video files have filenames that are no more than 8 characters long and include the suffix ".mov" or ".mp4." A caption for each video should be provided (preferably in a similarly named Word file submitted with the videos), stating clearly the content of the video presentation and its relevance to the materials submitted.

IMPORTANT: One to four traditional still images from the video **must** be provided. These still images may be published with the article and will act as thumbnail images in the electronic edition that will link to the full video file. Please indicate clearly in your text whether a figure has a video associated with it, and be sure to indicate the name of the corresponding video file. A brief figure legend should also be provided.

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Regular Article

Abstract length: 250 words or fewer (structured, as noted below)
Article length: 3,000 words or fewer
Regular Articles are original research contributions that aim to inform clinical practice or the understanding of a disease process. Regular Articles include but are not limited to clinical trials, interventional studies, cohort studies, case-control studies, epidemiologic assessments, and surveys. Components of a Regular Article include:

- **What's Known on This Subject; What This Study Adds**

These brief summaries are each limited to 40 words. Please use precise and accurate language in paragraph form (i.e., not bullet points). For manuscripts accepted as Regular Articles, these summaries will become a highly visible part of your published paper, with prominence on the first page. Moreover, these summaries may be highlighted and

presented in other areas of the journal. It is therefore paramount that you use language of the same caliber as the rest of your paper.

- **Structured Abstract (four paragraphs with headings in boldface type; single-spaced)**

The abstract should consist of: Background (or Objectives, or Background and Objectives), Methods, Results, and Conclusions. The Objective should clearly state the hypothesis; Methods, inclusion criteria and study design; Results, the outcome of the study; and Conclusions, the outcome in relation to the hypothesis and possible directions of future study.

- **Body of Article**

For the body of your article, follow this general outline:

- Introduction

A 1- to 2-paragraph introduction outlining the wider context that generated the study and the hypothesis.

- Patients and Methods

This section should detail inclusion criteria and study design to ensure reproducibility of the research. All studies that involve human subjects must be approved or deemed exempt by an official institutional review board; this should be noted here.

- Results

This section should give specific answers to the aims or questions stated in the introduction. The order of presentation of results should parallel the order of the methods section.

- Discussion

The section should highlight antecedent literature on the topic and how the current study changes the understanding of a disease process or clinical situation, and should include a section on the limitations of the present study.

- Conclusion

A brief concluding paragraph presenting the implications of the study results and possible new research directions on the subject.

General submission instructions (including cover letter, title page requirements, contributors' statement page, journal style guidance, and conflict of interest statements) apply to Regular Articles.

- **Download and view a sample Regular Article manuscript (PDF) here.**

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Case Report

Abstract length: 250 words or fewer (unstructured: no headings, run in a single paragraph)
Article length: 1,600 words or fewer
Author limit: Seven (7) authors or fewer
Case Reports highlight unique presentations or aspects of disease processes that may expand the differential diagnosis and improve patient care. In general, case reports will include 10 cases or fewer. For a manuscript to be considered a Case Report, it must meet at least one of the following three criteria:

1. Challenge an existing clinical or pathophysiologic paradigm.
2. Provide a starting point for novel hypothesis-testing clinical research.
3. Focus on topics pertinent to the pediatric generalist, allowing pediatrics colleagues to provide improved care. (Manuscripts meeting this criterion will be prioritized over other submissions.)

Case Reports should consist of an unstructured abstract that summarizes the case(s), a brief introduction (recommended length, 1-2 paragraphs), a section that details patient presentation, initial diagnosis and outcome, as well as a discussion that includes a brief review of the relevant literature and describes how this case brings new understanding to the disease process.

Authors may find the criteria for case reports as contained in the CARE guidelines useful in preparing their manuscript.
The general submission instructions (including cover letter, title page, contributors' statement page, journal style guidance, and conflict of interest statements) also apply to Case Reports.

- **Download and view a sample Case Report manuscript (PDF) here.**

References

1. J of Clin Epidem. Vol. 67, 1, pg 46-51

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Commentary

Abstract length: no abstract
Article length: 400 to 800 words

Commentaries are opinion pieces consisting of a main point and supporting discussion. These contributions usually pertain to and are published concurrently with a specific article; the commentary serves to launch a broader discussion of a topic. Commentaries may address general issues or controversies in the field of pediatrics.

Commentaries are solicited by the editors. Unsolicited opinion pieces are published asPediatrics Perspectives. **Responses to published articles should be submitted as online Comments.**
The general submission instructions (including cover letter, title page, contributors' statement page, journal style guidance, and conflict of interest statements, also apply to commentaries).

- **Download and view a sample Commentary manuscript (PDF) here.**

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Diagnostic Dilemmas and Clinical Reasoning

Abstract length: 250 words or fewer (unstructured: no headings, run in a single paragraph)
NOTE: ***Abstracts must not reveal the final diagnosis***
Article length: 3,500 words or fewer
Author limit: Seven (7) authors or fewer
Diagnostic Dilemmas and Clinical Reasoning articles are interactive case studies, with comments inserted by generalists and specialists asked to comment on the case, simulating what might occur in an oral case presentation.

The goal of this feature is to present clinical cases that are diagnostic dilemmas and that involve the input of both generalists and subspecialists who comment as segments of the case are presented, similar to Ethics Rounds feature articles. Each case presented should generate a dialogue about unusual or complicated disease processes and stimulate discussion about clinical reasoning. The initial case description should include the chief complaint and enough information to generate an initial differential diagnosis. Clinical details should alternate with input from generalists and from subspecialists as the case evolves and as the ultimate diagnosis is made. The case should culminate with a brief (750–1,000) summary of the key points of the case and of the ultimate diagnosis. Use of media, such as radiology studies, pathology specimens, or video clips as, is encouraged to complement the discussion.

- Authors may come from any institution. The case may be one that was discussed in the hospital's teaching rounds (many hospitals have sessions entitled Case Conference, CPC, Professorial Rounds, or something similar).
- The authors may choose to solicit experts on their own and/or to write the entire manuscript as a team. Authors may also choose to submit a case to our journal, and the editors will solicit experts to comment on the case.

- Manuscripts will be submitted for peer review, with acceptance contingent on positive peer reviews and input from the editorial board.
- All cases should be real cases. Written consent from the family and from the providers who cared for the patient is required before a manuscript can be published. (The consent can be in the form of an email.) On submission, authors must attest that they have written consent from the family. Instances where there are extenuating circumstances in which family consent may be problematic will be handled on a case-by-case basis. If a case is published without family consent, enough elements should be changed so that the patient and family are not recognizable. If the case is too unique to be disguised, then those involved in the care of the patient cannot be authors, and the published paper must have no link to the institution where the case took place.
- The requirements of local institutional review boards should be followed.
- Authorship: All authors must fulfill the ICJME criteria for authorship.

Questions can be addressed to Rachel Moon, M.D., section editor for Diagnostic Dilemmas and Clinical Reasoning, at RYM4Z@hscmail.mcc.virginia.edu.

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Ethics Rounds

Ethics Rounds present discussions of cases that illustrate ethical dilemmas in patient care, research, or administration. Authors who have a case that raises ethical issues and who want to submit a paper for Ethics Rounds should email Assistant Editor John Lantos (jlantos@cmh.edu).

The general submission instructions (including cover letter, title page, contributors' statement page, journal style guidance, and conflict of interest statements, also apply to Ethics Rounds).

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Family Partnerships

Abstract length: No abstract
Article length: 2,000 words or fewer
Author limit: Four (4) authors or fewer
Reference limit: 10 references or fewer

Pediatrics is interested in publishing articles that reflect the joint perspective of patients, families, and the health care professionals taking care of the family and child. These articles should be written collaboratively and reflect their shared thoughts about a topic related to children's health care. Examples of topics that articles could address include shared decision-making, use of the Internet or other technologies to improve care, family-centered rounds, health care disparities, or issues related to medical education. These are just examples; the Executive Editorial Board would be willing to consider any relevant manuscript as long as it represents the voices of patients/families and healthcare providers. The manuscript should reflect a partnership amongst the authors.
If an individual patient's story is to be shared as a narrative, the article should not just focus on that patient's story and what went right or wrong, but reflect a broad perspective so that the lessons learned can be generalizable to others. The audience for these articles will primarily be health care professionals, but these articles will also be made free to the public so everyone can potentially benefit from reading the manuscript.

Specific points to consider: It would be acceptable for authors to write sections individually from their unique viewpoint. The article should contain a jointly written introduction and conclusion to ensure an overall collaborative voice.

Specific questions may be directed to Lewis First, MD, editor in chief of *Pediatrics* at lewis.first@uvm.edu.
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Monthly Feature

Abstract length: no abstract
Article length: 1,200 words or fewer
The Monthly Feature column offers an opportunity to gain insight into aspects of our field: past, present, and future. Alternating monthly, the column will provide ongoing updates from four standing groups: (1) Global Health; (2) the Council on Medical Student Education in Pediatrics (COMSEP); (3) the Section on Pediatric Trainees (SOPT); and (4) the Historical Archives Advisory Committee for the AAP.

While many of the Monthly Features are invited, any queries or proposals should be directed to the editors of their respective columns: Jay Berkelhamer, MD (jberkelhamer@aap.net) for Global Health; Robert Dudas, MD (rdudas@jhmi.edu) for COMSEP; Kristin Schwarz, MD (SOPTpediatrics@aap.org) for SOPT; and Jeffrey Baker, MD (jeffrey.baker@dm.duke.edu) for the AAP Historical Archives Advisory Committee.
The general instructions regarding submission (including cover letter, title page requirements, contributors' statement page, journal style guidance, and conflict of interest statements) also apply to Monthly Features.

SOPT *Pediatrics* Monthly Feature

This section publishes insightful updates and opinion articles on all aspects of pediatrics, written from the unique perspective of the trainee.

The goal of the editorial board of the AAP Section on Pediatric Trainees (SOPT) Monthly Feature is to work with trainee authors to develop thoughtful and timely articles related to pediatrics that appeal to everyone from medical students to well-seasoned practitioners. Topic content that focuses on training in pediatric medicine is preferred, but a range of other content areas will be considered. Topics should be relevant to students, residents and fellows, but also of general interest to the readership of *Pediatrics*. The issue being discussed must be *uniquely viewed from the trainee's perspective*, not from that of the supervisor, educator or attending.
A few questions to consider when writing include: Why is the issue important? What is causing the problem to persist? How might it be corrected? How is this issue important to pediatricians in training? How might it affect pediatric medicine in the future? We are looking for authors who take a stand and support it with evidence from the literature, and for articles with an "edge". A narrative thread that engages the reader and includes observations drawn from the author's clinical and professional experiences is recommended.

Points To Consider:

- The first author must be a resident, fellow, or medical student, but does not need to be a SOPT member. Collaborating authors at any career level are welcome.
- One article will be published up to every 4 months as the Monthly Feature in *Pediatrics*. High quality articles not selected for publication in *Pediatrics* will have other publication opportunities through SOPT.
- Word Limit: 1,200 words
- Reference Limit: 10 references
- Author limit: 4 authors

Specific questions may be directed to Section Editor Kristin Schwarz, MD, atSOPTpediatrics@aap.org

Historical Perspectives Monthly Feature

The historical perspectives Monthly Feature is intended to attract concise and engaging historical articles of interest to clinicians. These articles are more akin to a commentary than an original article, and cannot be expected to provide the kind of in-depth analysis expected in professional historical journals. The content may draw from original research or develop a particular insight from existing scholarship. These articles are typically qualitative, and not divided into the conventional sections appropriate for original scientific contributions. Articles are peer reviewed by professionals with both medical and historical expertise.

Consider the following points as you develop your article:

- Frame a clear question or central argument. Historical articles do not just recite chronologies or lists of persons and dates, they investigate a particular question and develop an argument, backed up by sources.
- Set your article in historical context—in its own time and place. Don't judge the past by the standards of the present. Secondary sources can be very helpful. Search for articles or books that can provide historical background. If you are not familiar with historical scholarship, see "resources" on the Pediatric History Center page of the American Academy of Pediatrics Web site.
- Will your article be of interest to pediatricians (the main audience for Pediatrics)? Is the writing clear, organized, and easy to follow?
- Is it original? Authors who have completed longer historical projects may wish to submit a short article related to a bigger project that may attract new readers to their other scholarship.
- Are assertions in the paper accurate and supported with appropriate references? Most articles will have about 10 to 20 references. Follow the AMA Manual of Style. Specific references in longer sources may require page numbers to be noted in parentheses.

  Primary sources (produced by participants or contemporaries) are preferred when possible. The goal is to provide enough information that a reader could independently confirm the assertions in the text. Secondary sources (books and reviews written by historians or physician-historians) should be cited to provide context (to frame the story in space and time) and scholarly background.

Specific questions may be directed to Section Editor Jeffrey P. Baker, MD, PhD, (jeffrey.baker@dm.duke.edu.)
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Pediatrics Perspectives

Abstract length: no abstract
Article length: 1,200 words max
Author limit: Three (3) authors or fewer
Figure/table: No more than one (1) figure or table allowed
Pediatrics Perspectives are unsolicited opinion pieces that focus on issues of policy, public health, or other research and clinical topics related to infant, child, and/or adolescent health. These articles should be 1200 words maximum, be written by no more than three authors and have no more than 7 references. Pediatrics Perspectives may include one figure or one table.

The general instructions regarding submission (including cover letter, title page requirements, contributors' statement page, journal style guidance, and conflict of interest statements) also apply to Pediatrics Perspectives.

- **Download and view a sample Pediatrics Perspectives manuscript (PDF) here.**

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Quality Report

Abstract: 250 words or fewer (structured: see Regular Articles)
Article: 3,000 words or fewer
Supplemental content: appropriate for figures, tables, multimedia, measurement tools
Quality Reports are intended to add to our understanding of how to improve the quality, safety, and value of child health care. Submissions that describe replicable and sustainable initiatives undertaken and evaluated using rigorous quality-improvement methods will be given highest priority. Uncontrolled pre-post studies will be given low priority. Reports of clinical trials to assess whether interventions are effective and reports of the development and testing of improvement-related tools to assess validity and reliability are better suited as Regular Articles. Pilot projects of interventions to improve quality of care may be acceptable if there are important lessons that can inform further quality-improvement efforts. If you are uncertain whether your manuscript is appropriate as a Quality Report, e-mail Dr. John Patrick T. Co, MD, MPH, FAAP (jco@partners.org).
Authors should review their institution's guidelines around quality improvement projects. If the authors did not obtain IRB approval and/or formal IRB exemption after review, they must state how the project described in their submission met criteria for not being reviewed by their institution's IRB.

One of the hallmarks of a Quality Report is a description of tests of change over time. Priority will be given to those manuscripts that have multiple tests of change. Reports should provide descriptions of the change process, whether successful or unsuccessful, and include insights regarding why planned interventions did or did not lead to improvement. Figures are helpful in illustrating changes over time (e.g., run charts, statistical process control charts). These figures should be annotated to show when the interventions were implemented.

Descriptions of initiatives undertaken by collaborative quality-improvement networks should include both description of overall collaborative findings and key lessons learned (both positive and negative) from individual sites in relation to improvement approaches and outcomes. Submissions that have uniform outcome assessment across sites will be given higher priority.

Authors are expected to generally follow the Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) Guidelines for reporting their quality improvement projects. The SQUIRE guidelines are described in detail on the SQUIRE website at www.squire-statement.org. Format the submission to follow the IMRaD (Introduction, Methods, Results, Discussion) format consistent with the rest of the journal.
The SQUIRE guidelines suggest specific areas that need to be addressed in each section, with recognition that every report will have different areas of emphasis.

Some key aspects of SQUIRE 2.0 include:

Introduction: Why did you start?
Summarizes problem description, available knowledge, rationale, and specific aims.

Methods: What did you do?
Describes context, intervention(s), study of the intervention(s), measures (e.g., outcomes, balance measures, costs), analysis, and ethical considerations. The methods section should have information about how any run/control charts were developed and analyzed (e.g., rules governing changes in center lines and confidence intervals). If costs are included in the measures, the method of cost assessment and evaluation should be clear and rigorous.

Results: What did you find?
Describes the actual course of the intervention, including contextual elements, as well as changes in process and outcomes (including balance measures and any cost assessment). The results should include a description of and interpretation of any chart findings.

Discussion: What do the findings mean?
Begins with a summary of findings in relation to specific aims/key measures, followed by interpretation of findings in relation to interventions, existing literature, expected outcomes (including the effect of context), and cost information, if available. The discussion should conclude with discussion of limitations, and conclusions/next steps.

The general instructions to authors regarding submission (including cover letter, title page requirements, contributors' statement page, journal style guidance, and conflict-of-interest statements) also apply to Quality Reports.

- **Download and view a sample Quality Reports manuscript (PDF) here.**

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Review Article, Systematic Reviews and Meta-Analyses

Abstract length: 250 words or fewer (structured or unstructured, depending on review type)
Article length: 4,000 words or fewer
Review Articles combine and/or summarize data from the knowledge base of a topic. Preference is given to systematic reviews and meta-analyses of clearly stated questions over traditional narrative reviews of a topic. Both types of review require an abstract; the abstract of a narrative review may be unstructured (no headings, run in a single paragraph). **See below for abstracts of systematic reviews and meta-analyses.**

The general instructions regarding submission (including cover letter, title page requirements, contributors' statement page, journal style guidance, and conflict of interest statements) also apply to Review Articles.

Systematic Reviews and Meta-Analyses

Reports of systematic reviews and meta-analyses should use the PRISMA statement (http://www.prisma-statement.org/) as a guide, and include a completed PRISMA checklist and flow diagram to accompany the main text. Blank templates of the checklist and flow diagram can be downloaded from the PRISMA Web site (http://www.prisma-statement.org/statement.htm).
Structured abstracts for systematic reviews are recommended. Headings should include: Context, Objective, Data Sources, Study Selection, Data Extraction, Results, Limitations, and Conclusions (see Iverson et al[1[pp22-23]]).

- **Download and view a sample Narrative Review manuscript (PDF) here.**
- **Download and view a sample Systematic Review/Meta-analysis manuscript (PDF)here.**

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Special Article

Abstract length: 250 words or fewer (unstructured: no headings, run in a single paragraph)
Article length: 4,000 words or fewer
Special Articles reflect topics or issues of relevance to pediatric health care that do not conform to a traditional study format. Special Articles may address broad social and ethical issues, scientific methodology, or other scholarly topics, and may include reports from consensus committees and working groups. These articles should not include specific guidelines or recommendations for practice. Guidelines and recommendations from groups outside of the AAP must be approved through the AAP and may be published at the discretion of the AAP in the Academy's dedicated section of the journal (see below).

The general instructions regarding submission (including cover letter, title page requirements, contributors' statement page, journal style guidance, and conflict of interest statements) apply to Special Articles.

- **Download and view a sample Special Article manuscript (PDF) here.**

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State-of-the-Art Review Article

Abstract length: 250 words or fewer (unstructured: no headings, run in a single paragraph)
Article length: 4,000 words or fewer
State-of-the-Art Review Articles provide a comprehensive and scholarly overview of an important clinical subject with a principle focus on developments in the past 5 years. State-of-the-Art Articles are usually invited. If you are interested in submitting a State-of-the-Art Review, please email Associate Editor Dr. Steven Zeichner(zeichner@virginia.edu) and copy Publications Editor Mark Plemmons (mplemmons@aap.org).
The general instructions regarding submission (including cover letter, title page requirements, contributors' statement page, journal style guidance, and conflict of interest statements) also apply to State-of-the-Art Reviews.

- **Download and view a sample State-of-the-Art Review manuscript (PDF) here.**

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"From the American Academy of Pediatrics"- For AAP Use Only

The editorial process and manuscript selection for publication in *Pediatrics* are separate from the processes and materials that are produced or endorsed by the AAP. These materials are published in print and online in a visually distinct section of the journal. AAP Clinical Practice Guidelines, Policy Statements, Clinical Reports and other AAP-produced or endorsed materials that are intended to help guide practice are highly valued by membership, and are published in this section of the journal at the sole discretion of the AAP. Content produced or endorsed by the AAP is reviewed and approved outside of the*Pediatrics* editorial process.
Do *not* select an AAP Clinical Report, AAP Policy Statement, or other AAP article type for your submission. These are reserved for internal AAP use only.
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Cover Letter

The cover letter serves to assure the editors that the article and the authors meet the conditions of publication. A brief paragraph that provides any additional information that may be useful to the editors is welcome, but keep in

mind that the need for a long cover letter may indicate that the article does not speak for itself. Reviewers will not see the cover letter; cover letters are not a Title Page.

All authors are required to affirm the following in their cover letter (in Step Five: Details & Comments as described here) before their manuscript is considered:

- That the manuscript is being submitted only to *Pediatrics*, that it will not be submitted elsewhere while under consideration, that it has not been published elsewhere, and, should it be published in *Pediatrics*, that it will not be published elsewhere—either in similar form or verbatim—without permission of the editors. These restrictions do not apply to abstracts or to press reports of presentations at scientific meetings.
- That all authors are responsible for reported research.
- That all authors have participated in the concept and design; analysis and interpretation of data; drafting or revising of the manuscript, and that they have approved the manuscript as submitted.

If a manuscript uses the same or similar data contained in previously published articles, the authors must state this in the cover letter (and provide citations to the related or possibly duplicative materials).

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Getting Started

1. Go to Manuscript Central (https://mc.manuscriptcentral.com/pediatrics) and sign in, or click the "Register here" option if you are a first-time user.
2. Sign in and select "Author Center."
3. After logging in, click the blue star displaying "Click here to submit a new manuscript."

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Submitting Your Manuscript

You must complete each step to submit your manuscript into Manuscript Central. Use proper capitalization - Do not use all CAPS, or all lowercase, or HTML. Click on the "Save and Continue" button on each screen to save your work and advance to the screen.

Step One: Type, Title, and Abstract. Select your article type and enter the title, short title, and abstract. Review your article type earlier in these guidelines for further details on abstracts. The Table of Contents Summary and the What's Known/What's Added summaries are required for Regular Articles only (if this does not apply, input "n/a" to skip).

For published articles, the Table of Contents Summary will appear under the author names in the table of contents to give the reader a brief insight into what the article is about. It should entice the reader to read the full article. Summarize your article in 25 words or less. For example: "Through linkage of state Medicaid and Child Protective Services databases, this study captures similarities and differences in health care expenditures based on a history of child maltreatment."

Step Two: Attributes. Enter the appropriate keywords/categories for your submission.
Step Three: Authors & Institutions. All authors must be listed here. Before adding a new author, check to see if the author is already in the database (enter the author's e-mail address and click "Find"). It is important that these e-mails be up-to-date, since copyright forms and other important correspondence will sent to them if the article is provisionally accepted. If the author is found, their information will be automatically filled out for you. For an author that is not found, enter the information, then click "Add to My Authors."
Be sure your author listing is correct. Except in instances where the editorial office has determined that a person does not qualify for authorship, Pediatrics does not allow changes to the author order, including adding or removing authors from a paper or any subsequent revisions.

Step Four: Reviewers & Editors. To indicate any preferred and non-preferred reviewers, enter the reviewer's information and click the appropriate designation button.
Step Five: Details & Comments (with Cover Letter). Input or attach your cover letter here, including all required affirmations. This step also allows you to check a box indicating that, should your manuscript not be accepted by Pediatrics, you would like it transferred to*Hospital Pediatrics* for consideration.
Transfers to *Hospital Pediatrics:* If your manuscript is not accepted by *Pediatrics* and the editors feel the topic is appropriate for *Hospital Pediatrics,* you will receive an email indicating that your manuscript is ready to transfer, along with additional instructions on how to proceed. Please note that if your manuscript has been reviewed by *Pediatrics*reviewers, those reviews will transfer to *Hospital Pediatrics* along with your manuscript. Your manuscript will undergo additional peer review by *Hospital Pediatrics* reviewers and editors. If you have any questions about this transfer, please contact the editorial office atPediatricsEditorial@aap.org.
Step Six: File Upload. In this step, you will be prompted to upload your files.
To designate the order in which your files appear, use the drop-downs in the "order" column. The first file should be your manuscript in .RTF or .DOC format (this includes the Title Page(s), followed by the Contributors' Statement Page, a copy of the Abstract, the body of the article, any Acknowledgments, References, and any legends for tables/figures/etc. Do not split your manuscript into multiple files.) Include any other files below your manuscript file.

Step Seven: Review & Submit. Review your submission (in PDF and HTML formats) before sending it to the editors. Click the “Submit” button when you are done reviewing.

You may halt a submission at any step and save it to submit later. After submission, you will receive an email confirmation. You can log-on to Manuscript Central any time to check the status of your manuscript. The editors will inform you via email once a decision has been made.

Open Access

Pediatrics has a 12 month embargo on articles (followed by a 4 year open access period) and does not allow articles to be opened for Creative Commons or similar licenses. If your funding body has open access requirements, please contact the Editorial Office prior to submission.

Copyright Forms

At the time of provisional acceptance, all authors will receive instructions for submitting an online copyright form. No paper will be scheduled for an issue and move onto production until all authors have completed their copyright forms.

We do not accept copyright forms via fax, e-mail, or regular mail unless a technical problem with the online author account cannot be resolved. Every effort should be made for authors to use the online copyright system. Corresponding authors can log in to the submission system at any time to check on the status of any co-author's copyright form.

All accepted manuscripts become the permanent property of the American Academy of Pediatrics and may not be published elsewhere, in whole or in part, without written permission from the Academy (with certain exceptions: authors retain certain rights including the right to republish their work in books and other scholarly collections). Authors who were employees of the United States Government at the time the work was done should so state on the copyright form. Articles authored by federal employees remain in the public domain.

Note: *Pediatrics* cannot accept any copyright that has been altered, revised, amended, or otherwise changed. Our original electronic copyright form must be used as is.

Disclosure Forms

At the time of provisional acceptance, all authors are required to submit a disclosure form.*Pediatrics* adheres to ICMJE policy and uses an online disclosure e-form in order for authors to do so. The collection of forms is

automated within the online submission system.**Note: *Pediatrics* cannot accept any disclosure that has been altered, revised, amended, or otherwise changed. Our original electronic disclosure form must be used as is.**

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Reader Comments

Pediatrics welcomes reader comments on published articles. To submit a comment, click on the "Comments" tab that appears with each article, then click on "Submit a Comment." Comments submitted via e-mail or regular mail will not be considered for posting or returned.
The editors review all comments submitted online; comments are not peer-reviewed. The decision regarding whether to post a comment is at the sole discretion of the editors; all editorial decisions are final. Once a comment has been posted on the website, you will not have the right to have it removed or edited. *Pediatrics* shall, however, be able to remove any comment at its discretion.
Note: Comments are online responses only. They are not published, nor cited in Medline/PubMed.
Be sure to follow all of the consideration criteria below; you will **not** be able to modify your comment after submission.

Consideration Criteria for Posting of Reader Comments:

- To ensure timely discussion, comments are limited to articles published within the previous 6 months.

- The editors will consider posting comments that contribute substantially to the discussion of the original article to which the reader is responding. All editorial decisions are final.
- We will consider posting comments from all readers regardless of professional background. Decisions about posting are made based on the content, not the professional background of the respondent.
- *Pediatrics* does not allow multiple comment submissions from the same reader for a particular article
- Comments must be in English and not exceed 500 words, not including references.
- Comments must have no more than 3 authors.
- Comments must have no more than 5 references.
- Comments cannot include web links. We will remove any web links from responses chosen for posting.
- *Pediatrics* will not post comments that are, or appear in the opinion of the editor to be obscene, libelous, incomprehensible, defamatory, or rude; that include advertising, address personal health questions about the respondent or family members; or that give personal health information about identifiable individuals.
- In general, we do not edit reader comments prior to or after posting. The editors may, at their discretion, modify submitted comments either before or after posting the comment.

How to Submit Reader Comments for Consideration

1. Locate the article online using the “Current Issue” or “eArchives” links.

2. To respond to the article, click the “Comments” tab. Pediatrics only allows one comment per author per article.

3. Click on the "Submit a Comment" bar.

4. Compose your comment and add your author information. (Note that no HTML tags are allowed. Lines and paragraphs are automatically recognized. The
 line break, paragraph and close paragraph tags are inserted automatically. If paragraphs are not recognized simply add a couple of blank lines.)

5. Click "Submit".

How to View Comments

1. To read comments on an article that have been posted, click on the "Comments" tab.

2. Recent comments also located on the home page in the "Recent Comments" box.

How to Cite a Comment

Example:
Quartermain, Michael D., Prenatal Diagnosis Data [comment], Pediatrics (October 27, 2015), http://pediatrics.aappublications.org/content/136/2/e378.comments#prenatal-diagnosis-data (accessed November 2, 2015).
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Letters to the Editor

Selected comments may be chosen for publication in the indexed edition of *Pediatrics* as “Letters to the Editor.” The editors may choose to abridge and edit a comment prior to publication as a Letter to the Editor in *Pediatrics* without notifying or seeking approval from the author. Only these selected responses will be cited in MedLine.
At the time of provisional acceptance, the comment author will receive instructions for submitting an online copyright form. No comment will be scheduled for an issue’s Letters to the Editor section and move onto production until the copyright form is complete.

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Errata

The corresponding author of an article can request a correction to a published manuscript. The editors will decide if an erratum is in order. If the error is an author-generated error, the cost of publishing the erratum will be billed to the author.

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Supplements to *Pediatrics*

Supplements are sponsored sets of articles on a single topic or a theme pertinent to*Pediatrics*. Such sets of articles may come from the proceedings of sponsored meetings, reports from task forces or committees, organizations interested in a particular topic, or research groups. Please note: *Pediatrics* does not accept supplements financed by for-profit corporations if the topics in the supplement bear close relation to the products sold by the corporation. *Pediatrics* also does not accept submissions of supplements with sponsorship from pharmaceutical companies. All supplements are peer-reviewed. The contents of all supplements are open-access from the date of publication.

Supplement Costs

- The cost to sponsor a printed supplement to *Pediatrics* is $975 per page, with a minimum of 32 pages. This estimate includes all costs for production, copyediting, press, distribution and postage, and online production and hosting of the supplement. A budget contract estimate will be issued for your approval prior to scheduling. The final price includes 100 complimentary copies of the supplement. Additional printed copies can be purchased by contacting Kate Larson, Managing Editor, at klarson@aap.org.
- We offer the option of publishing online-only supplements to *Pediatrics*. The submission and production processes are exactly the same as those supplements that are published both in print and online. The difference is that no copies of the supplement are printed, thereby eliminating costs associated with printing and postage. The cost to sponsor an online-only supplement is $485 per page.
- A 50% deposit is required at budget contract and scheduling.

Conceptual Approval

Approval of the topic of a supplement must be obtained from Alex Kemper, MD, MPH, MS, Deputy Editor, prior to submission. To facilitate this process, we ask for a brief letter outlining the supplement, a proposed table of contents listing titles and authors of prospective papers, and a statement describing who will underwrite the cost of the supplement. This material should be sent to the deputy editor (supplements@aap.org) during the planning stages of the supplement, ideally several months prior to submission.

Submission Requirements

To submit the supplement after conceptual approval, you must submit using Manuscript Central. The supplement should begin with several pages of introductory information that can be uploaded as multiple Word files, such as: COVER (Title, Sponsored by…); TITLE PAGE (Title, Sponsored by..., Date of symposium (if any), Location of symposium, Corresponding Editor(s) of supplement); PARTICIPANTS (if applicable; Conference participants names, institutions, cities); TABLE OF CONTENTS; and INTRODUCTION.
Research articles within the supplement should follow the Special Article format. The general submission instructions (including title page, contributors' statement page, abstract, journal style guidance, and conflict of interest statements) also apply to these individual supplement articles.
You may also wish to find a recently published supplement to *Pediatrics* and use it as a guide, or view supplements at http://pediatrics.aappublications.org/content/supplemental.

- **Download and view a sample Supplement (PDF) here.**

Upload each individual article as a separate Word file. Unless you have received other instructions from the editorial office, all articles within the supplement must have a complete Title Page as shown in the Title Page guidelines. Be sure that each author's conflict of interest, funding, and financial disclosure (on the title page) is complete and accurate. These will have to match the copyright and disclosure forms required later in the process. There is no word limit for articles in a supplement, but they should be concise. Include a contributors' statement page and abstract for all articles. Please collate uploaded files submitted (as necessary) to match the order in which they should appear.
Be sure to enter every author in the Authors & Institutions section (Step 3 of your online submission). This step allows you to search email addresses for authors already in our system; please check with co-author(s) to see if they have an address already in our system - otherwise a duplicate account might be added. All authors will need an account in order to log into the system and complete their required copyright and disclosure forms later in the process.

Once the supplement is received by the deputy editor, it is sent out in its entirety to reviewers. If the supplement is provisionally accepted, revisions may be required. If revisions cannot be made to the satisfaction of the editors, the supplement may be rejected.

We estimate 120 days from final acceptance to publication. However, this timeline can vary depending on the number of other supplements already scheduled for publication.

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ANEXO 6

CARTA DO EDITOR DO PERIÓDICO – RECEBIMENTO DO ARTIGO

12-Feb-2017

Manuscript ID: 2017-0499

Vomiting for More than 2.5 Days Is Independently Associated With Poor Evolution in Bronchiolitis

Dear Dr. Vivian Lorenzo and Colleagues:

Thank you for submitting your article(s) to Pediatrics. This is an automated reply that has been sent to all authors on the manuscript so that everyone designated as an author is aware of the submission. If you feel that you do not meet author criteria, or were unaware that you were listed as an author, please contact PediatricsEditorial@aap.org. All future correspondence will be directly with the submitting author.

If you submitted a new MANUSCRIPT, it will be screened and possibly peer-reviewed. The peer-review process may take eight weeks or more. If your manuscript is accepted, it will be published online. The editors determine later if an accepted paper also will appear in the print edition.

If you submitted a REVISED manuscript or supplement, your submission retains its previous ID number but is appended with ".R1" or ".R2" depending on the version.

If you submitted a SUPPLEMENT (single article or multiple articles), it will be peer-reviewed. The submitting author will be notified of a decision within approximately two months.

The submitting author can review the status of the submission online by logging in at https://mc.manuscriptcentral.com/pediatrics and checking their author center.

We will contact the submitting author as soon as possible with our decision.

Sincerely,

Lewis R. First, MD

Editor-in-Chief

Pediatrics Editorial Office

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ANEXO 7

CARTA DE ENVIO AO EDITOR DO PERIÓDICO

Salvador, 12th February, 2017.

Prof. Lewis R. First, MD

Pediatrics

Editor-in-Chief

Dear Editor,

I am submitting the manuscript Vomiting for more than 2.5 days is independently associated with poor evolution in bronchiolitis to Pediatrics Journal as a Regular Article.

Bronchiolitis is a leading cause of acute illness and hospitalization among young children. The variable course of disease and the uncertainty of determining the appropriate level of supportive care for children with bronchiolitis often result in hospital admission even when symptoms are not severe. In contrast, current scoring systems have limited effectiveness in predicting whether illness will progress to severe complications that would necessitate intensive care. Currently, the group of children with subsequent clinical deterioration after admission is poorly defined in available literature. Herein, we found that prolonged duration of vomiting is an independent predictor of ICU admission in children hospitalized with bronchiolitis. Vomiting for ≥2.5 days may be used in clinical practice as an alert sign for children hospitalized with bronchiolitis.

This manuscript is being submitted only to Pediatrics. It has not been submitted elsewhere while under consideration, it has not been published elsewhere, and, should it be published in Pediatrics, it will not

be published elsewhere—either in similar form or verbatim—without permission of the editors.

All authors are responsible for reported research. All authors participated in the concept and design; analysis and interpretation of data; drafting or revising of the manuscript, and approved the manuscript as submitted.

Yours Truly,

Vivian Botelho Lorenzo

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