Application of 4 birthweight curves and local reference range at a University Hospital of Rio de Janeiro, Brazil

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BACKGROUND: Numerous fetal growth curves have been developed from various subpopulations and geographic locations worldwide.
OBJECTIVE: To determine the birthweight standard at the Maternity School and compare it to currently used standards in the clinical practice services.
STUDY DESIGN: Cross-sectional, observational, and descriptive study. Data from infants born between 2011 and 2016 were collected from the Maternity School Hospital of the Federal University of Rio de Janeiro to define the 10th, 25th, 50th, 75th, and 90th percentiles of the birthweight by gestational age. It was determined the performance of the INTERGROWTH-21st, Fenton, Alexander, and Lubchenco for the Maternity School standards.
RESULTS: After the 33rd week of pregnancy, the INTERGROWTH standard was similar to the local standard for small-for-gestational-age infants and Fenton for large-for-gestational-age infants at Maternity School Hospital. The INTERGROWTH standard was found to be inadequate to classify small-for-gestational-age infants, which are babies at major risk for morbidity and mortality at the onset of the 33rd week of pregnancy.
CONCLUSION: It was possible to define reference values for birthweight for the maternal school hospital considering at least 33 weeks of pregnancy with a 95% confidence interval. The comparison of the INTERGROWTH, Fenton, Alexander, and Lubchenko standards to the maternal school hospital curve showed that the Fenton curve was the most suitable for the diagnosis of small for gestational age.

Key words: adequate for the gestational age, birthweight pattern, large for the gestational age newborn baby, small for the gestational age

Introduction

It is a worldwide consensus that birthweight variation for gestational age is an important clinical indicator of newborn health. Low birthweight (LBW), a term used to describe babies born with a weight of <2500 g, is a potential indicator better than any other characteristic, and its incidence varies according to the country.[1] This condition is strongly linked to premature births that occur before 36 weeks of pregnancy and with babies who are small for gestational age (SGA), which refers to babies born with a weight below the 10th percentile for their gestational age. It is associated with increased fetal and neonatal mortality and increased infant morbidity.[2] The level of LBW in developing countries (16.5%) is more than double that in developed regions (7%). In Brazil, the incidence of LBW was 10% in 1996.[2]

Newborn babies diagnosed with SGA have several complications that can be classified into short- and long-term consequences. Large-for-gestational-age (LGA) infants also show an increased risk for complications that are more frequent in the group above the 97th percentile for gestational age.[3]

According to birthweight, infant management by all health and medical providers may change. Thus, using an

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This study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki and submitted to the Research Ethics Committee of the Maternity School Hospital of the Federal University of Rio de Janeiro (protocol number 2.529.818).

The data supporting this study's findings are available from the corresponding author (K.B.C.R.) upon reasonable request.

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Why was this study conducted?

To define a local reference curve of birthweight and compare these standards to 4 international curves: INTERGROWTH, Fenton, Alexander, and Lubchenko, showing their performance in the population of the Maternity School.

Key findings

None of the 4 international curves are accurate for our population. A local curve was defined from 33 weeks of pregnancy.

What does this add to what is known?

The study shows that the international curves are not suitable for the local standard. For small for gestational age, Fenton is the most suitable curve.

appropriate local standard for this purpose is crucial to avoiding the risk of neglecting high-risk babies with worse perinatal outcomes, a higher rate of morbidity and mortality, and a waste of human, material, and financial resources when adequate-for-gestational-age (AGA) infants are classified as a high-risk baby.

Several studies have been published on fetal growth curves, and different standards have been used to determine whether this would be adequate,[3,4] including a curve for premature babies.[5–7] The International Fetal and Newborn Growth Consortium for the 21st Century, or INTERGROWTH-21st, is a global, multidisciplinary network dedicated to improving perinatal health and reducing preventable newborn deaths that proposed standard curves.[8] However, studies show that each population has a specific curve.[9–11]

Developing a reference chart for birthweight for the population attending the Maternity School Hospital of the Federal University of Rio de Janeiro (ME-UFRJ) will allow comparison with international standards for better health assistance. The major objective of this study was to define a reference range of birthweight on the basis of births at the ME-UFRJ. Therefore, it was compared with applying the 4 reference birthweight curves (Lubchenco, Alexander, Fenton, and INTERGROWTH-21st) to diagnose SGA and LGA newborns.

Materials and Methods

A cross-sectional, observational, and descriptive study was conducted. Data from infants born between 2011 and 2016 were collected from the hospital maternity records. ME-UFRJ is a nonprofit hospital that assists pregnant women from all Brazilian regions and Rio de Janeiro city. Infants born with at least 24 weeks of gestation were considered inclusion criteria for the present study.

The statistical software Stata (version 13, StataCorp, College Station, TX, 2013) was used for data analyses. The local Ethics Committee approved the final study protocol (identification number 2.529.818, March 2018).

To define the reference range of birthweight, it was considered as exclusion criteria: stillborn, chromosomal abnormality, multiple pregnancies, fetal malformations, hypertensive syndromes of pregnancy, diabetes mellitus or gestational, autoimmune diseases such as Lupus Erythematosus or Antiphospholipid Antibody Syndrome, and cases with inaccurate gestational age annotation.

Different exclusion criteria were considered to compare the application of the 4 reference birthweight curves: chromosomal abnormality, multiple pregnancies, fetal malformations, inaccurate gestational age annotation, and stillborn. This difference is necessary to evaluate the performance of the curves in the entire population, including pregnancies with associated morbidities.

Gestational age was considered as described in the medical records at delivery time. It was estimated by the last menstrual period when the differences between the estimates of gestational age by last menstrual period and by first- or second-trimester ultrasound were <7 days or <14 days, respectively. If this is not the case, the gestational age will be corrected using the ultrasound date. The gestational age at delivery was considered inaccurate when there was no obstetric ultrasound before 28 weeks of gestation.

The criterion of newborn classification was based on the weight adequacy for gestational age. According to that, a neonate was classified as SGA when birthweight was at or below the 10th percentile, AGA when birthweight was between the 10th and 90th percentile, or LGA when birthweight was at or >90th percentile. Data were divided into 4 groups. The first group presented the performance of the curves in the population at usual risk from the 24th to the 32nd week of gestation. A second group included the population at usual risk from the 33rd to the 42nd week of gestation. Then, 2 groups with the same gestational age range as the first 2, including newborns with high-risk pregnancies.

To define the standard birthweight in the institution, the sample was stratified by gestational age, as mentioned above. After observing the weight distribution of the newborns in each GA, the 5th, 10th, 50th, 90th, and 95th percentiles of each GA were determined. After all, reference values for birthweight were established in each GA at the ME-UFRJ.

To compare the application of the 4 references birthweight curves (Lubchenco, Alexander, Fenton, and INTERGROWTH-21st) for the diagnosis of SGA and LGA in natives and stillborns, all newborns were classified as SGA, AGA, or LGA according to the referenced curves. Afterward, the SGA, AGA, and LGA proportions of the above curves were compared with the local birthweight curve. Differences between proportions were considered statistically significant when 95% confidence interval (CI) limits did not include the null value.

Results

A total of 10,847 newborns were considered eligible for the present study.

TABLE 1
Patients eligible for the present study considering gestational age

Gestational age (wk)	Patients (n)
24	2
25	4
26	9
27	7
28	11
29	11
30	12
31	21
32	18
33	35
34	74
35	86
36	142
37	413
38	1011
39	1675
40	1508
41	961
42	56

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However, 1427 cases were excluded because of incomplete data. Moreover, subjects were excluded as a result of inaccurate annotation (n=538), multiple gestations (n=199), stillborn (n=88), fetal pathologies (n=173), and maternal morbidities (n=2360). The final sample was 6062 cases.

All patients selected for the present study were divided into groups considering gestational age at birth, as shown in Table 1.

Table 2 shows the weights in grams of the fifth, 10th, 25th, 50th, 75th, 90th, and 95th percentiles for each gestational age, and the respective 95% CI is shown in Table 3. Table 4 presents the proportion of SGA, AGA, and LGA for 24 to 32 weeks of gestation classified by the INTERGROWTH, Fenton, Alexander, and Lubchencho standard (95% CI). For pregnancies up to 32 weeks, the Fenton standard showed results closer to 10% expected, with proportions of SGA and LGA of 4.95% and 10.89%, respectively. The Alexander and Lubchencho standards showed similar results, underestimating the rate of SGA, with the same rate of SGA of 3.96% and LGA of 3.96% and 4.95%, respectively.

Considering normal and low-risk pregnancies from week 33 to week 42, the performance of the growth curve elaborated in this study was evaluated, with 9.59% SGA and 10.35% LGA. From this sample, it was impossible to determine the weight standards with a 95% CI for infants born until 33 weeks of gestation because the number of cases required was not reached. For pregnancies with >33 weeks, there was no overlapping of CI values for the percentiles studied (Table 3). Table 5 shows the proportion of SGA, AGA, and LGA for pregnancies of 33−42 weeks classified by our growth curve, INTERGROWTH, Fenton, Alexander, and Lubchencho standard (95% CI). When assessing the INTERGROWTH standard, 7.16% of SGA and 9.61% of LGA were observed. For SGA, the Fenton curve showed a result closer to the expected, with 10.85%. For LGA, the result was 5.48%. The performance of the Alexander and Lubchenco curves was similar: 4.94% and 5.08% of SGA and 13.40% and 12.46% of LGA, respectively.

After considering cases with maternal morbidities, the proportions of SGA, AGA, and LGA of newborns between 33 and 42 weeks were recalculated. The results are shown in Table 6. The Fenton standard offered a performance close to that expected for SGA (11.30%) but only 6.08% for LGA.

Discussion

Principal findings

The study sought to determine the birthweight standard for infants born at the ME-UFRJ and compared it with the performance of the previously used curves (Fenton and Alexander) and the one currently used in clinical practice, INTERGROWTH. This was established in a worldwide multicenter study by the World Health Organization (WHO).[6−8] Constructing a table specific to the institution's population allowed us to assess the most appropriate chart, directing resources to treat newborns properly. The Maternity School curve up to 32 weeks of gestation showed an insufficient number of cases to achieve statistically significant results; therefore, the performance of the curve at these gestational ages was not presented here.

Results in the context of what is known

Infants born between the 24th and 32nd week of gestation are considered premature and with a relatively lower prevalence. A prevalence of 1.5% was found in the present study, which is in accordance with the consolidated data of 1.5% of deliveries with gestational age <31 weeks in Brazil.[12] In addition to the low prevalence, premature births could be associated with the exclusion criteria for determining the weight pattern, such as multiple pregnancies and maternal and fetal pathologies. From

TABLE 2
Birthweight by gestational age from infants born at the ME-UFRJ

	Percentiles (birthweight in g)						
Gestational age (wk)	5th	10th	25th	50th	75th	90th	95th
24	650.0	650.0	650.0	675.0	700.0	700.0	700.0
25	730.0	730.0	730.0	737.5	936.3	1000.0	1000.0
26	800.0	800.0	827.5	940.0	1160.0	1180.0	1180.0
27	730.0	730.0	820.0	1030.0	1130.0	1365.0	1365.0
28	630.0	706.0	1065.0	1170.0	1265.0	1320.0	1330.0
29	1180.0	1213.0	1316.3	1452.5	1591.3	1631.5	1645.0
30	1015.0	1172.5	1392.5	1557.5	1706.3	1797.0	1895.0
31	1208.5	1258.0	1427.5	1600.0	1822.5	1989.0	2045.0
32	1515.0	1555.5	1732.5	1945.0	2141.3	2378.0	2585.0
33	1243.0	1481.0	1750.0	2010.0	2375.0	2600.0	2742.0
34	1571.3	1795.0	1975.0	2265.0	2522.5	2932.5	3141.3
35	2027.8	2085.0	2312.5	2565.0	2815.0	3143.5	3365.0
36	2098.8	2363.0	2607.5	2784.5	3065.0	3338.5	3489.3
37	2423.5	2512.0	2735.0	2975.0	3237.5	3543.0	3741.5
38	2534.0	2665.0	2895.0	3165.0	3440.0	3725.0	3897.0
39	2680.0	2805.0	3030.0	3275.0	3550.0	3775.0	3970.0
40	2782.3	2915.0	3140.0	3400.0	3685.0	3975.0	4175.0
41	2845.5	2966.0	3212.5	3520.0	3790.0	4068.0	4230.0
42	2703.0	2907.0	3292.5	3715.0	3925.0	4184.0	4487.5

ME-UFRJ, Maternal School Hospital of the Federal University of Rio de Janeiro.

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6062 cases, only 135 (1.24%) were delivered until the 32nd week. Thus, the CI of all the percentiles defined up to 33 weeks overlapped, making any inference impossible.

After analyzing the performance of the curves in the interval from 24 to 32 weeks of pregnancy, the INTERGROWTH curve presented only 1.98% of SGA and 2.97% of LGA. Even with the considerable variation observed in the CI of these proportions (0.48%−7.74% and 0.94%−8.96%), it was observed that the curve showed a low index of diagnosis of both SGA and LGA. The classification of newborns by the INTERGROWTH curve was significantly below expectations.

In the same group (<33 weeks), the Fenton curve also showed a result lower than expected for SGA (4.95%), although with a 95% CI from 2.04% to 11.50%. Thus, the curve performed better than the INTERGROWTH curve, reaching what was expected in the CI. The result was adequate for LGA, with 10.89% (95% CI, 6.07−18.76). The Fenton curve showed the best performance for diagnosing SGA and LGA in pregnancies up to 33 weeks.

The performances of the Alexander and Lubchenco curves for the group up to 33 weeks of pregnancy were similar. Regarding the SGA, both reached 3.96% of the result (95% CI, 0.84−9.60 and 1.46−10.23, respectively). They also showed low SGA detection, reaching close to the 10% index at the upper limit of the CI. A similar result was also found for LGA: 3.96% for Alexander (1.46%−10.23%) and 4.95% (2.04%−11.50%) for Lubchenco.

Evaluating all the results obtained for pregnancies up to 33 weeks, a low SGA and LGA detection rate was observed. The curve that presented the most inferior performance was INTERGROWTH, the one currently used in the institution, with results consistently below the adequate level. With slightly superior and remarkably similar performance, Alexander and Lubchenco also presented a low SGA and LGA detection index. For this group, the Fenton curve showed the best result. Among the cases of LGA, a rate close to the expected was revealed, and despite the still low rate for SGA, it is closer to the expected result.

Considering the results from the group with more than 33 weeks of pregnancy, the Maternity School Hospital showed a proportion of 9.59% of SGA (95% CI, 8.87−10.37), as expected. The same was observed for LGA, with a ratio of 10.35% (95% CI, 9.60−11.15). Both results confirmed the suitability of the standard to classify infants from the Maternity School Hospital. There was a performance improvement when evaluating the INTERGROWTH standard in this group. Despite this improvement, the detection rate for SGA was still below expectations: 7.16% (6.53%−7.84%). For LGA, the INTERGROWTH standard showed 9.61% (95% CI, 8.88−10.38), with a good detection rate. The Fenton curve was the closest to the local standard, with 10.85% (95% CI, 10.80−11.66) of SGA. When evaluating the result among the LGA group, the curve deviates to the right, with a low detection rate of LGA 5.48% (95% CI, 4.93−6.09). The Alexander and Lubchenco standards showed similar rates, with a low rate of SGA diagnosis (4.94% and 5.08%, respectively). Regarding the LGA, both curves resulted in a detection rate above expectations (13.40% and 12.46%, respectively), as if they were shifted to the left.

Considering the third group (pregnancy associated with morbidities from 33 to 42 weeks), it was possible to reach an adequate number of cases for analysis. An acceptable pattern was observed when evaluating the Maternity School Hospital curve, with 10.27% SGA and 10.93% LGA. There was a slight

TABLE 3
Percentiles of 95% CIs birthweight according to each gestational age

	95% CIs						
Gestational age (wk)	5th	10th	25th	50th	75th	90th	95th
24	650–688	650–695	650–700	650–700	650–700	654.16–700	661–700
25	730–730	730–738	730–885	730–1000	730–1000	736–1000	761–1000
26	800–828	800–845	800–1007	825–1168	887–1180	1087–1180	1155–1180
27	730–891	730–971	730–1108	758–1291	982–1365	1126–1365	1130–1365
28	630–1058	630–1096	630–1178	1049–1269	1166–1330	1219–1330	1266–1330
29	1180–1313	1180–1320	1180–1455	1315–1596	1449–1645	1562–1645	1600–1645
30	1015–1339	1015–1422	1078–1539	1405–1696	1575–1855	1685–1895	1722–1895
31	1205–1366	1205–1439	1249–1536	1470–1812	1618–1994	1819–2050	1845–2050
32	1515–1626	1515–1777	1540–1940	1789–2131	1961–2453	2135–2585	2149–2585
33	1075–1610	1075–1740	1595–1930	1910–2246	2116–2570	2403–2810	2561–2810
34	1477–1802	1563–1920	1864–2128	2188–2382	2455–2666	2641–3231	2856–3553
35	1593–2085	2008–2175	2146–2382	2442–2635	2669–2878	2875–3365	3102–3460
36	1835–2332	2123–2486	2515–2671	2729–2883	2990–3146	3224–3484	3340–3784
37	2389–2465	2465–2570	2665–2785	2945–3035	3188–3302	3478–3627	3627–3845
38	2471–2580	2625–2700	2860–2927	3130–3190	3417–3485	3680–3773	3840–3960
39	2655–2715	2775–2830	3005–3055	3250–3295	3525–3580	3745–3820	3910–4015
40	2758–2824	2880–2957	3108–3168	3380–3430	3658–3715	3922–4045	4120–4225
41	2805–2890	2915–3020	3175–3261	3483–3555	3765–3835	3990–4110	4168–4299
42	(2310–2986)	(2660–3064)	(3041–3562)	(3558–3796)	(3792–4060)	(4022–4553)	(4062–4890)

CI, confidence interval.

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TABLE 4
Proportion of SGA, AGA, and LGA for pregnancies with 24–32 wk classified by the INTERGROWTH, Fenton, Alexander, and Lubchenco standard (95% CI).

	INTERGROWTH	Fenton	Alexander	Lubchenco
SGA	1.98 (0.48–7.74)	4.95 (2.04–11.50)	3.96 (0.84–9.60)	3.96 (1.46–10.23)
AGA	95.04 (88.49–97.95)	84.15 (75.52–90.14)	92.07 (84.79–96.03)	91.08 (83.59–95.35)
LGA	2.97 (0.94–8.96)	10.89 (6.07–18.76)	3.96 (1.46–10.23)	4.95 (2.04–11.50)

AGA, appropriated-for-gestational-age; *CI*, confidence interval; *LGA*, large-for-gestational-age; *SGA*, small for gestational age.

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increase in these percentages when births were included with risk factors (ie, a higher SGA and LGA index). The INTERGROWTH curve showed a low detection rate for SGA (7.60%). For LGA, the detected rate was adequate (10.64%). The Fenton curve showed a deviation to the right for LGA (6.08%), with better performance for SGA (11.30%). The Alexander and Lubchenco curves presented similar results, with a deviation on the right for the SGA (6.13% and 5.58%, respectively) and a deviation on the left for LGA (13.29% and 13.62%, respectively). Significant results were observed by considering the results of each curve for all 3 experiments.

In 2014, the WHO published the INTERGROWTH chart[6] to determine birthweight standards and recommend its worldwide intent to improve newborn care. The INTERGROWTH standard adopted in the institution's clinical practice showed low detection rates for SGA. This result is in accordance with a study in England.[10] Research studies published in New Zealand and the United States have also demonstrated this low detection rate.[11,13] One of the main targets of newborn healthcare is identifying the baby at risk and preventing possible adverse events. The detection rate of SGA by the INTERGROWTH standard was low compared with the Maternity School Hospital curve. Regarding the

TABLE 5
Proportion of SGA, AGA, and LGA for pregnancies of 33–42 wk classified by the maternal school hospital standard, INTERGROWTH, Fenton, Alexander, and Lubchenco standard (95% CI), excluding high-risk pregnancies

Variables	Maternity School Hospital	INTERGROWTH	Fenton	Alexander	Lubchenco
SGA	9.59 (8.87–10.37)	7.16 (6.53–7.84)	10.85 (10.08–11.66)	4.94 (4.42–5.52)	5.08 (4.55–5.67)
AGA	80.05 (79.01–81.04)	83.22 (82.25–84.15)	83.66 (82.69–84.57)	81.64 (80.64–82.61)	82.45 (82.25–84.15)
LGA	10.35 (9.60–11.15)	9.61(8.88–10.38)	5.48 (4.93–6.09)	13.40 (12.56–14.29)	12.46 (11.64–13.32)

AGA, appropriated-for-gestational-age; *CI*, confidence interval; *LGA*, large-for-gestational-age; *SGA*, small for gestational age.

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TABLE 6
Proportion of SGA, AGA, and LGA for pregnancies of 33–42 wk classified by the maternal school hospital standard, the INTERGROWTH, Fenton, Alexander, and Lubchenco standard (95% CI), including high-risk pregnancies

Variables	Maternity School Hospital	INTERGROWTH	Fenton	Alexander	Lubchenco
SGA	10.27 (9.57–11.02)	7.60 (6.99–8.26)	11.30 (10.57–12.08)	6.13 (5.58–6.72)	5.58 (5.06–6.16)
AGA	78.78 (77.79–79.74)	81.74 (80.81–82.65)	82.60 (81.68–83.48)	80.52 (79.56–81.45)	80.79 (79.83–81.71)
LGA	10.93 (10.21–11.70)	10.64 (9.93–11.40)	6.08 (5.54–6.68)	13.29 (12.51–14.12)	13.62 (12.82–14.45)

AGA, appropriated-for-gestational-age; *CI*, confidence interval; *LGA*, large-for-gestational-age; *SGA*, small for gestational age.

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diagnosis of LGA, the INTERGROWTH pattern showed results as expected.

The Fenton standard showed more satisfactory results for SGA diagnosis than INTERGROWTH. Regarding LGA, it was below expectations. The Alexander and Lubchenco standards showed a low SGA detection rate, and that LGA detection was above expectations.

Clinical implications

Despite the advantages of using a birthweight standard, we needed more suitable curves for our population. A false diagnosis of normality was observed using published curves, especially concerning SGA, considering a newborn infant as low risk for adverse events, consequently placing this group at greater risk of morbidity and mortality.

This is particularly challenging in premature newborns, where those with growth restriction exacerbate the common complications of prematurity.

Research implications

Our research showed no standard weight curves suitable for our sample. It is necessary to increase the number of cases in the utilized sampling group to define the birthweight pattern and to establish the most appropriate curve for our population, especially for lower gestational ages from 24 to 32 weeks. Other nearby populations have not published their data, which helps keep the unit at the forefront of research into maternal and child health.

Strengths and limitations

According to the results presented here, it is essential to increase the sample analyzed, especially for the group associated with prematurity as a risk factor. A larger study group would allow for measuring the performance of the curves at all gestational ages. Increasing the sample size by including other maternity hospitals in Rio de Janeiro or increasing the period analyzed at the same hospital would define a complete pattern for the population assisted at healthcare units in Rio de Janeiro.

A limitation of the present study is that all data were retrospectively collected. In addition, some maternal information, such as smoking during pregnancy, was somehow compromised because it was only available for mothers who attended Maternity School Hospital for prenatal assistance.

Conclusions

This cross-sectional, observational, and descriptive study defined reference local birthweight values considering at least 33 weeks of pregnancy with a 95% CI. For premature deliveries (24–33 weeks of pregnancy), the reference values were not defined with a 95% CI.

The comparison of the INTERGROWTH, Fenton, Alexander, and Lubchenco standards to the Maternity School Hospital curve considering SGA, AGA, and LGA showed that the Fenton curve was the most suitable for the diagnosis of SGA. ■

CRediT authorship contribution statement

Fabio G. Da Matta: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Data curation, Conceptualization. **Karina Bilda de Castro Rezende:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Maria Isabel M.P. Cardoso:** Writing –

review & editing, Writing – original draft, Visualization, Methodology, Data curation. **Luiza P. Ladeira:** Writing – review & editing, Writing – original draft, Visualization, Validation. **Rita G. Bornia:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Methodology. **Joffre Amim:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision.

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