Nurses’ knowledge about Berardinelli-Seip Congenital Lipodystrophy

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Abstract

Berardinelli-Seip Congenital Lipodystrophy (BSCL) is a rare autosomal recessive disease characterized by the almost complete absence of adipose tissue. Due to a strong founder effect that resulted in a higher prevalence of BSCL in Rio Grande do Norte (RN), a state in northeastern Brazil, it has been essential that health professionals develop knowledge about this disease. Nurses are often the first point of contact with patients during health care assistance. The purpose of this study was to investigate the knowledge of these professionals about BSCL in two main hospitals in the RN state. A questionnaire was applied to 199 nurses working in the Hospital Regional Mariano Coelho—HRMC (Regional Hospital Mariano Coelho), in Currais Novos–RN, and in the Hospital Universitário Onofre Lopes—HUOL (University Hospital Onofre Lopes), in Natal–RN. This study showed that most nursing professionals do not know about the disease, although they have already received patients with BSCL in those hospitals. The nurses from HRMC and HUOL lacked knowledge of BSCL and the healthcare of these patients requires immediate improvement. Significant efforts are required to close the gap between current and needed practice patterns.

Introduction

Berardinelli-Seip Congenital Lipodystrophies (BSCLs) are autosomal recessive disorders characterized by a generalized loss of adipose tissue from birth, hypertriglyceridemia, hyperinsulinism, glucose intolerance, hepatic steatosis, diabetes mellitus, prominent musculature, hypertrophic cardiomyopathy, bone cysts, umbilical protrusion, acanthosis nigricans, and other clinical features [1–6].

The prevalence rate of BSCL in different countries has been estimated in the literature. In the US and Norway, the prevalence of this disease is 1 in 10 million and 1 in 1 million people, respectively [3,7]. However, in Lebanon, Portugal, and Oman, the prevalence rates are 1 in 200,000, 1 in 500,000, and 1 in 25,000 people, respectively [7]. Despite the absence of a regular
registration system for BSCL at the national level, our research found that RN presents a high BSCL prevalence (3 in 100,000), mainly in Seridó territory due to consanguineous marriages [8]. Clinical and laboratory data for BSCL patients from RN were reported by Lima et al [9].

As an extremely rare lipodystrophy, BSCL is almost unknown by the health professionals. However, the great prevalence in RN, compared with the rest of the world, raises the necessity of specialized knowledge by those professionals. Besides, financial and human resources are still necessary to manage patients with lipodystrophies in RN. Thus, the ASPOSBERN (Associação de Pais e Pessoas com a Síndrome de Berardinelli do Estado do Rio Grande do Norte —Association of Parents and People with Berardinelli Syndrome of Rio Grande do Norte) Association was founded as a non-profit organization aiming to improve the quality of life of BSCL patients and their families, by performing an important role in the management of BSCL patients diagnosed by qualified physicians [8,9].

Brazilian nursing teams are essentially comprised of three occupational groups, according to the nurse training levels: nurses with higher education (referred to here as 'nurses'), ‘nursing technician’ with secondary education, and ‘nursing aid’ with basic education. In Brazil, nurse technicians and nurses represent most of the nursing workforce. These workers are mainly responsible for activities that involve direct contact with patients. However, these two different nursing categories comprise different responsibilities and roles: Nurses are in charge of teaching, supervision, and management, while technical and auxiliary staff carry out most care activities [10].

Nursing care for patients with BSCL is essential from birth and requires specialized knowledge to ensure the safety of the patients and their families. The care and surveillance of BSCL patients by nurses should include blood pressure monitoring; periodic screening for glycosuria and proteinuria; glucose, glycated hemoglobin, triglyceride, insulin, leptin, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels; bone age, signs of precocious puberty, and genetic counseling may also be taken into account [11–13].

Since nurses are the largest care workforce for BSCL patients in hospitals, a valid and reliable instrument to evaluate their knowledge, skills, and attitudes is essential to help the Brazilian Health System promote strategies and genetic counseling for families, and improving the management of individual abnormalities of this type of lipodystrophy is a priority. For this purpose, this study aimed to evaluate the knowledge, skills, and practice related to BSCL of nurses at two hospitals located in Rio Grande do Norte state, Northeast Brazil.

Materials and methods
Study design and data collection
In this cross-sectional study, 199 nurses were randomly selected from two community hospitals from Rio Grande do Norte state, Northeast Brazil. The Hospital Regional Mariano Coelho —HRMC (Regional Hospital Mariano Coelho) and the Hospital Universitário Onofre Lopes—HUOL (University Hospital Onofre Lopes) are located in the cities of Currais Novos and in Natal, respectively (Fig 1).

The study data were collected from January to August 2015. All participants were requested to complete a questionnaire aiming to evaluate their knowledge, attitude, and skills related to BSCL. All nurses were verbally informed about the study by the principal investigator, and signed a written consent before participation.

An appropriate instrument which could measure the knowledge of BSCL by nurse professionals was developed specifically for this study and was divided into two parts: The first included general information on the participants (gender, age, occupation, educational level, job titles, specialty, clinical experience time); and the second concerned the participants’
knowledge about BSCL (S1 and S2 Data Sets). Then, this questionnaire was pre-tested and an expert consultation verified the validity of the content.

Statistical analysis
The variables of this study were age, sex, level of education, and clinical experience time. The data were analyzed using Statistical Package for Social Sciences software (SPSS Inc., Chicago, USA), version 20.0. The number of participants was expressed in absolute number and percentage. Data were presented as number (%) for categorical variables. Continuous and normally distributed variables were expressed as mean ±SD. The Fisher’s exact test was performed to verify the differences between both hospitals and between nurses and technicians. The level of significance was set at 0.05.

Ethical statement
The consent procedure and research were approved by the Ethics and Research Committee of Faculdade de Ciências da Saúde do Trairi—FACISA (Faculty of Health Sciences of Trairi) of Universidade Federal do Rio Grande do Norte—UFRN (Federal University of Rio Grande do Norte) with study number 36182614.1.0000.5568. The data did not contain any personal identifiers. The confidentiality of all information was preserved.

Results
General information of participants
199 questionnaires were included in this research: 75 completed by nurses and 124 by nursing technicians from both hospitals. Of the 199 participants, there were 111 (56%) females, aged from 20 to 59 years old, with a mean of 37.8 ± 9.8 years. When we analyzed the data of the two hospitals separately, 155 and 44 participants were from HUOL and HRMC (nurses and technicians), respectively. For HUOL, there were 64 nurses (38.6±9.9 years old, 60 females) and 91 technicians (33.7±7.8 years old, 13 females). For HRMC, there were 11 nurses (36.5 ± 8.2 years
old, 9 females) and 33 technicians (47.4±7.9 years old, 29 females) (Table 1). The mean age of nurses at HUOL and HRMC was not different (p = 0.5). However, technicians from HRMC were older than those from HUOL (p < 0.0001). On the other hand, when we verified the mean age of participants from HUOL, we observed that the nurses were older than technicians (p = 0.0010), while for HRMC the data showed that technicians were older than nurses (p < 0.0004). In fact, for HUOL, the age group ≥ 50 years was 8% and 3% for nurses and technicians, respectively, whereas for HRMC we found that 18% and 48% of nurses and technicians, respectively, were in the age group of ≥ 50 years (Table 1). Taken together, these data reflect the similarity in the age pattern between nurses of HUOL and HRMC but not between technicians, and a contrasting age pattern between nurses and technicians who work in the same hospital.

Concerning the education level, of the 199 nurses who participated in this study, 28% had specialization and only 7% had a master or higher degree, resulting in 35% professionals with a postgraduate degree (Table 1). When we analyzed the clinical experience time, 41% of the nurses from HUOL and 64% of the nurses from HRMC had between 0 to 10 years of clinical experience. However, when we analyzed this status for technicians at the respective hospitals, the results showed that 43% and 6% were professionals with 0 to 10 years of clinical experience. Additionally, we found that 36% of the nurses from HUOL and 9% of the nurses from HRMC had between 11 to 20 years of clinical experience. For technicians at the respective hospitals, 10% and 16% had between 11 to 20 years of clinical experience. 36% of the technicians at HRMC and 9% of those at HUOL had between 21 to 30 years of clinical experience. For more than 30 years of experience, HUOL presented 6% of nurses, but no technicians. At HRMC, no nurses and only 3% of technicians presented more than 30 years of experience. Together, these data suggest that nurses from HUOL had higher clinical experience time than those from

Table 1. Personal status between nurses and technicians from HUOL (N = 155) and HRMC (N = 44).

| N (%)                          | Nurses HUOL (N = 64) | Nurses HRMC (N = 11) | Nurses Total (N = 75) | Technicians HUOL (N = 91) | Technicians HRMC (N = 33) | Technicians Total (N = 124) | Total number (N = 199) |
|--------------------------------|----------------------|----------------------|-----------------------|---------------------------|---------------------------|-----------------------------|----------------------|
| Gender                         |                      |                      |                       |                           |                           |                             |                      |
| Male                           | 4 (6.0)              | 2 (18)               | 6 (8.0)               | 78 (87)                   | 4 (12)                    | 82 (66)                     | 88 (44)              |
| Female                         | 60 (94)              | 9 (81)               | 69 (92)               | 13 (13)                   | 29 (88)                   | 42 (34)                     | 111 (56)             |
| Age Group (Mean ± SD)          | 38.6±9.9             | 36.5±8.2             | 38.35±9.7             | 37.7±7.5                  | 47.4±7.9                  | 37.57±10.0                  | 37.86±9.8               |
| ≤35 Years                      | 26 (40)              | 6 (55)               | 32 (43)               | 57 (63)                   | 3 (9)                     | 60 (49)                     | 92 (47)              |
| 36–49 Years                    | 28 (44)              | 3 (27)               | 31 (41)               | 27 (30)                   | 14 (42)                   | 41 (33)                     | 72 (36)              |
| ≥50 Years                      | 5 (8.0)              | 2 (18)               | 7 (9.0)               | 3 (3.0)                   | 16 (48)                   | 19 (15)                     | 26 (13)              |
| Unknown                        | 5 (8.0)              | 0 (0.0)              | 5 (7.0)               | 4 (4.0)                   | 0 (0.0)                   | 4 (3.0)                     | 9 (4.0)              |
| Education Level                |                      |                      |                       |                           |                           |                             |                      |
| Technical secondary school graduates or below | 0 (0.0)              | 0 (0.0)              | 0 (0.0)               | 91 (100)                  | 33 (100)                  | 124 (100)                   | 124 (62)             |
| Specialization                 | 48 (75)              | 08 (72)              | 56 (75)               | 0 (0.0)                   | 0 (0.0)                   | 0 (0.0)                     | 56 (28)              |
| Master or higher degree        | 15 (23)              | 0 (0.0)              | 15 (20)               | 0 (0.0)                   | 0 (0.0)                   | 0 (0.0)                     | 15 (7.0)             |
| Unknown                        | 01 (2.0)             | 03 (28)              | 04 (5.0)              | 0 (0.0)                   | 0 (0.0)                   | 0 (0.0)                     | 4 (3.0)              |
| Clinical experience time (years)|                      |                      |                       |                           |                           |                             |                      |
| 0–10                           | 26 (41)              | 7 (64)               | 33 (44)               | 39 (43)                   | 2 (6.0)                   | 41 (33)                     | 74 (37)              |
| 11–20                          | 23 (36)              | 1 (9.0)              | 24 (32)               | 9 (10)                    | 5 (16)                    | 14 (11)                     | 38 (20)              |
| 21–30                          | 6 (9.0)              | 1 (9.0)              | 7 (9.0)               | 0 (0.0)                   | 12 (36)                   | 12 (10)                     | 19 (10)              |
| >30                            | 4 (6.0)              | 0 (0.0)              | 4 (6.0)               | 0 (0.0)                   | 1 (3.0)                   | 1 (1.0)                     | 5 (2.0)              |
| Unknown                        | 5 (8.0)              | 2 (18)               | 7 (9.0)               | 43 (47)                   | 13 (39)                   | 56 (45.0)                   | 63 (31)              |

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HRMC, while technicians from HRMC had more clinical experience time than those from HUOL.

BSCL knowledge

When nurses and technicians answered questions about BSCL morpho-physiological features, the data showed opposite results between HUOL and HRMC (Tables 2 and 3). While 64% of the nurses and 79% of the technicians from HRMC had knowledge about the morpho-physiological aspects of BSCL (p = 0.4247), only 36% of the nurses and 10% of the technicians from HUOL affirmed to recognize these features (p = 0.0001). When we verified their knowledge about the genetic causes of BSCL, 36% of the nurses and 21% of the technicians from HRMC were knowledgeable of such causes of BSCL (p = 0.4247). For HUOL, 11% of the nurses and 4.0% of the technicians had any information about BSCL genetic causes (p = 0.2019). Afterward, they were asked about their ability to recognize a BSCL patient. While 64% of the nurses and 70% of the technicians from HRMC informed that they could recognize a patient with BSCL (p = 0.7222), 19% of the nurses and 4% of the technicians from HUOL affirmed that they had the ability to recognize these patients (p = 0.0060). Subsequently, when they were asked if they had assisted the treatment of a BSCL patient in their hospital, 45% of the nurses and 42% of the technicians from HRMC answered positively (p = 0.1000), while only 19% of the nurses and 2% of the technicians from HUOL had assisted the treatment of a BSCL patient (p = 0.0009).

When we asked about their skills to better inform a family of a recently born BSCL patient regarding the morpho-physiological features and genetic causes, 18% of the nurses and 6% of the technicians from HRMC answered positively (p = 0.2565). On the other hand, only 7.8% of the nurses and 1% of the technicians from HUOL confirmed the same (p = 0.0822). With regard to providing health care to BSCL patients, 27% of the nurses and 24% of the technicians from HRMC affirmed that they had the necessary knowledge and skills to offer BSCL patients the proper health care (p = 1.000). On the other hand, only 7.8% of the nurses and 1% of the

Table 2. The knowledge of nurses and technicians from HRMC about Berardinelli-Seip Congenital Lipodystrophy (BSCL).

| Question                                                                 | Nurses HRMC (N = 11) | Technicians HRMC (N = 33) | Total HRMC (N = 44) | P     | OR    | 95% CI   |
|------------------------------------------------------------------------|----------------------|---------------------------|---------------------|-------|-------|----------|
| Q1. Have knowledge about the morpho-physiological aspects of BSCL.     | 7 (64)               | 26 (79)                   | 33 (75)             | 0.4247| 0.4712| (0.1155, 1.793) |
| Q2. Have knowledge about the genetic causes of BSCL.                   | 4 (36)               | 7 (21)                    | 11 (25)             | 0.4247| 2.122 | (0.5576, 8.654) |
| Q3. Can recognize a BSCL patient.                                      | 7 (64)               | 23 (70)                   | 30 (68)             | 0.7222| 0.7609| (0.2061, 2.755) |
| Q4. Had any BSCL patient in your hospital.                             | 5 (45)               | 14 (42)                   | 19 (43)             | 0.1000| 1.131 | (0.2931, 3.898) |
| Q5. Can explain to the parents of a new baby with BSCL the morpho-physiological and genetic causes of this disease. | 2 (18)               | 2 (06)                    | 4 (9)               | 0.2565| 3.444 | (0.4713, 23.55) |
| Q6. Can properly source the health care for a BSCL patient.            | 3 (27)               | 8 (24)                    | 11 (25)             | 1.0000| 1.172 | (0.2818, 4.799) |
| Q7. Have heard about ASPOSBERN.                                        | 6 (55)               | 19 (58)                   | 25 (57)             | 1.0000| 0.8842| (0.2565, 3.411) |

OR: Odds Ratio.
95% CI: 95% Confidence Interval.
All statistical tests were performed using p-value < 0.05 as the level of significance.

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technicians from HUOL affirmed that they had the ability to provide BSCL patients the proper health care (p = 0.0822). Finally, when they were asked about their knowledge regarding the ASPOSBERN association, 55% of the nurses and 58% of the technicians from HRMC affirmed their having knowledge about the activities performed by this association (p = 1.000), while only 5% of the nurses and 4.4% of the technicians from HUOL had the same knowledge (p = 1.000). All of these data are summarized in Tables 2 and 3. When the data were analyzed together for each hospital, we observed that HRMC nurses and technicians had more knowledge for almost all questions compared to their counterparts at HUOL (Table 4).

After responding to all of the questions, all of the participants were invited to discuss BSCL morphology, physiology, genetic causes, treatment, and the importance of multi-professional assistance for these patients. However, 33% (n = 50) and 50% (n = 22) of nursing professionals from HUOL and HRMC, respectively, participated in those discussions.

**Discussion**

In the current study, the knowledge of nurses and technicians in two hospitals from Rio Grande do Norte state (RN), Brazil, regarding BSCL was determined. Although we have previously estimated a high BSCL prevalence rate of 3.23 per 100,000 people in RN [8], we found that the nurses and technicians from HUOL, located in the capital city of RN, lacked knowledge concerning the BSCL morpho-physiological and genetic causes. It should be noted that HUOL is the main hospital in RN that promotes the health care of BSCL patients and serves as the major reference for qualified physicians on the treatment of BSCL [9]. On the other hand, nurses and technicians from HRMC, in Currais Novos, located in Seridó territory in RN, presented more knowledge concerning BSCL than those from HUOL: 75% had knowledge about

### Table 3. The knowledge of nurses and technicians from HUOL about Berardinelli-Seip Congenital Lipodystrophy (BSCL).

| Question                                                                 | Nurses HUOL (N = 64) | Technicians HUOL (N = 91) | Total HUOL (N = 155) | P       | OR   | 95% CI     |
|-------------------------------------------------------------------------|----------------------|---------------------------|----------------------|---------|------|------------|
| Q1. Have knowledge about the morpho-physiological aspects of BSCL       | 23 (36)              | 9 (10)                    | 32 (21.0)            | 123 (79.0) | 0.0001 | 5.111     | (2.146, 11.94) |
| Q2. Have knowledge about the genetic causes of BSCL                     | 7 (11)               | 4 (4.0)                   | 11 (7.0)             | 144 (93) | 0.2019 | 2.671     | (0.7925, 8.404)  |
| Q3. Can recognize a BSCL patient.                                       | 12 (19)              | 4 (4.0)                   | 16 (11.3)            | 139 (89.7) | 0.0060 | 5.019     | (1.675, 14.68)   |
| Q4. Had any BSCL patient in your hospital.                              | 12 (19)              | 2 (2.0)                   | 14 (10)              | 141 (90) | 0.0009 | 10.27     | (2.389, 46.91)   |
| Q5. Can explain to the parents of a new baby with BSCL the morpho-physiological and genetic causes of this disease. | 5 (7.8)              | 1 (1.0)                   | 6 (4.0)              | 149 (96.0) | 0.0822 | 7.62      | (0.992, 90.71)   |
| Q6. Can properly source the health care for a BSCL patient.              | 5 (7.8)              | 1 (1.0)                   | 6 (4.0)              | 149 (96.0) | 0.0822 | 7.62      | (0.992, 90.71)   |
| Q7. Have heard about ASPOSBERN.                                          | 3 (5.0)              | 4 (4.4)                   | 7 (4.5)              | 148 (95.5) | 1.000  | 1.07      | (0.262, 4.1)     |

OR: Odds Ratio.
95% CI: 95% Confidence Interval.

All statistical tests were performed using p-value < 0.05 as the level of significance.

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the morpho-physiological aspects; they could recognize a patient with BSCL; almost 45% had participated in a patient treatment; and 57% knew about the ASPOSBERN Association (Table 4). This is the first study to screen the knowledge of nurses from Rio Grande do Norte state (RN), Brazil, regarding BSCL.

Although the responsibilities of nurses and nursing technicians are determined according to their education level, we found a greater lack of BSCL knowledge between these two categories only at HUOL, the main hospital in RN that promotes the regular surveillance and therapeutic management of BSCL patients. Since HRMC and ASPOSBERN are both located in Currais Novos city, we believe that the ASPOSBERN activities could explain the higher knowledge of both nurses and technicians from that location. Another explanation is that HRMC technicians were older than those at HUOL (47.7 ± 7.9 vs 33.7 ± 7.8) and 48% of them were 50 years. Although technicians presented only a secondary education, these age data could also explain why this HRMC category presented higher knowledge concerning BSCL, since they lived in the Seridó territory, which has presented many BSCL cases since the end of the 20th century. We believe that the higher level of knowledge found in Currais Novos municipality was due to both the elevated age of HRMC technicians and ASPOSBERN actions in that RN territory. Taken together, these findings highlight the urgent requirement to develop efforts directed at offering education and training to ensure that health care providers have suitable knowledge and skills to properly treat BSCL patients mainly at HUOL.

This lipodystrophy was initially described in 1954 by a Brazilian doctor, Waldemar Berardinelli [1], and in 1959 by a Norwegian doctor, Martin Seip [14]. RN patients with this type of lipodystrophy present a phenotype very well characterized: acromegaloid facial appearance, atrophic cheeks, prognathism, prominent musculature, umbilical protrusion, acanthosis nigricans, phlebomegaly, and others [6,9,15–18]. These morphological characteristics can be easily identified and in the last years an increase in the number of diagnosed patients has been observed [6,8,9,15].

Depending on the case, the diagnosis of BSCL can be established by associating clinical characteristics with biochemical and/or genetic exams. The characteristics that determine the

| Table 4. The knowledge of nurse professionals from HUOL and HRMC about Berardinelli-Seip Congenital Lipodystrophy (BSCL). |
|---|
| **Yes—N (%)** | **HUOL (N = 155)** | **HRMC (N = 44)** | **Total (N = 199)** | **P** | **OR** | **95% CI** |
| Q1. Have knowledge about the morpho-physiological aspects of BSCL. | 32 (20.6) | 33 (75.0) | 65 (32.7) | 134 (67.3) | < 0.0001 | 0.08672 (0.04166, 0.1927) |
| Q2. Have knowledge about the genetic causes of BSCL. | 11 (7.1) | 11 (25.0) | 22 (11.1) | 177 (88.9) | 0.0021 | 0.2292 (0.09209, 0.5731) |
| Q3. Can recognize a BSCL patient. | 16 (10.3) | 30 (66.2) | 46 (23.1) | 153 (76.9) | < 0.0001 | 0.05372 (0.02529, 0.1206) |
| Q4. Had any BSCL patient in your hospital. | 14 (9.0) | 19 (43.2) | 33 (15.6) | 166 (83.4) | < 0.0001 | 0.1306 (0.05775, 0.302) |
| Q5. Can explain to the parents of a new baby with BSCL the morpho-physiological and genetic causes of this disease. | 06 (3.9) | 04 (9.0) | 10 (5.0) | 189 (95.0) | 0.2325 | 0.4027 (0.1073, 1.321) |
| Q6. Can properly source the health care for a BSCL patient. | 06 (3.9) | 11 (25.0) | 17 (8.5) | 182 (97.5) | < 0.0001 | 0.1208 (0.04152, 0.3698) |
| Q7. Have heard about ASPOSBERN. | 07 (4.5) | 25 (57) | 32 (16) | 167 (84) | < 0.0001 | 0.3595 (0.01485, 0.09315) |
| OR: Odds Ratio. |
| 95% CI: 95% Confidence Interval. |
| All statistical tests were performed using p-value < 0.05 as the level of significance. |

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The majority of the criteria are acromegaloïd facial appearance, hepatomegaly, high concentration of triglycerides (> 150 mg/dL), and insulin resistance. The characteristics of the minor criteria are hypertrophic cardiomyopathy, mild psychomotor retardation or moderate cognitive deficit, hirsutism, and puberty in pre-school girls. However, due to its rarity, most clinical physicians and health care providers are not familiar with its diagnosis and management [12]. Figs 2 and 3 show the physical appearance of type 1 and type 2 BSCL patients from RN. Also provided is a schematic overview (Fig 4) highlighting the main morphological features found in BSCL from RN to emphasize that nurses must be aware of those features to help the recognition of those patients, which can have great implications for health care based on body images.

Fig 2. Physical appearance of type 1 BSCL patient from RN. (A) Anterior view of a 24-year-old Brazilian female with type 1 BSCL due to A712T mutation in the AGPAT2 gene. (B) Anterior view of face showing acromegaloïd facies, atrophic cheeks, and prognathism. (C) Anterior view of right arm and abdomen showing phlebomegaly and umbilical protusion, respectively, as previously described by Lima and co-workers [6,9].

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According to data from the literature [9,12,15], the BSCL surveillance needs to be achieved periodically during the year to monitor hepatic complications and the clinical parameters of occurrence/progression of diabetes mellitus. Furthermore, since BSCL is a metabolic disease that affects several systems, a multidisciplinary team composed of physicians, nurses, nutritionists and dietitians, physical therapists, geneticists, and others is required to ensure the suitable surveillance.

Nutritional advice can also be employed by nurses to help families. These professionals can inform the requirement to consult a dietitian to acquire a specialized diet, with a focus on balanced macronutrient composition comprising 50–60% carbohydrate, 20–30% fat, and 10–20% protein, as well as including the adequacy of micronutrient intakes. To reduce
hypertriglyceridemia, the nurses can suggest the intake of medium chain triglyceride-based formulas in infants and older individuals. Cis-mono-unsaturated fats and long chain omega-3 fatty acids should be the main form of fat intake. This is critical conduct that needs to be offered after birth since diet is a basis to prevent or ameliorate the metabolic comorbidities of BSCL [19–24]. According to the World Health Organization (WHO) and Instituto Brasileiro de Geografia e Estatística—IBGE (Brazilian Institute of Geography and Statistics) [25,26], more than 50% of Brazilian adults are overweight and 20% are obese. Additionally, it is important to note that RN is one of the Brazilian states with a higher number of overweight and obese individuals [27]. Since Seridó territory in RN is known for its typical fatty food, such as coalho’s cheese, animal by-products, sugar cookies, and others, BSCL individuals need to avoid this type of food and the nurses can promote actions to ensure the nutrition and hydration requests of BSCL patients to improve their quality of life.

The importance of knowledge about the genetic causes of BSCL is crucial to predict the future course of the disease since specific symptoms can be associated with the type of mutation in certain genes. Mutations in genes AGPAT2, BSCL2, CAV1, and CAVIN1 give rise to 4 subtypes of BSCL: type 1, 2, 3, and 4, respectively [5]. In RN state from Brazil, only type 1 and

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**Fig 4. A schematic overview of the main morphological features of type 1 and type 2 BSCL patients.** Acanthosis nigricans, acromegaloïd facies, atrophic cheeks, prognathism and phlebomegaly, and metabolic comorbidities are shown, as previously described by Lima and co-workers [9].

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Type 2 of BSCL were described [8]. Type 1 BSCL occurs due to mutations in the gene AGPAT2 that encode 1-acylglycerol-3-phosphate O-acyltransferase 2 (1-AGPAT2), while type 2 BSCL is caused by mutations in the gene BSCL2 that encode seipin [28,29].

Concerning genetic consequences, mutations in the AGPAT2 gene are associated with the occurrence of bone cysts [12,30], while mutations in the BSCL2 gene are associated with cognitive deficits and a higher incidence of premature death [8,31]. According to Brown et al., genetic diagnosis is crucial for prenatal diagnosis and genetic counseling [12]. Thus, the genetic knowledge of BSCL should help the healthcare providers to offer better surveillance and to direct the correct choice of specific therapeutic tools. Here, we found that the nurses from HUOL and HRMC lacked knowledge about the genetic causes of BSCL and this finding was more significant for HUOL.

Nursing professionals can also offer some advice on the importance of the practical physical exercises to ameliorate the metabolic complications of BSCL patients. Since the lack of physical exercise is a central mechanism in the development of diabetes mellitus [32–34], they should be encouraged to exercise, taking into account the comorbidities previously described, such as cardiomyopathies, bone cysts, hepatosplenomegaly, and others [9,15–18,35]. For patients presenting bone cysts and hepatosplenomegaly, contact sports are not appropriate. Protective shoes can be suggested in the case of patients with fractures in bone cysts. On the other hand, patients who have cardiomyopathy need to be evaluated before starting an exercise regimen [12]. In this context, the morphological, metabolic, and genetic knowledge of this generalized lipodystrophy can help to offer better exercise advice for each patient.

Even though the nursing professionals do not have the competence to supply the clinical diagnosis of any disease, it is extremely important that these professionals present the proper knowledge and skills to help the BSCL families concerning the health care required to the management of the individual abnormalities of this lipodystrophy.

This study has some limitations. Firstly, the survey was conducted in both urban and rural hospitals, but we need to improve the number of participants from HUOL, since after 2015 the number of nurse professionals increased in this hospital. Secondly, not all knowledge of BSCL management was assessed in the test questionnaire. Despite these limitations, a reasonably high response rate of 55% and 89% at HUOL and HRMC, respectively, was attained; therefore, the results represent nurses’ current knowledge of BSCL and healthcare for BSCL patients.

Conclusions

Taken together, our data emphasize that nurses from HRMC and HUOL clearly lacked knowledge regarding Berardinelli-Seip Congenital Lipodystrophy. However, this finding was more pronounced for HUOL than for HRMC. Our data demonstrate that the healthcare of BSCL patients urgently needs to be improved and significant efforts are required to close the gap between current and desirable nursing practice patterns.

Supporting information

S1 Data Set. Questionnaire in Portuguese.
(DOCX)

S2 Data Set. Questionnaire in English.
(DOCX)

S3 Data Set. Individual participant data.
(XLSX)
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References
1. Berardinelli W. An undiagnosed endocrinometabolic syndrome: report of 2 cases. J Clin Endocrinol Metab. 1954; 14: 193–204. https://doi.org/10.1210/jcem-14-2-193 PMID: 13130666
2. Seip M, Trygstad O. Generalized lipodystrophy, congenital and acquired (lipoatrophy). Acta Paediatr Suppl. 1996; 413: 2–28. https://doi.org/10.1111/j.1651-2227.1996.tb14262.x PMID: 8783769
3. Garg A. Lipodystrophies. Am J Med. 2000; 108: 143–152. https://doi.org/10.1016/S0002-9343(99)00414-3 PMID: 11126308
4. Garg A, Agarwal AK. Lipodystrophies: Disorders of adipose tissue biology. Biochim Biophys Acta. 2009; 1791: 507–513. https://doi.org/10.1016/j.bbalip.2008.12.014 PMID: 19162222
5. Haghighi A, Kavehmanesh Z, Haghighi A, Salehzadeh F, Santos-Simarro F, Van Maldergem L, et al. Congenital generalized lipodystrophy: Identification of novel variants and expansion of clinical spectrum. Clin Genet. 2015; 89: 434–441. https://doi.org/10.1111/cge.12623 PMID: 26072928
6. Lima JG, Lima NN, Oliveira CF, Dantas REFC, Baracho MFP, Nobrega LHC, et al. Umbilical Hernia in Patients with Berardinelli-seip Syndrome: Is it Really Hernia. J Clin Mol Endocrinol. 2015; 1. https://doi.org/10.21767/2572-5432.10001
7. Van Maldergem L. Berardinelli-Seip Congenital Lipodystrophy. GeneReviews®. 2016; 1–2. Available: https://www.ncbi.nlm.nih.gov/books/NBK1212/
8. Medeiros LBA, Dantas VKC, Sarmento ASC, Agnez-Lima LF, Meireles AL, Nobre TTX, et al. High prevalence of Berardinelli-Seip Congenital Lipodystrophy in Rio Grande do Norte State, Northeast Brazil. Diabetol Metab Syndr. 2017; 9: https://doi.org/10.1186/s13098-017-0280-7 PMID: 29046728
9. Lima JG, Nobrega LHC, Lima NN, Santos MGN, Baracho MFP, Jeronimo SMB. Clinical and laboratory data of a large series of patients with congenital generalized lipodystrophy. Diabetol Metab Syndr. 2018; 8. https://doi.org/10.1186/s13098-016-0140-x PMID: 26989241
10. Gottems LBD, Alves ED, Sena RR. Brazilian nursing and professionalization at technical level: a retrospective analysis. Rev Lat Am Enfermagem. 2007; 15: 1033–1040. https://doi.org/10.1590/S0104-11692007000500023 PMID: 18157459
11. Jéru I, Vatier C, Araújo-Vilar D, Vigouroux C, Lascols O. Clinical utility gene card for: Congenital generalized lipodystrophy. Eur J Hum Genet. 2016; 24: 5–8. https://doi.org/10.1038/ejhg.2016.53 PMID: 27189019
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12. Brown RJ, Chair C, Araujo-Vilar D, Cheung PT, Dunger D, Garg A, et al. The diagnosis and management of lipodystrophy syndromes: A multi-society practice guideline. J Clin Endocrinol Metab. 2016; 101: 4500–4511. https://doi.org/10.1210/jc.2016-2466 PMID: 27710244

13. Gupta N, Asri N, Farah W, Almasri J, Barrionuevo PM, Alsawas M, et al. Clinical features and management of non-HIV related lipodystrophy in children: a systematic review. J Clin Endocrinol Metab. 2016; 102: 363–374. https://doi.org/10.1210/jc.2016-2271 PMID: 27967300

14. Seip M. Lipodystrophy and gigantism with associated endocrine manifestation: a new dienecephalic syndrome. Acta Paediatr. 1959; 48: 555–574. PMID: 14444642

15. Lima JG, Nobrega LHC, Lima NN, Santos MCF, Baracho MFP, Winzenrieth R, et al. Normal bone density and trabecular bone score, but high serum sclerostin in congenital generalized lipodystrophy. Bone. 2017; 101: 21–25. https://doi.org/10.1016/j.bone.2017.03.053 PMID: 28390904

16. Ponte CMM, Fernandes VO, Gurgel MHC, Vasconcelos ITGF, Karbage LB de AS, Liberato CBR, et al. Early commitment of cardiovascular autonomic modulation in Brazilian patients with congenital generalized lipodystrophy. BMC Cardiovasc Disord. 2018; 18: 6. https://doi.org/10.1186/s12872-017-0738-4 PMID: 29329523

17. Guedes Do Rêgo A, Mesquita ET, De Faria CA, Álvares M, Do Rêgo G, De Fátima M, et al. Cardiometabolic abnormalities in patients with berardinelli-seip syndrome. Arq Bras Cardiol. 2010; 94: 102–110.

18. Lima JG, Nobrega LHC, Lima NN, dos Santos MCF, Baracho M de FP, Bandeira F, et al. Bone Density in Patients With Berardinelli-Seip Congenital Lipodystrophy Is Higher in Trabecular Sites and in Type 2 Patients. J Clin Densitom. Elsevier; 2018; 21: 61–67. https://doi.org/10.1016/j.jcd.2016.10.002 PMID: 27894728

19. Thomas L V, Jenkins G, Belton J, Clements S, Jacob C, Johnson N, et al. Nutritional advice for community patients: insights from a panel discussion. Br J Community Nurs. MA Healthcare London; 2016; 21: 130–137. https://doi.org/10.12968/bjcn.2016.21.3.130 PMID: 26940615

20. Mackay L. The nurse’s role in giving nutritional advice. Prof Nurse. 1995; 10: 427–8. PMID: 7724629

21. Tappenden KA, Quatara B, Parkhurst ML, Malone AM, Fanjiang G, Ziegler TR. Critical Role of Nutrition in Improving Quality of Care: An Interdisciplinary Call to Action to Address Adult Hospital Malnutrition. J Acad Nutr Diet. Elsevier; 2013; 113: 1219–1237. https://doi.org/10.1016/j.jand.2013.05.015 PMID: 23871528

22. Bloomfield J, Pegram A. Improving nutrition and hydration in hospital: the nurse’s responsibility. Nurs Stand. 2012; 26: 52–56. https://doi.org/10.7748/ns2012.04.26.34.52.c9065 PMID: 22787874

23. Moore SA. Educating the family and the patient about nutrition. Prim Care. 1994; 21: 69–83. PMID: 8197258

24. Hussain I, Garg A. Lipodystrophy Syndromes. Dermatol Clin. 2008; 26. https://doi.org/10.1016/j.det.2008.05.004 PMID: 18793991

25. Helping people with diabetes manage their health and lives in Brazil [Internet]. [cited 24 Apr 2018]. Available: http://www.who.int/en/news-room/feature-stories/detail/helping-people-with-diabetes-manage-their-health-and-lives-in-brazil

26. Instituto Brasileiro de Geografia e Estatística—IBGE. Pesquisa nacional de saúde: 2013: ciclos de vida: Brasil e grandes regiões [Internet]. [cited 24 Apr 2018]. Available: http://www.abeso.org.br/uploads/downloads/102/59496cc2f9561d.pdf

27. Instituto Brasileiro de Geografia e Estatística—IBGE. Estimativas sobre frequência e distribuição socio-demográfica de fatores de risco e proteção para doenças crônicas nas capitais dos 26 estados brasileiros e no distrito federal em 2016 [Internet]. [cited 24 Apr 2018]. Available: www.saude.gov.br/svs

28. Garg A, Wilson R, Barnes R, Arioglu E, Zaidi Z, Gurakan F, et al. A Gene for Congenital Generalized Lipodystrophy Maps to Human Chromosome 9q34. J Clin Endocrinol Metab. 1999; 84: 3390–3394. https://doi.org/10.1210/jcem.84.9.6103 PMID: 10487716

29. Magré J, Delépine M, Khallouf E, Gedde-Dah T, Van Maldergem L, Sobel E, et al. Identification of the gene altered in Berardinelli-Seip congenital lipodystrophy on chromosome 11q13. Nat Genet. 2001; 28: 365–370. https://doi.org/10.1038/ng585 PMID: 11479539

30. Fu M, Kazlauskaite R, Baracho MDFP, Santos MGDN, Brandão-Neto J, Vilares S, et al. Mutations in Gng3lg and AGPAT2 in Berardinelli-Seip congenital lipodystrophy and Brunzell syndrome: Phenotype variability suggests important modifier effects. J Clin Endocrinol Metab. 2004; 89: 2916–2922. https://doi.org/10.1210/jcem.84.9.6103 PMID: 10487716

31. Van Maldergem L, Magré J, Khallouf TE, Gedde-Dah T, Delépine M, Trygstad O, et al. Genotype-phenotype relationships in Berardinelli-Seip congenital lipodystrophy. J Med Genet. 2002; 39: 722–33. https://doi.org/10.1136/jmg.39.10.722 PMID: 12362029

32. Asano RY, Sales MM, Browne RAV, Moraes JFVN, Coelho Júnior HJ, Moraes MR, et al. Acute effects of physical exercise in type 2 diabetes: A review. World J Diabetes. Baishideng Publishing Group Inc; 2014; 5: 659–65. https://doi.org/10.4239/wjd.v5.i5.659 PMID: 25317243
33. Stanford K, Goodyear LJ. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ. American Physiological Society; 2014; 38: 308–14. https://doi.org/10.1152/advan.00080.2014 PMID: 25434013

34. Caouza E, Hanusch-Enserer U, Strasser B, Ludvik B, Metz-Schimmerl S, Pacini G, et al. The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. Arch Phys Med Rehabil. 2005; 86: 1527–1533. https://doi.org/10.1016/j.apmr.2005.01.007 PMID: 16084803

35. Hasani-Ranjbar S, Soltani A, Hadavi M, Ejtahed H-S, Mohammad-Amoli M, Radmard AR. Congenital Generalized Lipodystrophy in a Youth Presented with Sclerotic and Lytic Bone Lesions; a Family with AGPAT2 Mutation. Int J Pediatr. 2017; 5. https://doi.org/10.22038/ijp.2016.7849

36. SMART—Servier Medical ART—3000 free medical images [Internet]. [cited 24 Apr 2018]. Available: https://smart.servier.com/