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Associação entre o ganho de peso excessivo e o crescimento linear na infância: Estudo de coorte.

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Orientador: Márcia Regina Vitolo

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SUMÁRIO

1. RESUMO

Introdução: O crescimento linear é um processo biológico, influenciado por diversos fatores extrínsecos e intrínsecos. A estatura é considerada um marcador das condições nutricionais de longo prazo na infância, no entanto, a grande maioria dos estudos explora somente a baixa estatura como consequência da desnutrição e carência de nutrientes epecíficos. **Objetivo:** Verificar a relação entre o ganho de peso excessivo e a sua influência no z-score de estatura por idade aos 6 anos, entre meninos e meninas. **Métodos:** Foram analisados dados oriundos de ensaio de campo randomizado por conglomerados com crianças do Sul do Brasil, acompanhandas dos 6 meses aos 6 anos de idade. Dados antropométricos foram obtidos por meio de aferição de peso e estatura, e os indicadores nutricionais, foram classificados utilizando os padrões de crescimento definidos pela Organização Mundial da Saúde. O teste U de *Mann-Whitney* foi utilizado visando comparar as medianas de E/I entre as crianças com e sem excesso de peso aos 6 anos de idade. A relação entre o Δ-Índice de massa corporal po idade e o z-score de estatura por idade aos 6 anos foi analisada por meio de regressão linear *e* ANOVA utilizada a análise multivariada de regressão linear. **Resultados:** Avaliou-se *n*= 294 crianças ao longo do período do estudo. Verificou-se que crianças que ganharam peso excessivamente dos 6 meses aos 6 anos apresentam uma probabilidade de 47% de serem significativamente mais altas do que aquelas que apresentaram ganho de peso adequado (p=0,00). **Conclusão:** Crianças com ganho de peso excessivo sofrem aceleração no processo de crescimento e são mais altas quando comparadas aos seus pares de peso saudável, resultando em prejuízo na expressão do potencial de crescimento linear.

Palavras chave: Crescimento; Obesidade; Índice de Massa Corporal; Estatura-Idade; Estudos de Coortes; Fases do Ciclo de Vida.

2. ABSTRACT:

Introduction: Linear growth is a biological process, influenced by several extrinsic and extrinsic factors. Height is considered a marker of long-term nutritional conditions in childhood, however, the vast majority of studies only explore short stature as a consequence of malnutrition and lack of specific nutrients. **Objective:** To verify the relationship between excessive weight gain and its influence on the Stature/Age z-score at 6 years, between boys and girls. **Methods:** We analyzed data from a randomized field trial by conglomerates with children from southern Brazil, from 6 months to 6 years of age. Anthropometric data were obtained by means of weight and height measurement, and nutritional indicators were classified using the growth patterns defined by the WHO. The Mann-Whitney U test was used to compare the Stature/Age medians between the overweight and obese children at 6 years of age. The relationship between Δ-BMI / Age and the 6-year Stature/Age z-score was analyzed using linear regression and ANOVA using the linear regression multivariate analysis. **Results:** *n*= 294 children were evaluated over the study period. It was found that children who gained weight excessively from 6 months to 6 years were 47% more likely to be significantly taller than those who presented adequate weight gain (*p*= 0.00). **Conclusion:** Children with excessive weight gain experience an acceleration in the growth process and are taller when compared to their healthy weight peers, resulting in impaired expression of linear growth potential.

Keywords: Growth; Obesity; Body Mass Index; Stature by Age; Cohort Studies; Life Cycle Stages.

Lista de abreviaturas e siglas

CT	Colesterol Total
DP	Desvio Padrão
NAFLD	Doença Hepática Gordurosa Não Alcoólica
FGF	Fator de Crescimento de Fibroblastos
TNF-α	Factor de Necrose Tumoral Alfa
GJ	Glicemia de Jejum
GH	Hormônio do Crescimento
IGF-I	Fator De Crescimento Semelhante À Insulina Tipo 1
IL-6	Interleucina 6
IMC	Índice de Massa Corporal
HDL	Lipoproteína de Alta Densidade
LDL	Lipoproteína de Baixa Densidade
OMS	Organização Mundia da Saúde
PA	Pressão Arterial
PCR	Proteína C - Reativa
CNP	Peptídeo C - Natriurético
POF	Pesquisa de Orçamento Familiar
BMP	Proteínas Morfogenéticas Ósseas
SISVAN	Sistema de Vigilância Alimentar e Nutricional
SPSS *Statistical*	*Package for Social Sciences*
TCLE	Termo de Consentimento Livre e Esclarecido
Z-score de IMC/I	Z-score Curva de Crescimento (Índice de Massa Corpora/ Idade)
Z-score de E/I	Z-score Curva de Crescimento (Estatura/ Idade)

3. REVISÃO DA LITERATURA

3.1. Epidemiologia da obesidade infantil no Brasil e no mundo

O sobrepeso e a obesidade infantil são considerados importantes problemas de saúde pública (MENDIS *et. al*., 2015; FAROOQI *et al*., 2015; BASS *et. al*., 2015; WHO, 2016; DOHERTY *et al*., 2017). Atualmente, cerca de 42 milhões de crianças com idade inferior a cinco anos, apresentam excesso de peso em todo o mundo, das quais 31 milhões vivem em países em desenvolvimento (WHO, 2016). De acordo com o *National Health and Nutrition Examination Survey* III (NHANES 1988 - 1994), e IV (NHANES 2013 – 2014), nas últimas décadas, o excesso de peso infantil vem aumentando substancialmente. Estes achados mostram que entre crianças e adolescentes norte americanos, de dois a 19 anos, 17,0% apresentam obesidade e 5,8% obesidade extrema. (OGDEN *et al*., 2016). Além disto, dados mostram que nos EUA, o peso médio das crianças aumentou mais de 5kg, nos últimos 30 anos (LOBSTEIN *et al*., 2015).

Evidências atuais sugerem elevadas proporções de excesso de peso infantil em todo o mundo (WHO, 2016). Dados de estudo, realizado na região ocidental da África Central, revelaram que 18% das crianças entre cinco e 12 anos, estudantes de escolas públicas e privadas, urbanas e rurais, apresentaram excesso de peso (NAVIT *et al*., 2015). Além disto, na Inglaterra, dados recentes da pesquisa nacional, mostraram que a obesidade infantil apresentou índices alarmantes, entre os anos de 2015 a 2016, ela esteve presente em uma, a cada três crianças, com seis anos de idade (NSH DIGITAL, 2017). Ainda neste sentido, resultados do estudo de SIDDIQUI *et al*. (2016) na Índia, indicaram que entre crianças e adolescentes de dois a 17 anos, a prevalência de excesso de peso foi de 23,9%. Recentemente, WANG *et al.* (2017) realizou estudo com dados da pesquisa nacional *Chinese National Surveyon Students Constitutionand Health*, a qual avaliou a evolução dos percentuais de excesso de peso em estudantes chineses entre os anos de 1985 – 2014, resultados apontaram prevalência de 24,2% de excesso de peso nesta população.

Corroborando com esses dados, Fleming e colaboradores (2014) publicaram artigo de revisão, cujo objetivo foi investigar a evolução do excesso de peso infantil, entre 1980 a 2013. A revisão incluiu 1.769 estudos, realizados em 188 países. As prevalências de excesso de peso variaram de 8 para 24%. No Brasil, a prevalência de excesso de peso aumentou de 16% para 24%, nos períodos estudados. Na região sul do Brasil, estudo de base populacional avaliou o estado nutricional de 335 crianças em

idade escolar (seis – dez anos), residentes do município de Pelotas – RS, os pesquisadores identificaram prevalências de 26% de sobrepeso, 15% de obesidade e 10% de obesidade grave, mostrando que o excesso de peso esteve presente em mais de 50% desta população (PASSOS *et al*., 2015). Recentemente, estudo longitudinal brasileiro, intitulado "Coorte de 2004" realizado no município de Pelotas – RS, com 3.350 crianças do nascimento à idade escolar, avaliou o estado nutricional infantil, por meio do uso da curva de IMC/ I, da Organização Mundial da Saúde (OMS), e identificou a prevalência de 40% de excesso de peso na população estudada (SANTOS *et al*., 2016). Além disso, dados da última Pesquisa de Orçamento Familiar (POF 2008/ 2009), constataram prevalências de excesso de peso semelhantes, variando entre 32 a 40%, entre crianças de cinco e nove anos, seguida de modesta taxa de baixo peso (4%) (IBGE, 2010).

Neste contexo, evidências científicas indicam que atualmente o Brasil enfrenta um processo de transição nutricional, o qual é caracterizado pela redução da prevalência de baixo peso e expressivo aumento do excesso de peso infantil e outras doenças crônicas, coexistindo nas mesmas comunidades (RAMOS *et al*., 2015). Esses dados são alarmantes, considerando que a obesidade na infância tende a permanecer na fase adulta, aumentando assim o risco de morbimortalidade (THE LANCET, 2015; SAHOO *et al*., 2015; SANDERS *et al*., 2015; SIMMONDS *et al*., 2015; SIMMONDS *et al*., 2016).

3.2. Consequências da obesidade infantil

De um modo geral, a obesidade pode ser definida como o acúmulo de tecido adiposo localizado ou generalizado, provocado por desequilíbrio nutricional associado ou não a distúrbios genéticos ou endocrinometabólicos (ABESO, 2016; OGDEN, *et. al.*, 2010), enquanto o conceito de excesso de peso infantil refere-se à medida de IMC superior ao valor recomendado para uma determinada estatura e sexo (OGDEN, *et. al.*, 2010). Há consenso na literatura sobre as consequências da obesidade infantil e o ganho de peso excessivo, admitindo-se que sua presença pode gerar potenciais efeitos nocivos à saúde, (ONG *et al.*, 2000; POLLOCK *et al.*, 2015; BACHA *et al*., 2016; AFRICA *et al.*, 2016; KUMAR *et al.*, 2017) afetando, portanto, o bem-estar social e emocional, a autoestima, a educação e a qualidade de vida infantil (ROSIEKA *et al*., 2015; SAHOO *et al*., 2015; MILLER *et al*., 2015; SANDERS *et al*., 2015; BASS *et al*., 2015; WHO, 2016).

3.2.1. Consequências psicossociais

Há relativo consenso sobre a contribuição da obesidade no que tange a dificuldades comportamentais e emocionais na infância, como por exemplo, a ansiedade-depressão (MORRISSON *et al*., 2015; CRUZ *et al*., 2017), associando-se a estigmatização, socialização superficial, insatisfação com a imagem corporal e prejuízo no desempenho escolar (MILLER *et al*., 2015; ROSIEKA *et al*., 2015; GOUVEIA *et al*., 2016; SAHOO *et al*., 2015; BLACK *et al*., 2015). Ainda nessa perspectiva, Rankin e colaboradores (2016) realizaram revisão sistemática de estudos publicados a partir de 2006, que avaliaram a associação entre comorbidades psicológicas e o excesso de peso e obesidade infantil. Os autores descreveram 53 estudos de diferentes países, sendo 13 longitudinais, e concluíram que as evidências dão suporte à hipótese de que, em crianças com excesso de peso, parece haver risco consistente do surgimento de depressão, ansiedade, distúrbios comportamentais, transtornos psiquiátricos, psicológicos e psicossociais, redução de autoestima e de qualidade de vida. Podendo perdurar na adolescência e na vida adulta.

3.2.2. Consequências neurocognitivas

Atualmente, a literatura científica tem explorado os efeitos da obesidade e do ganho de peso excessivo no desenvolvimento neuronal. Evidências atuais suportam que a ocorrência da obesidade infantil está amplamente associada ao desenvolvimento de anormalidades na função e na estrutura cerebral, particularmente no lobo frontal, e nas microestruturais da substância branca do cérebro. Diversos autores associam tais alterações, a desfechos negativos para o desenvolvimento infantil, como atraso do desenvolvimento de habilidades motoras e habilidades cognitivas prejudicadas (SWEAT *et al*., 2017; Alarcón *et al.*, 2016; MARTIN *et al*., 2016; CATALDO *et al.*, 2015; YANOVSKI *et al*., 2016; MESTRE *et al*., 2017).

Estudo recente indicou, que as crianças obesas, em relação às de pesos adequados, experimentaram significativa redução de volume do hipocampo, associado à alteração do seu funcionamento (MESTRE *et al*., 2017). Essa situação é preocupante, dado as evidências consolidadas de que o hipocampo interliga as informações do contexto externo (sensoriais), e interno (estímulos gastrointestinais e endócrinos, informações mnemônicas e cognitivas, sinais endócrinos periféricos: leptina, GLP-1 e grelina), que por sua vez atuam sobre os seus receptores neuronais, resultando na redução ou aumento potencial do mecanismo de estímulo de ingestão alimentar (MESTRE *et al*., 2017; SCOTT, *et al*., 2017).

3.2.3. Consequências endócrino metabólicas

Evidências indicam que o tecido adiposo é um órgão endócrino, multifuncional, capaz de armazenar energia e mobilizá-la quando necessário, além de produzir e secretar moléculas biologicamente ativas denominadas adipocinas, as quais são capazes de desempenhar diferentes papéis no organismo (CAO *et al*., 2014; DECLÈVES *et al.*, 2015). As adipocinas promovem um ambiente pró-inflamatório ou anti-inflamatório que contribui para o aparecimento de doenças relacionadas à obesidade e ao ganho de peso excessivo, devido à lipotoxicidade e disfunções orgânicas que são ocasionadas pelo acúmulo excessivo de lipídios (DECLÈVES *et al*., 2015; VALLES *et al*., 2015). A obesidade, em especial a obesidade visceral, leva ao aumento da produção de citocinas pró-inflamatórias incluindo, proteína c-reativa (PCR), interleucina 6 (IL-6) e fator de necrose tumoral alfa (TNF-α). Este padrão é observado em adultos e também em crianças obesas (CAO *et al*., 2014; IZAOLA *et al*., 2015; MINIHANE *et al*., 2015; TOEMEN *et al.*, 2015; VALDEARCOS *et al*., 2015). Além disto, há evidências de que atualmente a inflamação sistêmica subclínica, seja um fator crucial para o desenvolvimento da maioria das complicações metabólicas, e das comorbidades secundárias decorrentes à obesidade (MINIHANE *et al*., 2015; TOEMEN *et al*., 2015; VALLES *et al*., 2015; YU *et al*., 2015; WENSVEEN *et al*., 2015).

Corroborando com esses dados, no sul do país, Bertotto e colaboradores (2012) avaliaram o índice de massa corpórea por idade de 338 crianças entre um e quatro anos de idade, de baixa condição socioeconômica. Os resultados mostraram que a mudança no z escore de IMC/idade > 0,67 no primeiro ano de vida, (a qual é considerada o ponto de corte utilizado para classificação do ganho de peso excessivo na infância) (ONG *et al*., 2000), associou-se com o excesso de peso e a presença de adiposidade abdominal na idade pré-escolar. No mesmo grupo de crianças, outro estudo demonstrou que o ganho de peso excessivo durante a infância, está associado ao desfecho de resistência insulínica já na idade escolar (COSTA *et al*., 2017). Ainda neste sentido recentemente, diversos estudos têm associado à obesidade infantil a desfechos fisiopatológicos que se estendem também à vida adulta, tais como, desenvolvimento de diabetes mellitus, síndrome metabólica e obesidade abdominal (SABIN *et al.*, 2015; LIANG *et al*., 2015; AJALA *et al*., 2017).

3.2.4. Consequências cardiovasculares

A obesidade e o ganho de peso excessivo na infância estão associados ao surgimento de doenças cardiovasculares e eventos cardíacos a curto e longo prazo

(BASS *et al.*, 2015; COTE *et al.*, 2015; WHO, 2016; BACHA *et al*., 2016; LLEWELLYN *et al*., 2016; LI *et al*., 2016). Sabe-se também que a obesidade em crianças e adolescentes, é preditora para a elevação dos níveis de pressão arterial (PA), colesterol total (CT), triglicerídeos, da lipoproteína de baixa densidade (LDL) e da glicemia de jejum (GJ). Está associada a redução dos níveis daLipoproteína de alta densidade (HDL), desenvolvimento precoce de aterosclerose, comprometimento da resistência cardiovascular, rigidez arterial, e desenvolvimento de fatores de risco cardiometabólicos (XI *et al.*, 2015; BASS *et al*., 2015; YANG *et al.*, 2016; BACHA *et al.*, 2016; DING *et al.*, 2016; LI *et al.*, 2016; DATHAN-STUMPF *et al.*, 2016; VACCARO *et al.*, 2016; COTE *et al.*, 2015; GENONI *et al*., 2017).

No Brasil, estudo seccional de base escolar, intitulado “ERICA”, avaliou 73.399 estudantes entre 12 e 17 anos, os pesquisadores observaram que um quinto da prevalência de hipertensão arterial em adolescentes escolares, pode ser atribuída à obesidade. Os maiores percentuais de hipertensão arterial e obesidade foram observados na região sul do país, sendo Porto Alegre a capital com as maiores prevalências. Diante disso, fica evidente que a obesidade infantil determina uma série de complicações para a criança, gerando impacto na tendência de qualidade e expectativa de vida (BLOCH *et al.*, 2016). Ainda nesse sentido, intervenções precoces iniciadas ainda na infância, são de grande valia para auxiliar na redução dos desfechos fisiopatológicos e metabólicos, decorrentes à obesidade (MCCRINDLE *et al.*, 2015; KUMAR *et al.*, 2017).

3.2.5. Consequências na função renal

Evidências recentes indicam que a obesidade é preditora independente do desenvolvimento de comprometimento renal, tanto em adultos, como em crianças (DING *et al*., 2015; COSTA *et al.*, 2015; SCHIFFL *et al.* ,2017). A obesidade em decorrência do acúmulo excessivo de tecido adiposo, promove o início de uma cascata de eventos celulares progressivos, que incluem hiperfiltração glomerular compensatória, hiperatividade do sistema nervoso simpático e a falta de sensibilidade à insulina, que por sua vez, aumenta os efeitos da angiotensina II, exacerba a proteinúria, e induz a produção de citocinas inflamatórias. Juntos, estes processos contribuem para alterações deletérias na função e na estrutura renal, podendo ocasionar danos nos rins (DECLÈVES *et al.*, 2015; DING *et al*., 2015; ZURITA-CRUZ *et al.*, 2016; KOVESDY *et al.*, 2017). Assim, parece razoável postular a necessidade da implementação de medidas que previnam o desenvolvimento da obesidade, particularmente no início da vida e, consequentemente, retardem ou evitem a ocorrência de morbidades relacionadas

à obesidade e doenças crônicas relacionadas (SILVA *et al.,* 2016). Neste contexto, a promoção de um estilo de vida saudável é um elemento essencial dessas intervenções, uma vez que nefropatias induzidas por obesidade, são basicamente evitáveis, e que a redução de peso contribui consideravelmente na melhora da taxa de filtração glomerular, nos estágios iniciais de danos renais (SCHIFFL *et al.,* 2017).

3.2.6. Consequências gastrointestinais

Perspectivas recentes sobre lipotoxicidade identificam a obesidade pediátrica como um potencial fator de risco para manifestações da doença gordurosa hepática não alcoólica (NAFLD) (CLEMENTE *et al.,* 2016; UBIÑA-AZNAR *et al.,* 2017). Além disto, há evidências de que a NAFLD represente a doença hepática crônica mais frequente em crianças que vivem em países industrializados (GOYAL *et al*., 2016). A NAFLD é caracterizada pelo acúmulo de gordura no hepatócito, sabe-se que ela varia da esteatose até a cirrose avançada (BUZZETTI *et al*., 2016), passando por estágios intermediários de esteato-hepatite e fibrose (CLEMENTE *et al.,* 2016; POVERO *et al.*, 2016). A forma mais agressiva da doença é conhecida como estato-hepatite não alcoólica (NASH), sua incidência é de 3% à 5% em crianças obesas (CLEMENTE *et al*., 2016). A NASH caracteriza-se por inflamação lobular e/ ou portal, fibrose, morte de hepatócitos e angiogênese patológica, em casos graves há necessidade de transplante de fígado (FITZPATRICK *et al.,* 2015). Ainda neste sentido, Goyal e cols. (2016) publicaram revisão sistemática que incluiu estudos que avaliaram a progressão e história natural da doença hepática gordurosa não alcoólica pediátrica. A revisão incluiu 59 estudos, os autores concluíram que indivíduos acometidos pela obesidade na infância, apresentam fator de risco para o desenvolvimento de carcinoma hepatocelular na idade adulta.

3.2.7. Consequências pulmonares

A obesidade está vinculada ao aumento do risco de sintomas respiratórios, morbimortalidade infantil e redução de qualidade de vida (LI *et al.,* 2016; VIJAYAKANTHI *et al.,* 2016). Um estudo recente realizado com jovens obesos entre oito e 18 anos de idade demonstrou que crianças e adolescentes obesos são acometidos por alterações da função pulmonar. Os autores sugerem que a diminuição da capacidade residual funcional (FRC) foi a anormalidade da função pulmonar mais comum, presente em 64,4% das crianças e adolescentes obesos avaliados (KONGKIATTIKUL *et al*., 2015).

Também já foi demonstrado que entre a população pediátrica obesa as complicações pulmonares mais frequentes incluem apneia obstrutiva do sono (TAMANYAN *et al.*, 2016) e asma (VIJAYAKANTHI *et al.*, 2016; MANION *et al.*, 2017). A redução da aptidão cardiorrespiratória em crianças obesas é um fator limitante para a prática de exercício físico e pode contribuir para o desencadeamento de problemas de saúde (TSIROS *et al.*, 2015; LEINAAR *et al.*, 2016). Além disso, estudo de coorte alemão, conduzido por Bazzano e colaboradores (2016), que acompanhou indivíduos dos nove aos 35 anos de idade, constatou que crianças que experimentaram o excesso de peso na infância, se tornaram adultos com alto risco de desenvolver apneia obstrutiva do sono, independente do estado nutricional apresentado na idade adulta.

3.3. Obesidade infantil e crescimento linear

O conceito de crescimento proposto atualmente pelo Ministério da Saúde (2012) refere-se ao processo biológico, dinâmico e contínuo de multiplicação (hiperplasia) e aumento do tamanho (hipertrofia) celular, observado desde a concepção até o final da vida, considerando-se os fenômenos de renovação tecidual e orgânica. De forma geral, termo crescimento linear, também denominado como crescimento longitudinal, ou popularmente “aumento da estatura”, é compreendido como o processo que se dá do momento do nascimento até a adolescência, cessando quando o indivíduo atinge a sua altura final, resultante da interação entre sua carga genética e dos fatores do meio ambiente, que juntos permitirão a maior ou menor expressão do seu potencial genético (JEE *et al.*, 2016).

3.3.1 Processo fisiológico do crescimento linear

Evidências indicam que o crescimento linear infantil é um processo biológico, conduzido pela condrogênese da placa epifisária (ou placa de crescimento) (JEE *et al.*, 2017). A placa de crescimento é uma estrutura de cartilagem hialina, localizada na metáfise da terminação óssea (de ossos longos, ossos tubulares curtos das mãos e dos pés e das vértebras), de crianças e adolescentes (OVALLE *et al.*, 2014).

Sabe-se que a placa de crescimento compreende três camadas/zonas distintas, com papéis diferenciados entre si. A zona de repouso tem a função de reservatório de condrócitos progenitores. A zona proliferativa é o local da proliferação celular rápida. Na borda da zona proliferativa próxima da metáfise, as células param de se dividir e inicia-se a hipertrofia celular dos condrócitos. Este processo, combinado com a secreção

da matriz extracelular, resulta na condrogênese e no crescimento ósseo (BARON *et al.*, 2015; MELROSE *et al*., 2016; JEE *et al*., 2017).

Muitos sistemas regulam e controlam a condrogênese na placa de crescimento, de uma forma geral, o crescimento normal na infância depende de hormônios múltiplos, fatores parácrinos, moléculas de matriz extracelular e proteínas intracelulares (BARON *et al.*, 2015; JEE *et al.*, 2017).

- *Sistema hormonal:* O hormônio tireoidiano, o hormônio do crescimento (GH), glicocorticoide, andrógenos e estrogênio regulam positivamente o crescimento linear (BARON *et al*., 2015).
- *Sistema parácrino*: Múltiplos fatores de crescimento parácrinos são produzidos localmente na placa de crescimento, estão inclusos o fator de crescimento semelhante à insulina tipo 1 (IGF-I), GH (BARON *et al.*, 2015), peptídeo C-natriurético (CNP) (NAKAO *et al.*, 2015), proteínas morfogênicas ósseas (BMPs) e fatores de crescimento de fibroblastos (FGFs), juntos eles interagem com oscondrócitos adjacentes, atuando sobre receptores específicos da superfície celular. Há evidências de que cada um desses fatores endócrinos regulamenta o crescimento ósseo por ação direta na placa de crescimento (BARON *et al.*, 2015).
- *Matriz extracelular:* A estrutura da cartilagem é crucial para o crescimento linear. Ela é composta por colágenos (incluindo colágeno II e X), proteoglicanos (incluindo aggrecan e perlecan) e proteínas não colágenas (incluindo proteína da matriz oligomérica cartilaginosa) (MYLLYHARJU *et al.*, 2014).
- *Fatores de transcrição:* Está bem estabelecido na literatura a amplitude de rotas intracelulares que desempenham papéis importantes na condrogênese da placa de crescimento (BARON *et al*., 2015). Dentre elas, pode-se citar os fatores de transcrição RUNX2 (SUN *et al.*, 2016), SOX9 (LEFEBVRE *et al.*, 2016) e SHOX, os quais desempenham papéis fundamentais para a formação da placa de crescimento (JEE *et al.*, 2017).

3.3.1. Perfil antropométrico, crescimento linear a sua relação com a obesidade infantil

Atualmente, a literatura científica tem explorado os efeitos dos “primeiros 1000 dias”, período entre a concepção e o fim do segundo ano de vida, para o crescimento e o desenvolvimento saudável das crianças (CUNHA *et al*., 2015). Tradicionalmente, o crescimento é considerado um ótimo indicador de saúde infantil (BRNIČEVIĆ *et al.*,

2015; BEER *et al.*, 2015), ao longo desse processo, a criança experimenta amplamente a influência de fatores que influenciam na regulação do crescimento linear, tais como, fatores extrínsecos (Ministério da Saúde – Brasil, 2012) e intrínsecos (JEE *et al.*, 2017).

Nos últimos 40 anos, estudos publicados abordando a descrição dos padrões antropométricos infantis, vêm mostrando o declínio expressivo da prevalência de déficit estatural no Brasil (IBGE, 2010). A redução contínua na frequência de meninos e meninas com déficit de estatura ocorreu em todas as regiões do País. Entre 1974-1975, 1989 e 2008-2009, destaca-se a impressionante redução na prevalência de déficit de estatura no sexo masculino, de (38,5%, 23,2%, para 12,2%) na região Norte; (44,4%, 24,5% para 7,9%) na região Nordeste; (22,7%, 11,1% para 6,8%) na região Centro-Oeste; (20,2%, 9,6% para 6,2%) na região Sudeste e (20,8%, 8,2% para 4,7%) na região Sul. E no sexo feminino de (36,5%, 18,6% para 10,3%) na região Norte; (40%, 23,6% para 6,9%) na região Nordeste; (23,4%, 6,8% para 7,4%); (18,9%, 5,8% para 5,3%) e (18,8%, 6,8% para 4%) na região Sul, respectivamente (IBGE 2010; Diretoria de Pesquisas, Coordenação de Trabalho e Rendimento, Estudo Nacional da Despesa Familiar 1974-1975; Pesquisa de Orçamentos Familiares 2008-2009; Instituto Nacional de Alimentação e Nutrição, Pesquisa Nacional sobre Saúde e Nutrição 1989).

No Sul do Brasil, Barros e colaboradores (2008), publicaram estudo de coorte, cujo intuito foi investigar a prevalência de déficits antropométricos em crianças com um ano de idade, participantes dos estudos intitulados “Coorte de 1982”, “Coorte de 1993” e “Coorte de 2004”. O estudo incluiu 1.449 crianças em 1982, 1.359 em 1993 e 3.907 em 2004. As prevalências de déficits de comprimento/idade encontradas variaram discretamente entre (8,3% - 6,3% - 6%) nos períodos estudados. Os autores concluíram que os motivos que explicam o estacionamento das prevalências de déficit de estatura precisam ser mais bem investigados. Posteriormente, dados da última Pesquisa de Orçamento Familiar (POF 2008/ 2009) mostraram as frequências de baixa estatura entre as crianças menores de cinco anos, segundo as regiões do Brasil. Foram observados déficits de estatura de 8,5% na região Norte, 5,9% na região Nordeste, 6,1% na região Sudeste e Centro-Oeste, e 3,9% na região Sul do país.

Por outro lado, a situação epidemiológica atual, acentua crescentes prevalências de excesso de peso infantil. Sabe-se que a ingestão nutricional inadequada, é um fator extrínseco que gera alterações no crescimento ósseo longitudinal (BARSTOW *et al.*, 2015). Dado da literatura revela que crianças obesas são geralmente mais altas, do que os seus pares com pesos saudáveis (HATTORI *et al*., 2002). Além disto, evidências indicam que a obesidade infantil, está amplamente associada ao processo de

crescimento linear acelerado, resultando em estatura alta para idade (BARSTOW *et al.*, 2015), idade óssea avançada (FENNOY *et al*., 2013) e puberdade com início e maturação precoces (LEE *et al.,* 2016), devido ao aumento dos níveis de leptina, insulina e andrógenos e redução de GH no organismo (SHALITIN *et al*., 2017).

Os estudos disponíveis que avaliam os efeitos da obesidade e do ganho de peso infantil são, portanto, consistentes com a hipótese de que a lipotoxicidade afeta nocivamente todos os sistemas do organismo da criança, inclusive no que diz respeito ao seu crescimento linear. Nota-se, entretanto, lacuna na literatura científica quanto a real dimensão do impacto que o ganho de peso excessivo, pode exercer, no indicador z-escore de Estatura/idade, durante o período do crescimento linear.

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5. OBJETIVOS

5.1. Objetivo geral:

Verificar a relação entre o ganho de peso excessivo e o crescimento linear.

5.2. Objetivo específico:

Verificar a correlação entre o aumento do z-score IMC/I e a sua influência na variação do indicador z-score E/I, entre meninos e meninas, de maneira individual para cada uma das idades.

Verificar a correlação entre o Δ-IMC/I dos 6 meses aos 6 anos e a sua influência no z-score de E/I aos 6 anos, entre meninos e meninas.

6. ARTIGO ORIGINAL

Journal of Nutrition and Metabolism

Association between excessive weight gain and linear growth in childhood: a cohort study

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6.1. Abstract

Long-term nutritional conditions in childhood are often measured by stature; however, the vast majority of studies explore only short stature as a consequence of malnutrition and specific nutrient deficiencies. **Objective:** To verify the relation between excessive weight gain and linear growth. **Methods:** Data from a cluster-randomized field trial with children from the South of Brazil, followed from 6 months to 6 years of age, were analyzed for the study. Anthropometric data were obtained by measuring weight and stature, and nutritional indicators were classified using the growth standards defined by the WHO. The Mann-Whitney U test was used to compare the median S/A (*Stature/Age*) between overweight and non-overweight children at 6 years of age. The relation between Δ-BMI/A (Δ-Body Mass Index/ Age) and S/A z-score at 6 years of age was analyzed using linear regression and ANOVA used the multivariate linear regression analysis. **Results:** Throughout the study period *n*= 294 children were assessed. The median z-score of stature-for-age at 6 years of children who had excessive weight gain was 0.62 (IQ= -0.02 - 1.12), significantly higher when compared to those who did not have excessive weight gain, which was 0.06 (IQR= -0.625 - 0.85) (p=0.000). Through the multiple linear regression model adjusted for confounding variables, it was found that an increase of 1 unit in the BMI/Age z-score from 6 months to 6 years impacts a 0.19 z-score increase in the S/A indicator at 6 years, when considering both genders (p=0.00). **Conclusion:** Children with excessive weight gain suffer acceleration in the growth process and present higher stature when compared to their healthy weight peers.

6.2. Introduction

Obesity is a public health problem and current evidence shows that, in many cases, its onset occurs in childhood. [1] Over the past 40 years, population-based studies have shown that a nutritional transition process has been occurring in the country. During this period, in southern Brazil, a 24% increase in childhood overweight rates was observed, coexisting with a 16% decline in the prevalence of stature deficit, and with a low percentage of weight deficit (4%), oscillating around 1%. [2] Currently, about 42 million children under the age of five are overweight, of which 31 million live in developing countries. [3]

Current evidence indicates that childhood's overweight has been associated with several complications, including type II diabetes mellitus [4], insulin resistance [5], and increased blood pressure levels [6-7], thus affecting children's health and quality of life. In addition, more recent studies show that excessive weight gain interferes with the production of hormones, such as leptin, androgen hormones, and growth hormone (GH) [8], which may result in older bone age [9] and early onset and pubertal maturation process [10], which consequently may result in greater stature when compared to their appropriate weight peers [11]. Thus, hypotheses indicate that excessive weight gain may interfere with the linear growth process [08, 10, 11] and not only overweight, but also accelerated linear growth, are possible indicators of metabolic changes among children, serving as an alert for the need to request laboratory tests and more frequent or specialized follow-up.

However, to our knowledge, there are no studies in Brazil that have researched the relation between the impact of excessive weight gain/overweight and linear growth in childhood. Cross-sectional studies may direct the results in this direction, but they do not show the dimension of the impact of weight gain on stature increase. Given the above, the aim of this study is to investigate the association between excessive weight gain and its effect on linear growth.

6.3. Materials and Methods

6.3.1 Study Design

Prospective cohort study, conducted with data from children accompanied from six months to six years of age, participating in a cluster randomized field trial conducted in the capital city of *Rio Grande do Sul*, Brazil, in which 20 Health Centers (HCs) from all district zones of the city were randomized into "intervention" and "control" groups. The

intervention consisted of an update on the "ten steps to healthy eating for children under two years of age", offered to all HC staff, and the supply of educational material on breastfeeding and complementary feeding to be delivered to pregnant women in prenatal care and mothers of children in childcare in the health centers of the "intervention" group. The project number 30741714.7.0000.5345 was approved by the Research Ethics Committee of the *Universidade Federal de Ciências da Saúde de Porto Alegre - UFCSPA*. (Federal University of Health Sciences of Porto Alegre).

The sample size was calculated based on the primary objective of the randomized field trial, which was to increase breastfeeding rates through the intervention. An estimated 720 mother-child pairs were needed in order to achieve the sample size. [12]

6.3.2 Recruitment and Data Collection

The recruitment process was carried out from April to December 2008 and included the identification of pregnant women registered in the health centers of the study and who were in their last trimester. The pregnant women who agreed to participate in the study were informed about the procedures involved in the research, signed the Free and Informed Consent Form (FICF), answered a structured questionnaire about maternal and family characteristics, health conditions and sociodemographic data, besides providing contact information to be used in the later stages of data collection from the children.

Data collection occurred through home visits and involved four stages: 1) between November 2008 and September 2009, when children were 6 to 9 months old, 2) between December 2009 and April 2010, when children were 12 to 16 months old, 3) between August 2011 and March 2012, when children were 2 to 3 years old, and 4) between August 2014 and June 2015, when children were 6 to 7 years old.

During the home visits for data collection, structured questionnaires were applied, in addition to the measurement of anthropometric parameters of the children, performed by nutritionists and nutrition students previously trained to perform this task.

6.3.3 Anthropometric Measurements

At 6 and 12 months, the children were weighed without clothes or diapers, on the mother's lap using a digital scale with precision of 100g, Techline ® (*São Paulo/SP, BR*) duly calibrated. To extract the weight of the baby, the differential weight was calculated by subtracting the mother's weight from the total weight of the mother with the baby. To measure the length, the child was placed lying down, without diapers, on a

straight, flat, hard surface. With the help of the mother, the baby's head was positioned on the fixed base of the ruler, and the researcher extended both baby's legs, pressing lightly at the knees, and brought the movable base of the ruler closer until it was parallel to the base of the feet. The length was evaluated using a wooden pediatric ruler, Serwital Inc®.

At 2 - 3 years and 6 - 7 years the children were weighed barefoot and wearing light clothing on calibrated digital scales of the brand *Lider* ® with a variation of 100g. The children were measured standing using a stadiometer of the brand *Alturaexata* ® with its own base where the child was positioned and measured according to national standards. [13]

The anthropometric measurements were made in duplicate in all the steps, and in cases of divergence, a third measurement was made and the average of the three measurements was calculated.

6.3.4 Research Procedures

Children's body mass index (BMI) was calculated in all stages of the study and the nutritional status was classified with the help of the software Anthro version 3. 2 and Anthro Plus version 1.0.4. To evaluate the children's growth, we used the curves of stature-for-age and BMI-for-age, specific for sex and age of each child. The curves developed in 2006 were used for children aged zero to three years old, and the 2007 curves were used for children aged six to seven years old.

Children with a Length/Stature for Age (S/A) z - score < - 2 were considered to have low stature, and those with a z-score ≥ - 2 were considered to have adequate stature. All children with a z-score > +1 were classified as overweight, and those with > + 2 with obesity, according to the World Health Organization criteria.

The weight gain of children during the study period was calculated by varying the BMI/Age z - score from six months to six years (Δ- BMI/A), that is, subtracting from the BMI/Age z-score value at six years the BMI/Age z - score value at six months. Values greater than 0.67 were considered as excessive weight gain. [14]

6.3.5 Statistical Analysis

For the analyses of this study, children who did not have their anthropometric measurements taken were excluded, and those with premature birth (<37 weeks) and with congenital diseases that affect growth, such as Sickle Cell Anemia, Down

Syndrome, Congenital Heart Disease, and Congenital Adrenal Hyperplasia were considered ineligible.

For the statistical analysis we used the Statistical Package for Social Sciences (SPSS) version 21.0. Data collected from the variables were submitted to double typing and later validated. The results were presented as median and interquartile range (IQR) for continuous variables and absolute numbers and percentages for categorical variables.

The univariate analysis expressed the frequency of children with short stature, overweight, and with excessive weight gain. The Mann-Whitney U-test was used for the initial analyses to compare the medians of S/A between overweight and non-overweight children at each age and to check the effect of weight gain during the study period on children's stature at 6 years to compare the medians of the z-score of S/A at 6 years between children with and without excessive weight gain.

The relation between Δ-BMI/A from 6 months to 6 years and the z-score of S/A at 6 years was analyzed by linear regression and ANOVA to verify the significance level of the regression. In addition, cross-sectional analyses to verify the relation between BMI/A z-score and S/A z-score were also performed by means of linear regression, performed individually for each age. The effects of exposures were adjusted for the following confounding variables: breastfeeding, family income, maternal education, pre-gestational BMI, maternal stature, and birth weight in all multivariate analyses.

To assess whether the intervention had an impact on the study outcome (stature), we used the generalized estimating equations (GEE) method, which analyzed the difference between children's S/A values taking into account their initial allocation to the "intervention" or "control" groups. One child was considered an outlier and was excluded from the analyses. Values of $p < 0.05$ were considered significant in all statistical tests implemented.

6.4. Results

A total of 715 pregnant women were enrolled in this research, of which, 577 children at 6 months, 492 at 12 months, 430 at 3 years and 297 at 6 years were included in the study sample. Follow-up losses in this cohort occurred due to refusal to participate, address change, maternal and/or infant death, congenital disease, premature birth, and absence of anthropometric data (**Figure 1**).

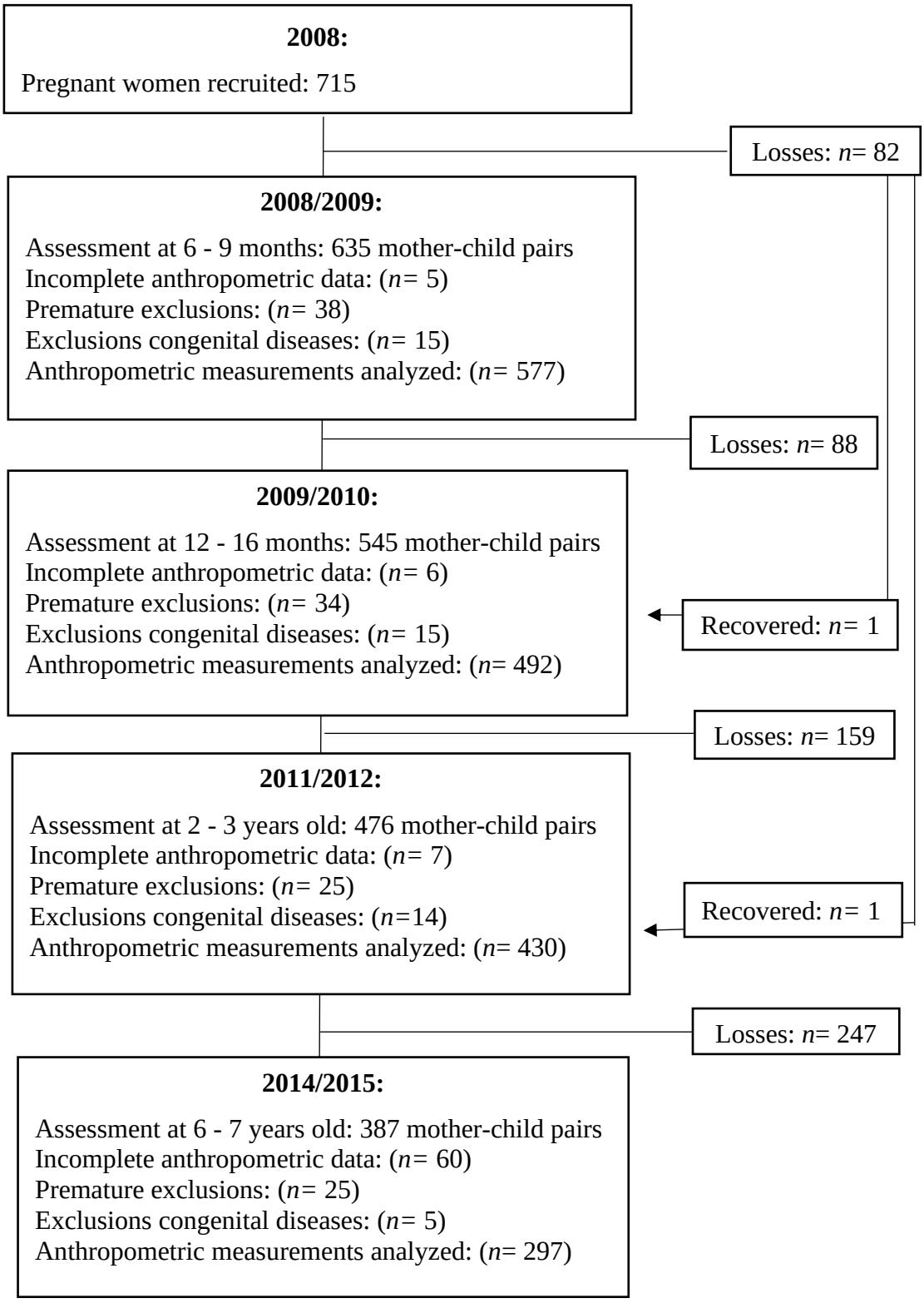

Figure 1. **Collection flowchart** [a]

[a] Note: Description of all data collection phases, from the recruitment of pregnant women to the period when the children were 6 years old.

Regarding maternal and family characteristics obtained during enrollment of pregnant women, 21.2% of mothers (*n*= 123) were less than 20 years old, 30.8% (*n*= 179) had less than eight years of schooling, and 67.3% (*n*= 391) had no secular work. From the maternal anthropometric evaluation, a 37% prevalence of overweight was detected pre-pregnancy (*n*= 212).

In 70.1% of families (n=397) monthly income was less than R$1,245.00, equivalent to three minimum wages in 2008. No difference was found between the Intervention and Control groups regarding the stature of the children assessed in all stages of the study. The gender distribution of the sample was homogeneous, with 52.5% of children being males (*n=305*) at the beginning of the study.

Figure 2 describes the anthropometric growth characteristics of the children evaluated in each of the data collection stages.

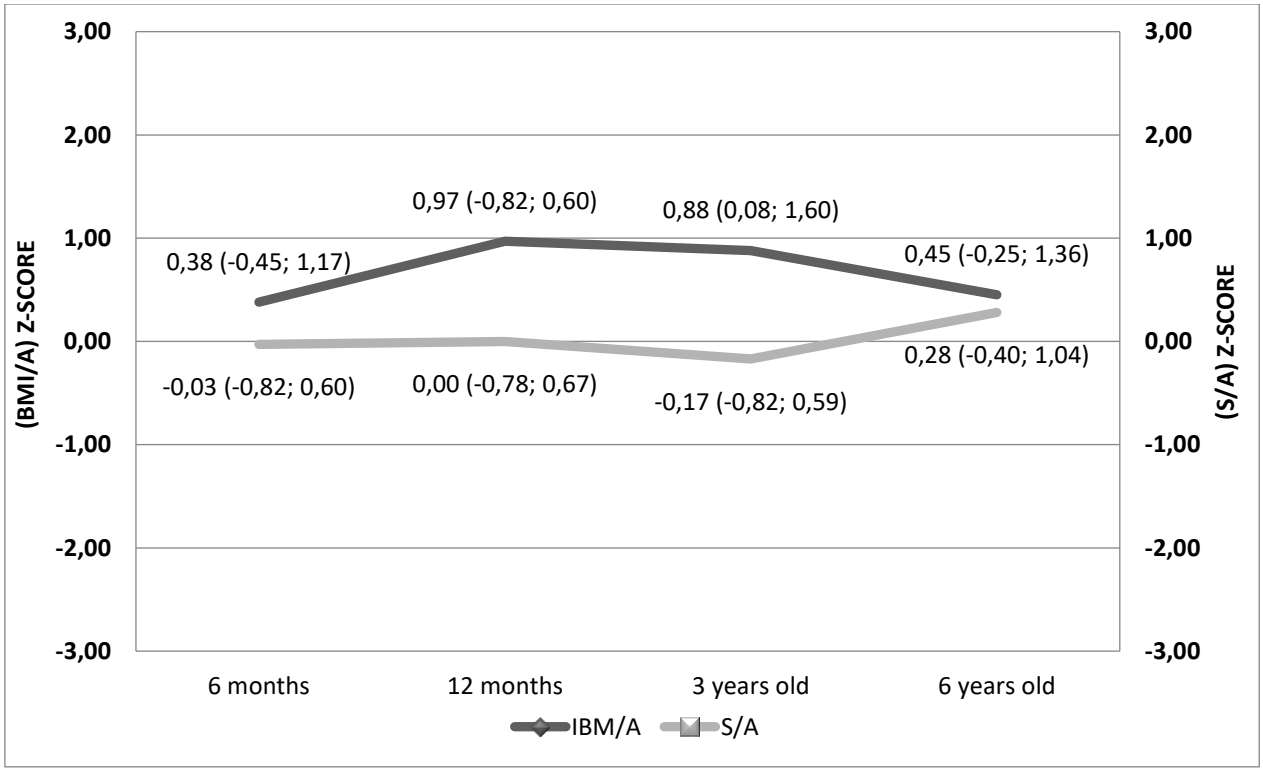

Figure 2. Median of nutritional indicators over the follow-up period of the study (2008 - 2015).

Note: Values presented as Median and Percentile (P. 25; P. 75)

BMI/A Z-score= Z-score Growth curve (Body Mass Index/Age) - WHO

S/A Z-score= Z-score Growth curve (Stature/Age) - WHO

The proportion of overweight children was 29.3% at 6 months (*n=169*), 48.3% at 12 months (*n=237)*, 44.3% at 3 (*n=190*) and 33.4% at 6 years (*n=99*). Obesity was observed in 8.5% of children at 6 months (*n=49*), 17.5% at 12 months (*n=86),* 18.6% at 3 years (*n=80*) and 17.9% at 6 years (*n=53*). Throughout the study follow-up, we observed the prevalence of stature deficits of around 3.6% of children at 6 months (*n=21*), 3.2% at 12 months (*n=16),* 4% at 3 years (*n=17*), and 1.4% at 6 years (*n=4).* The comparison of stature between overweight and non-overweight children is shown in Table 1.

Table 1. Comparison of the H/A z-score between overweight and non-overweight children:

	Overweight		Non-overweight		*p*
	n	**Median (P. 25; P.75)**	***n***	**Median (P. 25; P.75)**	
6 months	169	0,04 (-0,81; 0,66)	407	-0,15 (-0,85; 0,55)	0,189
12 months	237	0,00 (-0,85; 0,69)	254	0,00 (-0,73; 0,68)	0,479
3 years old	190	-0,32 (-0,97; 0,42)	239	0,05 (-0,67; 0,72)	0,025
6 years old	99	0,11 (-0,65; 0,72)	197	0,83 (0,20; 1,29)	0,000

Test employed= U Mann Whitney

Values presented as Median and Percentile (P. 25; P. 75)

p - values considered significant = ($p < 0.05$)

It was found that among those classified as overweight, the median z-score of S/A were significantly higher when compared to their peers with appropriate weights at 3 and 6 years of age. Analyses stratified by sex were performed, however no statistically significant difference was found (Data not shown in table). From the analysis of the multiple linear regression model adjusted for confounding factors, whose results are presented in Table 2, it is observed that the BMI/A z-score values in all phases are correlated to the S/A values, and the variation in the BMI/A z-score is associated with 20% of the stature variation at 3 years of age, and 31% at 6 years of age. It was also observed that, at 3 years of age, the increase of 1 unit in the z-score of BMI/A indicator had repercussions in the increase of 0.07 units more in the z-score of S/A indicator (p=0.00) and 0.27 units at 6 years of age (p=0.00).

Table 2. Cross-sectional analysis of the effect of the BMI/A indicator on the S/A indicator[a]:

	Both sexes			Masculine			Feminine		
	R^2	**B**	***p***	**R^2**	**B**	***p***	**R^2**	**B**	***p***
6 months	0,23	-0,08	0,000	0,27	-0,08	0,000	0,20	-0,08	0,001
12 months	0,19	0,04	0,000	0,26	0,01	0,000	0,16	0,04	0,000
3 years old	0,2	0,07	0,000	0,19	0,01	0,000	0,25	0,17	0,000
6 years old	0,31	0,27	0,000	0,33	0,28	0,000	0,32	0,26	0,000

Note: Test employed= Multiple linear regression model, adjusted for confounding variables.

BMI/A Z-score = Z-score Growth curve (Body Mass Index/Age) – WHO.

p - values considered significant= ($p < 0.05$).

Regarding weight gain from 6 months to 6 years, 294 children had sufficient data for the calculation of this variable, and 41.5% (n=122) had a Δ-BMI/A value greater than 0.67, considered as excessive weight gain. The median z-score of stature-for-age at 6 years of children who had excessive weight gain was 0.62 (IQR= -0.02 - 1.12), significantly higher when compared to those who did not have excessive weight gain, which was 0.06 (IQR= -0.625 - 0.85) (p=0.000).

Through the multiple linear regression model adjusted for confounding variables, it was verified that children who gained excess weight from 6 months to 6 years had a 47% probability of being significantly taller than those who had a BMI/A variation of less than 0.67 (p=0.00), regardless of the child's gender. Additionally, it was observed that Δ-BMI/A was associated with 26% of the variation in the S/A indicator at age 6 when considering both sexes, 30% among boys and 24% among girls. It is also observed that an increase of 1 unit of BMI/A z-score from 6 months to 6 years would lead to an increase of 0.19 z-score in the S/A indicator at 6 years, when considering both sexes (p=0.00). There was no significant difference between genders, however, among boys this increase would be 0.22 (p=0.00) and among girls 0.13 z-score of S/A (p=0.025).

6.5. Discussion

Upon analyzing the anthropometric characteristics of growth of the children evaluated, it was noted that excessive weight gain is associated with greater stature in childhood. It was also observed that the increase in BMI/A resulted in acceleration in the children's growth at six years of age.

6.5.1. Short stature

The present study also revealed that the prevalence of short stature decreased from 3.6% at 6 months to 1.4% at 6 years. Studies published in Brazil, showed a decrease in the prevalence of stunting and underweight. Between 1974 - 1975, 1989 and 2008-2009, stands out the impressive reduction in the prevalence of stunting among boys (20.8%, 8.2% to 4.7%) and girls (18.8%, 6.8% to 4%), aged five to nine years, from the southern region. [3]

It is noteworthy that, in the present study, the prevalence of overweight was high in all age groups and that this condition may be influencing the results of short stature in the evaluated population. Once the BMI/A z-score values at all ages are correlated to the S/A values, and at three years of age, the increase of one unit in the BMI/A z-score indicator would cause the increase of 0.07 z-score units in the S/A indicator and 0.27 units at six years of age. Consequently, as it is known that the proportion of overweight has steadily increased, and that it is associated with higher child stature, such a hypothesis justifies the declining trend in the prevalence of stature deficit in the assessed population. [15 - 20]

6.5.2. Weight gain and linear growth

When analyzing the study data, it was observed that among those classified as overweight at three and six years of age, the median stature was significantly greater when compared to their eutrophic peers. Similar results to those found in the present study have been observed in research conducted with children in schools, and clinics for childhood obesity treatment, showing that obese children are generally taller, than those with healthy weights. [21-22]

In addition, 41.5% of children were found to have gained excess weight from 6 months to 6 years of age, who were 47% more likely to be significantly taller than those who had a BMI/A range of less than 0.67. Literature data indicate that the mechanisms that promote advanced linear growth in overweight children are complex, and several changes in hormone levels have been proposed as responsible for this phenomenon. Evidence supports the hypothesis that high BMI in childhood is correlated with such changes. Among the elevated hormones one can mention, leptin, dehydroepiandrosterone sulfate (DHEAS) and Delta 4-androstenedione (AD). [15-17, 23] Still in this regard, the review that analyzed studies conducted with children shows that overweight affects the GH / IGF-I axis, and may trigger accelerated linear growth and puberty with early onset. [10, 15, 24-26] However, it is important to highlight that one of the outcomes that can occur in the body of the obese child is the premature

completion of the linear growth process, which occurs due to advanced bone age, resulting in decreased final linear growth potential. [09, 15, 27-29] Thus, hypotheses indicate that excessive weight gain can accelerate the process of linear growth [08, 10, 11] being not only the excess weight, but also the accelerated statural growth, possible indicators of metabolic changes among children, serving as an alert for the need to request laboratory tests and more frequent or specialized follow-up.

Among the limitations of this study, it should be noted that all participants were of low socioeconomic status, thus, our findings cannot be extrapolated to other populations, limiting the external validity of the results obtained. Another limitation that must be considered is that the sample was studied up to the age of seven years, so it is not possible to evaluate the impact of the increase in BMI/A z-score at other stages of life.

The results of the present study suggest that children with excessive weight gain may show accelerated linear growth. It should be considered that the mechanisms of childhood obesity risk impact the expression of linear growth potential, which may lead to a reduction in final stature.

Thus, studies investigating stature data in children, especially those aiming to show prevalence of short stature, should contextualize the results as to the condition of overweight and excess weight gain of the studied population.

6.6. Conclusions

The results of the present article allow the conclusion that children with excessive weight gain and overweight are taller when compared to their peers with healthy weights. The analysis of the results allowed us to observe that at 3 years, the increase of 1 unit in BMI/A z-score would cause the increase of 0.07 z-score units in the S/A indicator and 0.27 units at 6 years. Additionally, it was observed that increasing the BMI/age z-score by 1 unit from 6 months to 6 years would lead to an increase of 0.19 z-score in the S/A indicator at 6 years, when considering both sexes.

The importance of supporting a healthy environment throughout childhood is evident, as a priority in public health strategies, in order to prevent the emergence of harmful effects of overweight on children's health, highlighting the possible impact on the expression of linear growth potential, and the outcome of reduced final stature.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Supplementary Materials

No Supplementary Material is provided.

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7. Conclusões e considerações finais

Os resultados da presente dissertação permitem concluir que crianças com ganho de peso excessivo e excesso de peso são mais altas, quando comparadas aos seus pares com pesos saudáveis. Além disto, o presente estudo também elucidou a compreensão quanto a real dimensão do impacto do ganho de peso excessivo e do excesso de peso no indicador z-escore de Estatura/ idade. A análise dos resultados permitiu observar que aos 3 anos, o aumento de 1 unidade no indicador de z-score de IMC/I causaria o aumento de 0,07 unidades de z-score no indicador de E/I e 0,27 unidades aos 6 anos. Adicionalmente, observou-se que o aumento de 1 unidade de z-score de IMC/Idade dos 6 meses aos 6 anos levaria ao aumento de 0,19 z-score no indicador de E/I aos 6 anos, quando considerando ambos os sexos.

Por fim, a análise dos resultados da presente dissertação evidência a importância de apoiar um ambiente saudável durante toda a infância, como uma prioridade nas estratégias de saúde pública, a fim de prevenir o surgimento de efeitos nocivos à saúde infantil, destacando-se o aceleramento do crescimento linear, que ocorre em detrimento ao processo deletério a qual o organismo da criança com ganho de peso excessivo e consequente excesso de peso é submetido.

8. ANEXOS:

8.1. Anexo 1. Guide for authors of the Journal of Nutrition and Metabolism

Instructions for Contributors

Journal of Nutrition and Metabolism is a peer-reviewed, Open Access journal that publishes original research articles and review articles covering the broad and multidisciplinary field of human nutrition and metabolism. The journal welcomes submissions on studies related to obesity, diabetes, metabolic syndrome, molecular and cellular biology of nutrients, foods and dietary supplements, as well as macro- and micronutrients including vitamins and minerals.

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