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Original article

A systematic comparison between infant formula compositions using the Bray-Curtis Similarity Index

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ABSTRACT

Background: Making an informed choice between the available infant formulas is challenging, as there is no unbiased tool allowing a systematic comparison between the very long lists of infant formula compositions.
Aim: The aim is to present the Bray-Curtis Similarity Index (BCSI) as a tool for systematic comparison between standard stage-1 infant formula (SS-1-IF) compositions.
Methods: We obtained the nutrient levels from the packaging labels of 23 SS-1-IFs available in Al-Ahsa, Saudi Arabia, in April 2018. The international legislations that launched infant formula standards endorse targeting the minimum rather than the maximum proposed nutrients levels. Thus, we blindly compared between displayed nutrients levels on each of the 23-studied SS-1-IF and the minimum international proposed nutrient levels via using the BCSI.
Results: The range of the total displayed components was 38–57. Except for docosahexaenoic acid, all displayed components were within the standard recommended range. The BCSI summarized all displayed nutrients in a single number. The BCSI of the studied SS-1-IF ranged from 0.4141 to 0.79730. We ranked the 23 studied SS-1-IFs based on the higher BCSI is the closer to the minimum proposed nutrient levels. A dendrogram segregated the SS-1-IFs into four clusters based on their BSCI and total numbers of all displayed components.
Conclusions: We think the BCSI is an appropriate tool for a systematic comparison between SS-1-IFs compositions and may help for choosing a SS-1-IF.

1. Introduction

Breast milk (BM) is the ideal nutrition for infants during their first 6 months of life [1]. However, when BM is not feasible, infant formula (IF) is the recommended alternative. [1] Globally, approximately 60% of infants are IF fed during their first 6 months of life [2,3]. The 2007 revised CODEX STAN 72–1981 (Codex, hereafter) is the international standard for IF launched by the Codex Alimentarius Commission [4]. The International Expert Group of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) updates the standards for the Codex Alimentarius Commission [5]. The European Commission and its companion, the European Food Safety Authority Panel on Dietetic Products, Nutrition and Allergies (EFSA-NDA), also established IF standards similar to the Codex [6,7]. This legislative framework recommends that manufacturers of IFs display the nutrients levels on the packaging labels of IFs. Manufactures of IFs display energy, nutrients levels, moisture, and ash on the packaging using different headings, including nutritional information, nutritional value, composition, average composition, average analysis, approximate analysis, or standard analysis. Hereafter, we are using the term nutritional information (NI) when referring to this part of the packaging label.

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The IF that is used for feeding 0- to 6-month-old healthy term infants is commonly called standard stage-1 IF (SS-1-IF) [8]. There are many brand names for cow milk-based powder SS-1-IF available in the market. No clinical comparison is available for the SS-1-IFs [9,10]. Two reasons contribute to this lack of knowledge. First, it is difficult, if not impossible, to conduct such a clinical study [11]. Second, clinical studies are not a prerequisite for manufacturing or adding new nutrients to SS-1-IFs [11,12]. Nutrients just need to be "Generally Recognized As Safe" to be added to SS-1-IFs [11,12].

The information displayed on the NI is supposed to facilitate making an informed choice of the SS-1-IF brand [13]. However, it is challenging to use the NI data to compare between SS-1-IFs [3,14,15], possibly due to the absence of an unbiased tool allowing a systematic comparison between NI data [16]. Previous studies conducted to compare NI data of IFs SS-1-IFs were descriptive and included few of the SS-1-IF available in the market. A study identified 10 IFs in the Iraqi market, but the comparison was performed with only four IFs [17]. Another study identified more than 18 IFs in the Saudi market but compared only five IFs [18].

Of 436 surveyed mothers, 20% responded "No" and 38.8% responded "sometimes" regarding "whether they believed pediatricians are well aware of the best formula for their babies" [9]. This study found that most of the surveyed mothers are confused when choosing the best IF [9]. Another study reported that caregivers found NIs difficult to comprehend irrespective of their educational level or ethnicity [3]. The caregivers wanted to compare nutrients in IFs to assist them in making an informed choice of the most suitable IF. However, this is not possible because NIs display a very long list of similar items without displaying their reference limits. This study recommended the development of an understandable and effective tool to assist in comparing IFs.

Researchers in biodiversity and ecology use several compositional similarity indices for comparing species abundance in two different assemblages [19–21]. The Bray-Curtis Similarity Index (BCSI) is a frequently used abundance-based index [19,21]. The BCSI is expressed as $[2M/(A+B)]$, where M is the sum of the lower (minimum) of the two abundances for species found in both assemblages and A and B are the sums of the abundances of all species in both assemblages. The BCSI ranges from 0 to 1, where 0 means the two sites are completely dissimilar and 1 means the two sites are completely similar [21]. The BCSI is also used in scientific areas other than biodiversity and ecology. For example, the BCSI was used to compare bacterial colonization profiles in various human organs [22,23] and the nutritional composition of seed of various harvests [24,25]. Another advantage is that the BCSI supports performing a cluster analysis [26].

As finding a safe and suitable IF is important globally, we agree with others that supporting breastfeeding should not prevent educating health care givers and health care providers to find a safe and suitable IF [27]. We presume that BCSI can be a useful tool for a systematic comparison of IFs [10]. The BCSI equation is rephrased to fit this purpose as follows:

$$BCSI = \frac{2 \times (\text{sum of lower level of each displayed level and its corresponding benchmark level})}{(\text{sum of all displayed and their corresponding benchmark levels})}$$

As an example, suppose the levels of three items in an SS-1-IFs are 1.8, 1.5, and 0.8 and their corresponding benchmark levels (BL) are 2, 1, and 0.5, respectively. From these data, we create three pairs: (1.8, 2), (1.5, 1) and (0.8, 0.5). The lower level of each pair are as follows: 1.8, 1, and 0.5.

$BCSI = \frac{2\times(1.8+1+0.5)}{(1.8+1.5+0.8+2+1+0.5)} = 0.87$ The interpretation of the BCSI result is that the SS-1-IF is 87% similar to the BL. The aim of the study is to demonstrate how the BCSI can be used to compare SS-1-IFs.

2. Material and methods

We conducted a cross-sectional study in the Al-Ahsa, Saudi Arabia. Three of the authors (AA, JA, FA) identified all SS-1-IFs available in pharmacies and supermarkets in April 2018. The packaging of each SS-1-IF was photographed after obtaining permission. The displayed information on the NI packaging was entered into Excel Microsoft software. Quality control was performed by two authors (MA and AZ) by double-checking the data extraction and entry. The remaining author (SA), blinded to the brand names of the SS-1-IFs, calculated the BCSI, performed the analysis, and wrote the first draft of the manuscript.

2.1. Benchmark levels (BL)

We selected 42 components of the information displayed on the NI panels for the BCSI calculation. The selection criteria for the 42 components were as follows: (1) mandatory components; (2) nutrients considered by the Codex as objectional nutrients (i.e., should not be added to IFs); and (3) nutrients that were displayed by $\geq$ 50% of the study IFs and not a component of essential nutrients. Author SA made seven assumptions to create the BL for these 42 nutrients.

The Codex considers 34 components with their minimum and maximum levels as mandatory [4]. These 34 components are energy, protein, total fat, linoleic acid, α-Linolenic acid, total carbohydrates, 13 vitamins, 12 minerals and trace elements, choline, myo-Inositol, and L-carnitine. The first assumption was that the BL for the 34 components are the Codex-proposed minimum levels. The basis for choosing the minimum rather than the maximum nutrients levels was the ESPGHAN and EFSA-NDA statements. The ESPGHAN [5,28] and EFSA-NDA [6] state that unnecessary amounts of nutrients may be a burden on an infant's metabolic and physiologic functions and may reduce the safety margin. The EFSA-NDA endorses targeting the minimum rather than the maximum proposed nutrients levels [6]. The proposed maximum nutrients levels appear to be more controversial than the proposed minimum levels [28]. Some experts assert that the maximum levels may be driven by commercial interests rather than by infants' nutritional requirements [28]. A large randomized control trial found that adolescents who were fed with an IF with 2.3 mg/L iron at 6–12 months of age had better cognitive outcomes than their counterpart who were fed an IF fortified with 12 mg/L iron [29]. We chose the Codex for benchmarking, as more than 160 countries globally are members of the Codex [5].

The second assumption was that the BL for glucose and fluoride should be 'zero'. The basis of this assumption is that the Codex [4], the ESPGHAN [5], and the EFSA-NDA [6] are against adding glucose and fluoride to SS-1-IF (objectional nutrients).

The Codex and the EFSA-NDA consider docosahexaenoic (DHA), arachidonic (ARA), and eicosapentaenoic (EPA) acids as optional nutrients [4, EFSA-NDA6]. However, recently, the European Commission considered the DHA as a mandatory nutrient and proposed 0.02 g/100 kcal as the minimum level [7]. The third assumption was therefore that the BL for DHA is accepted as 0.02 g/100 kcal. The Codex endorses that if DHA is added to IF, ARA should at least be the same as DHA [4,30]. The Codex and the European Commission endorse that if DHA is added to IF, EPA should not exceed the DHA [4,7]. The fourth assumption was that the prescribed DHA level is accepted as the BL for ARA and EPA.

The Codex and the ESPGHAN [4,5] as well as the European Commission and the EFSA-NDA [EFSA-NDA6, 7] consider some nutrients as optional. They propose only maximum levels of some of these nutrients. These optional nutrients are potentially beneficial as they are present in BM. Oligosaccharides, the third most abundant nutrients in BM, is one of these optional nutrients [EFSA-NDA6]. The European Commission via the EFSA-NDA allows one of two combinations of oligosaccharides added to IFs [EFSA-NDA6, EFSA-NDA7, EFSA-NDA] [31]. The first combination is a 9:1 ratio of galacto-oligosaccharide (GOS) to fructo-oligosaccharide (FOS) with 0.8 g/dL as the total proposed maximum. Two of the study SS-1-IFs displayed the GOS:FOS combination. The GOS:FOS ratio was 9:1 and the total 0.3 g/dL in one SS-1-IF. In the second SS-1-IF, the GOS:FOS ratio was 6:1 and the total 0.27 g/dL. Only one SS-1-IF declared that it contains 0.02 g/dL of 2-Fl without LNnT. The fifth assumption was that 0.3 g/dL is accepted as the BL for the two SS-1-IFs declared GOS and FOS combination, 0.18 for the SS-1-IF declaring 2-FL, and 0.8 g/dL for the remaining SS-1-IFs.

For taurine and nucleotides, there are only proposed maximum levels [5, EFSA-NDA6, 7]. The 6th assumption was therefore that the maximum proposed levels of taurine and nucleotides are their BL. The 7th assumption was if any of the selected nutrients was not displayed on the NI, the score is 'zero'.

2.1.1. *Statistical analysis*

The Codex expresses the proposed levels of macronutrients in gram (g)/100 kcal [4]. Nucleotides, taurine, L-carnitine, and some minerals are expressed in milligram (mg)/100 kcal and vitamins, some minerals, and trace elements in μg/100 kcal. The proposed oligosaccharides levels are only expressed in g/dL. Levels of BLs ranged from 60 (energy) to 0.0000001 (B12). The high value, different scales of measurement, and outliers distort the BCSI [20,26,32]. Thus, all nutrients levels, except energy and oligosaccharides, were expressed in g/dL, and the appropriate unit conversions were performed as the first step in resolving the problem. Despite these units, conversation boxplots detected 6 severe outliers (Supplementary graphs). A power transformation was the second step to resolve the problem [26,32]. A fourth-root (power = 0.25), a tenth-root (power = 0.10), and a twentieth-root (power = 0.05) were assessed in terms of numbers and magnitude of outliers and normalizing the distribution of the components levels. The normal distribution was assessed by visual examination of the histograms, mean, median, skewness, kurtosis, and a Shapiro-Wilk test. The normality plots and tests as well as boxplots indicated that 0.10 power transformation is more suitable than 0.25 and 0.05 power transformation (supplementary graph). Thus, the BCSI for each SS-1-IF was calculated with a 0.10 power transformed component level (Supplementary Excel Workbook). Subsequently, the BCSI results were back-transformed by a power of 10 to report the actual BCSI [33].

A hierarchical cluster analysis (HCA) was used to classify the SS-1-IFs based on their BCSIs and total number of displayed components on the NI panels. The first large jump in the agglomeration coefficients was considered the 'best-cut' at which to stop the clustering process [34]. An Excel Microsoft and an IBM-SPSS (version 20, Chicago, IL) were used for the statistical analysis.

3. Results

We identified 23 SS-1-IFs available in the Al-Ahsa area. Table 1 depicts remarks on all displayed components on the NI panel of each SS-1-IF. The range of the displayed NI components was 38–57. Sixteen (70%) SS-1-IFs displayed more than 42 components on their NI panels. Nutrients were expressed in the Codex-required units in only 5 (22%) SS-1-IFs (Table 1). The concertation of the nutrients was listed as average concentration in 14 SS-1-IFs, as nutritional information in 4, as standard analysis in 2, and as approximate analysis, nutritional value, and composition in 1 SS-1-IF each.

Half of the SS-1-IFs (n = 21) displayed all 34 essential nutrients listed in the Codex and 2 SS-1-IFs displayed 33 essential nutrients but not L-carnitine. Six SS-1-IFs included fluoride and 3 included glucose. Three SS-1-IFs, Aptamil, Bebelac, and Humana Bebemil, indicated both fluoride and glucose.

Seventeen SS-1-IFs displayed DHA/ARA, including two who displayed EPA. Of this group, only one SS-1-IF complied with the European Commission's minimum proposed DHA level. Except for DHA, all other nutrients were within the standard recommended range.

Six SS-1-IFs included total saturated fats, one displayed total trans fatty acids and one had total saturated fats and trans fatty acids as one component. Five SS-1-IFs indicated total polyunsaturated fats. Almost half (n = 18) SS-1-IFs indicated a subtotal of polyunsaturated fats as all had linoleic and α-Linolenic acids and 12 SS-1-IFs displayed DHA/ARA, with two also displaying EPA.

The Whey: Casein ratio was available or could be calculated in 15 SS-1-IFs. Just over half (n = 22) had taurine and 18 displayed oligosaccharides. Nineteen SS-1-IFs displayed total nucleotides of which 8 also displayed levels for the 5 nucleotide types added to their SS-1-IFs.

Ten SS-1-IFs displayed ash levels ranging from 2.1 to 3.6 g/100g of powder. Nine SS-1-IFs displayed moisture levels, all were ≤2.0%–3.0%. Lutein, β-carotene, and carotenoids were displayed on the NI panels of 5, 3, and 1 SS-1-IFs, respectively.

The range of the BCSI of 0.10 power transformed component levels was 0.4141–0.7970 (Table 1). The HCA indicated that the first large jump in the agglomeration coefficients 'best-cut' was at 7.5 cluster distances. Stopping the clustering process at this 'best cut' segregated the studied SS-1-IFs into four clusters (Fig. 1).

4. Discussion

BM is the best nutrition for infants with SS-1-IF as the recommended alternative when the BM is unavailable or not an option. There are many brand names of SS-1-IFs available in the market. Making an informed choice between the available infant formulas is challenging, as there is no unbiased tool allowing a systematic comparison between the very long lists of infant formula compositions. We demonstrated that the BCSI can be used as an unbiased tool for a systematic comparison between SS-1-IFs. We could rank the SS-1-IFs based on the higher BCSI, the closer to the minimum proposed nutrient levels. This ranking will help informed decision-making when choosing a SS-1-IF.

The ESPGHAN and EFSA-NDA endorse targeting the minimum rather than the maximum proposed nutrients levels [5,6, 28]. Thus, we blindly compared between displayed nutrients levels on each of the 23-studied SS-1-IF and the minimum proposed nutrient levels by the Codex, ESPGHAN, EFSA-NDA, or the European Commission via using the BCSI BLs are required to calculate the BSCI. We made seven assumptions to create the BLs. Most of the assumptions were based on the international standard. The similarity between the BLs

Table 1
The 23 identified standard stage-1 infant formula (SS-1-IF) ranked in order of decreasing Bray-Curtis similarity indices (BCSIs) and remarks on displayed components.

SS-1-IF ranked in order of decreasing BCSIs	BCSI	Remarks on displayed components
1. Supramil Premium	0.7970	Number of all displayed components: 48 Galacto-oligosaccharide (GOS): Fructo-oligosaccharide (FOS) ratio 9:1 Docosahexaenoic (DHA), (below recommended level) Arachidonic (ARA) Taurine Total nucleotides and its 5 components Ash (2.4 g/100 g of powder)
2. S-26 PRO Gold	0.7865	Number of displayed components: 47 α-lactalbumin DHA (below recommended level) ARA FOS Taurine Lutein Carotenoids Total nucleotides Ash (3.3 g/100 g of powder)
3. Illuma	0.7759	Number of all displayed components: 48 α-lactalbumin β-Palmitate DHA (within recommended range) ARA Whey: Casein ratio 64:36 FOS Taurine Lutein β-carotene Total nucleotides Moisture Highest Ash (3.6 g/100 g of powder)
4. Bright-51	0.7707	Number of all displayed components: 44 DHA (below recommended level) ARA Whey: Casein ratio 60:40 GOS Taurine Lutein Total nucleotides Ash (2.5 g/100 g of powder)
5. Fabimilk	0.7691	Nutrients were expressed in the Codex-required units Number of all displayed components: 53 α-lactalbumin Total Saturated fats Trans fatty acids Total Monounsaturated fats Total Polyunsaturated fats DHA (below recommended level) ARA Whey: Casein ratio 60:40 FOS Taurine Total nucleotides and its 5 components Moisture Ash (2.4 g/100 g of powder)
6. Lactonic Gold	0.7561	Number of all displayed components: 50 Total Saturated fats DHA (below recommended level) ARA Whey: Casein ratio 60:40 GOS: FOS ratio 6:1 Taurine Total nucleotides and its 5 components
7. Frisolac Gold	0.7552	Number of all displayed components: 52 Total Saturated fats Total Monounsaturated fats Total Polyunsaturated fats DHA (below recommended level) ARA Whey: Casein ratio 60:40 GOS Taurine Total nucleotides and its 5 components Moisture
8. Similac Intelli-Pro	0.7472	Number of all displayed components: 44

Table 1 (*continued*)

SS-1-IF ranked in order of decreasing BCSIs	BCSI	Remarks on displayed components
		DHA (below recommended level) ARA GOS Taurine Lutein β-carotene Total nucleotides Ash (2.9 g/100 g of powder)
9. NAN OPTIPRO	0.7386	Number of all displayed components: 43 DHA (below recommended level) ARA Lactose only as carbohydrates 2′-O-fucosyllactose Taurine Total nucleotides Ash (2.7 g/100 g of powder)
10. Nuralac	0.7277	Number of all displayed components: 42 DHA (below recommended level) ARA GOS Taurine Total nucleotides
11. Primalac Premium	0.7237	Nutrients were expressed in the Codex-required units Number of all displayed components: 44 DHA (below recommended level) ARA Whey: Casein ratio 60:40 Lactose only as carbohydrates GOS Taurine Total nucleotides Fluoride
12. Liptomil Plus	0.7204	Nutrients were expressed in the Codex-required units Number of all displayed components: 50 DHA (below recommended level) ARA Eicosapentaenoic Whey: Casein ratio 60:40 Lactose only as carbohydrates GOS Taurine Total nucleotides and its 5 components Fluoride
13. Blemil Plus	0.7010	Number of all displayed components: 50 DHA (below recommended level) ARA Whey: Casein ratio 60:40 Lactose only as carbohydrates FOS Taurine Lutein Total nucleotides and its 5 components Highest Fluoride Ash (2.5 g/100 g of powder)
14. Maeil MAM'MA	0.6856	Number of all displayed components: 45 α-lactalbumin DHA (below recommended level) ARA Eicosapentaenoic Whey: Casein ratio 60:40 GOS Taurine β-carotene Total nucleotides Moisture Ash (3.3 g/100 g of powder) No L-carnitine
15. Babywell	0.6227	Number of all displayed components: 40 GOS Taurine Total nucleotides No DHA/ARA
16. Aptamil	0.6173	Number of all displayed components: 57 Animal fats

(*continued on next page*)

Table 1 (*continued*)

SS-1-IF ranked in order of decreasing BCSIs	BCSI	Remarks on displayed components
		Total Saturated fats (including trans fatty acids) Total Monounsaturated fats Total Polyunsaturated fats DHA (below recommended level) ARA Whey: Casein ratio 60:40 Glucose Maltose Polysaccharides GOS + FOS Taurine Total nucleotides and its 5 components Fluoride Moisture
17. Bebelac	0.6134	Same as Aptamil except it contained DHA/ARA of ≈0.6 that in Aptamil
18. Ronalac	0.5324	Number of all displayed components: 42 Whey: Casein ratio 60:40 Maltodextrin Taurine Total nucleotides Lowest moisture (2%) No oligosaccharides
19. Humana Bebemil	0.4965	Number of all displayed components: 45 DHA (below recommended level) ARA Whey: Casein ratio 60:40 Glucose Dextrins GOS Taurine Fluoride No nucleotides
20. Novalac	0.4641	Nutrients were expressed in the Codex-required units Number of all displayed components: 41 Total Saturated fats Total Monounsaturated fats Total Polyunsaturated fats Taurine No DHA/ARA No nucleotides No oligosaccharides
21. Biomil Plus	0.4543	Number of all displayed components: 38 Taurine Lowest ash (2.1 g/100 g of powder) Moisture No DHA/ARA No nucleotides No oligosaccharides
22. Larilac	0.4498	Nutrients were expressed in the Codex-required units Number of all displayed components: 41 Whey: Casein ratio 60:40 Maltodextrin Taurine Moisture No DHA/ARA No nucleotides No oligosaccharides
23. Nactalia	0.4141	Number of all displayed components: 41 α-lactalbumin Whey: Casein ratio 60:40 Maltodextrin Total nucleotides No DHA/ARA No Taurine No L-carnitine No oligosaccharides

and the selected 42 components on the NI panels varied widely (41%–80%). Except for DHA, all displayed components were within the standard recommended range. The reason underlying the low DHA level in all except one SS-1-IF declaring its level, is because the mandatory proposed minimum DHA level stipulated in 2016 will only be mandatory from 22 February 2020 [7].

The BSCIs facilitates a comparison between the components of SS-1-IFs and support making an informed choice. The advantage of the BCSI summarizing the result in a single number is the ability to rank the SS-1-IFs and to perform the HCA. The results of the BCSI

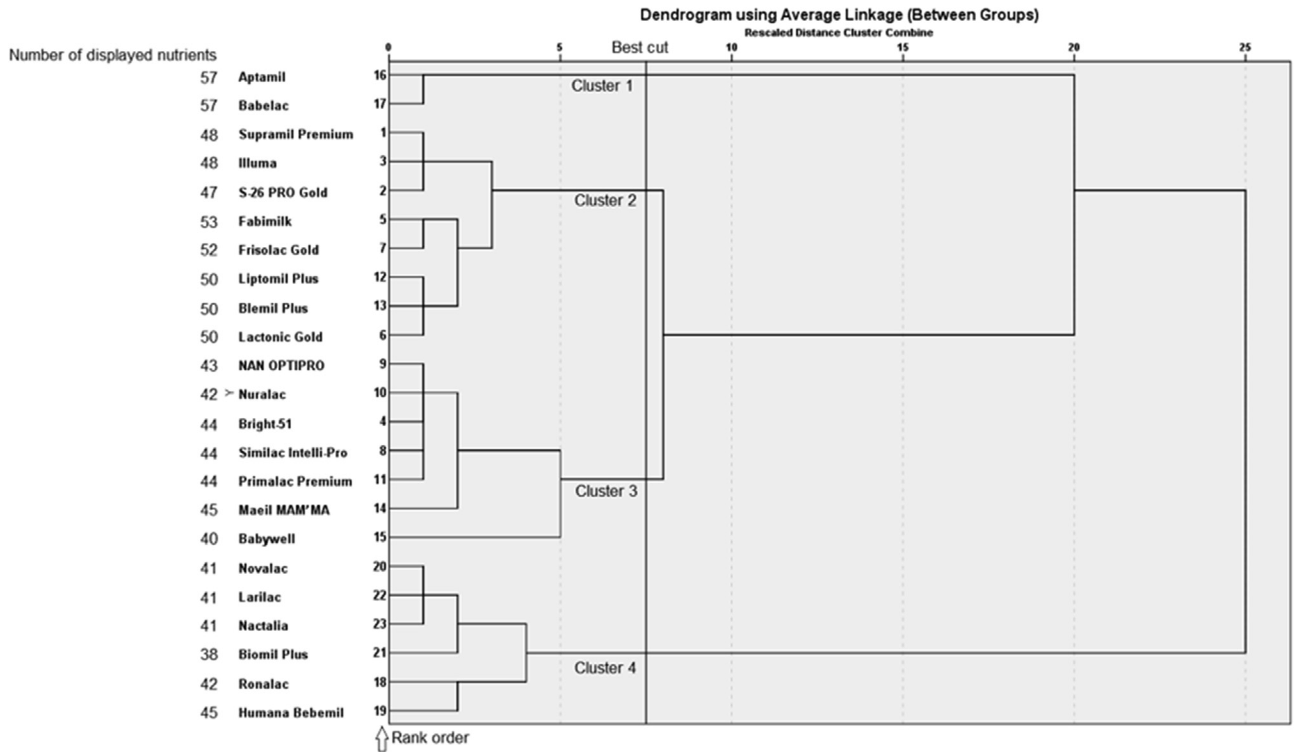

Fig. 1. Dendrogram based on Bray–Curtis similarity indices calculated on 0.10 power transformed components levels and total numbers of all displayed components.

provide a solid evidence base from which to prescribe or choose a SS-1-IF. It is prudent to choose a SS-1-IF from the top 4 BCSIs. However, if a specific nutrient is required, it would be prudent to choose a SS-1-IF with the highest BCSI among the group containing that nutrient. Some people support displaying more rather than less components [3]. The dendrogram in Fig. 1 may be a useful tool to make an informed choice. Cluster 2 contained the most balanced SS-1-IFs in terms of both BCSIs and the total number of displayed components. However, the perceptions of healthcare providers and caregivers regarding the usefulness of the BSCI should be explored in a future study. Until then, we recommend that healthcare providers prescribing IFs or local legislators calculate BCSI for all IFs available in their setting to be able to determine to what extent the IFs they prescribe is similar to the BLs. A BCSI Excel calculator is available as a supplementary file. Users have to enter the level of nutrients in the IF and the BCSI will be calculated. It may be required to convert the unit of measurement of the IF to match that of the calculator.

There is no limit to the number of items that may be included in the BCSI. However, we chose only 42 components. Two-thirds of the 23 studied SS-1-IFs declared more than 42 components. The unselected components are most likely present in all the studied SS-1-IFs but were not declared by more than half of the SS-1-IFs included in the study. It is not feasible, and difficult, to use one of the standard statistical techniques to replace the undeclared (missing) levels, as they were not randomly missing [35]. In addition, these levels cannot be included in HCA as HCA generally cannot analyze variables with missing data [36]. We calculated BCSIs based on the displayed components. There may be a discrepancy between the actual and displayed components of IFs [37]. It would be more accurate to calculate BCSIs based on the actual components, but the data is not readily available. We did not include quality components in the BCSI. Moisture was the only displayed quality component but was displayed by only 8 SS-1-IFs. Including the moisture in BCSI would yield a lower BCSI for SS-1-IFs that did not display the moisture. However, the displayed range of moisture was very close (2%–3%) and below the maximum allowed (5%) [38].

The BL for fluoride may need modification to suit a setting external to Saudi Arabia. The quality of water used for SS-1-IFs reconstitution is important in terms of its fluoride level [EFSA-NDA6]. The vast majority of mothers in Saudi Arabia reconstitute SS-1-IFs with bottled drinking water. It has been shown that the fluoride level in the labels of most of the local and imported bottled drinking water brands in Saudi Arabia is inaccurate and may be higher than the recommended fluoride level of 0.7 parts per million for Saudi Arabia [39,40]. Using bottled water to reconstitute the SS-1-IFs containing fluoride may increase the risk of dental and skeletal fluorosis if the total fluoride became > 1.5 parts per million [39]. We adopted the Codex recommendation “fluoride should not be added to infant formula” [4] and we considered ‘zero’ as the BL for fluoride. A recent study supports the Codex recommendation. This study has showed that higher levels of fluoride in tap water was associated with decreased non-verbal intellectual capabilities and this association was more noticeable among IF-fed children [41].

The BCSI, similar to other abundance based indices, has few inherit disadvantages [20]. One important disadvantage is that the BCSI is strongly affected by high-level components. Paradoxically, this abundance-sensitivity may be an advantage in our case as macronutrients has to be weighted more than micronutrients. The BCSI covers only certain aspects of SS-1-IFs composition. It ignores the structural aspects such as how the components interact.

In summary, BM is the best nutrition for infants and IF is the recommend alternative. We indicated that the BCSI can be used as an unbiased tool for a systematic comparison between SS-1-IFs. The SS-1-IFs can be ranked based on their BCSIs. Knowledge of the ranking will support informed decision-making when choosing SS-1-IFs. We recommend healthcare providers prescribing IFs or local legislators to calculate the BCSI for all IFs available in their setting.

Ethical statement

The Institutional Review Board Committee at the Ministry of the National Guard-Health approved the study with a consent waiver, as this study did not involve research on human subjects or animals.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

SA proposed the study, calculated the BCSI, performed the analysis, and wrote the first draft of the manuscript. AA, JA, and FA identified and photographed all SS-1-IFs available in pharmacies and supermarkets. The packaging of each SS-1-IF was photographed after obtaining permission. The displayed information on the NI packaging was entered into Excel Microsoft software. MA and AZ performed the quality control by double-checking the data extraction and entry. All authors provided critical feedback, helped in shaping the manuscript, and approved the final manuscript.

Declarations of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpam.2020.01.004.

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