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# Bioelectrical Impedance in Premature Newborns and Its Relationship with Diet Therapy in a Neonatal Intensive Care Unit

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# Bioelectrical Impedance in Premature Newborns and Its Relationship with Diet Therapy in a Neonatal Intensive Care Unit

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**Abstract:** (1) Background: To estimate resistance, reactance and phase angle values among moderate preterm infants and their variation according to neonatal and maternal characteristics and nutritional intake. (2) Methods: This was a cohort that evaluated 43 moderate preterm infants using bioelectrical impedance analysis. The study variables included resistance, reactance and PA measurements, in addition to classification of nutritional intake. (3) Results: The mean resistance was 602.0+118.2 Ω, reactance was 57.2 Ω (IIQ = 42.6-65.2) and phase angle was 522° (IIQ = 4.1-6.6). Lower resistance values were found in the presence of risky pregnancy (532.2+111.9 Ω vs 650.9+97.9 Ω, p<0.001) and lower reactance values, in the presence of harmful maternal lifestyle habits at both the first (p=0.01) and second assessments (p=0.01). Eight preterm infants were considered to have insufficient nutritional intake (23.5%); 17, sufficient (50.0%) and 9, partially sufficient (26.5%). There was less reactance among preterm infants with insufficient nutritional intake (p < 0.001). (4) Conclusions: The bioelectrical impedance analysis measurements were within the range of values reported in other studies. There was an association between full diet and adequate nutritional intake with higher resistance values, and a lower reactance value was associated with the presence of risky pregnancy and harmful maternal lifestyle.

**Keywords:** electrical impedance; nutrition therapy; preterm birth; maternal behaviors; Intensive Care Units; Neonatal

## 1. Introduction

Providing adequate nutrition to promote the growth and development of premature newborns (PTNB), is one of the major challenges facing health workers in Neonatal Intensive Care units (NICU) on a daily basis.[1] Food intolerance, which is typical in this gestational age and becomes even more severe in more premature infants, often occurs and prevents full enteral nutrition.[2] Although there is still no consensus on its definition, the presence of more than 50% of gastric residuals of the offered diet, regurgitation, abdominal distension and/or emesis are some of the clinical signs that indicate the inability of the immature gastrointestinal tract to receive enteral nutrition. Its consequences are well known and have a great impact on the survival of these newborns (NBs), e.g., prolonged use of alternative feeding routes, including total parenteral nutrition and its related risks, as well as longer hospital stays and nutritional failure.[3] Although this is a common problem in the assistance of PTNBs, their growth is still monitored (since the 18th century) through anthropometric measurements, [4] and body composition measurements are not part of their routine care, although it is known that they can optimize nutrition and help promote better neonatal growth and development.[1]

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Premature newborns initially present growth restriction, and then they later show catch-up growth with higher fat mass (FM) accumulation, although they present lower fat-free mass gain (FFMG), higher adiposity and lower linear growth in the first two years of life. However, these metabolic and body composition differences are resolved and adequate nutrition in the NICU has been associated with weight gain and FFMG. This component of body composition has been pointed as a better predictor of neurodevelopment than weight, and these two indices are associated with better cognition in childhood.[1]

The problem lies in defining the best method of measuring body composition in NBs, for the sake of greater precision, fewer adverse effects and feasibility. Many of them, such as magnetic resonance and nuclear spectroscopy, dual energy X-ray absorption (DEXA) and isotopic techniques have already been studied and have their limitations, either for cost, impossibility of being performed at the bedside or for exposure to ionizing radiation.[1] The most promising methods are air displacement plethysmography (ADP), bioelectrical impedance (BIA), skinfold caliper measurements and ultrasonography. Only ADP is valid for use in PTNBs, but it has a high cost and cannot be used in severely ill NBs. The performance of ultrasound measurements may be affected by tissue compression and may lead to inconsistent results, while measurement of skinfolds is influenced by hydroelectrolytic status and has low accuracy. BIA is a non-invasive method, without exposure to radiation, that can be performed at the bedside, which has been promising for evaluation of body composition of NBs. However, further studies are needed in this population to better understand the values and behavior of BIA in this age group.[1]

The objective of this study was to make a contribution by presenting resistance (R), reactance (Xc) and phase angle (AF) values among moderate PTNBs in the first days of life, the variation of such values according to some neonatal and maternal characteristics, and their behavior according to nutritional intake in the second week of life.

## 2. Materials and Methods

This was a cohort conducted in a NICU of a tertiary university hospital in southern Brazil, between April 2018 and December 2021. The following inclusion criteria were considered: PTNBs (gestational age < 37 weeks) in need of intensive care and whose mothers agreed to participate in the study by signing an informed consent form. The following exclusion criteria were adopted: A) PTNBs with congenital malformation and genetic syndromes; b) cases of technical problems and errors in BIA measurements; c) PTNBs in a warm cradle at the time of measurement; d) unavailable limb areas for electrode placement, either by the presence of a catheter or by any other impediment; e) PTNBs transferred to another hospital or to their homes; f) absence of complete follow-up or g) absence of complete nutritional information.

Of 129 PTNBs initially eligible for the study, 79 were excluded because of transfer (3), inaccurate or wrong BIA measurements (7), moist-cradle bed (4), unavailable area for placement of BIA electrodes (4), absence of complete follow-up (44) and absence of complete nutritional information (17). There were a total of 50 eligible NBs: 43 moderate PTNBs, 4 extremely premature NBs and 3 late premature NBs, who were excluded from the study owing to the small number of cases. Thus, there were 43 moderate PTNBs left, whose BIA measurement was performed in the first and second weeks of life (Figure 1).

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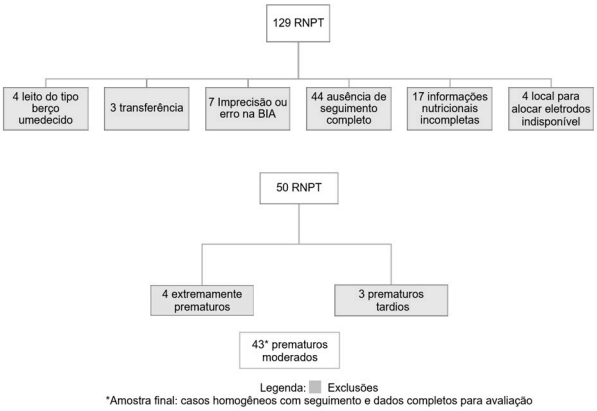


**Figure 1.** Flow chart for sample selection.

The study variables included BIA measurements, particularly, R and Xc [in Ohmns (Ω)], nutritional intake, classified as sufficient (energy ≥ 100kcal/kg/day and protein > 3g/kg/day), partial (energy ≥ 100kcal/kg/day and protein ≤ 3g/kg/day or < 100kcal/kg/day and protein > 3g/kg/day) or insufficient (energy < 100kcal/kg/day and protein ≤ 3g/kg/day).

R, Xc and PA values were determined with a *Bio Scan* Maltron 916 bio-electrical Impedance analyzer (50 kHz).[5] The test was always carried out on the same day of the week, before the newborn was fed the next diet and in two moments: between the 1st and 7th day of life and between the 8th and 15th day of life. The test was performed with PTNBs in the supine position, in the incubator itself and with electrodes positioned on the same side of the body (right or left, chosen according to the area available), with a spacing of at least four centimeters between them, measured with a sterile body tape measure. The electrodes were cut in half lengthwise to fit the placement area on the limb of the PTNBs and were not reused.[6] All procedures were performed after the materials had been sanitized with 70% isopropyl alcohol.

The weight of the newborns was measured on a Filizola® calibrated pediatric scale, with a minimum capacity of 125g and a maximum capacity of 15kg. The NBs were evaluated while being naked, positioned on the scale so that the body weight was distributed over the surface. For measuring length, standardization was followed in the NICU using the Frankfurt plan.[7] information on dietary therapy, neonatal data (sex, gestational age, birth weight, nutritional status, 1-minute a d 5-minute Apgar scores and respiratory distress syndrome) and maternal characteristics (age, schooling, smoking/alcoholism/drug addiction, number and type of deliveries, neonatal appointments, previous diseases, diseases during pregnancy, twin pregnancy and risky pregnancy) were collected from the medical records of the PTNBs. Dietary evolution was recorded for each PTNB from the beginning of the diet until they reached the energy target of 100/kcal/kg/day and of 3g/kg/day proteins.

Minimum sample size was estimated considering the type II error of 10%, significance level of 5% and effect magnitude of 60 points on average, indicating a minimum sample of 40 cases, with test power of 95%.

To estimate the difference between continuous variables with symmetric distribution, the t-test was applied for dependent samples, followed by analysis of variance (one-way ANOVA), while asymmetric distribution was checked by the Wilcoxon test and Kruskal-Wallis ANOVA, followed by Duncan and Mann-Whitney post-hoc tests, respectively. For all tests, a significance level of 5% was considered [*Statistics* 4.0 (*StatSoft Power Solutions*, Inc., Palo Alto, California, USA)]. The study was approved by the Research Ethics Committee of the institution under registration number 4.640.434.

## 3. Results

The study sample consisted of 43 moderate PTNBs, born to adult women with a mean age of 30.5 ± 7.7 years, 20 of whom (58.8%) were considered to have risk pregnancies (Table 1).

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**Table 1.** Maternal characteristics.

| Characteristics | Mean ± SD/n (%) |
|---|---|
| Age (years) | 30.5 ± 7.7 |
| Education - High School | 25 (73.5%) |
| Smoking/Alcoholism/Drug addiction | 7 (20.6%) |
| Primiparous | 4 (11.8%) |
| Abortions | 14 (41.2%) |
| Number of prenatal appointments < 6 | 2 (2.9%) |
| Previous diseases | 18 (52.9%) |
| Diseases during pregnancy | 15 (44.1%) |
| Cesarean section | 18 (52.9%) |
| Twin pregnancy | 14 (41.2%) |
| Risky pregnancy | 20 (58.8%) |

SD = Standard deviation / risky pregnancy = Maternal age > 35 years and/or disease during pregnancy.

The mean gestational age of the PTNBs was 33.3 ± 0.6 weeks and birth weight was 1.997.9 ± 542.0 grams, with proportional distribution of cases in relation to sex (1:1.2) (Table 2).

**Table 2.** Characteristics of premature newborns.

| Characteristics | N (%) /mean ± SD |
|---|---|
| Sex (M/F) | 25/21 (53.5%/46.5%) |
| Gestational age (weeks) | 33.3 ± 0.6 |
| Birth weight (grams) | 1997.9 ± 542.0 |
| Nutritional status | |
| SGA | 4 (11.8%) |
| SUGA | 26 (76.4%) |
| LGA | 4 (11.8%) |
| 1-minute Apgar score | |
| < 3 | 4 (11.8%) |
| 4- 6 | 4 (11.8%) |
| < 6 | 26 (76.4%) |
| 5-minute Apgar score | |
| < 6 | 34 (100.0%) |
| RDS | 24 (70.6%) |

SUGA = suitable for gestational age F = female LGA = large for gestational age M = male SGA = small for gestational age, RDS = respiratory distress syndrome.

In the first assessment, carried out in a median of 2 days (IIQ = 2-2), all NBs had not been fed a full diet and had a lower nutritional intake than desired for growth (< 100Kcal/kg/day and < 3g/kg/day of protein). Table 3 shows the BIA measurements of PTNBs in the first assessment.

**Table 3.** Resistance, reactance and phase angle measurements in the first assessment of bioelectrical impedance.

| Measures | Mean SD/median (IIQ) |
|---|---|

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| | |
|---|---|
| R (Ω) | 602.0 ± 118.2 |
| Xc (Ω) | 57.2 (42.6-65.2) |
| PA (°) | 5.22 (4.1-6.6) |

PA = Phase angle R = resistance XC = reactance.

Regarding maternal characteristics, there was a lower R value in the presence of risky pregnancy (532.2 ± 111.9 Ω *vs* 650.9 ± 97.9 Ω, p < 0.001). In addition, there were lower Xc values in the PTNBs of pregnant women with harmful life habits (smoking, alcoholism, drug addiction) in both the first (42.6 ± 14.2 Ω *vs* 61.3 ± 17.6 Ω, p = 0.01) and in the second assessments (44.0 ± 9.2 Ω *vs* 65.1 ± 20.1 Ω, p = 0.01).

For neonatal characteristics, no significant difference was found between the measurements of BIA according to gender, nutritional status, 1-minute Apgar score or RDS (p > 0.05 for all study variables).

The second assessment was carried out in a median of 8 days (IIQ = 8-9) and eight PTNBs were considered to have insufficient nutritional intake (23.5%), while 17 had sufficient (50.0%) and 9 had partially sufficient (26.5%) intakes, respectively.

There was a significantly lower R among PTNBs with insufficient intake, when compared to those with sufficient or partially sufficient intake (p (Table 4).

**Table 4.** Resistance, reactance and phase angle measurements according to nutritional intake in the second week of life.

| Measures | Insufficient NI (n = 8) | Partial NI (n = 9) | Sufficient NI (n = 17) | p |
|---|---|---|---|---|
| R (Ω) | 540.0 ± 120.2 | 611.2 ± 105.1 | 731.5 ± 101.9 | < 0.001[1] |
| Xc (Ω) | 53.6 (375-83.5) | 54.4 (49.2-86.9) | 54.9 (49.5-74.5) | 0.47[2] |
| AF (°) | 5.3 (3.6-9.3) | 5.4 (4.1-7.2) | 4.3 (3.8-5.9) | 0.53[2] |

PA = phase angle NI = nutritional intake R = resistance XC = reactance. [1]*One-way ANOVA , Duncan post-hoc* test [2]*Kruskal-Wallis ANOVA* .

There was also a significant increase in R between the first and second weeks of assessment only among PTNBs with sufficient nutritional intake (Table 5).

**Table 5.** Resistance, reactance and phase angle measurements in the first and second assessments according to nutritional intake.

| | Measures | 1st assessment | 2nd assessment | p |
|---|---|---|---|---|
| Insufficient NI (n = 8) | R (Ω) | 48.0 ± 114.7 | 540.0 ± 120.2 | 0.15[1] |
| | Xc (Ω) | 56.5 (42.3-69.6) | 55.1 (42.9-87.5) | 0.61[2] |
| | AF (°) | 5.9 (5.0-7.8) | 5.3 (3.9-11.5) | 0.73[2] |
| Partial NI (n = 9) | R (Ω) | 618.4 ± 146.0 | 61.2 ± 105.1 | 0.86[1] |
| | Xc (Ω) | 65.1 (61.7-8.6) | 56.2 (50.0-63.2) | 0.46[2] |
| | AF (°) | 6.6 (4.4-6.9) | 4.5 (4.1-5.0) | 0.68[2] |
| Sufficient NI (n = 17) | R (Ω) | 637.1 ± 69.0 | 731.5 ± 102.0 | **< 0.001**[1] |
| | Xc (Ω) | 49.0 (41.7-59.7) | 54.9 (49.5-70.2) | 0.14[2] |
| | AF (°) | 4.5 (3.7-5.2) | 4.3 (4.0-5.4) | 0.77[2] |

PA = phase angle NI = nutritional intake R = resistance XC = reactance [1]Dependent t-test [2] *Wilcoxon* test.

## 4. Discussion

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In the present study, the mean R in moderate PTNBs in the first days of life was 602.0 ± 118.2 Ω, Xc, with a median of 57.2 Ω (IIQ = 42.6-65.2) and median PA of 522° (IIQ = 4.1-6.6). There was a lower Xc value in the presence of risky pregnancy and harmful life habits and a higher R value among PTNBs with a full diet and sufficient nutritional intake; these values increased between the 1st and 2nd assessments in this group of NBs. Such values are similar to those reported by Coradine et al.[8], who also studied moderate PTNBs, but they were both lower than those found by Margutti et al.[9] with late PTNBs ($p < 0.001$) for R values. There was a significant variation in Xc values (48.7 to 67.9 Ω, $p < 0.001$) and similar PA values (4.7 to 5.2°, $p > 0.05$). In the studies by Piccoli et al.[6], Savino et al.[10], Margutti et al.[12] and Coradine et al.[8], there was a significant variation of the mean of R (466.0 to 684.8 Ω, $p < 0.001$), Xc (22.0 to 50.3 Ω; $p < 0.001$) and PA (2.5 to 5.1°; $p < 0.001$), even though all studies had focused on full term NBs (Chart 1). It is known that measurements of BIA may vary according to a number of factors, including age range, and among NBs, according to gestational age, clinical stability, fluid status, limb movement at the time of examination and imminence of feeding time[1], which may account for the different measures. Thus, there should be further studies on BIA, with a standardized design for this specific population, to establish more accurate reference values in Neonatology. Margutti et al.[11] also found that R values were significantly lower in male NBs, who seem to have a higher amount of FFM, total body water and cell membranes. Nehab et al.[12] suggested that their postnatal growth is higher, with greater muscle mass gain. In the study sample, there was no significant difference in the measurements of BIA between male and female NBs.

In relation to maternal characteristics, there was a lower Xc value in the presence of a risky pregnancy in the present study. Nehab et al.[12] found that gestational factors, susceptible to prevention, influence the amount of mass of neonatal fat, while demographic characteristics (mother's age, gestational age, and NB's sex) affect the amount of FFM at birth. Using ADP, they found that maternal morbidities such as diabetes mellitus and systemic arterial hypertension during pregnancy determined a higher percentage of body fat in full term NBs. FFM was also influenced by the newborn's sex, birth weight, gestational age and maternal age.

It is known that the use of tobacco, drugs and alcohol during pregnancy results in high rates of abortion, limited fetal growth, premature membrane rupture and premature delivery. In addition, there are higher mortality rates and lower birth weight.[13] In the present study, a lower Xc value was found in PTNBs whose mothers smoked and/or used drugs and/or drank alcoholic beverages. Whereas Xc is an indicator of cellular membrane integrity and intra- and extracellular water distribution, this finding may be indicative of cellular death and/or decreased cellular integrity, and Xc can be used as a marker to determine the intensity of the harmful effects of tobacco, alcohol, drugs on the body of NBs whose mothers maintained these habits during pregnancy. Zhou et al.[14] also reported the impact of smoking on the growth and body composition of NBs, possibly attributed to higher energy expenditure, maternal malnutrition, lower maternal weight gain during pregnancy, placental dysfunction and possible direct effects of tobacco on maternal and fetal metabolism.

Studies have shown that early deficits in protein and energy intake during the first two weeks of life affect neonatal growth and long-term neurocognitive development in infants.[15,17] Gerritsen et al.[18] found that only 58% of moderate PTNBs reached the recommended protein intake on the seventh day of life and that the average increase of 1g/kg/day in protein intake in the first week of life resulted in a significant increase in weight, Baillat et al.[19] also found that early energy and protein intake positively influences neonatal growth and that 60% of children did not reach such nutritional intake at the end of the first week of life. They indicated that for every increase of 10Kcal/kg/d at the end of the first week of life there was a 27% lower chance of delayed extrauterine growth in PTNBs (or = 0.73; 95% CI = 0.66-0.82). In the present sample, similarly, there was an increase in R only among PTNBs who were fed a full diet and had the recommended nutritional intake of proteins in the second week of life.

In a randomized study carried out in Spain with 38 non-breastfed PTNBs, who were divided into three groups and received different amounts of protein through infant formulas for PTNBs, it was found that the groups that had received the highest amount of protein (4.2 g/kg/day or 4.7 g/kg/day) presented higher FFM gain than the control group with non-supplemented formula.[19]

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Mól et al.[20] assessed the difference in body composition between PTNBs fed breastmilk or infant formula in comparison to those born at term. They found that those fed formula presented higher R, which may represent a greater amount of adipose tissue and lower FFM. However, PTNBs fed breastmilk did not present differences in body composition in comparison with the control group of term infants.

PTNBs have a high metabolic rate and biochemical immaturity, which affects metabolic functions and leads to high nutritional risk.[21] The assessment of nutritional status in the first days of life allows a better understanding of intrauterine development and enables better dietary therapy intervention [22], with a view to promoting neurodevelopment and reducing metabolic risks in the long term. The anthropometric assessment is used to measure weight loss in the first days of life and check if the subsequent weight gain and length are within the values considered as normal according to the literature. However, this form of assessment does not distinguish adipose, muscle and physiological tissues.[1,23]

BIA has been applied in research with PTNBs; however, there are many are in the use of it in this age group. BIA measures the opposition (or impedance) of the body tissues to the flow of an alternating, low-intensity electric current, which passes through the body through the use of electrodes that are in contact with the skin. Thus, it is a portable and easy-to-use device.[5] BIA measurements help determine the values of R, Xc and PA, and the values of R are inversely proportional to the quantity of intra- and extracellular fluids. Muscle tissues present lower R; owing to the large amount of water and electrolytes, electric current conduction is good. On the other hand, the adipose tissue is not a good conductor of electric current because of the low amount of water and electrolytes; thus, R is higher. By means of these indicators, it can be inferred that higher values of R indicate a greater amount of adipose tissue and a lower amount of muscle tissue.[24] Because PA indicates the presence of a healthy or disease-affected membrane, it can be used as a prognostic marker in different clinical situations, whose low values may be associated with poor nutritional status.[25,26]

In the first two weeks of life of PTNBs, especially between the 4th and 9th days of life, there is physiological loss of neonatal weight of up to 15% of body weight. After that period, there is a growth peak with a speed that attempts to reproduce intrauterine rates. Dietary therapy and assessment of body composition at these critical moments of oscillating weight deserve special attention in the quest for growth and nutritional quality.[27]

Body weight in NICUs is the most commonly used measure for the nutritional assessment of PTNBs, although it does not evaluate body composition. With increased survival of these NBs, there has been greater interest in nutritional assessment, as feeding in the first weeks of life has a direct impact on their development.[28,29]

A limitation of the present study was that it did not estimate the nutritional intake of macronutrients. It is known that there is variation of breastmilk donors and interindividual variation and changes in the composition of breastmilk according to lactation stage, in addition to the difference of macronutrients in milk and supplementation with nutritional formulas. Therefore, it is impossible to assess the profile of each macronutrient.

It is worth pointing out that there was no attempt to insert the data found in prediction equations for FFN and FM, because the use of BIA in NBs needs to be standardized and the existing equations have methodological limitations and still lack validation in Brazilian NBs.[5]

## 5. Conclusions

This section is not mandatory but can be added to the manuscript if the discussion is unusually long or complex. The BIA measurements made in this sample are within the range of values reported in other studies with PTNBs and full-term NBs, with significant variation, which possibly reflects the lack of standardization in the design of studies using this method of assessing body composition in NBs. There was an association between full diet and adequate nutritional intake with higher R values, as well as a lower Xc value associated with the presence of a risky pregnancy and harmful life habits, such as smoking.

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**Conflicts of Interest:** The authors declare no conflicts of interest.

## Appendix A

**Chart A1** - Resistance, reactance and phase angle values in the literature

| **Authors** | **Piccoli et al. (2002)** | **Savino et al. (2003)** | **Margutti et al. (2010)** | **Margutti et al. (2012)** | **Coradine et al. (2021)** | **Coradine et al. (2021)** | **Tortorella et al. (2023)** |
|---|---|---|---|---|---|---|---|
| Town/City (Country) | Turin (Italy) | Turin (Italy) | Ribeirão Preto (Brazil) | Ribeirão Preto (Brazil) | Curitiba (Brazil) | Curitiba (Brazil) | Curitiba (Brazil) |
| n | 163 | 58 | 109 | 68 | 76 | 17 | 43 |
| GA | Term | Term | Term | 35.0 ± 1.6 | 32.8 ± 2.6 | 37.9 ± 1.1 | 33.0 ± 0.6 |
| R | 505 ± 60 | 466 ± 64 | 684.8 ± 53.5 | 794.7 ± 124.3 | 569.0 ± 113.1 | 524.8 ± 96.2 | 602.0 ± 118.2 |
| Xc | 43 ± 14 | 22 ± 12 | 37.5 ± 5.3 | 67.9 ± 31.9 | 48.7 (26.6-103.2) | 50.3 (18.5-93.4) | 57.2 (42.6 – 65.2) |
| PA | 4.86 ± 1 | 2.5 ± 1.5 | 3.14 ± 0.43 | 4.92 ± 2.18 | 4.7 (2.5-12.1) | 5.1 (2.7-10.7) | 5.2 (4.1 – 6.6) |

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