SUGAR COMPOSITION AND LEVEL OF COMMERCIALLY AVAILABLE INFANT FORMULAE IN THE UNITED ARAB EMIRATES

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ABSTRACT

Sugar Composition and Level of Commercially Available Infant Formulae in the United Arab Emirates

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Background: Infant formulae are a primary source of nutrition during the first years of life. Frequently, sugar is added to these formulae, which can lead to different adverse health problems including early childhood caries, if consumed excessively or with bad feeding habits.

Aim: To assess the amount and type of dietary sugars in commercially available infant formulae in the UAE.

Materials and Methods: This study involved measuring sucrose, glucose, and fructose in 71 different brands of commercially available infant formulae for retail sale in the UAE. Organic and non-organic milk-based, and soy-based formulae recommended for healthy infants from birth until three years of age were included. Hydrolyzed rice, lactose-free, and goat milk formulae were also included. The experimental analysis was conducted in a private laboratory in Dubai. The process of quantifying sugars was performed using high-performance liquid chromatography with refractive index detection (HPLC-RI), with the limit of detection (LOD) set at 0.1 g/100ml. Sugar values were determined and compared with nutritional labels. Descriptive analysis was performed using tables. Comparison between this study's findings, data on the products' labels, World Health Organization (WHO) standards, and The European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) Standards for infant formulae was done.

Results: Out of the 71 samples, 23 had detectable sugar levels. 12 samples had glucose, one sample had fructose, and 10 samples had sucrose. Of all infant formulae products that were analyzed, 10 were found to have sugars contributing to more than 5% of total energy intake.

All infant formulae packages had carbohydrates levels mentioned on the labels, but very few mentioned details about the added sugar content.

Conclusions: Many infant formulae products consumed by infants and young children in the UAE were found to contain sugars that exceed the standard recommended intake. Tighter regulations that monitor the amount of sugar in infant formulae are needed. Guidelines for a comprehensive labelling system that accurately discloses the sugar levels are required to reduce adverse health problems secondary to excess sugar consumption in early childhood.

DEDICATION

I am dedicating this thesis to people who have meant and continue to mean so much to me.

To my mother, Dr Elham Atalla, whose love for me knows no bounds and who taught me the value of hard work and determination. You set the bar high for me to succeed by being an example of a loving, caring, and a hard-working person.

To my father, Dr Osama Awad, my best friend and personal superhero. Thank you for encouraging me and having my back to follow and achieve my dreams. No matter how big I grow, or how successful I become, I will always strive to make you both proud.

I owe a debt of gratitude to Dr. Manal Al Halabi for the endless support and guidance throughout my journey. You always believed in me and showed me what it means to be dedicated. You were an encouraging mentor, a caring mother, a supportive friend, and someone I will forever look up to.

DECLARATION

I declare that all the content of this thesis is my own work. There is no conflict of interest with any other entity or organization

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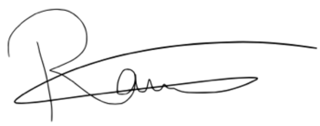
Signature: 

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ABBREVIATIONS

(AAP) - American Academy of Pediatrics

(AAPD) - American Academy of Pediatric Dentistry

(ADFSA) - Abu Dhabi Agriculture Food and Safety Authority

(EAPD) - European Academy of Pediatric Dentistry

(ECC) - Early Childhood Caries

(FAO) - Food and Agriculture Organization

(FOS) - Fructo-oligosaccharides

(GC) - Gas chromatography

(GCC) - Gulf Cooperation Council

(HPLC-RI) - High-performance liquid chromatography with refractive index detection

(ICDAS) - International Caries Detection and Assessment System

(LOD) - Limit of detection

(LOQ) - Limit of quantitation

(MBF) - Milk-based formulae

(NMES) - Non-milk extrinsic sugars

(PHF) - Protein hydrolysate formula

(S-ECC) - Severe early childhood caries

(SACN) - Scientific Advisory Committee on Nutrition

(SBF) - Soy-based formulae

(SES) - Socioeconomic status

(SM) - Streptococcus Mutans

(UAE) - United Arab Emirates

(WHO) - World Health Organization

1. INTRODUCTION

Tooth decay is a multifactorial disease that results from a complex interaction occurring over time between bacteria capable of producing acids and fermentable sugars in food in the biofilm in contact with the tooth surface (Featherstone, 2004). Early Childhood Caries (ECC), in specific, has been on the increase across the world and has become a major health problem (Anil and Anand, 2017). In the United Arab Emirates (UAE), the prevalence of caries in preschool children was reported to be 74.1% (Kowash *et al.*, 2017) and 80.95% in the Gulf Cooperation Council (GCC)(Al Ayyan *et al.*, 2018). Evidence examining possible various risk factors known to cause ECC are scarce (Kirthiga *et al.*, 2019). However, there is evidence that night-time use of the bottle, especially when prolonged, may be associated with early childhood caries (AAPD, 2013).

Infant formulae are primary sources of nutrition during the first years of life. Their composition is often altered to either add or remove a few components such as corn syrup, sucrose, lactose, etc. Due to their carbohydrate content, infant formulae are anticipated to have a high-cariogenic potential. The potential cariogenicity of milk and infant formulae, which are the most common bottle contents, remain uncertain and largely inconclusive (Aarthi *et al*., 2013; Tan *et al*., 2016). According to the international standards, the recommended minimum total carbohydrate content is 9.0 g/100 kcal and maximum carbohydrate content of 14.0 g/100 in infant formula (CODEX Alimentarius, 1981; Koletzko *et al.*, 2005). However, investigations into the level of added sugar to this essential part of an infant diet has been carried out worldwide (Tan *et al.*, 2016) and revealed that many products contain sugar levels that are different from the nutritional labels and are often above the recommended daily levels (Walker and Goran, 2015). To the best of our knowledge, the level of dietary sugars in commercially available infant formulae in the UAE has not been assessed before. As this is an important public health topic, the present study is intended to assess the sugar content in all infant formulae commercially available in the UAE, targeted for children up to three years of age.

2. REVIEW OF THE LITERATURE

2.1 Dental Caries: An Overview

Dental caries is a progressive disease that affects the dental hard tissues. It is the most prevalent chronic disease (Al Agili, 2013) and has been on the increase worldwide, especially in low socio-economic populations (Anil and Anand, 2017). Its prevalence is increasing in developing countries due to multiple factors; including the intake of cariogenic food, lack of exposure to fluoride and oral health services, and other lifestyle factors (Miura *et al.*, 1997). In the UAE, the prevalence of caries in preschool children was reported to be 74.1% (Kowash *et al.*, 2017). The process of dental caries is now well-established and has been studied over the past decades. Acids produced by oral bacteria and ferment carbohydrates consumed, diffuse into dental hard tissues dissolving crystals of hydroxyapatite, the main dental hard tissue component. Calcium and phosphate minerals leave the tooth structure, a process called demineralization. This demineralization process can be reversed by these minerals, calcium, and phosphate, along with fluoride, diffusing back into the tooth, in a process called remineralization (Pitts *et al.*, 2017). The balance between demineralization and remineralization is what determines oral equilibrium. However, if the pathological process predominates, caries will develop. These pathological factors are the intake of fermentable carbohydrates, the presence of cariogenic bacteria, and disturbed salivary function (Featherstone, 2004).

Caries diagnosis is achieved after air-drying teeth, in the presence of adequate light, and the use of a blunt probe to remove debris and plaque. The World Health Organization (WHO) recommends using the decayed, missing, and filled teeth (DMFT, dmft) index for permanent and primary teeth, respectively (WHO, 2013). The WHO criteria for caries diagnosis is a valid method in epidemiological studies. However, it is only efficient in detecting cavities, but not non-cavitated lesions, which would largely result in underestimating caries prevalence.

Another valid criteria for caries detection is The International Caries Detection and Assessment System (ICDAS criteria) as defined in the ICCMS^{TM} Guide for Practitioners and Educators (CCMS, 2014). The full ICDAS codes are as follows; 0; No evidence of caries, 1; Initial caries, 2; Distinct visual change in enamel, 3; Localized enamel breakdown due to caries with no visible dentine, 4; Underlying dark shadow from dentine, 5; Distinct cavity with visible dentine, 6; Extensive distinct cavity with visible dentine. Hence, it allows more precise monitoring of caries rather than simply excluding non-cavitated lesions.

2.2 Early Childhood Caries (ECC)

2.2.1 Definition

Early childhood caries (ECC) remains a major health problem globally. According to The European Academy of Pediatric Dentistry (EAPD) The term ECC corresponds to the presence of any sign of dental caries on any tooth surface during the first three years of life (EAPD, 2008). On the other hand, The American Academy of Pediatric Dentistry (AAPD) defines ECC as the presence of one or more decayed (non-cavitated or cavitated lesions), missing (due to caries), or filled tooth surfaces in any primary tooth in a child under the age of six (AAPD, 2018). Moreover, the AAPD also defines severe early childhood caries (S-ECC) as *"any sign of smooth-surface caries in a child younger than three years of age, and from ages three through five, one or more cavitated, missing (due to caries), or filled smooth surfaces in primary maxillary anterior teeth or a decayed, missing, or filled score of greater than or equal to four (age 3), greater than or equal to five (age 4), or greater than or equal to six (age 5)*" (AAPD, 2018). In other words, if a child has carious lesions by one more than his age, they are said to have severe ECC. Early childhood caries was formerly known as nursing bottle caries, baby bottle tooth decay, nursing caries, rampant caries, baby bottle caries, milk bottle syndrome, and prolonged nursing habit caries (Anil and Anand, 2017); however, studies over the past decades proved that ECC is not solely dependent on bottle-feeding habits. Therefore, the term ECC was adopted to reflect the disease etiology's multifactorial nature (Tinanoff and O'Sullivan, 1997). It has typical unique characteristics such as the presence of many carious lesions (cavitated or non-cavitated) in the primary dentition that develop rapidly and can affect teeth as soon as they erupt in the primary dentition (Fontana, 2015; Kühnisch *et al.*, 2016).

2.2.2 Prevalence

Although the prevalence of dental caries declined in western countries, caries in preschoolers remain a major health problem worldwide (Masumo *et al.*, 2012). The prevalence of ECC greatly varies with several factors like race, culture, and ethnicity; socioeconomic status, lifestyle, dietary pattern, and oral hygiene practices. Moreover, the difference in caries detection methods contributes to the varied prevalence. In most developed countries, the prevalence of ECC is between 1 and 12% (Congiu *et al*., 2014). In the United States of America (USA) specifically, data from a 2011-2012 national survey reported that ECC remains highly prevalent in poor and near-poor USA preschool children (AAPD, 2018). As measured by decayed and filled tooth surfaces (dfs), the prevalence of ECC has not changed from previous surveys. Still, the filled component (fs) has considerably increased, indicating that more treatment is being provided (Dye *et al.*, 2015). A prevalence of about 40% has been reported in the USA among 2–11-year-old children (Bugis, 2012).

On the other hand, ECC is more prevalent in low socioeconomic groups, with a prevalence as high as 70% (Ismail *et al.*, 2008). In the Middle East, a high prevalence of ECC has been reported. In Palestine, for example, it was reported to be 76% (Azizi, 2014). In the UAE, the prevalence of caries in preschool children was 74.1% (Kowash *et al.*, 2017) and 80.95% in the GCC (Al Ayyan *et al.*, 2018). Gomez et al. (Ramos-Gomez *et al.*, 2002) state that the highest prevalence of ECC is reported in the 3- to 4-year-old age group and that boys are more affected than girls. It was also reported that children with existing carious lesions are 5-6 times more likely to develop new carious lesions compared to children with no previous caries (Milsom *et al*., 2008).

2.2.3 Risk Factors

It is well understood that ECC has a multifactorial etiology. These factors can broadly be classified into cariogenic bacteria, fermentable carbohydrates, and susceptible teeth. Streptococcus Mutans (SM) and Lactobacillus species are the main microbial risk markers for ECC (Zero *et al*., 1992; Kanasi *et al*., 1992). SM ferment carbohydrates and produce acids that demineralize tooth structure. Depending on frequency and exposure, it can be transmitted vertically from the mother to the child by salivary contact (Li and Caufield, 1995). SM is mainly acquired from the mothers during the first 12-24 months, and transmission increases with poor maternal oral hygiene and frequent sugar consumption (Berkowitz, 2006). Horizontal transmission of SM can also occur between siblings or from caregivers. Other bacterial species may also be associated with ECC; however, SM is the main bacteria strongly associated with the initiation of caries, while other bacteria might be associated with caries progression (Kawashita *et al*., 2011). Diet also is a major risk factor for dental caries, especially one that includes high levels of fermentable carbohydrates (Moynihan and Kelly, 2014). As ECC is exclusive for younger children, our focus is inappropriate feeding practices. According to the AAPD, bottle feeding with milk at night, especially if prolonged, and *ad libitum* breastfeeding are associated with ECC initiation in children (AAPD, 2018; Reisine and Douglass, 1998). Although studies have shown that cow milk has virtually low cariogenicity due to its low lactose level (Bowen and Lawrence, 2005), children sleeping with sweetened milk bottles are at high risk for having ECC. The combined effect of prolonged exposure to cariogenic sugars with an inadequate clearance of sugars as they are consumed during night time increase the likelihood of fermenting these sugars by cariogenic bacteria into acid and therefore demineralizing enamel (Gupta *et al.*, 2013). Not only milk but also bottle feeding with juice throughout the day or at night increases the risk of caries (Tinanoff *et al.*, 2011). Likewise, frequent use of a sippy or no-spill cup, and snacking on sugary foods and drinks increase caries risk (Tinanoff, Kanellis and Vargas, 2002). On the other hand, ECC does not arise from breastfeeding independently (Iida *et al.*, 2007). However, when breastfeeding is combined with other carbohydrates, it is highly cariogenic in vitro (Erickson and Mazhari, 1999). According to the AAPD, on-demand breastfeeding after the first primary tooth begins to erupt is associated with ECC (AAPD, 2018). A systematic review concluded that breastfeeding for more than a year, especially if nocturnal, could be associated with a high risk for caries (Valaitis *et al.*, 2000). In general, frequent snacking, frequent exposure to sugars, sleeping with a baby bottle, in addition to maternal oral hygiene and dietary habits; all predispose to higher caries risk (Paglia *et al.*, 2016). Other risk factors for the development of ECC have been reported in the literature. Low socioeconomic status (SES), poor parental education, and several lifestyle factors are associated with ECC (Dabawala *et al.*, 2017). Although many studies revealed that ECC could affect children from both low-SES and high-SES population groups (Colak *et al.*, 2013; Meyer *et al.*, 2017), other studies concluded that children from low-SES are twice more likely to have dental caries than those from a higher-SES (Gaur and Nayak, 2011). Unemployment and migration background can be considered more specific risk factors for a high ECC prevalence (Meyer *et al.*, 2017). Children with immigrant backgrounds were found to have three times higher caries rate (Nunn *et al.*, 2009). Another sociodemographic variable is the history of parental cavities and abscessed teeth (Southward *et al.*, 2008). Social status, ethnicity, poor parental education, and dental insurance coverage are all factors that can influence the severity of ECC (Aida *et al.*, 2006). Moreover, poor oral hygiene habits promote the development of ECC. Irregular toothbrushing or brushing without supervision also increases the risk of developing ECC (Prakash *et al.*, 2012). A recent meta-analysis revealed that the two most important oral hygiene factors related to ECC were visible plaque and toothbrushing less than once daily (Kirthiga *et al.*, 2019). It is well known that saliva has a protective role against caries development. Salivary flow rate, buffering capacity, antimicrobial characteristics, and clearance of foods from tooth surfaces all play a role in preventing caries development (Jiang *et al.*, 2016). The salivary flow tends to decrease at night, particularly when children feed on high sugar-containing food or drinks at bedtime (Silva *et al.*, 2016). Susceptible teeth surfaces also increase the risk for developing ECC, and these include newly erupted teeth due to immature enamel, teeth with hypoplastic enamel (Caufield, Li, and Bromage, 2012; AAPD, 2018). Kirthiga et al. concluded that the strongest risk factors associated with ECC were the presence of enamel defects, dentinal caries, and high levels of streptococci mutans (Kirthiga *et al.*, 2019). In summary, ECC develops as soon as there is ineffective mechanical plaque removal, combined with a sugary diet, especially when sweetened food and beverages are consumed (Meyer and Enax, 2018).

2.3 Infant Formulae

2.3.1 Composition

Although human milk and breastfeeding are considered the ideal form of infant feeding as it provides many benefits for the child's wellbeing; including nutritional, developmental, and psychological advantages (AAP, 2012), in addition to the fact that it has not been epidemiologically associated with caries (Mohebbi *et al.*, 2008), however, many infants cannot be breast-fed or for whom breast milk is not available and therefore need infant formula milk. Infant formula is considered an important part of many children's diet, if not the only source of nutrition. Milk formulae can be divided into three groups: infant formulae, follow-up formulae, and whole milk formulae. Infant formulae are intended for infants during the first 4-6 months or until 12 months if complementary food is introduced (Chaudhary *et al.*, 2011). It can be further classified by protein content into three subgroups; milk-based formulae (MBF), soy-based formulae (SBF), and protein hydrolysate formula (PHF). MBF is made from cow's milk and is modified in a way to mimic human breast milk. These modifications include dilution of the protein to accommodate the infants' immature renal system and substitution of animal fat and animal protein (casein) with vegetable oils and proteins found in breast milk (whey). A modification also includes minerals; addition of iron, and adjustment of calcium: phosphorus ratio (Denne, 2015). SBF is made from soy proteins and used for children with lactose intolerance or cow's milk allergy. They are lactose-free, and contain sucrose and/or corn syrup as the main carbohydrate. PHF, also known as hypoallergenic infant formulae, contain hydrolyzed protein and amino acids, making them appropriate for infants with protein sensitivity or allergies (AAP, 2000). Soy-based and protein hydrolysate formulae both contain extrinsic sugars such as glucose and sucrose syrup. The follow-on formula is modified cow's milk covering infants' nutritional needs during 6 months to the age of two. The third group is whole milk formula, cow's milk with added necessary vitamins without added sugar restriction. This is usually recommended for children after the first year of life. To ensure infants are receiving safe products that meet their normal nutritional requirements, global standards by international committees were developed for that purpose. An example is The Codex Alimentarius Commission, which was created by the Food and Agriculture Organization (FAO) of the United Nations and the WHO, in order to develop food standards and guidelines in the area of food quality and safety, which aim to protect public health. Codex Standard 72 on Infant formula (CODEX Alimentarius, 1981) was adopted as a worldwide standard in 1981, which was then reviewed as ESPGHAN Recommended Standards for the Composition of Infant Formula (Koletzko *et al.*, 2005). This standard was divided into two main sections;

Section A defining the requirements in infant formulae that purposed to meet the normal nutritional requirements for infants. Section B defining formulae for special medical purposes intended for infants with special dietary requirements. It defines infant formula as a breast milk substitute that is specially manufactured to satisfy, by itself, the nutritional requirements of infants until the introduction of complementary feeding. It is a product based on cow milk or other animals' milk, or a combination thereof and/or other ingredients, all of which should be gluten-free. These products are physically processed only and packaged in a way to prevent spoilage and contamination under all normal conditions of storage and distribution. Their nutritional safety should be scientifically demonstrated and proven to support normal development and growth of infants. Infant formula should contain 60-70 kcal (250-295 kJ) of energy per 100 ml, after preparation according to manufacturer's instructions. Some ingredients could be added to the formula to provide substances naturally found in breast milk and to ensure that it is appropriate as the sole source of nutrition for the infant. These added ingredients, should not be added for their mere presence, but their addition should show a real benefit. Of particular interest is the total carbohydrates level, which should optimally be between 9-14 g/100kcal. As stated in the standard, lactose and glucose should be the preferred carbohydrate in formula based on cow's milk protein and hydrolyzed protein. Although not an absolute requirement for a healthy growth, lactose is the preferred carbohydrate in infant formulae (EFSA, 2014). This preference is due to the fact that lactose is predominant in human milk and to newborns' ability to hydrolyze it. Lactose is considered to have many advantages for the gut, including prebiotic effects, softening of stool, enhancement of water and calcium absorption. A specific need of infants for lactose has not been demonstrated, but its possible beneficial effects made it prudent to include lactose in infant formula. Therefore, no minimum or maximum lactose levels were set based on the available evidence (Koletzko *et al.*, 2005). Comparatively, glucose is present in low levels in human breast milk and therefore unsuitable for routine use in infant formula. It may react with protein during heat treatment of formula and form Maillard products (LSRO, 1998). Its addition to infant formula may also lead to an increased osmolality, which can cause unwanted effects in infants, such as diarrhea. The addition of 1g glucose per 100 ml formula increases osmolality by 58 mOsm/kg, and therefore, glucose addition is not recommended (Koletzko *et al.*, 2005). However, small amounts of glucose may help mitigate the disagreeable taste on infant formulae (EFSA, 2014). Furthermore, fructose addition may lead to severe side effects, including death in young infants with hereditary fructose intolerance, a hereditary disease that can lead to severe symptoms, including poor feeding, vomiting, and failure to thrive (Coffee and Tolan, 2010). Sucrose is a disaccharide containing glucose and fructose, so it is considered to have similar side effects as fructose. Feeding infants affected by this condition with fructose or sucrose containing formulae can develop hypoglycemia, vomiting, malnutrition, liver cirrhosis, and most extremely sudden death (Koletzko *et al.*, 2005). Given the possibility of life-threatening symptoms in infants with hereditary fructose intolerance in early infancy, sucrose and fructose should not be added to infant formulae. However, fructose addition to follow-on formulae may be acceptable, as most infants will be already exposed to these sugars from complementary foods (EFSA, 2014). The addition of fructose or sucrose does not have any advantage over lactose, but in fact, due to their greater sweetness, may increase the preference of sweet taste in infants. Moreover, it may be necessary to add starches to infant formulae for technical reasons. Considering the ability of infants to digest starches, precooked or gelatinized starches that are gluten-free by nature may be added to infant formula up to 30% of total carbohydrates and up to 2 g/100 ml (Koletzko *et al.*, 2005).

2.3.2 Cariogenic Potential of Milk and Infant Formulae

The cariogenicity of various bottle contents is controversial. For instance, solutions containing lactose can produce a quick drop in pH. However, in addition to lactose, milk is considered a complex solution containing calcium, phosphorus, proteins, and other vitamins (Peres *et al.*, 2002). Cow's milk is deemed to be protective against caries due to high calcium and phosphorus content. Moreover, it contains protein in the form of casein micelles, which form very stable calcium phosphate complexes, and also contains vitamin D and fluoride, which strengthens tooth development (Westover *et al*. 1989).

On the other hand, human milk cariogenicity is controversial (Bowen and Lawrence, 2005). Some studies demonstrated that it is noncariogenic, while others reported that it could be related to dental caries (Erickson and Mazhari, 1999). Breast milk has a low mineral content, a higher lactose concentration, and lower protein than cow's milk. Lactose concentration in breast milk is 7%, whereas in cow's milk, it is around 4% (Coppa *et al*., 1993; Andreas *et al*., 2015). However, the prevalence of dental caries caused by breastfeeding alone was reported to be relatively low. This is mainly due to continued breastfeeding, during the day and night, until two years of age (Valaitis *et al.*, 2000).

Conversely, the cariogenic potential of sucrose-containing solutions in the baby bottle has been well reported (Tinanoff and O'Sullivan, 1997). A high cariogenic potential of infant formulae can be expected, owing to their varied carbohydrate content (Sheikh, 1996). The available evidence on the cariogenicity of different types of infant formulae in humans is scarce. However, a systematic review (Tan *et al.*, 2016) compared the cariogenicity between different infant formulae with various sugars types. Sugars are generally divided into "intrinsic" and "extrinsic sugars" based on their availability for metabolism, with the latter further subdivided into milk and non-milk extrinsic sugars (NMES)(Hussein *et al.*, 1996). The main measures of formulae cariogenicity studied were changes in plaque pH and salivary buffering capacity (Tan *et al.*, 2016). In general, SBF was more likely to be cariogenic and produces more considerable plaque changes than MBF (Danchaivijitr *et al.*, 2006). Other studies compared the effect of types of sugar on cariogenicity of infant formulae. According to the sugar content, infant formulae are categorized into: formulae containing lactose only, formulae containing NMES, which include sucrose, glucose, honey, oligofructose, etc., and formulae containing both lactose and NMES. Formulae containing only NMES are more cariogenic as they produce more remarkable plaque pH changes than formulae containing only lactose, while formulae containing both lactose and NMES produce significant plaque pH changes greater than both previous formulae (de Mazer Papa *et al.*, 2010; Raju *et al.*, 2012). Although infant formulae were reported to be as cariogenic as sucrose in some studies, their cariogenic potential varied across other studies, and no definite conclusions could be drawn (Aarthi *et al*., 2013). However, the systematic review concluded that the cariogenicity of different infant formulae types remained inconclusive. Studies' findings were either contradictory or based on a limited level of evidence. On the other hand, an in vitro study, which compared the effects of human breast milk and infant formulae on enamel mineral content in primary teeth, concluded that breast milk was protective against demineralization, whereas infant formulae promote loss of minerals from enamel surface (Aly *et al*., 2019). Moreover, it was demonstrated that sucrose containing formulae result in more significant increase in biofilm growth compared to lactose-based formulae (Hinds *et al.*, 2016).

2.3.3 Nutritional Labels

Many products are frequently marketed and consumed by infants worldwide. Since 1981, the WHO adopted the International Code of Marketing of Breast-milk Substitutes (WHO, 1981), which aims to provision of safe and adequate nutrition for infants by ensuring proper use of breast milk substitutes, when necessary, based on adequate information through suitable marketing and distribution. It recommends that labels be designed to provide transparent information about the appropriate use of the products and not discourage breastfeeding. The label should state the ingredients used, the composition, analysis of the product, the storage conditions required, and the batch number with an expiry date. As previously mentioned, the global standard requirements for infant formulae are based on the ESPGHAN guidelines (Koletzko *et al.*, 2005). It is assumed that manufacturers of infant formulae comply with these standards. However, studies comparing the actual nutritional values with the labeled values are scarce. A Saudi study compared the package labels of infant formulae with ESPGHAN standards (Almazrooy *et al.*, 2017) and found all formulae studied were safe and nutritionally adequate. However, in terms of sugar specifically, it was reported in another study that the nutrient label data can underestimate or overestimate actual sugar levels (Walker and Goran, 2015) and that many products contain sugars in amounts that exceed the recommended daily levels and differ from nutrition labels. To the best of our knowledge, the level and type of dietary sugars in commercially available infant formulae in the UAE have not been studied before. Neither the comparison between labeled and measured sugar content, hence the purpose of this study.

3. AIM

The aim of this study is to assess the amount and type of dietary sugars in commercially available infant formulae in the UAE.

3.1 Specific Objectives

1. To compare the labeled and measured levels of glucose, fructose, and sucrose and determine whether they are accurately identified on the infant formulae products' labels.
2. To calculate the total calories of measured sugars consumed from the infant formulae per day and compare them against the recommended intake.

3.2 Hypothesis

The sugar content in infant formulae available in the UAE market is optimum according to the international recommendations for the maximum daily intake of infants and young children and is accurately labeled.

4. MATERIALS AND METHODS

This study involved measuring sucrose, glucose, and fructose in 71 different brands of commercially available infant formulae for retail sale in the baby food sections in major supermarkets in the UAE.

4.1 Inclusion Criteria

I. Organic and non-organic milk-based and goat milk formulae
II. Soy-based, hydrolyzed rice, and lactose-free formulae
III. Formulae recommended for healthy infants from birth until three years of age

4.2 Exclusion Criteria

Infant formulae for special medical purposes (except lactose-free formulae).

4.3 Experimental Analysis

The experimental analysis was conducted in a private laboratory in Dubai (Geoscience Testing Laboratory). Samples were sent to the lab, each in a coded container, to assure the laboratory chemist's blinding to the brand and nutritional labels of the formulae tested. Quantifying sucrose, glucose, and fructose was performed using high-performance liquid chromatography with refractive index detection (HPLC-RI). The machine used Agilent HPLC 1260™WITH RI Detector™ (Figure 1), was calibrated before being used to test the samples. Calibration was performed by a trained laboratory chemist assigned by the distributing company. Study and control cycle were run using HPLC RID VWD Software™. Before preparing the samples for testing, the mobile phase for chromatographic separation was done by mixing 800 ml of acetonitrile and 200 ml of water. This mixture was sonicated for 15 minutes and degassed before use. Calibration was done using a stock standard consisting of 1g of glucose, 1g of fructose, 1g of sucrose, 1g of lactose, and 10.4g of maltose monohydrate mixed with HPLC grade water up to 10 ml marking in a volumetric flask. From this stock standard, five calibration standards were made; 1) calibration level-1: 10 ml solution of 0.1 ml of the stock standard with water, 2) calibration level-2: 10 ml solution of 0.5 ml of the stock standard with water, 3) calibration level-3: 10ml solution of 1 ml of the stock standard with water, 4) calibration level-4: 10ml solution of 2 ml of the stock standard with water, 5) calibration level-5: 10ml solution of 4 ml of the stock standard with water. All calibration standards were placed in glass vials and put in a vortex mixer for homogeneity (Figure 2). Samples were then prepared; the infant formulae were reconstituted according to the manufacturers' instructions using distilled water, as detailed in Table 1.

Figure 10: Agilent HPLC 1260™ WITH RI Detector™

Figure 11: Calibration standards in vortex mixer

According to sugar content, infant formulae were categorized into: a) formulae containing lactose only (L), b) formulae containing non-milk extrinsic sugars (NMES), and c) formulae containing both lactose and NMES (L+NMES). Each formula was measured and stirred manually in a glass beaker, then transferred into a sonicator (Ultrasonic bath XUBA3™) for

15 minutes to ensure homogeneity of the prepared samples (Figure 3). Two ml of the homogenized sample was taken and added to 1.5 ml of distilled water (Figure 4), and incubated at 60 degrees Celsius for 10 minutes. Samples were then allowed to cool before adding 0.25ml of Carrez solution I, 0.25ml of Carrez solution II, and 1ml of acetonitrile. The samples were then centrifuged again for 10 minutes (Figure 5).

Figure 12: Infant formulae samples stirred manually and transferred into a sonicator

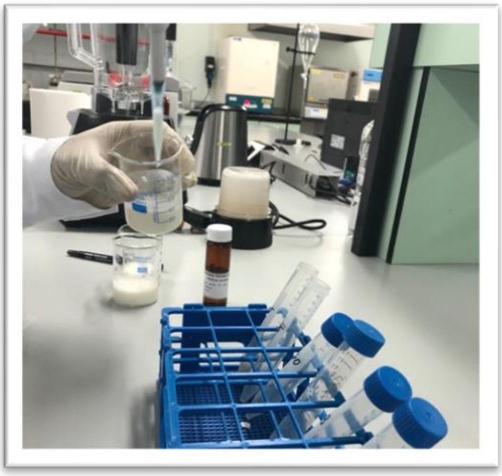

Figure 13: 2ml of the sample added to 1.5 ml of distilled water

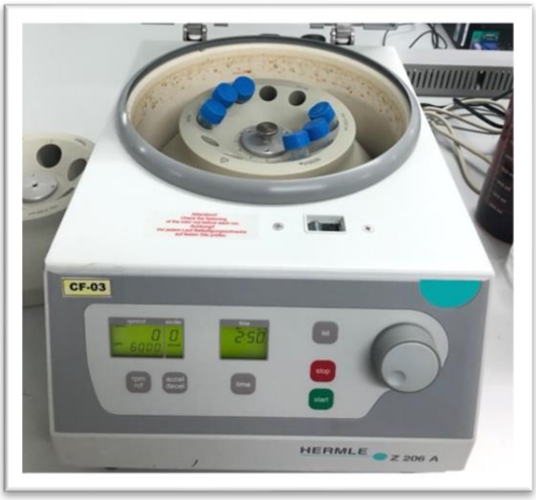

Figure 14: Samples centrifuged for 10 minutes

The resultant upper aqueous layer was removed by filtration, using a 0.45 microliter nylon filter, injected into a 2ml HPLC vial (Figure 6), and then into the HPLC (Figure 7). To ensure accuracy of the results, a duplicate sample was taken from each sample at this point, with resultant two vials of the same sample injected into the HPLC.

Figure 15: Aqueous layer (pointed with red arrow) injected into HPLC vial by filtration

Figure 16: Samples placed in HPLC

Moreover, a quality control sample was performed simultaneously to ensure that laboratory analysis results are consistent, comparable, and accurate within specified limits of precision. During every batch of testing, verification standards were run along with the sample, and the response was measured. If the response varied by more than 20% from the initial calibration peak, the instrument was calibrated. A blank sample was injected between every two consecutive samples to ensure stability and to allow the refractive index to return to baseline between samples. The measured readings of sucrose, fructose, and glucose appeared on the software at the end of the testing cycle. The HPLC machine used for testing is run by the limit of quantitation (LOQ) and limit of detection (LOD) methods. LOD is the smallest concentration of an analyte in a test sample that can be distinguished from zero, whereas LOQ is the smallest concentration of an analyte in a test sample that can be determined with acceptable repeatability. LOD is set at 0.1, which means that the lowest concentration of any of the three sugars tested that can be reliably detected was 0.1 g/100ml.

4.4 Data analysis

Descriptive analysis was performed using tables. Comparison between this study's findings, data on the products' labels, WHO standards, and ESPGHAN Standard for infant formulae was done.

Brand Name	Age Range (months)	Manufacturing Country	Manufacturers' Instructions			Classification According to Labeled Sugar Content
			Scoop volume (g of powder/ml water)	Number of scoops/serving	Water volume (ml)/serving	
1. Aptamil 1	birth - 6	Holland	4.5 / 30	7	210	L + NMES
2. Aptamil Lactose-Free	birth - 6	Holland	4.3 / 30	7	210	NMES
3. Baby & Me Organic1	birth - 6	Denmark	4.3 / 30	6	180	L
4. Bebelac 1	birth - 6	Poland	4.087 / 30	7	210	L + NMES
5. Bebelac Lactose-Free	birth - 6	Holland	3.87 / 30	7	210	NMES
6. Biomil plus 1	birth - 6	France	N/A	7	210	N/A
7. Blemil Plus 1	birth - 6	Spain	4.5 / 30	7	210	L
8. Hipp Organic 1	birth - 6	Germany	4.3 / 30	7	210	L + NMES
9. Humana 1	birth - 6	Germany	4.5 / 30	6	180	L + NMES
10. Illuma 1	birth - 6	Ireland	8.8 / 60	3	180	L + NMES
11. Jovie Organic (goat infant milk) 1	birth - 6	Austria	4.3 / 30	6	180	L + NMES
12. Kabrita 1 (goat milk-based)	birth - 6	Holland	4.4 / 30	7	210	L + NMES
13. Liptomil plus 1	birth - 6	France	4.5 / 30	7	210	L

Brand Name	Age Range (months)	Manufacturing Country	Manufacturers' Instructions			Classification According to Labeled Sugar Content
			Scoop volume (g of powder/ml water)	Number of scoops/serving	Water volume (ml)/serving	
14. Nan Optipro 1	birth - 6	Netherlands	4.37 / 30	7	210	L
15. Nan Supreme HA 1	birth - 6	Switzerland	4.367 / 30	7	210	L + NMES
16. Novalac 1	birth - 6	Germany	4.37 / 30	6	180	N/A
17. Nutrilac 1	birth - 6	USA	8.5 / 60	4	240	NMES
18. Primilac premium 1	birth - 6	Holland	4.3 / 30	7	210	L + NMES
19. S-26 Lactose-Free Gold	birth - 6	Netherlands	4.4 / 30	7	210	NMES
20. S-26 Pro Gold 1	birth - 6	Singapore	8.6 / 60	3	180	L + NMES
21. Similac Gold 1	birth - 6	Ireland	N/A	3	180	NMES
22. Similac Total Comfort 1	birth - 6	Spain	8 / 60	3	180	L + NMES
23. Liptomil plus Lactose-Free	From birth onwards	France	4.5 / 30	7	210	N/A
24. SMA Pro 1	From birth onwards	Europe	4.4 / 30	6	180	N/A
25. Blemil plus HR 1 (hydrolyzed rice protein)	from 1st day	Spain	4.5 / 30	7	210	L + NMES

Brand Name	Age Range (months)	Manufacturing Country	Manufacturers' Instructions			Classification According to Labeled Sugar Content
			Scoop volume (g of powder/ml water)	Number of scoops/serving	Water volume (ml)/serving	
26. Nan Lactose-Free	birth - 12	Netherlands	4.39 / 30	7	210	N/A
27. Nanny Care (goat milk-based)	birth - 12	New Zealand	4.3 / 30	8	240	L
28. Primilac Lactose-free	birth - 12	Holland	4.3 / 30	7	180	NMES
29. SMA Pro 2	6+	Europe	4.6 / 30	6	180	N/A
30. Isomil 2 (soy follow on formula)	from 6	Netherlands	N/A	4	240	N/A
31. Blemil plus HR 2 (hydrolyzed rice protein)	from 6th month onwards	Spain	4.7 / 30	8	240	L + NMES
32. Aptamil 2	6-12	Holland	4.9 / 30	7	210	L + NMES
33. Baby & Me Organic2	6-12	Denmark	4.6 / 30	7	210	L + NMES
34. Bebelac 2	6-12	Poland	4.47 / 30	7	210	L + NMES
35. Biomil plus 2	6-12	France	N/A	7	210	N/A
36. Blemil Plus 2	6-12	Spain	4.7 / 30	8	240	L + NMES
37. Hipp Organic 2	6-12	Germany	4.5 / 30	6	180	L + NMES

Brand Name	Age Range (months)	Manufacturing Country	Manufacturers' Instructions			Classification According to Labeled Sugar Content
			Scoop volume (g of powder/ml water)	Number of scoops/serving	Water volume (ml)/serving	
38. Humana 2	6-12	Germany	4.5 / 30	6	181	L + NMES
39. Jovie Organic (goat infant milk) 2	6-12	Austria	4.5 / 30	7	210	L + NMES
40. Kabrita 2 (goat milk-based)	6-12	Holland	4.6 / 30	6	180	L + NMES
41. Liptomil plus 2	6-12	France	4.5 / 30	6	180	L + NMES
42. Nan Optipro 2	6-12	Switzerland	4.597 / 30	7	210	L
43. Nan Supreme HA 2	6-12	Switzerland	4.527 / 30	7	210	L + NMES
44. Novalac 2	6-12	Germany	4.37 / 30	7	210	N/A
45. Primilac premium 2	6-12	Holland	5 / 30	6	180	L + NMES
46. S-26 Promil Gold 2	6-12	Singapore	9.27 / 60	3	180	L + NMES
47. Similac Total Comfort 2	6-12	Spain	9.1 / 60	3	180	L + NMES
48. Nutrilac 2	6-12	USA	9.2 / 60	4	240	NMES
49. Similac Gold 2	6-12	Ireland	N/A	3	180	NMES
50. Illuma 2	6-12	Ireland	7 / 45	4	180	L + NMES

Brand Name	Age Range (months)	Manufacturing Country	Manufacturers' Instructions			Classification According to Labeled Sugar Content
			Scoop volume (g of powder/ml water)	Number of scoops/serving	Water volume (ml)/serving	
51. Jovie Organic (goat infant milk) 3	12+	Austria	4.5 / 30	5	150	L + NMES
52. Aptamil 3	12-36	Holland	4.9 / 30	6	180	L + NMES
53. Baby & Me Organic3	12-36	Denmark	4.5 / 30	7	210	L
54. Bebelac 3	12-36	EU	4.67 / 30	6	180	L + NMES
55. Hipp Organic 3	12-36	Germany	4 / 30	6	180	L
56. Humana 3	12-36	Germany	4.7 / 30	6	182	L + NMES
57. Illuma 3	12-36	Ireland	8.11 / 42	5	210	L + NMES
58. Kabrita 3 (goat milk-based)	12-36	Holland	4.8 / 30	6	180	L + NMES
59. Nan Optipro 3	12-36	Switzerland	4.67 / 30	7	210	L + NMES
60. Nan Supreme HA 3	12-36	Switzerland	4.527 / 30	7	210	L + NMES
61. Nestle NIDO one plus	12-36	UAE	N/A	6	210	N/A
62. NovalacGenio vanilla flavor	12-36	Germany	4.37 / 30	7	210	N/A
63. Primilac premium 3	12-36	Holland	5.5 / 30	6	180	NMES

Brand Name	Age Range (months)	Manufacturing Country	Manufacturers' Instructions			Classification According to Labeled Sugar Content
			Scoop volume (g of powder/ml water)	Number of scoops/serving	Water volume (ml)/serving	
64. S-26 Progress Gold 3	12-36	Singapore	8.4 / 42	5	210	L + NMES
65. SMA Pro 3	12-36	Europe	4.6 / 30	6	180	N/A
66. Nutrilac 3	12-36	USA	8.8 / 44	4	175	NMES
67. Biomil plus 3	12-36	France	N/A	6	180	NMES
68. Similac Gold 3	12-36	Ireland	N/A	3	180	NMES
69. Similac Total Comfort 3	12-36	Spain	9.1 / 60	4	240	N/A
70. Blemil Plus 3	12-36	Spain	4.8 / 30	8	240	L + NMES
71. Lipto Growl plus 3	12-48	France	4.5 / 30	6	180	L + NMES

Table 1: Infant formulae samples tested with manufacturer's instructions as labeled on packages. (L+NMES: lactose and non-milk extrinsic sugars, NMES: non-milk extrinsic sugars only, L: lactose only, N/A: sugar labeling unavailable).

5. RESULTS

5.1 Sugar Content of the Infant Formula Samples

The total number of infant formulae tested was 71. These were tested for sucrose, glucose, and fructose. All tested samples were manufactured outside the UAE, except one (Nestle Nido One Plus). Out of the 71 samples, 23 had detectable sugar levels. Twelve samples had glucose and ranged for use between birth and 36 months. Only one sample had detectable fructose (Similac Total Comfort 1) with a value of 4.6 g/100ml. This sample belonged to the infant formulae category, intended for use between birth and six months of age. Sucrose was detected in 10 samples. All these 10 samples belonged to the follow-on formulae category, intended for use in the range of 6-12 and 12-36 months. The infant formulae in which the three sugars were detected are listed in table 2, arranged in ascending order according to levels of glucose, fructose, and sucrose measured.

Brand Name	Age Range (months)	Classification According to Sugar Content	Measured Sugar Levels (g/100ml)		
			Glucose	Fructose	Sucrose
1. Humana 1	birth - 6	L + NMES	**0.17**	<0.1	<0.1
2. Aptamil 2	6-12	L + NMES	**0.17**	<0.1	<0.1
3. Aptamil 1	birth - 6	L + NMES	**0.18**	<0.1	<0.1
4. Aptamil 3	12-36	L + NMES	**0.18**	<0.1	<0.1
5. Bebelac 3	12-36	L + NMES	**0.18**	<0.1	<0.1
6. Aptamil Lactose-Free	birth - 6	NMES	**0.18**	<0.1	<0.1
7. Bebelac 1	birth - 6	L + NMES	**0.2**	<0.1	<0.1
8. Nan Lactose-Free	birth - 12	N/A	**0.2**	<0.1	<0.1
9. Bebelac Lactose-Free	birth - 6	NMES	**0.21**	<0.1	<0.1
10. Bebelac 2	6-12	L + NMES	**0.22**	<0.1	<0.1
11. Primilac Lactose-Free	birth - 12	NMES	**0.23**	<0.1	<0.1
12. Humana 3	12-36	L + NMES	**0.28**	<0.1	<0.1
13. Similac Total Comfort 1	birth - 6	L + NMES	<0.1	**4.6**	<0.1

Brand Name	Age Range (months)	Classification According to Sugar Content	Measured Sugar Levels (g/100ml)		
			Glucose	Fructose	Sucrose
14. Blemil Plus 3	12-36	L + NMES	<0.1	<0.1	**0.8**
15. Illuma 2	6-12	L + NMES	<0.1	<0.1	**1.01**
16. Similac Total Comfort 3	12-36	N/A	<0.1	<0.1	**1.05**
17. Similac Gold 3	12-36	NMES	<0.1	<0.1	**1.07**
18. Similac Gold 2	6-12	NMES	<0.1	<0.1	**1.12**
19. Isomil 2 (soy follow on formula)	from 6	N/A	<0.1	<0.1	**1.16**
20. Nutrilac 2	6-12	NMES	<0.1	<0.1	**1.42**
21. Similac Total Comfort 2	6-12	L + NMES	<0.1	<0.1	**1.47**
22. Biomil plus 3	12-36	NMES	<0.1	<0.1	**1.47**
23. Nutrilac 3	12-36	NMES	<0.1	<0.1	**2.87**

Table 2: Infant formulae samples in which sugar (glucose, fructose, sucrose) was detected

Of these 23 infant formulae, 12 samples belong to the L+NMES category, and eight belong to the NMES category. None belong to the lactose-only group. Three infant formulae packages did not have a clearly labeled sugar content and were classified as N/A. Figure 8 demonstrates these results.

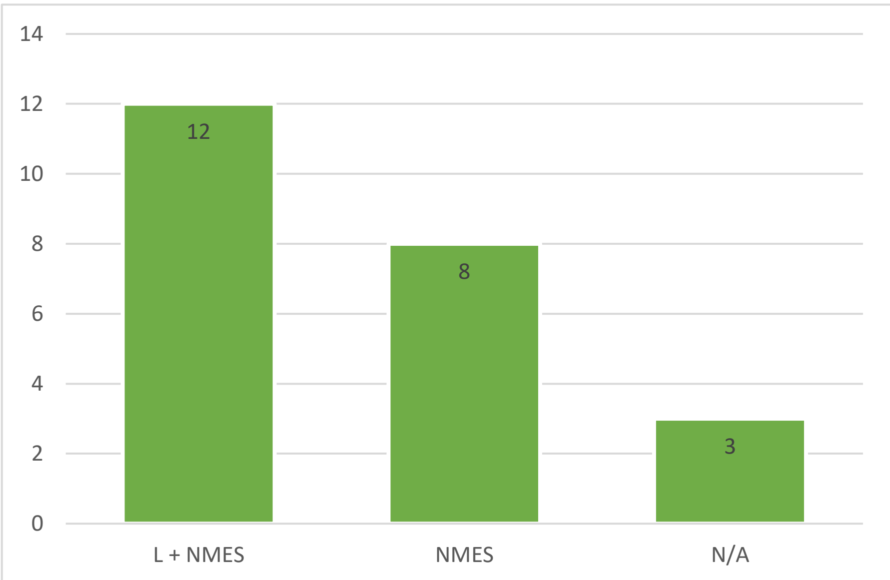

Figure 17: Classification of infant formulae in which sugar was detected, according to their labeled sugar content. (L+NMES: lactose and non-milk extrinsic sugars, NMES: non-milk extrinsic sugars only).

5.2 Daily Sugar Consumption from the Tested Samples

Following the daily recommended manufacturers' preparation guidelines, the daily sugar consumption from the 23 samples where sugar (glucose, fructose, sucrose) was detected was calculated and compared with the recommended intake, as mentioned in Table 3.

The total grams of measured sugar per serving and per day were calculated for each infant formula according to the manufacturers' recommendations, and values were obtained from the following equation: grams of sugar per serving = [(water volume per serving (ml) x measured sugar (g)) / 100ml]. This value was then multiplied by the recommended number of servings per day to get the total grams of measured sugar per day. One sample (Similac Total Comfort 1) contained above 30 g of sugar per day, and this was the only sample with fructose detected.

In order to compare the labeled carbohydrate levels against the standard, the labeled carbohydrate level per 100 kcal was calculated for each sample. According to the international standards, the recommended total carbohydrate content in infant formulae is 9.0-14 g/100 kcal (CODEX Alimentarius, 1981; Koletzko *et al.*, 2005). Only one sample (Nutrilac 3) exceeded the recommendation with a value of 24.14 g of carbohydrate per 100 kcal.

Moreover, the total calories in kcal per 100ml were recorded from the package labeling, then the total calories per serving and per day were calculated. The percent of total calories from sugar was derived from the following equation: % total calories from sugar = [(total g of sugar per day x 4) / total calories per day] x 100. Figure 9 presents the percentages of the contribution of sugars to the daily caloric intake. Of all infant formulae products that were analyzed, eight were found to have sugars contributing to more than 5% of total energy intake, and two samples to more than 10% (Similac Total Comfort 1 and Nutrilac 3).

Brand Name	Measured Sugar Levels (g/100ml)			Daily Sugar Consumption					
	Glucose	Fructose	Sucrose	g of sugar per serving	g of sugar per day	g of (labeled) carbohydrate/100kcal	kcal per serving	kcal per day	% of total calories from sugar
1. Humana 1	0.17	<0.1	<0.1	0.31	1.53	10.44	122	612	1.00
2. Aptamil 2	0.17	<0.1	<0.1	0.36	1.07	11.49	141	422	1.01
3. Aptamil 1	0.18	<0.1	<0.1	0.38	1.51	11.23	137	546	1.11
4. Aptamil 3	0.18	<0.1	<0.1	0.32	0.97	11.75	113	340	1.14
5. Bebelac 3	0.18	<0.1	<0.1	0.32	0.97	11.88	124	373	1.04
6. Aptamil Lactose-Free	0.18	<0.1	<0.1	0.38	1.51	11.06	139	554	1.09
7. Bebelac 1	0.2	<0.1	<0.1	0.42	2.10	11.23	137	683	1.23
8. Nan Lactose-Free	0.2	<0.1	<0.1	0.42	1.26	11.64	141	422	1.19
9. Bebelac Lactose-Free	0.21	<0.1	<0.1	0.44	2.21	11.36	139	693	1.27
10. Bebelac 2	0.22	<0.1	<0.1	0.46	1.39	11.64	141	422	1.31
11. Primilac Lactose-Free	0.23	<0.1	<0.1	0.41	1.24	11.06	119	356	1.39
12. Humana 3	0.28	<0.1	<0.1	0.51	1.02	12.24	122	244	1.67
13. Similac Total Comfort 1	<0.1	4.6	<0.1	8.28	49.68	10.44	122	734	**27.06**
14. Blemil Plus 3	<0.1	<0.1	0.8	1.92	3.84	11.59	166	331	4.64

Brand Name	Measured Sugar Levels (g/100ml)			Daily Sugar Consumption					
	Glucose	Fructose	Sucrose	g of sugar per serving	g of sugar per day	g of (labeled) carbohydrate/100kcal	kcal per serving	kcal per day	% of total calories from sugar
15. Illuma 2	<0.1	<0.1	1.01	1.82	9.09	12.09	121	603	6.03
16. Similac Total Comfort 3	<0.1	<0.1	1.05	2.52	7.56	10.82	178	533	5.68
17. Similac Gold 3	<0.1	<0.1	1.07	1.93	5.78	10.41	133	400	5.78
18. Similac Gold 2	<0.1	<0.1	1.12	2.02	10.08	10.81	133	666	6.05
19. Isomil 2 (soy follow on formula)	<0.1	<0.1	1.16	2.78	11.14	12.17	166	662	6.72
20. Nutrilac 2	<0.1	<0.1	1.42	3.41	10.22	7.12	175	701	5.84
21. Similac Total Comfort 2	<0.1	<0.1	1.47	2.65	13.23	10.82	133	666	7.95
22. Biomil plus 3	<0.1	<0.1	1.47	2.65	7.94	11.04	121	362	8.78
23. Nutrilac 3	<0.1	<0.1	2.87	5.02	15.07	**24.14**	152	457	**13.20**

Table 3: Daily consumption of sugar as per manufacturers' preparation instructions and labels' data.

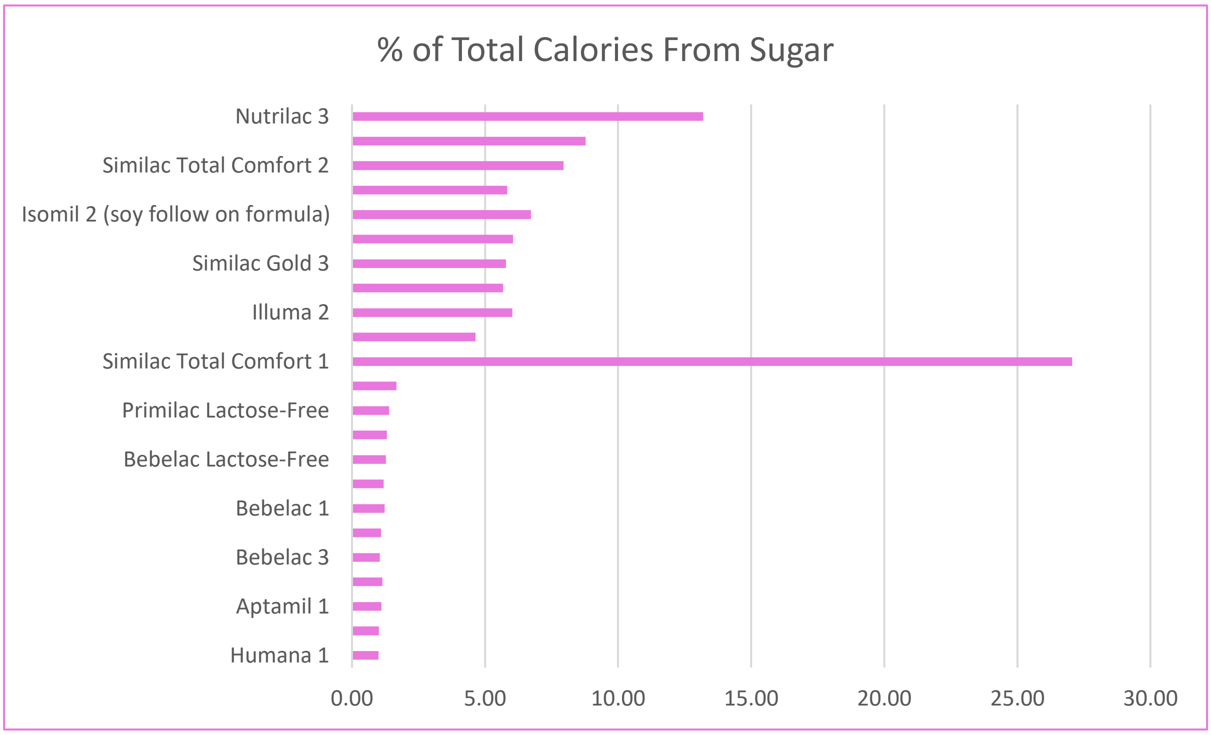

Figure 18: Percent of total calories from sugars available in the infant formulae tested.

5.3 Comparison Between Labeled and Measured Sugar Content

All tested samples had the total carbohydrate level mentioned on the label. Out of the 23 samples where the glucose, fructose, or sucrose were detected, only four had the fructose level labeled. Fructose was reported on the labels as fructo-oligosaccharides (FOS) or oligofructose. Glucose was reported on the label of 10 samples. Sucrose, also labeled as saccharose, was found on the label of only one sample, and the labeled level was higher than tested. Table 4 compares the labeled and measured glucose, fructose, and sucrose levels, respectively, for samples in which sugar was detected. All the labeled and the measured sugar levels in the rest of the samples are summarized in table 5.

Brand Name	Measured Glucose	Labeled Glucose
1. **Humana 1**	0.17	0.2
2. **Aptamil 2**	0.17	0.2
3. **Aptamil 1**	0.18	0.2
4. **Aptamil 3**	0.18	0.3
5. **Bebelac 3**	0.18	0.2
6. **Aptamil Lactose-Free**	0.18	0.2
7. **Bebelac 1**	0.2	0.2
8. **Nan Lactose-Free**	0.2	N/A
9. **Bebelac Lactose-Free**	0.21	0.2
10. **Bebelac 2**	0.22	0.2
11. **Primilac Lactose-Free**	0.23	N/A
12. **Humana 3**	0.28	0.2
	Measured Fructose	**Labeled Fructose**
13. **Similac Total Comfort 1**	4.6	N/A

	Measured Sucrose	Labeled Sucrose
14. Blemil Plus 3	0.8	2.1
15. Illuma 2	1.01	N/A
16. Similac Total Comfort 3	1.05	N/A
17. Similac Gold 3	1.07	N/A
18. Similac Gold 2	1.12	N/A
19. Isomil 2 (soy follow on formula)	1.16	N/A
20. Nutrilac 2	1.42	N/A
21. Similac Total Comfort 2	1.47	N/A
22. Biomil plus 3	1.47	N/A
23. Nutrilac 3	2.87	N/A

Table 4: Comparison between labeled and measured sugar levels in samples in which sugar was detected.

Brand name	Age range (months)	Labeled sugar content (g/100ml)		Measured Sugar Levels (g/100ml)		
				Glucose	Fructose	Sucrose
1. Baby & Me Organic1	Birth-6	**Carbohydrates**	6.6	<0.1	<0.1	<0.1
		Lactose	6.5			
2. Biomil plus 1	Birth-6	**Carbohydrates**	7.62			
3. Blemil Plus 1	Birth-6	**Carbohydrates**	7.1			
		Lactose	7.1			
4. Hipp Organic 1	Birth-6	**Carbohydrates**	7			
		of which sugars	7			
		of which lactose	6.9			
5. Illuma 1	Birth-6	**Carbohydrates**	7.5			
		Lactose	7.2			
		Oligo-fructose	0.3			
		2'-O-fucosyllactose	0.03			
6. Jovie Organic (goat infant milk) 1	Birth-6	**Carbohydrates**	7.1			
		Lactose	6.9			
7. Kabrita 1 (goat milk based)	Birth-6	**Carbohydrates**	7.5			
		Lactose	6.9			
8. Liptomil plus 1	Birth-6	**Carbohydrates**				
		Lactose	7.18			
9. Nan Optipro 1	Birth -6	**Carbohydrates**	7.5			
		lactose	7.5			
10. Nan Supreme HA 1	Birth-6	**Carbohydrates**	7.6			
		lactose	5.2			
11. Novalac 1	Birth-6	**Carbohydrates**	7.5			
		Sugars	5.3			
12. Nutrilac 1	Birth-6	**Carbohydrates**	7.2			
		GOS	0.4			
13. Primilac premium 1	Birth-6	**Carbohydrates**	7.3			
		Lactose	6.9			
		Maltodextrin	0.31			
		GOS	0.25			
14. S-26 LF Gold	Birth-12	**Carbohydrates**	7.8			
		Lactose	<0.007			
15. S-26 Pro Gold 1	Birth-6	**Carbohydrates**	7.4			
		Lactose	6.9			
		Sucrose	0.0			
		Oligofructose	0.5			

		2’-0-Fucosyllactose	0.03			
16. Similac Gold 1	Birth-6	**Carbohydrates**	6.7			
		Fructo-oligosaccharides	0.2			
		2’-fucosyllactose	0.2			
		Sugars	6.6			
17. Liptomil plus LF	From birth onwards	**Carbohydrates**	7.94			
18. SMA Pro 1	From birth	**Carbohydrates**	7.1			
		of which, sugars	7.1			
19. Blemil plus HR 1 (hydrolyzed rice protein)	From 1st day	**Carbohydrates**	7.7			
		Maltodextrin	6			
		Corn starch	1.6			
20. Nanny Care (goat milk based)	Birth-12	**Carbohydrate**	7.4			
		of which sugars	7.4			
		of which lactose	7.4			
21. SMA Pro 2	6+	**Carbohydrates**	7.9			
		of which, sugars	5.5			
22. Blemil plus HR 2 (hydrolyzed rice protein)	From 6th month onwards	**Carbohydrates**	8.1			
		Maltodextrin	6.4			
		Corn starch	1.7			
23. Baby & Me Organic2	6-12	**Carbohydrates**	7	<0.1	<0.1	<0.1
		Lactose	5.2			
		Maltodextrin	1.6			
24. Biomil plus 2	6-12	**Carbohydrates**	8.22			
25. Blemil Plus 2	6-12	**Carbohydrates**	7.3			
		Lactose	6.5			
		Maltodextrin	0.8			
26. Hipp Organic 2	6-12	**Carbohydrates**	7.2			
		of which sugars	7.2			
		of which lactose	7			
27. Humana 2	6-12	**Carbohydrates**	7.6			
		Glucose	0.2			
		Lactose	5.2			
		Maltose	0.1			
		Dextrins	1.0			
		Starch	1.1			
28. Jovie Organic (goat infant milk) 2	6-12	**Carbohydrates**	6.9			
		Lactose	6.7			
		Friendly advice: make sure your baby’s teeth are cleaned after the last feeding				

29. Kabrita 2 (goat milk based)	6-12	**Carbohydrates**	7.8	<0.1	<0.1	<0.1
		Lactose	7.1			
30. Liptomil plus 2	6-12	**Carbohydrates**	7.74			
		Lactose	5.58			
		Maltodextrin	2.16			
31. Nan Optipro 2	6-12	**Carbohydrates**	8			
		lactose	8			
32. Nan Supreme HA 2	6-12	**Carbohydrates**	7.8			
		lactose	4.9			
33. Novalac 2	6-12	**Carbohydrates**	7.2			
		Sugars	5.3			
34. Primilac premium 2	6-12	**Carbohydrates**	8.3			
		Lactose	7.8			
		Maltodextrin	0.41			
		GOS	0.39			
35. S-26 Promil Gold 2	6-12	**Carbohydrates**	8.1			
		Lactose	7.6			
		Sucrose	0			
		Oligofructose	0.5			
		2'-0-Fucosyllactose	0.03			
36. Jovie Organic (goat infant milk) 3	12+	**Carbohydrates**	6.9			
		Lactose	6.7			
		Friendly advice: make sure your baby's teeth are cleaned after the last feeding				
37. Baby & Me Organic3	12-36	**Carbohydrates**	7			
		Lactose	7			
38. Hipp Organic 3	12-36	**Carbohydrates**	6			
		of which sugars	6			
		of which lactose	6			
39. Illuma 3	12-36	**Carbohydrates**	10.8			
		Lactose	7.9			
		Maltodextrin	2.6			
		Oligo-fructose	0.3			
		2'-O-fucosyllactose	0.03			
40. Kabrita 3 (goat milk based)	12-36	**Carbohydrates**	8			
		Lactose	7.3			
41. Nan Optipro 3	12-36	**Carbohydrates**	8.1			
		Lactose	5.6			

42. Nan Supreme HA 3	12-36	**Carbohydrates**	7.6			
		lactose	4.7			
43. Nestle NIDO one plus	12-36	**Carbohydrates**	7.88			
		No Sucrose added				
44. Novalac Genio vanilla flavor	12-36	**Carbohydrates**	7.5			
		Sucrose free				
45. Primilac premium 3	12-36	**Carbohydrates**	9.8			
		GOS	0.4	<0.1	<0.1	<0.1
46. S-26 Progress Gold 3	12-36	**Carbohydrates**	10.7			
		Lactose	9.4			
		Sucrose	0			
		Oligofructose	0.5			
		2’-0-Fucosyllactose	0.03			
47. SMA Pro 3	12-36	**Carbohydrates**	9			
		of which, sugars	6.6			
48. Lipto Grow plus 3	12-48	**Carbohydrates**	7.64			
		Lactose	5.75			
		Maltodextrin	1.89			

Table 5: Comparison between labeled and measured sugar levels in samples in which sugar was not detected.

6. DISCUSSION

This study examined an aspect related to an important building block in many infants' lives, namely the use of milk formula. Many mothers resort to using infant formulae early in their babies' lives alone or combined with breastfeeding (Grummer *et al*., 2008). This practice may continue into the primary dentition phase and beyond, thus negatively affecting teeth (Chaudhary *et al.*, 2011). The introduction of formulae milk goes against most international guidelines and associations, including The American Academy of Pediatrics (AAP), which recommend exclusive breastfeeding for the first six months of life, and the introduction of complementary foods *along* with breastfeeding during the first year of life (AAP, 2019). This is because human milk and breastfeeding are considered the ideal form of infant feeding as they provide many benefits for the child's wellbeing; including nutritional, developmental, and psychological advantages (AAP, 2012), in addition to the fact that it has not been epidemiologically associated with caries (Mohebbi *et al.*, 2008). However, many infants cannot be breastfed and therefore need infant formula milk partially or solely.

The present study specifically investigated the levels of glucose, fructose, and sucrose in commercially available infant formulae in the UAE. As mentioned above, infant formula is considered an essential part of many children's diet, if not the only source of nutrition for the early months of life, and hence the importance of investigating this issue. These specific types of sugar were selected in this study due to their well-known implication in dental caries. In descending order of cariogenicity, sucrose, glucose, and fructose have been well established as cariogenic sugars (Sheiham, 1983).

Several techniques have been developed to evaluate the sugar content in food. One of the methods is analysis by gas chromatography (GC) (Mason and Slover, 1971). Even though GC is a sensitive and reliable method for sugar analysis, its process is strenuous and lengthy. GC was the dominant technique for analyzing carbohydrates until the mid-1970 when the high-performance liquid chromatography (HPLC) method started to become the leading method. This technique is used for its accuracy and rapidity compared to the GC method. Due to its reported satisfactory precision and sensitivity, the HPLC method was used in our study.

A total of 71 different brands of commercially available infant formulae available for retail sale in the UAE were analyzed for sucrose, fructose, and glucose levels. Organic and non-organic milk-based and soy-based formulae recommended for healthy infants from birth until three years of age were included. Hydrolyzed rice, lactose-free, and goat milk formulae were also included. Because our study aimed to assess the amount and type of dietary sugars in infant formulae for infants in general, formulae for special medical purposes (except lactose-free formulae) were excluded. Although the list of products included might not be comprehensive, it is likely to be representative of products available commercially.

As reported in the literature, formulae containing only non-milk extrinsic sugars (NMES) are more cariogenic as they produce more remarkable plaque pH changes than formulae containing only lactose (de Mazer Papa *et al.*, 2010). Whereas formulae containing both lactose and NMES produce significant plaque pH changes greater than both other formulae categories (de Mazer Papa *et al.*, 2010; Raju *et al.*, 2012). Based on the labels' data of our 71 infant formulae samples tested, 38 samples belonged to the L+NMES category, 12 belonged to the NMES category, and eight to the lactose only category. Thirteen formulae packages did not have a clearly labeled sugar content. Having most samples available in the UAE market that belong to the L+NMES followed by the NMES categories suggests that almost 70% of the samples are cariogenic. The fact that 13 samples had no labeled sugar content is another issue that requires attention as it might be assumed that a certain infant formula product does not have added sugar simply because it is not mentioned on the label. The Abu Dhabi Agriculture Food and Safety Authority (ADFSA) regulates the quality of infant formulae products sold in the UAE. Although it states that infant formulae labels should include the nutritional value and product ingredients including: energy, protein, carbohydrates, vitamins, and minerals (ADFSA, 2019); it is not required by law to disclose the specific sugar content. On a broader scale, the WHO developed The International Code of Marketing of Breast-milk Substitutes (WHO, 1981), which includes regulations for the marketing of feeding bottles. It states that the label of infant formulae should state the ingredients used, the composition/analysis of the product, the storage conditions required, and the expiry date, however, it does not impose disclosing sugar content specifically. This is an important issue for future research, and it can be argued that the level of carbohydrates, in general, is not enough and can be misguiding in terms of sugar consumption.

Out of the 71 samples, 23 had detectable sugar levels, and none of these samples had any combination of detected sugars. These results differ from Walker and Goran's study, where it was found that sugar content in infant formulae was distributed amongst lactose, sucrose, maltose, or glucose (Walker and Goran, 2015). According to the ESPGHAN Recommended Standards for the Composition of Infant Formula (Koletzko *et al.*, 2005; CODEX Alimentarius, 1981), lactose and glucose should be the preferred carbohydrate in formula based on cow's milk protein and hydrolyzed protein. The current study did not analyze the lactose content because lactose has virtually low cariogenicity (Bowen and Lawrence, 2005). However, 12 samples had glucose and ranged for use between birth and 36 months. Glucose levels ranged from 0.17 to 0.28 g/100ml. As stated in the standard, glucose is present in low levels in human breast milk, thus, based on that it is unsuitable for routine use in infant formula. Its addition to infant formula may also lead to an increased osmolality, which can cause unwanted effects in infants, such as diarrhea (Koletzko *et al.*, 2005). A major point of interest is its implications in dental caries. Even if present at fairly low levels, Glucose increases caries' rate (Sheiham, 1983; Gupta *et al*., 2013).

According to the ESPGHAN recommendations, fructose addition may lead to severe side effects, including death in young infants with hereditary fructose intolerance. Given these serious complications, fructose should not be added to infant formulae intended for use during the first six months of life. Still, its addition to follow-on formulae may be acceptable since infants will be exposed to it from complementary foods (Koletzko *et al.*, 2005). In this study, one sample had detectable fructose (Similac Total Comfort 1) with a value of 4.6 g/100ml. This is of primary concern as this sample belonged to the infant formulae category, which is intended for use between birth and six months of age, and this contradicts the above-mentioned recommendation. Not to mention that although fructose is less cariogenic than sucrose, it is still considered a cariogenic sugar (Sheiham, 1983).

Sucrose, which is also known as saccharose, is a disaccharide containing glucose and fructose, so the EPSGHAN standards also recommend that sucrose should not be added to infant formula until six months of age (Koletzko *et al.*, 2005). The current study results demonstrated compliance with this recommendation, as the ten samples where sucrose was detected belonged to the follow-on formulae category, intended for use in the range of 6-12 and 12-36 months. Nine of these samples were milk-based formulae (MBF), and only one was a soy-based formula (SBF).

As mentioned in the literature, unlike milk-based formulae (MBF), soy-based formulae (SBF) are lactose-free and contain sucrose as the main carbohydrate (Pediatrics, 2000). Isomil 2 (soy follow on formula) was the only SBF in our study and had a sucrose level of 1.16 g/100ml. Although its addition does not have any benefits over lactose, sucrose tends to be added to mitigate the potentially unpleasant taste of infant formulae (EFSA, 2014). A note of caution is due here as, because of the greater sweetness and the innate preference for sweet taste in infants, it can be assumed that infants might develop a form of attachment to infant formulae and lose the bond to breastmilk. This in turn is alarming since it is widely known that human milk and breastfeeding are considered the ideal form of infant feeding, as it provides many benefits for the child's wellbeing; including nutritional, developmental, and psychological advantages (AAP, 2012).

From a dental perspective, sucrose has been described as the most cariogenic sugar (Anderson *et al.*, 2009). One of the issues that emerge from our findings is that sucrose was detected in 10 samples in the range of 0.8-2.87 g/100ml. The cariogenic potential of sucrose-containing solutions in the baby bottle has been well reported (Tinanoff and O'Sullivan, 1997). Moreover, sucrose-containing formulae result in a more significant increase in biofilm growth than lactose-based formulae (Hinds *et al.*, 2016). Although ECC has a multifactorial etiology, bottle feeding with milk at night, especially if prolonged, is associated with ECC initiation in children (AAPD, 2018). Children sleeping with sweetened milk bottles are at a higher risk for having ECC. It is important to bear in mind that not only exposure to cariogenic sugars but also the added effect of inadequate clearance of sugars as they are consumed during night time increase the likelihood of fermenting these sugars by cariogenic bacteria into acid and therefore demineralizing enamel (Paglia *et al.*, 2016).

An objective of this study was to calculate the total calories of measured sugars consumed from the infant formulae per day and compare them against the recommended intake. The results of this study show that eight of the infant formulae tested were found to have sugars contributing to more than 5% of total energy intake, and two samples to more than 10%. The WHO has a strong recommendation for both adults and children that added sugar should provide less than 10% of total energy intake, or less than 60 grams per person per day, whichever is lesser, and a conditional recommendation for a further reduction of the intake of free sugars to below 5% of total energy intake (WHO, 2015). Similarly, the Scientific Advisory Committee on Nutrition (SACN) recommends that for all age groups from two years and above, the intake of free sugars should not exceed 5% of total dietary energy intake (SACN, 2015). There are no specific recommendations for infants; however, the ESPGHAN Committee on Nutrition states that free sugar intake in infants and toddlers should be even lower than 5% of energy intake (ESPGHAN, 2017). The high percentages of total energy intake calculated in the present study (eight samples > 5% and two samples > 10%), were based on the values of detected sugars and following manufacturers' recommendations for numbers of servings per day. These findings may somewhat be limited by the possibility that not all infants might be on a feeding regimen that follows these recommendations; some infants might be exclusively formula-fed, others might be formula-fed along with breastfeeding (mixed feeding). Therefore, it is possible that although some infant formulae in this study contain added sugar in amounts that contribute to more than 5% of the total energy intake, infants that are mixed fed might not be consuming more than the recommendation. Moreover, infants may be weaned and introduced to complementary feeding from six months, so other food products contribute to the total energy intake. However, it is safe to assume that these findings are applicable for infants that are exclusively formula-fed.

It is also worth mentioning that in this study, only three types of sugars were tested, namely, sucrose, glucose, and fructose. There are perhaps other added sugars that will also increase the percentage of added sugars' contribution to the total energy intake.

As mentioned in the literature review, global standards by international committees were developed to ensure infants are receiving safe products that meet their normal nutritional requirements (CODEX Alimentarius, 1981). ESPGHAN Recommended Standards for the

Composition of Infant Formula (Koletzko *et al.*, 2005) state that the total carbohydrates level should optimally be between 9-14 g/100 kcal. There are no recommendations for each sugar, and for that reason, it was not possible to correlate this value with our tested sugar values. However, we compared the labeled carbohydrate levels mentioned on the package against the standard. Only one sample (Nutrilac 3) exceeded the recommendation with a value of 24.14 g of carbohydrate per 100 kcal. Almazrooy *et al.* compared five types of infant formula brands, and they all were compliant with the standard, with a carbohydrate content of 9-14 g/100 kcal (Almazrooy *et al.*, 2017). However, this finding has been based on a relatively small sample size.

This brings us to another objective, comparing the labeled and measured glucose, fructose, and sucrose levels for samples in which sugar was detected. It is assumed that manufacturers of infant formulae comply with standards. Very few studies have been conducted to determine the possible discrepancy between the actual and labeled sugar levels. A Saudi study compared the package labels of infant formulae with ESPGHAN standards (Almazrooy *et al.*, 2017) and reported that all formulae studied were safe and nutritionally adequate. Unlike our study, their comparison was done between the information written on the formulae's containers and ESPGHAN standards, and no laboratory testing was involved. A similar study investigated the labeling, energy, carbohydrate, and sugar content of formula milk products (Bridge, Lomazzi and Bedi, 2020). Their data were collected from the information reported in the packaging of products and concluded that most of the sampled products were high in total carbohydrates. In 2015, Walker and Goran conducted a similar study and reported that the nutrient label data can underestimate or overestimate actual sugar levels and that many products contain sugars in amounts that exceed the recommended daily levels and differ from nutrition labels (Walker and Goran, 2015). This present study's results are consistent with the latter study, in which a range of differences was noted. It is worth noting that all infant formulae packages had carbohydrate levels mentioned on the labels, but very few mention details about the added sugar content. In infant formulae in which glucose was detected, the difference between the labeled and measured glucose levels was very minimal, ranging between 0.03 and 0.12, with some of these samples having more detected glucose than labeled, and other with less. Two of these samples did not have any labeled glucose level so comparison was not possible. Likewise, for the infant formula in which fructose was detected, no fructose level was labeled on the package. Most infant formulae – all except one – in which sucrose was detected, no sucrose level was labeled. In the only product which had the sucrose level mentioned on the package, the labeled sucrose was higher than that measured. These finding are rather disappointing, because although total carbohydrate level is labeled, not mentioning sugars and their values on labels can be misleading to parents. As mentioned earlier, the ADFSA regulates the quality of infant formulae products sold in the UAE, and although it states that infant formulae labels should include carbohydrates value (ADFSA, 2019); companies are not mandated by law to disclose the specific sugar content. Another cause of concern is the usage of unclear terms on the package labeling. Fructose, for example was reported on the labels as fructo-oligosaccharides in the abbreviated form (FOS) or oligofructose, and this confusing labeling may be difficult to interpret by parents. In accordance with the present results, Bridge *et al.*, have also reported that nutritional information on the infant formula products were unclear and inconsistent (Bridge *et al*., 2020) .

To the best of our knowledge, this is the first comprehensive study to use laboratory analysis to test the actual content and levels of sugars in infant formulae available in the UAE. Our findings agree with other studies, which suggest that children could be exposed to more added daily sugars than expected (Walker and Goran, 2015). It was demonstrated that total sugars, in some products, contribute to more than 5% of total calories, and this represents a significant risk to infants and toddlers. A major area of interest was the unavailable sugar labeling on most of the products. This is particularly alarming because even if it was not labeled, these products still contain sugars and are consumed by infants whose parents are not aware of the actual sugar content. To help prevent future adverse health outcomes, including ECC, which are secondary to the overconsumption of sugar, having international guidelines and standards for informing the public of the actual sugar content by having adequate labeling is necessary. It is also important to emphasize in addition to overconsumption of sugar, bad feeding habits such as bottle feeding at night contribute to the development of ECC, and advise should be given to parents on this matter. Interestingly, only one infant formulae brand (Jovie Organic goat infant milk 2 and 3) noted a friendly advice to parents: “make sure your baby’s teeth are cleaned after the last feeding”.

There may be some possible limitations in this study. The first is a limitation related to the HPLC method used in our study. The limit of detection (LOD) was set at 0.1, which means that any sugar value below 0.1 g/100ml was just recorded as <0.1 and not precisely detected. Another limitation is the unawareness of the methods used by each infant formula company to measure the sugar level disclosed. Different techniques might have led to discrepancies between the labeled and measured sugar levels in the study samples. Moreover, we specifically investigated the levels of sucrose, glucose, and fructose, and in commercially available infant formulae, due to their well-established cariogenic potential. However, other types of sugar might also be present, leading to an increased caries risk and an increased contribution of sugars to the total caloric intake. Additionally, although the calculated values of sugar contribution to the total energy intake are applicable for exclusively formula-fed infants, they must be interpreted with caution for infants who are mix-fed or introduced to complementary feeding.

7. CONCLUSIONS AND RECOMMENDATIONS

In the sample of studied infant milk formulae commercially available in the UAE, it was found that:

- Many infant formulae products consumed by infants and young children contained sugars contributing to the total dietary energy intake in amounts exceeding the recommended intake.
- There were many discrepancies between the labeled and measured sugar levels in the study samples
- Sugar was not listed on the label of some products.

Despite the importance of early childhood nutrition and the need to limit added sugar intake, no regulations mandate manufacturers to disclose added sugars. Therefore, there is a definite need to recommend tighter regulations that monitor the amount of sugar in infant formulae and have a comprehensive labeling system that accurately discloses the sugar levels. Having clear labeling on infant formulae packages alongside raising public awareness on the necessity to limit sugar intake during infancy allows parents to make informed decisions that may reduce adverse health problems secondary to excess sugar consumption in early childhood.

Determining pediatricians' and pediatric dentists' interpretation and understanding of guidelines related to bottle feeding and infants' oral health is a possible direction for future research. Further research could also be undertaken to investigate parents' compliance with weaning recommendations and oral hygiene practices in infants. Additionally, it would be of value to explore the popularity of different formulae brands both with parents and pediatricians.

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9. APPENDICES

APPENDIX I: Ethical Approval

27 February 2020

Dr Rawan Awad
Resident, Pediatric Dentistry
HBMCDM

Dear Dr Rawan,

This is with reference to the application titled "Sugar composition and level of commercially available infant formulae in United Arab Emirates (UAE)" for exempt review. The Board has reviewed the same at its meeting of February 25, 2020 and has agreed that the application does not require the approval of the IRB as human subjects are not involved in the study. However, as the study is on a commercial product, all personnel involved in the study will need to confirm that there is no conflict of interest by signing the conflict of interest forms.

For any questions, please contact the Institutional Review Board irb@mbru.ac.ae.

Thank you for your interest in MBRU's IRB.

Sincerely,

Dr Essa Kazim
Chairman, MBRU-IRB