Association of Dietary Intake of Polyphenols with an Adequate Nutritional Profile in Postpartum Women from Argentina

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ABSTRACT: HJ-Biplot analysis is a multivariate graphic representation that collects data covariation structure between variables and individuals to represent them in a low-dimensional space with the highest quality in the same reference system. Consequently, it is a promising technique for evaluating dietary exposure to polyphenols and accurately characterizing female nutrition. Herein, we hypothesized that polyphenol intake defines specific clusters with dietary impacts, which can be assessed using HJ-Biplot, based on a cross-sectional study in Argentina. The study included 275 healthy postpartum women who provided information about their food frequency intake and other conditions, which were then used to evaluate polyphenolic intake using the Phenol-Explorer database. Outcomes were established using HJ-Biplot for clustering and ANOVA to compare their impact on diet quality indicators. Two HJ-Biplot models were run (for intakes >20 mg/d and 5~20 mg/d, respectively) to identify three clusters per model with excellent statistical fitness to explain the data. Thus, specific polyphenolic clusters with potentially bioactive and safe compounds were defined despite significant inter-individual variability. In fact, women with the lowest polyphenolic intake exhibited worse dietary quality, body fat, and physical activity. As a result, HJ-Biplot proved to be an effective technique for clustering women based on their dietary intake of these compounds. Furthermore, cluster membership improved the intake of antioxidants, water, fiber, and healthy fats. Additionally, women with formal jobs and a higher educational level showed a better diet. Dietary polyphenols are critical during postpartum because they exert beneficial effects on women and breastfed infants.

Keywords: biostatistics, HJ-Biplot, nutrition assessment, polyphenols, postnatal care

INTRODUCTION

The nutritional status of women during postpartum is a major determinant of mother and infant health. Thus, global organizations highlight the significance of protecting and promoting public health by addressing this issue (Howlader et al., 2012; World Health Organization, 2016; Maitra, 2018). Breastfeeding provides newborns with the necessary nutrients and bioactive substances for healthy growth and development, and breast milk composition is dynamically associated with maternal diet (Keikha et al., 2017). For these reasons, healthcare systems should prioritize nutritional advice and assessment (diet, physical activity, and weight optimization) during postpartum (World Health Organization, 2016). Therefore, identify-ing dietary intake is critical for diagnosing nutritional needs and addressing health outcomes.

Polyphenols are bioactive compounds and potentially beneficial agents provided by the diet. They are derived from plants and have diverse chemical structures, which are classified into different groups, as follows: phenolic acids, flavonoids, stilbenes, and lignans (Miranda et al., 2018). These compounds are the most consumed non-nutrients (>1 g/d) and exert multiple biological effects (i.e., they are bioactive phytonutrients), including the prevention of oxidative stress, inflammation, and non-communicable diseases. Vulnerable populations, such as infants, women, and elders, benefit from an adequate dietary intake (Oesterle et al., 2021). In this sense, polyphenols exert certain beneficial effects during female re-

productive stages, such as the promotion of maternal mental health (Miranda et al., 2021), breastfeeding (Buntuchai et al., 2017), and pregnancy and postpartum well-being (de Boer and Cotingting, 2014). Furthermore, polyphenols in breast milk modulate infant gut microbiota, which improves immune system maturation and thus helps prevent chronic diseases in adulthood (Cortes-Macías et al., 2021). Nonetheless, because they are consumed with several other compounds, it is difficult to establish a relationship between dietary intake and health effects.

Nutritional epidemiology employs different methods to assess diet-health relationships. Traditional analyses, based on single-nutrient approaches that examine the outcomes of a nutrient or food intake, underestimate nutritional complexity and interaction mechanisms (Ocké, 2013). Conversely, multidimensional approaches, which study multiple dietary components simultaneously, may overcome these limitations. These statistical methods include principal component analysis, cluster analysis, and dietary indices, with several advantages and disadvantages (Reedy et al., 2010). The principal component analysis connects a set of variables (foods or nutrients) to obtain latent variables called principal components or latent dimensions (patterns), which are then used to predict a pattern adherence score with high statistical power. However, the resulting patterns can be abstract, unspecific, ineffective at identifying subpopulations, difficult to compare across studies, and inconsistent (McNaughton, 2010). Alternatively, cluster analysis uses classification methods to separate individuals into different groups based on their consumed foods. This enables an adequate description of the diet and is useful for characterizing subgroups, but large sample sizes may be required to identify significant outcomes (Tucker, 2010). Another multidimensional approach to nutrition research is by assessing compliance with diet quality indices based on dietary guidelines. Index-based methods are effective because they demonstrate both adherence to recommendations and their relationship to health events (Miller et al., 2010). However, dietary indices must be updated periodically, and demographic subgroups, such as ethnic minorities, could be underrepresented (Tucker, 2010).

The disadvantages of multidimensional methods for diet assessment are accentuated when large data matrices are used. To address these issues, multivariate techniques have been developed such as the HJ-Biplot, which represents individuals and variables in space and provides more information than other methods by exposing different relationships (e.g., individuals-individuals, variables-variables, and individuals-variables). Furthermore, the coordinates obtained in the HJ-Biplot can be used to calculate clusters (Carrasco et al. 2019; Frutos Bernal et al., 2020). Unlike traditional techniques or other biplot methods (JK-Biplot and GH-Biplot), the HJ-Biplot achieves optimal quality for both rows (individuals) and columns (variables) in the same reference system (Nieto-Librero et al., 2017). Thus, its use has increased over the last 20 years in multiple fields (food industry, health, and social sciences) because HJ-Biplot provides options for evaluating associations between multiple observations and variables, with fewer restrictions than conventional methods, and the advantage of being specifically designed for the inspection of data matrices (Martínez-Regalado et al., 2021). Ruiz et al. (2018) highlighted four main advantages: a simultaneous examination of multiple variables in the same graphical representational plane; different comparisons at individual and group levels; the relationship between measures of the same and/or different origins; and no need to perform *a posteriori* contrast.

Consequently, we propose using HJ-Biplot to explain the complexities of polyphenolic exposure and its outcomes in Argentinian postpartum women. The hypothesis is that polyphenol intake defines specific clusters and is associated with dietary and nutritional outcomes, which can be proven by the multivariate HJ-Biplot representation, to accurately characterize the nourishment of women during postpartum, a vulnerable and challenging stage of life, together with other statistical methods to establish epidemiological relationships.

MATERIALS AND METHODS

Study conditions

This cross-sectional study was conducted on 275 postpartum women in Córdoba province, Argentina, from April 2013 to February 2020. They voluntarily agreed to participate by signing an written informed consent form. Inclusion criteria were adult (≥ 18 years old), Córdoba's inhabitant, postpartum (first six months), and breastfeeding practice. Exclusion criteria were pregnancy and currently active diseases. This research was performed according to the Declaration of Helsinki and current Argentinian legislation. Also, the Ethics Committee of the National Hospital of Clinics of the National University of Córdoba approved this study, with the following registration codes: RENIS-IS000548, RENIS-IS001262, and RENIS-IS002045 for the national registry, REPIS-145, REPIS-2654, and REPIS-5554 for the provincial registry of Córdoba.

Dietary assessment

A validated quantitative food frequency questionnaire (FFQ) was used to record diet over the previous 12 months. The FFQ comprises 127 food items available in the country, grouped according to their nutritional profile and origin. Participants were interviewed face-to-face

by health professionals trained in nutritional assessment, who asked about the frequency (never or the number of times per month/week/day) and typical portion size of each consumed food (small, medium, or large). This instrument has shown adequate levels of validity and reproducibility for the Latin American population, with a moderate overestimation of 4% and the absence of constant bias (Cortez et al., 2021). Moreover, this FFQ has been applied in Argentina to identify dietary patterns in the general population and postpartum women (Pou et al., 2020; Cortez et al., 2021), with Argentinian women's dietary patterns being similar to those of other Latin American countries (Caire-Juvera et al., 2007; Gomes et al., 2019). A validated photographic atlas based on standard portion sizes in Argentina was used to assist participants in describing the quantity of foods consumed. Nutritional data was computed using a food composition-based

software (Cortez et al., 2021). Next, data were analyzed using the Phenol-Explorer database (version 3.6; Wishart Research Group, Edmonton, AB, Canada) (Rothwell et al., 2013). It provides values for about 500 different polyphenols in over 400 different foods in multiple forms, including raw, cooked, and processed ones. These compounds were classified as displayed in Table 1.

Briefly, after each food consumption has been estimated (in g or mL), individual intakes of each polyphenolic compound were calculated by multiplying it by the polyphenol content in 100 g or mL of the food. Total polyphenol content was calculated as the sum of all individual phenolics obtained by chromatography without hydrolysis, or by chromatography after hydrolysis, if data were not available (e.g., fennel), for all the classes of compounds considered. The total polyphenol content of prepared meals was calculated based on their ingredients. In the

Table 1. Dietary phenolic compounds estimated in the postpartum women intake in Argentina

Class	Subclass	n[1]	Example	Dietary source
Flavonoids	Anthocyanins	71	Malvidin	Grapes, berries, beans, wines
	Chalcones	2	Butein	Pod vegetables, beers
	Dihydrochalcones	5	Phloridzin	Pomes, herbs, fruit juices
	Flavanols	34	(−)-Epigallocatechin 3-*O*-gallate	Teas, nuts, fatty fruits, tropical fruits, berries
	Dihydroflavonols	3	Dihydroquercetin	Herbs, wines
	Flavanones	22	Hesperetin	Citrus, nuts, wines
	Flavones	49	Luteolin	Oils, shoot vegetables, olives, pulses, nuts
	Flavonols	78	Quercetin	Cocoa, wines, cereals, berries, teas, nuts, fruit vegetables, *yerba mate*
	Isoflavonoids	15	Daidzein	Soy products, nuts, beans
Phenolic acids	Hydroxybenzoic acids	29	5-*O*-Galloylquinic acid	Teas, berries, *yerba mate*, nuts
	Hydroxycinnamic acids	72	5-Caffeoylquinic acid	Coffee, *yerba mate*, tea, oils, nuts, cabbages, fruit vegetables, feaf vegetables, roots, tubers, beans, herbs, berries, drupes, pomes, wines, beers
	Hydroxyphenylacetic acids	5	Homovanillic acid	Oils, olives, beers
	Hydroxyphenylpropanoic acids	2	Dihydrocaffeic acid	Olives
Stilbenes		10	Resveratrol	Cocoa, nuts, berries, wines
Lignans		29	Lariciresinol	Cereals, dried fruits, berries, citrus, drupes, gourds, pomes, tropical fruits, coffee, teas, oils, nuts, beans, soy products, cabbages, fruit vegetables, leaf vegetables, pod vegetables, tubers, roots
Others	Alkylmethoxyphenols	3	4-Vinylguaiacol	Coffee, seeds, beers
	Alkylphenols	15	4-Methylcatechol	Coffee, cocoa, beers
	Curcuminoids	3	Curcumin	Spices
	Furanocoumarins	4	Bergapten	Citrus juices, herbs, stalk vegetables
	Hydroxybenzaldehydes	6	Vanillin	Cereals, cocoa, olives, oils, beers
	Hydroxybenzoketones	2	Paeonol	Beers
	Hydroxycinnamaldehydes	2	Sinapaldehyde	Wines
	Hydroxycoumarins	7	Umbelliferone	Beers, wines, cocoa
	Hydroxyphenylpropenes	6	Eugenol	Spices, infusions
	Methoxyphenols	1	Guaiacol	Coffee, seed oils
	Naphtoquinones	2	Juglone	Nuts
	Phenolic terpenes	7	Carnosol	Herbs
	Tyrosols	16	Oleuropein	Olives, oils, beers, wines
	Others	6	Pyrogallol	Cocoa, beers, coffee, pomes, olives

[1]Number of individual compounds constituting each subclass, based on the Phenol-Explorer database.

case of regional beverages (e.g., *yerba mate*), polyphenols were calculated based on previous studies (Cittadini et al., 2018). Polyphenols with a mean daily intake of ≥5 mg/d were considered for the analysis, as this amount has been reported as bioactive (Mervish et al., 2013; Bondonno et al., 2020).

Sample characterization

Self-reported information was registered about age, educational level, employment, partnership/marital status, parity, breastfeeding, postpartum days, and physical activity [in metabolic equivalents of the task−metabolic equivalent task (MET)−]. Body mass index was calculated from weight and height, and body fat percentage (BFP) was determined using hand-held bioelectrical impedance analysis. Table 2 shows the characteristics of women.

Diet quality assessment

The following set of validated indicators was analyzed:

Women's dietary diversity: The minimum dietary diversity for women (MDD-W) is a 10-item food-based indicator of nutrient intake adequacy among women of reproductive age in developing countries. It includes the following food groups: 1) grains, white roots and tubers, and plantains; 2) pulses; 3) nuts and seeds; 4) dairy; 5) meat, poultry, and fish; 6) eggs; 7) dark green leafy vegetables; 8) other vitamin-A rich fruits and vegetables; 9) other vegetables; and 10) other fruits. The scoring criteria are 1 point for each food group when the intake reaches ≥1 serving per

day and 0 for less (Gicevic et al., 2018).

Dietary total antioxidant capacity: The dietary total antioxidant capacity (TAC) is the sum of the ferric reducing antioxidant power of each beverage and food (Ledesma et al., 2019), which can exert health-protective effects in women (Stedile et al., 2016).

Glycaemic index: The glycemic index (GI) is a widely known index for evaluating and classifying carbohydrate-containing foods based on their impact on postprandial serum glucose levels (de la Iglesia et al., 2016). The daily GI was calculated based on an international base of 72 carbohydrate-containing foods from the FFQ (Haluszka et al., 2019).

Water intake: Hydration is essential for good health and breastfeeding (Zhou et al., 2019). Thus, plain water (PW-including tap water and bottled water) and water present in beverages and foods (WBFI-based on food composition tables, Mazzei and Puchulu, 1991) were used to calculate water intake.

Dietary fiber intake: Considering the importance of dietary fiber intake during postpartum to support gut microbiota and a healthy metabolism (Chan et al., 2019; Alderete et al., 2020; Hull et al., 2020), daily consumption of soluble dietary fiber intake (SDFI; e.g., pectin from fruits) and insoluble dietary fiber intake (IDFI; e.g., hemicellulose from cereal grains) were estimated.

Fat quality index: Fatty acids include saturated (SFA), monounsaturated (MUFA), and polyunsaturated (PUFA), which play several biological roles. Dietary recommendations suggest consuming moderate amounts of MUFA and PUFA instead of SFA to promote health and breastfeeding (Pollak, 2016). Thus, the fat quality index was calculated as FQI=(MUFA+PUFA)−SFA (Agnoli et al., 2019).

Protein to carbohydrate ratio: The macronutrient quality of diet is crucial during postpartum when requirements increase. Protein-rich foods are preferred over carbohydrate-rich foods because these dietary exposures affect maternal and infant health (Blumfield et al., 2015; Maslova et al., 2015; Bennett et al., 2017). Thus, the protein to carbohydrate ratio (PCR) was estimated.

Statistical analyses

First, continuous variables were described using means, standard errors, and medians, while the interquartile range and qualitative variables were described using frequencies and percentages. Then, Pearson's correlation coefficients (for continuous variables) and biserial-point coefficients (for categorical variables) were calculated to examine associations between women's sociodemographic characteristics and individual polyphenol intakes. These analyses were performed using the Stata 15 software (Stata Corp., LLC, College Station, TX, USA).

Subsequently, an HJ-Biplot multivariate analysis was

Table 2. Sociodemographic characteristics of the participants (n=275)

	Mean	SD	%	n
Age (yr)	29.12	6.00		
Postpartum day	91.57	56.43		
Body mass index (kg/m^2)	25.01	5.52		
Body fat percentage (%)	28.41	7.10		
Physical activity (MET)	407.63	721.81		
Partnership status				
In couple			89.09	245
Single			10.91	30
Educational level				
≥12 years			75.27	207
<12 years			24.73	68
Employment				
Employed			44.73	123
Informally employed or unemployed			55.27	152
Parity				
Primiparous			46.91	129
Multiparous			53.09	146
Breastfeeding				
Exclusive			62.18	171
Non-exclusive			37.82	104

SD, standard deviation; MET, metabolic equivalent task.

performed to discover correlations between polyphenols (Galindo-Villardón, 1986). This technique provides a graphical representation of rows (j_1, ..., j_n) and columns (h_1, ..., h_p) of a data matrix (X_{nxp}) in a low-dimensional subspace where their relative positions are interpretable. The markers are obtained from the singular value decomposition of the data matrix (represented as $X=UDV^T$, where U and V are orthogonal matrices and $D=diag$ (λ_1, ..., λ_p) containing the singular values), where the rows represent individuals (women) and the columns variables (polyphenols) so that both sets of markers can be overlaid in the same reference frame with the highest quality of representation. The HJ-Biplot graphic representation must be interpreted based on the following criteria (Carrasco et al., 2019):

- The distances between row markers are interpreted as an inverse function of their similarities, i.e., women close to each other are more similar, enabling clustering.
- The length of column markers (vectors) approximates the polyphenol standard deviation.
- The cosines of the angles between the column vectors approximate the correlations between the indicators so that acute angles are associated with indicators with high positive correlation, obtuse angles indicate negative correlation, and right angles indicate uncorrelated variables. Similarly, the cosines of the angles between the indicator markers and the axes (principal components) approximate the correlations between both.
- The order of the orthogonal projections of the row markers (points) onto a column marker (vector) approximates the order of row elements in that column. The greater the projection of a point on a vector, the more the woman deviates from the mean of that polyphenol.

Some additional measurements can be used for the correct interpretation of the graph (Díaz-Faes et al., 2013). In this sense, the HJ-Biplot uses the sum of the percentages of inertia as an indicator of overall representation quality, and as goodness-of-fit criteria of the individual representation of each of the column H markers and row J markers (contributions). The contribution is the relative variability of a variable explained by a factor or dimension. Furthermore, unlike classic biplots, the HJ-Biplot offers the highest quality of representation (QLR) for both types of markers, rows and columns. Only points with a high rendering quality can be interpreted correctly. In this study, QLR is assessed on a scale of 0 to 1,000 points.

The next step was to conduct a clustering analysis (Nieto-Librero et al., 2017). This multivariate classification technique is used to detect and describe subgroups (clusters) of subjects or homogeneous variables based on the values observed within a heterogeneous set, trying to achieve the maximum possible homogeneity in each group and significant differences between them. In this study, the clusters were calculated through the Biplot coordinates using the K-means method. In the K-means method, cosine similarity was used for similarity calculation between centroids and data points (i.e., women), allowing the variables responsible for the grouping of the different representations obtained by the HJ-Biplot to be identified (Carrasco et al., 2019). The K-means algorithm was selected because it is one of the simplest, most efficient, and widely used clustering algorithms in exploratory data analysis. It divides observations into K clusters so that the sum of their internal variances is as small as possible. The objective of this algorithm is to create groups that are homogeneous within and heterogeneous with each other (Calderón Cisneros et al., 2020). This is an unsupervised method because it requires setting the number of clusters *a priori* and selecting the solution with the lowest internal variance (Carrasco Oberto, 2020). Representation qualities of each cluster on the factorial plane were calculated. The HJ-Biplot analysis was performed using the MULTBIPLOT software package (MULTivariate analysis using BIPLOT) (Vicente-Villardón, 2015).

ANOVA with Fisher's *post-hoc* comparisons was used to test differences in dietary indicators among clusters, and effect sizes were calculated using Cohen's *d*. Effect sizes were interpreted as small (≥ 0.20), medium (≥ 0.50), large (≥ 0.80), and very large (≥ 1.30). The Skewness (S) and Kurtosis (K) distribution tests were used to determine whether the dietary indicators are suitable for normal distribution, with acceptable values between -2 and $+2$. *Post-hoc* power analysis was assessed using G*Power version 3.1.9.4 (Universität Düsseldorf, Düsseldorf, Germany), which revealed that the sample size used in each ANOVA test had power >0.82 at $\alpha=0.05$ and an effect size of 0.20.

A chemoinformatic-based analysis of the polyphenolic compounds that integrated the clusters was performed (Selby-Pham et al., 2018). Firstly, pharmacological properties were estimated using the Molinspiration property prediction tool (Molinspiration Cheminformatics, Slovensky Grob, Slovakia) with the corresponding Simplified Molecular Input Line Entry System (SMILES) notation (Varghese et al., 2019). Analyses provided information on bioactivity (the probability of a compound interacting with a pharmacological target) and pharmacokinetics predictors. Secondly, potential toxicity was assessed with the OSIRIS software (Osiris Software, Edmond, OK, USA), to predict mutagenic (M), tumorigenic (T), irritant (I), and reproductive (R) effects (Fonseca-Berzal et al., 2013).

RESULTS

General characterization of the polyphenolic intake

The mean intake of polyphenols was 1,040.06 (standard deviation: 622.58) mg/d. Among the 33 most consumed phenolic compounds listed in Table 3, 13 compounds were consumed in amounts higher than 20 mg/d, and the rest ranged from 5 to 20 mg/d. Chemically, they were hydroxycinnamic acids (55%), flavonoids-mainly flavanols (33%), hydroxybenzoic acids (6%), and lignans (6%).

As shown in Table 4, significant bivariate correlations existed between polyphenol intakes and the following sample characteristics: maternal age (variable depending on the compound type), postpartum days (positive), body mass index (BMI), BFP (inverse), and MET (positive). The biserial-point correlation for categorical data revealed that being employed was positively associated with the intake of most polyphenols, whereas educational level and parity were related to a lesser number of compounds.

Clustering of the polyphenolic intake by HJ-Biplot

Three axes were selected for HJ-Biplot analyses. The model with polyphenols consumed above 20 mg/d achieved a very high accumulated inertia (87.26%), indicating that it was adequate for the analysis. The explained variance was 63.17% for the first axis, 14.90% for the second axis, and 9.19% for the third axis. Moreover, 66.45% of the variance was explained by the three axes in the matrix of polyphenolic intake below 20 mg/d: 28.30% for the first axis, 23.04% for the second axis, and 15.11% for the third axis.

Table 5 shows the contributions of polyphenols to the axes and qualities of representation. Except for hesperetin and ferulic acid, which were better represented in planes 1 to 3, all variables for highly consumed polyphenols must be interpreted in factorial planes 1 to 2. Furthermore, polyphenols showed an adequate quality of representation (>200). Besides, naringenin and *trans*-ferulic acid were not represented in any axis, with low rep-

Table 3. Daily polyphenolic intake of Argentinian postpartum women (n=275)   (unit: mg/d)

Phenol	Family	Mean	SD	Median	Quartile 1	Quartile 3
5-Caffeoylquinic acid	Hydroxycinnamic acid	138.70	97.96	123.07	61.68	191.84
1,3-Dicaffeoylquinic acid	Hydroxycinnamic acid	88.62	97.01	56.84	5.68	142.11
1-Caffeoylquinic acid	Hydroxycinnamic acid	83.16	91.04	53.34	5.33	133.36
3-Caffeoylquinic acid	Hydroxycinnamic acid	66.61	58.60	51.98	13.58	102.30
4-Caffeoylquinic acid	Hydroxycinnamic acid	65.05	57.26	51.12	12.14	97.19
Ferulic acid	Hydroxycinnamic acid	61.22	71.01	40.17	19.14	71.57
Caffeic acid	Hydroxycinnamic acid	45.59	55.84	21.95	12.57	49.69
4,5-Dicaffeoylquinic acid	Hydroxycinnamic acid	35.69	39.07	22.89	2.29	57.23
1,4-Dicaffeoylquinic acid	Hydroxycinnamic acid	33.22	36.36	21.31	2.13	53.27
Hesperetin	Flavanone	23.16	30.40	12.70	0.00	35.95
Lariciresinol	Lignan	22.67	28.42	15.74	8.75	27.65
3,4-Dicaffeoylquinic acid	Hydroxycinnamic acid	21.82	22.32	16.23	3.02	33.48
Quercetin 3-*O*-rutinoside	Flavonol	20.56	19.70	15.81	4.52	30.49
Disuccinoylquinic acid	Hydroxycinnamic acid	17.61	19.28	11.30	1.13	28.25
Trans-ferulic acid	Hydroxycinnamic acid	14.90	18.56	8.78	0.00	22.57
Syringic acid	Hydroxybenzoic acid	13.84	29.15	5.14	1.05	14.66
Procyanidin dimer B2	Flavanol	12.48	11.19	10.14	4.08	17.61
3-Feruloylquinic acid	Hydroxycinnamic acid	11.91	11.52	10.73	2.23	19.28
(−)-Epicatechin	Flavanol	11.06	8.66	9.50	4.74	15.68
5-Feruloylquinic acid	Hydroxycinnamic acid	11.03	10.19	7.99	1.86	15.98
p-Coumaric acid	Hydroxycinnamic acid	9.23	8.76	6.86	3.00	12.06
(+)-Gallocatechin	Flavanol	9.17	16.93	0.08	0.00	12.09
Naringenin	Flavanone	8.50	11.18	4.99	1.34	11.80
4-Feruloylquinic acid	Hydroxycinnamic acid	8.46	7.80	6.22	1.41	12.43
Pinoresinol	Lignan	8.21	10.57	5.08	2.39	10.00
5-*O*-Galloylquinic acid	Hydroxybenzoic acid	7.55	13.99	0.00	0.00	9.95
Quercetin	Flavonol	6.84	3.94	5.94	4.15	9.17
(+)-Catechin	Flavanol	6.26	5.49	4.69	2.33	9.16
O-Coumaric acid	Hydroxycinnamic acid	6.17	11.28	1.18	0.00	8.31
(−)-Epigallocatechin 3-*O*-gallate	Flavanol	5.95	11.02	0.00	0.00	7.86
Caffeoyl-glucose	Hydroxycinnamic acid	5.27	5.77	3.38	0.34	8.45
Malvidin 3-*O*-glucoside	Anthocyanin	5.21	9.89	0.30	0.00	8.46
(−)-Epicatechin 3-*O*-gallate	Flavanol	5.13	8.83	0.77	0.00	6.43

Polyphenolic intakes higher than 5 mg/d are shown.
SD, standard deviation.

resentation qualities when running the analysis with the lower consumed phenols.

The cluster analysis was performed based on coordinates obtained from the HJ-Biplot (K-means method). Three clusters were formed with the sample data for each model, which were identified through the Convex-Hulls lines and graphed in Fig. 1 and 2. This analysis allowed us to identify the polyphenols that influenced the sets among the different sample points. Most women were adequately represented in both models, with only four and 14 individuals eliminated from models 1 and 2, respectively, for having QLR<200.

The clusters can be characterized as:
- Cluster 1: Women who have a low association with polyphenolic intake. In both models, this cluster showed an adequate quality of representation (99.93 and 91.50)

and mostly comprised the sample (44.6% and 39.1%).
- Cluster 2: From model 1 (>20 mg of polyphenols per day), it included women (20.7% of the sample) with high consumption of hesperetin, caffeic acid, lariciresinol, and ferulic acid. The cumulative quality of representation was 99.66. From model 2 (5~20 mg of polyphenols per day), it was constituted by women who consumed flavanols (4) and hydroxybenzoic acids (1), accounting for 24.1% of the sample with good quality of representation (95.16).
- Cluster 3: It was mainly related to hydroxycinnamic acids in model 1, with 34.7% of the women represented with QLR=99.78. However, the third cluster of polyphenols represented 36.8% of the sample, with moderate intake. Its quality of representation was 99.36, and women were mainly associated with the consumption

Table 4. Correlations between single polyphenolic intake and sociodemographic and health characteristics of Argentinian postpartum women (n=275)

Intake	Zero-order correlation					Biserial-point correlation			
	Age	PD	BMI	BFP	MET	E	EL	Parity	EBF
Malvidin 3-O-glucoside	0.121*	0.102	−0.145*	−0.096	0.000	0.059	−0.005	0.100	0.068
(−)-Epicatechin	−0.038	−0.029	−0.112	−0.120*	0.235*	0.018	0.028	0.015	0.053
(−)-Epigallocatechin 3-O-gallate	−0.128*	−0.024	0.013	−0.032	0.166*	−0.092	−0.048	0.028	−0.039
(−)-Epicatechin 3-O-gallate	−0.119*	−0.016	0.004	−0.037	0.169*	−0.088	−0.046	0.033	−0.035
(+)-Catechin	0.081	0.088	−0.151*	−0.116	0.184*	0.045	0.068	0.056	0.025
(+)-Gallocatechin	−0.128*	−0.024	0.013	−0.032	0.166*	−0.092	−0.048	0.028	−0.038
Procyanidin dimer B2	−0.008	−0.028	−0.095	−0.092	0.180*	0.017	0.045	−0.006	0.080
Hesperetin	−0.025	−0.112	0.029	0.004	0.120*	0.058	−0.084	0.001	−0.038
Naringenin	0.003	−0.096	0.022	0.002	0.155*	0.068	−0.037	−0.017	−0.005
Quercetin	0.040	0.073	−0.149*	−0.140*	0.239*	0.072	0.117*	−0.009	0.003
Quercetin 3-O-rutinoside	0.059	0.128*	0.015	−0.101	−0.038	0.127*	0.049	0.022	−0.051
5-O-Galloylquinic acid	−0.128*	−0.024	0.013	−0.032	0.166*	−0.092	−0.048	0.028	−0.039
Syringic acid	−0.044	0.123*	−0.101	−0.109	0.090	−0.028	0.092	−0.151*	−0.037
1-Caffeoyl quinic acid	0.061	0.122*	0.023	−0.092	−0.059	0.126*	0.046	0.017	−0.046
1,3-Dicaffeoylquinic	0.061	0.122*	0.023	−0.092	−0.059	0.126*	0.046	0.017	−0.046
1,4-Dicaffeoylquinic	0.061	0.122*	0.023	−0.092	−0.059	0.126*	0.046	0.017	−0.046
3,4-Dicaffeoylquinic acid	0.077	0.136*	0.013	−0.096	−0.053	0.137*	0.056	0.019	−0.044
3-Caffeoylquinic acid	0.166*	0.192*	−0.062	−0.121*	−0.001	0.169*	0.108	0.037	−0.030
Disuccinoylquinic acid	0.061	0.122*	0.023	−0.092	−0.059	0.126*	0.046	0.017	−0.046
3-Feruloylquinic acid	0.100	0.156*	−0.004	−0.104	−0.040	0.146*	0.069	0.023	−0.039
4,5-Dicaffeoylquinic acid	0.061	0.122*	0.023	−0.092	−0.059	0.126*	0.046	0.017	−0.046
4-Caffeoylquinic acid	0.156*	0.196*	−0.054	−0.111	0.011	0.160*	0.106	0.031	−0.020
4-Feruloylquinic acid	0.163*	0.199*	−0.057	−0.107	0.010	0.161*	0.108	0.029	−0.017
5-Caffeoylquinic acid	0.136*	0.177*	−0.052	−0.123*	0.006	0.164*	0.104	0.039	−0.035
5-Feruloylquinic acid	0.167*	0.201*	−0.061	−0.106	0.014	0.161*	0.110	0.029	−0.015
Caffeic acid	0.160*	0.171*	−0.119*	−0.065	0.112	0.096	0.117*	0.013	0.020
Caffeoyl-glucose	0.061	0.122*	0.023	−0.092	−0.059	0.126*	0.046	0.017	−0.046
Ferulic acid	0.028	−0.021	−0.032	0.049	0.033	0.103	0.035	−0.049	0.035
o-Coumaric acid	0.021	−0.059	−0.040	0.043	0.015	0.121*	0.037	−0.026	0.019
p-Coumaric acid	0.047	0.057	−0.119*	−0.062	0.089	0.091	0.130*	−0.102	−0.018
trans-Ferulic acid	−0.033	0.047	0.123*	0.120	0.054	−0.071	−0.102	−0.010	0.077
Lariciresinol	0.141*	−0.024	−0.106	−0.070	0.091	0.100	0.086	0.008	−0.049
Pinoresinol	0.152*	−0.030	−0.112	−0.067	0.073	0.099	0.085	0.012	−0.050

Zero-order correlations are presented as Pearson's r coefficients (*P<0.05).
PD, postpartum day; BMI, body mass index; BFP, body fat percentage; MET, metabolic equivalent task; E, employment; EL, educational level; EBF, exclusive breastfeeding.

of hydroxycinnamic acids.

The relationship between polyphenolic clusters and dietary indicators

Table 6 lists the descriptive statistics for the dietary quality indicators. The findings revealed that the S and K coefficients were between -2 and $+2$, indicating that the data had a normal distribution. Table 7 shows the ANOVA outcomes for comparing diet indicators with respect to cluster 1. In the range of 5 to 20 mg/d intake, cluster 2 showed higher means of TAC, WBFI (medium effects), SDFI, IDFI (small effects), and FQI (small effect). Cluster 3 also showed higher means of TAC (medium effect), WBFI (very large effect), SDFI (medium effect), and IDFI (small effect). In the case of cluster 2, polyphenol intake above 20 mg/d increased TAC (me-

dium effect), WBFI (large effect), SDFI (large effect), IDFI (large effect), FQI (small effect), whereas cluster 3 only increased WBFI (very large effect) and FQI (small effect). Finally, no differences were discovered in GI, MDD-W, PW, and PCR.

Chemoinformatic analysis of dietary polyphenols

Predictions about polyphenol properties are depicted in Fig. 3. For intakes >20 mg/d (Fig. 2), cluster 2 showed an appropriate score for both Lipinski's and Veber's rules (LR and VR, respectively). Although the cluster drug scores (DSs) were high, only hesperetin and lariciresinol had low scores as nuclear receptor ligand (NRL) and enzymatic inhibitors (EIs), respectively. However, cluster 3 showed less favorable pharmacokinetic potential. The hydroxycinnamic acids of this cluster evinced pharmaco-

Table 5. Contributions and representation qualities for each polyphenol on the first three axes

Polyphenol	Contribution			Quality of representation		
	Axis 1	Axis 2	Axis 3	Axis 1	Axis 2	Axis 3
Polyphenols consumed above 20 mg/d						
Hesperetin	17	142	478	17	159	637
Quercetin 3-*O*-rutinoside	948	33	7	948	981	988
1-Caffeoylquinic acid	948	45	6	948	993	999
1,3-Dicaffeoylquinic acid	948	45	6	948	993	999
1,4-Dicaffeoylquinic acid	948	45	6	948	993	999
3,4-Dicaffeoylquinic acid	977	19	2	977	996	998
3-Caffeoylquinic acid	830	128	31	830	958	989
4,5-Dicaffeoylquinic acid	948	45	6	948	993	999
4-Caffeoylquinic acid	762	170	58	762	932	990
5-Caffeoylquinic acid	861	87	9	861	948	957
Caffeic acid	21	784	179	21	805	984
Ferulic acid	3	156	235	3	159	394
Lariciresinol	2	236	172	2	238	410
Polyphenols consumed between 5 and 20 mg/d						
Malvidin 3-*O*-glucoside	24	256	167	24	280	447
(−)-Epicatechin	445	274	12	445	719	731
(−)-Epigallocatechin 3-*O*-gallate	710	8	242	710	718	960
(−)-Epicatechin 3-*O*-gallate	729	17	216	729	746	962
(+)-Catechin	305	419	36	305	724	760
(+)-Gallocatechin	711	9	241	711	720	961
Procyanidin dimer B2	198	242	46	198	440	486
Naringenin	0	93	49	0	93	142
Quercetin	409	235	104	409	644	748
5-*O*-Galloylquinic acid	710	8	242	710	718	960
Syringic acid	48	14	162	48	62	224
Disuccinoylquinic acid	317	391	182	317	708	890
3-Feruloylquinic acid	299	548	120	299	847	967
4-Feruloylquinic acid	177	725	15	177	902	917
5-Feruloylquinic acid	163	727	10	163	890	900
Caffeoyl-glucose	317	391	182	317	708	890
o-Coumaric acid	12	6	284	12	18	302
p-Coumaric acid	61	93	456	61	154	610
trans-Ferulic acid	11	0	52	11	11	63
Pinoresinol	11	150	205	11	161	366

The axes establish the HJ-Biplot reference system and represent latent factorial variables obtained from linear combinations of the initially observed variables.
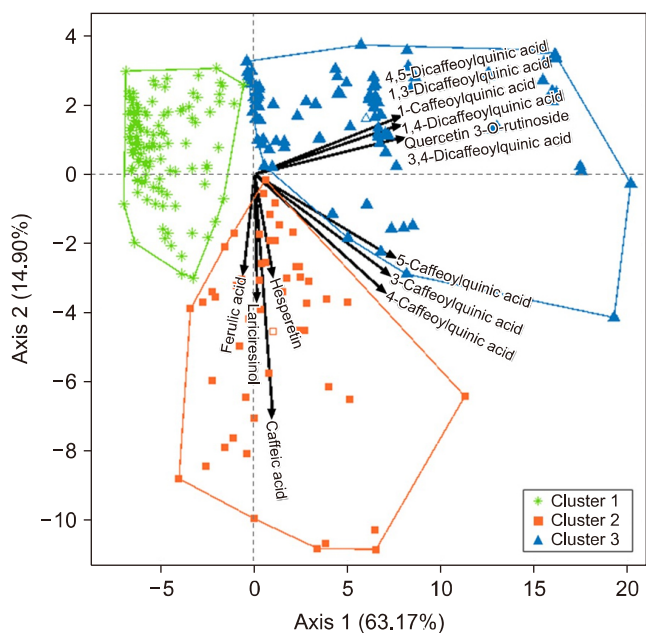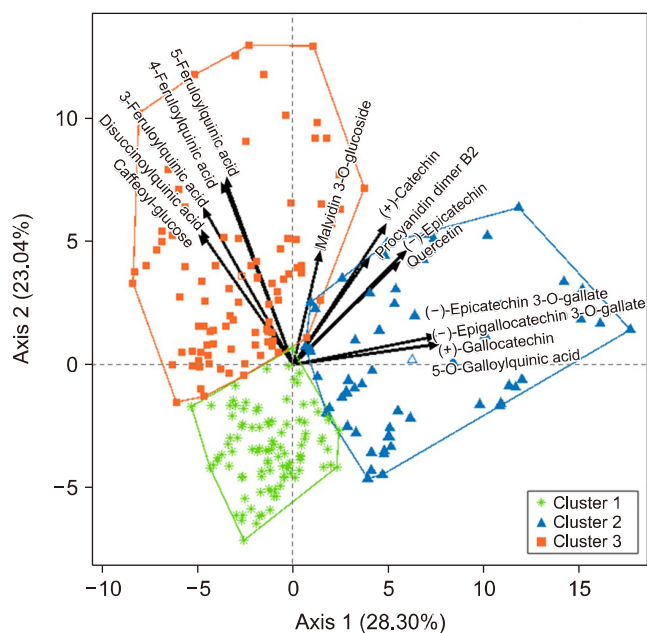
Fig. 1. A factorial representation of the HJ-Biplot for clusters in the main plane (axes 1~2) for the polyphenols consumed above 20 mg/d in Argentinian postpartum women. The axes define the reference system and represent latent factorial variables derived from linear combinations of the initially observed variables.

Fig. 2. A factorial representation of the HJ-Biplot for clusters in the main plane (axes 1~2) for polyphenols consumed at levels of 5~20 mg/d in Argentinian postpartum women. The axes define the reference system and represent latent factorial variables derived from linear combinations of the initially observed variables.

logical potential as NRL and EI (mainly 5- and 1-caffeoylquinic acids). Also, 5-caffeoylquinic, 1,3-dicaffeoylquinic, and 1-caffeoylquinic acids were identified as potential protease inhibitors (PIs), with the former acting as a G protein-coupled receptor ligand (GPCRL).

For intakes 5 to 20 mg/d, cluster 2 included several compounds with dissimilar pharmacokinetic properties. Catechins and 5-O-galloylquinic acid had high DS and scores as potential GPCRL (except for gallates), NRL, PI (except for gallates), and EI to different extents. Quercetin showed low scores as a kinase inhibitor (KI), NRL, and EI. Cluster 3 showed a discrepancy in its pharmacokinetic profile (good LR and poor VR). Its feruloylquinic acids showed better scores as NRL and EI than the other compounds in the cluster.

Overall, none of the polyphenols evaluated acted as ion

channel modulators or KI. Some toxicological risks were described for syringic acid, procyanidin dimer B2, naringenin, and quercetin. Disuccinoylquinic acid was excluded from the analysis for not having registered SMILES. Although the rest of the compounds showed certain potential bioactivity, this was limited because they did not belong to a cluster derived from the HJ-Biplot analysis.

DISCUSSION

This study aimed to establish the exposure to dietary polyphenols through HJ-Biplot and their relationship with several factors in healthy postpartum women from Córdoba, Argentina. Thirty-three polyphenolic compounds were consumed above 5 mg/d. The HJ-Biplot technique

Table 6. Descriptive statistics for dietary quality indicators of Argentinian postpartum women (n=275)

Dietary quality indicator	Mean	SD	Skewness	Kurtosis
Dietary total antioxidant capacity	7.91	4.64	1.24	1.89
Glycemic index	77.50	6.94	0.26	0.47
Minimum dietary diversity for women	8.08	1.79	−0.89	0.26
Water in beverage and food intake	2,219.59	1,178.93	1.21	1.99
Plain water	2,147.19	1,073.45	0.87	1.29
Soluble dietary fiber intake	6.15	3.25	1.08	1.61
Insoluble dietary fiber intake	16.85	9.16	0.88	0.70
Fat quality index	18.92	4.55	1.00	1.16
Protein to carbohydrate ratio	0.33	0.10	0.84	1.79

SD, standard deviation.

Table 7. ANOVA results and effect sizes for dietary quality variables among polyphenolic clusters (n=275)

Dietary variable	Polyphenols consumed from 5 to 20 mg/d				Polyphenols consumed above 20 mg/d			
	Cluster 1 (n=102)	Cluster 2 (n=63)	Cluster 3 (n=96)	Cohen's d (95% CI)	Cluster 1 (n=121)	Cluster 2 (n=56)	Cluster 3 (n=94)	Cohen's d (95% CI)
Dietary total antioxidant capacity	5.52±0.63	9.68±0.65*	10.56±0.80*	1<2: 0.705 (0.382~1.028) 1<3: 0.712 (0.425~0.999)	7.00±0.58	11.80±0.85*	7.82±0.66	1<2: 0.757 (0.431~1.084)
Glycemic index	77.38±1.04	75.82±1.32	75.39±1.07	—	76.12±0.95	74.33±0.95	77.63±1.08	—
Minimum dietary diversity for women	8.13±0.18	8.05±0.23	8.16±0.19	—	8.13±0.16	8.66±0.24	7.67±0.19	—
Water in beverage and food intake	1,481.42±85.77	1,982.37±111.28*	3,183.04±87.97*	1<2: 0.578 (0.257~0.898) 1<3: 1.979 (1.634~2.319)	1,414.70±75.49	2,452.71±109.12*	2,987.38±84.22*	1<2: 1.264 (0.921~1.607) 1<3: 1.917 (1.592~2.241)
Plain water	2,203.88±129.07	2,361.53±151.24	2,191.60±129.07	—	2,275.14±114.44	2,265.94±163.46	2,129.78±130.04	—
Soluble dietary fiber intake	5.23±0.30	6.59±0.38*	6.74±0.31*	1<2: 0.452 (0.135~0.770) 1<3: 0.503 (0.217~0.783)	5.37±0.27	8.39±0.40*	5.71±0.31	1.020 (0.686~1.354)
Insoluble dietary fiber intake	14.55±0.85	18.04±1.08*	18.36±0.88*	1<2: 0.409 (0.092~0.726) 1<3: 0.445 (0.163~0.727)	15.42±0.77	23.07±1.13*	14.94±0.87	0.909 (0.578~1.239)
Fat quality index	16.52±1.62	21.86±2.06*	20.75±1.68	1<2: 0.329 (0.012~0.644)	15.78±1.47	23.25±2.22*	21.75±1.67*	1<2: 0.461 (0.140~0.781) 1<3: 0.371 (0.100~0.643)
Protein to carbohydrate ratio	0.37±0.02	0.33±0.03	0.33±0.03	—	0.36±0.02	0.37±0.03	0.32±0.03	—

Data are expressed as mean±standard error.
Effect size threshold: small (0.20), medium (0.50), large (0.80), and very large (1.30).
*$P<0.05$.
CI, confidence interval.

Fig. 3. Pharmacokinetics, bioactivity, and toxicity of polyphenols. LR, pharmacokinetic score based on Lipinski's rule; VR, bioavailability score based on Veber's rule; DS, drug-score; GPCRL, G protein-coupled receptor ligand; ICM, ion channel modulator; KI, kinase inhibitor; NRL, nuclear receptor ligand; PI, protease inhibitor; EI, enzymatic inhibitor; M, mutagenic; T, tumorigenic; I, irritant; R, reproductive. For LR, the color indicates the number of violations to the rule: red ($\geq$2), yellow (1), green (0); for VR, green indicates abidance by the rule; for DS, red (<33%), yellow (33%~66%), green (>66%); for GPCRL, ICM, KI, NRL, PI, and EI, red (no activity), yellow (low activity), green (medium activity); for M, T, I, and R, green (no risk), yellow (moderate risk), red (high risk).

enabled the representation of women in rows and polyphenols in columns as multivariate superimposed data in the same reference system with adequate quality. Although the polyphenol intake varied greatly among participants, this technique allowed women to be clustered. Additionally, clusters were associated with different indicators of diet quality, which may be involved in nutritional outcomes.

The most consumed polyphenols were hydroxycinnamic acids, flavonoids, and lignans, which were in accordance with previous studies. Hydroxycinnamic acids are abundant in plant foods, including fruits (e.g., apple and orange), beverages (e.g., coffee and tea), and some root vegetables (e.g., carrot and potato) (El-Seedi et al., 2012), with a wide interindividual variability of intake due to dietary choices. For example, the daily intake of hydroxycinnamic acids was 151 mg/d in Italy, 705 mg/d in Poland, and 727 mg/d in Brazil (Coman and Vodnar, 2020). In all studies, coffee was the main contributor of hydroxycinnamic acids (above 60%), but several South American countries (Argentina, Uruguay, Paraguay, and Chile) consume *yerba mate* (a traditional product from *Ilex paraguariensis* drunk as an infusion). It is a significant source of polyphenols, which explains its nutritional value (Bracesco et al., 2011; Cittadini et al., 2018), with daily consumption of 1,011 mL/d in Argentinian postpartum women, resulting in an intake of 820 mg/d of hydroxycinnamic acids (Miranda et al., 2021).

Flavonoids are an abundant group of diverse phytochemicals with antioxidant and anti-inflammatory properties, which were the second most consumed polyphenol group in this study. Hesperetin had the highest in-

take among them, which is consistent with the Mediterranean healthy eating, lifestyle, and aging study in Europe (Godos et al., 2018). Our results also agree with regional studies. In this sense, Anacleto et al. (2019) reported that flavanones (hesperetin and naringenin) and proanthocyanins were the most consumed flavonoids in Brazil. Unlike these studies, our work discovered a significant exposure to flavanols, specifically gallate flavanols, which may be due to the high concentration of these compounds in *yerba mate* (Bracesco et al., 2011). Flavonoids are present in the Argentinian diet: tomato, orange, and lemon (flavanones); *yerba mate*, black tea, and pome fruits (flavanols); onion, apple, and black tea (flavonols); grape and berries (anthocyanidins) (Bracesco et al., 2011; Hejazi et al., 2020). Lignans, such as lariciresinol and pinoresinol, were also consumed according to the typical Latin American diet, which contains lignan-rich foods, including maize, potatoes, legumes, and whole grains (Rodríguez-García et al., 2019; Zarei et al., 2019), and to reports of Durazzo et al. (2018).

Growing epidemiological and clinical evidence associate polyphenols with health benefits (Leri et al., 2020). Thus, it is necessary to develop adequate statistical techniques to evaluate exposure to dietary polyphenols in a multidimensional manner because these compounds have biological interactions and synergistic effects (Herranz-López et al., 2012). In this regard, the effects of the 33 polyphenols discovered in the current study have been proposed, although most studies are based on group/subgroup or single-compound approaches (Del Bo' et al., 2019). It is difficult to identify polyphenol-rich dietary patterns with health outcomes. The HJ-Biplot technique

is a novel approach in nutritional epidemiology that offers high quality of representation for both specific polyphenols and individuals simultaneously. This unique advantage of HJ-Biplot, unlike other biplot techniques, facilitates the understanding of the multidimensionality of complex data sets, which has been validated in other scientific fields (Carrasco et al., 2019). Furthermore, when combined with clustering techniques, it enabled the recognition of conglomerates of individuals based on their projections on column markers (i.e., polyphenols), with adequate quality of representation. Due to the great variability of daily exposure, polyphenols were divided into two groups to improve representation in the HJ-Biplot hyperspace: compounds consumed between 5 and 20 mg/d and compounds consumed above 20 mg/d. Only polyphenols with an average intake above 5 mg/d were included in the analysis (Kesse-Guyot et al., 2012). HJ-biplot analyses were performed on each group, and three clusters were identified.

In Latin American countries, such as Argentina, a nutritional transition process has occurred over the last 20 years, characterized by a greater intake of ultra-processed foods and less consumption of fruits and vegetables (Pou et al., 2020). Therefore, to assess a possible nutritional transition in our sample, the intake of total polyphenols was compared, and there were no significant differences in the means between 2013~2016 and 2017~2020 (T= -1.19, $P>0.05$). Likewise, the cluster conformation by HJ-Biplot was not time-dependent, either for polyphenols above 20 mg/d ($\chi^2=4.91$, $d_f=2$, $P>0.05$) or for lower consumption ($\chi^2=0.92$, $d_f=2$, $P>0.05$).

Postpartum women in the cluster with the lowest polyphenolic intake presented worse indicators of dietary quality than the others due to exposure to a lower intake of antioxidants, water, fiber, and healthy fats, which must be modified given the cumulative and synergistic effects of these nutrients on multiple physiological pathways (Margină et al., 2020). Non-nutritional effects, such as the antioxidant and functional protection provided by phytochemicals (Saura-Calixto and Goñi, 2006), are also crucial in preventing non-communicable diseases (Nascimento-Souza et al., 2018). Because polyphenol source foods are also rich in other antioxidants, water, fiber, and unsaturated fatty acids, the results were as expected (Yahia et al., 2019). For example, the strongest cluster effect was on WBFI according to the water content of fruits and vegetables. Furthermore, *yerba mate* constitutes a highly consumed beverage by postpartum women, being the main source of polyphenols and water (Miranda et al., 2021). The study of water in foods has recently gained attention due to its health benefits, including gastrointestinal disease prevention and hydric balance maintenance, which questions traditional recommendations based solely on PW (Rosinger and Tanner, 2015). Sim-

ilarly, significant effects were discovered on TAC and dietary fiber. TAC considers the antioxidant activity of dietary compounds, both polyphenolic and non-polyphenolic (e.g., vitamins, lycopenes, carotenoids, among others), as well as their potential synergistic and redox interactions, which have been associated with positive health outcomes (Farhangi et al., 2020). Koehnlein et al. (2014) showed that infusions, cereals, legumes, fruits, and vegetables are the main sources of TAC and polyphenols in Brazil. Moreover, a study with cluster analysis of polyphenol intake conducted by Julia et al. (2016) proved that people with higher polyphenolic intake consumed more antioxidant vitamins, carotenoids, total fiber, and PUFAs, which was consistent with our findings. Collectively, these results indicate that different compounds share dietary sources, highlighting the importance of a diverse and plant-based diet in promoting health.

The chemical drug-likeness was assessed using LR and VR because a compound that does not comply with them may have poor pharmacokinetic properties (e.g., poor absorption, faster metabolism and excretion, unfavorable distribution, or toxicity) (Turner and Agatonovic-Kustrin, 2007). However, LR may not adequately predict the oral bioavailability of some compounds, such as small molecules (Leeson and Springthorpe, 2007). Therefore, many polyphenols violate LR and still achieve good bioavailability in animal and human studies (i.e., flavanols) (Yang et al., 2008). Hence, VR, which considers other factors that influence cellular permeability, distribution, and excretion (e.g., potential drug's topological polar surface area and molecular flexibility as determined by the number of rotatable bonds), is a complementary predictor of polyphenol bioavailability (Jablonsky et al., 2019; Sayed et al., 2020), with our findings suggesting pharmacokinetics of these compounds. Although hydroxycinnamic acids did not comply with LR and VR, as in previous studies (Basha et al., 2013), this can be offset by their elevated intake.

Hesperetin and lariciresinol, from cluster 2 of >20 mg/d intakes, showed potential bioactivity. The potential of hesperetin as an NRL has been established in biological models, enhancing cytoprotective and anti-inflammatory mechanisms (Muhammad et al., 2019). However, although some lignans are EI (Mason and Thompson, 2014), this should be confirmed for lariciresinol, whose known effects (e.g., anticancer, antimicrobial) depend on its action on biological lipid membranes (Ma et al., 2018). From cluster 3, the predicted NRL and EI roles of hydroxycinnamic acids have been established *in vitro* and *in vivo* in different pathways (Alfaro-Viquez et al., 2018; Bender et al., 2018). Additionally, 5-caffeoylquinic acid has been proposed as a modulator of signaling pathways associated with protein G receptors (Stefanello et al., 2019). Conversely, predicted PI bioactivity needs to be

confirmed experimentally.

Predicted bioactivities of the catechin derivatives of cluster 2 (5~20 mg/d polyphenol intake) have already been determined *in vitro* (Li et al., 2012; Moreno-Ulloa et al., 2015; Peluso and Serafini, 2017; Arif, 2022). This cluster also included quercetin and 5-*O*-galloylquinic acid, both compounds with widely recognized biological effects (Karas et al., 2017; Ulusoy and Sanlier, 2020). Although the potential of cluster 3's feruloylquinic acids was in accordance with the biological effects of hydroxycinnamic acids, they have been scarcely investigated (Dokli et al., 2013). Malvidin-3-*O*-glucoside and caffeoyl-glucose are well known EI (Huang et al., 2018; Błaszczak et al., 2020).

Although there are experimental reports on the toxic effects of syringic acid, procyanidin dimer B2, naringenin, and quercetin, they have not been replicated in humans. Additionally, high doses are required to exert toxicity, which is far above the dietary exposure levels described in this study (Yamakoshi et al., 2002; Harwood et al., 2007; Ortiz-Andrade et al., 2008; Mirza and Panchal, 2019). Consequently, all clusters were considered safe based on polyphenol intake ranges.

Some limitations need to be addressed. The cross-sectional nature of the study limits the inference on causality among variables. However, the current findings contribute to existing evidence and raise new questions for future research using longitudinal designs. Another potential limitation is the use of FFQ because it can cause difficulties in estimating the intake of polyphenols that depend on several factors, including harvest season, food processing and cooking, assessment biases, and measurement errors. However, we used an instrument that showed adequate validity and reproducibility for the Latin American population, with a moderate overestimation of 4% and absence of constant bias, and we considered seasonal variations and cooking methods (Cortez et al., 2021). Similarly, the use of large databases, such as the Phenol-Explorer, can represent a disadvantage (e.g., by underestimating the dietary intake of less studied compounds and foods, or by inconsistency in analytical methods) (Hill et al., 2021). However, Phenol-Explorer uses the most detailed and extensive global database with proven validity for quantifying polyphenolic compounds. Other methodological approaches, such as combining Phenol-Explorer with other valid databases (e.g., United States Department of Agriculture), direct quantification of compounds in food, and polyphenolic metabolite dosing, could potentially benefit future research (Xu et al., 2021). Finally, although chemoinformatics can be used as a black box, the benefits it has provided are well known. The pharmacological property prediction tools are accessible and cost effective, and they can help select optimal candidates with sufficient bioactivity, good bioavailability, metabolic stability, and no structure-related toxicity. Also, chemoinformatics contributes to the development of multi- and transdisciplinary science (Medina-Franco et al., 2021). Despite these limitations, this study provides significant evidence on how to approach the consumption of polyphenols statistically and on the associations of these with nutritional health outcomes of postpartum women.

Conclusively, HJ-Biplot is a technique that overcomes methodological limitations in accurately studying the dietary intake of diverse compounds, including polyphenols. It identifies multiple relationships between polyphenols and reduces them to a low-complexity, high quality system. Furthermore, it provides a spatial solution for finding women with similar polyphenolic intakes, ensuring the multidimensional study of these compounds. In this study, Argentinian postpartum women were divided into clusters based on their intake of the following polyphenolic families: hydroxycinnamic acids, flavonoids, and lignans. Additionally, the identified clusters include compounds with biological potential that are consumed within safe ranges. In fact, polyphenol intake is associated with improved nutritional status (BFP, BMI, and level of physical activity), which can be promoted by socioeconomic factors, such as employment and education. Their nutritional benefits could also be mediated by cluster dietary implications, given that they have higher diet quality indicators, such as the intake of antioxidants, water, fiber, and healthy fats.

AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Concept and design: ARM, AVS, MVC. Analysis and interpretation: ARM, AVS, NGG, MPGV. Data collection: ARM, AVS, MVC. Writing the article: ARM, AVS. Critical revision of the article: MVC, EAS, NGG, MPGV. Final approval of the article: all authors. Statistical analysis: ARM, AVS, NGG, MPGV. Obtained funding: EAS. Overall responsibility: EAS.

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