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Perception about pediatric hypertension

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ABSTRACT

Pediatric hypertension is prevalent and it may appear silently in childhood where the diagnosis is based on regular blood pressure measurements, which vary with age, sex, and height. It can progress to adulthood and be associated with potentially severe organ damage, so it is important to be aware of its existence and apply an early intervention. To evaluate the population's knowledge of the disease, we provided a questionnaire to the caregivers of pediatric patients at the Hospital de Santa Maria and the results were statistically analyzed in order to infer possible associations between sociodemographic variables (age, sex, race, residence, graduation level, and occupation) and theoretical knowledge of the disease. There were significant statistical associations between age, graduation level, and occupation with the knowledge of the possible silent emergence of the disease in childhood, the existence of risk factors, and the age from which the blood pressure should be checked. In this preliminary study, we used an experimental questionnaire. We employed generalized linear models to obtain statistical models. In future research, we will use more elaborate techniques, such as multivariate analysis (factorial analysis, correspondence analysis), as well as other suitable methods for analyzing the data obtained.

1. Introduction

High arterial blood pressure (BP) is a condition that is traditionally considered a disease of adults, but it may emerge in pediatric subjects and silently in most cases. The diagnostic criteria for pediatric hypertension (HT) mainly reference the normal BP distribution in healthy children [1] and they are based on the concept that the pediatric BP increases with age and with body mass [2]. Thus, considering that there is a strong correlation between body mass index and BP [2], HT has become highly prevalent among children and teens [3] due to parallel growth in the epidemic of childhood obesity [4], which suggests that obesity is a major risk factor for the development of pediatric HT [3,5]. Despite the wide variety of estimated HT incidence rates, a recent study determined high–normal BP prevalence values in 16% of cases and HT in 3.2% [6], which are consistent with other reports that 25% of all pediatric patients have BP levels that meet the criteria for the diagnosis of pediatric HT [7]. However, in the same study by Hansen et al. in [7], they also showed that despite the high estimated prevalence, this disease remains under-diagnosed.

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The present study was designed to assess whether caregivers (parents or their legal representatives) in the Portuguese population are aware of the existence of this pathology and the importance of assessing BP in this age group, as well as determining whether the results are influenced positively or negatively by characteristic sociodemographic parameters. In addition, we aimed to determine whether the regular measurement indication for BP is usually fulfilled according to current recommendations.

The questionnaire data were analyzed in three steps. Initially, we used descriptive statistics to summarize all of the information. In the next stage, we verified the suitability of the questionnaire. Finally, we employed generalized linear models (GLM) to obtain statistical models which relate the questionnaire answers and the sociodemographic information.

The remainder of this paper is organized as follows. In the next section, we discuss the questionnaire in detail and introduce GLM as a statistical method. Section 3 deals with the data. Questionnaires were given to 128 random individuals and 107 were completed correctly. The estimated models and the estimates of interesting likelihoods for some individual characteristics are presented. In the final two sections, we discuss the results and give some conclusions.

2. Preliminaries

2.1. Questionnaire

A questionnaire is an instrument that can be very informative when designed correctly. Thus, an experimental questionnaire was provided to the caregivers of children aged between three and 18 years to identify whether the caregivers of children and young people had any knowledge of high BP in children.

The questionnaire was designed as a "minimal" scheme to be completed within a short period of time. The information requested by questionnaire is described as follows.

- Sociodemographic characteristics such as age, sex, race, residence area, level of education, and profession.
- Five dichotomic questions to easily answer Yes/No in a short period of time:
  1. Can HT arise in pediatric subjects?
  2. Is HT a silent disease in the majority of cases?
  3. Should BP measurements be collected during routine health surveillance visits (routine visits) from three years of age?
  4. Are risk factors such as obesity, lack of physical activity, or overeating associated with HT?
  5. Please respond if you have children. Is your child's BP usually measured during health surveillance visits?

2.2. GLM approach

In 1972, [8] first described the use of GLM as a powerful method in statistics by standardizing the theoretical and applied aspects of the structure of linear regression up to that time. Due to the large number of available models as well as the simple and rapid computational analysis using this method, GLM play important roles in statistical analysis. The aim of GLM is to establish a functional relationship between the variable for prediction (dependent variable) and a set of other exogenous variables (explanatory variables or covariates). This relationship can then be used to predict the dependent variable. The dependent variables and the explanatory variables can be of any type, i.e., continuous, discrete, dichotomous, quantitative, qualitative, stochastic, and non-stochastic. The response variable can also be a proportion, positive, and have a non-normal random component. In 1935, Bliss proposed the probit model for proportions, while in 1944, Berkson developed logistic regression. Log-linear models for contingency tables were introduced by Birch in 1963. In 1972, Nelder and Wedderburn proved that all of these models are particular cases of a general family: the GLM. In GLM, the random component belongs to an exponential family and a transformation of the expected value of the response variable is related to the explanatory variables. The simplest models where the explanatory variables are nonrandom and the disturbances are Gaussian white noise can be estimated by ordinary least squares, but they can be extended to more general models where the disturbances are autocorrelated, heteroscedastic, not Gaussian, etc., or when some of the explanatory variables are stochastic. Thus, linear regression models can be estimated by generalized least squares.

In the classical linear model, a vector X with p covariates $X = (X_1, X_2, \ldots, X_p)$ can explain the variability of the variable of interest Y (response variable), where $Y = Z\beta + \epsilon_i$. Z is a specification matrix with size $n \times p$ (usually $Z = X$, considering an unitary vector in first column), β is a parameter vector, and ϵ is a vector of random errors ϵ_i, which are independent and identically distributed as a reduced Gaussian.

The data are in the form (y_i, x_i), $i = 1, \ldots, n$ because the observations (Y, X) are made n times. The response variable Y has an expected value of $E[Y|Z] = \mu$.

In GLM, the model is an extension of the classical model, but the response variable does not need to be Gaussian and it follows an exponential family distribution[1] [9].

[1] A random variable Y belongs to an exponentially distributed family if its probability density function (or probability mass function) can be represented as

$$f(y|\theta, \phi) = e^{\frac{y\theta - b(\theta)}{a(\theta)}} + c(y, \phi), \tag{1}$$

Another extension from the classical model is that the function relating the expected value with the covariates can be any differentiable function. Y_i has an expected value of $E[Y_i|x_i] = \mu_i = b'(\theta_i),\ i = 1, \ldots, n$.

A differentiable and monotone link function is also defined as g, which relates the random component with the systematic component of the response variable. The expected value μ_i is related to the linear predictor $\eta_i = z_i^T \beta_i$ according to the relationship

$$\mu_i = h(\eta_i) = h(z_i^T \beta_i), \quad \eta_i = g(\mu_i), \tag{2}$$

where

- h is a differentiable function;
- $g = h^{-1}$ is the function link;
- β is a vector of parameters with size p (the same size as the number of explanatory variables); and
- z_i is a specification vector with size p.

Different link functions can be used in GLM. When the random component of the response variable has a Poisson distribution, the link function is logarithmic and the model is log-linear. In particular, when the linear predictor $\eta_i = z_i^T \beta_i$ coincides with the canonical parameter θ_i, $\theta_i = \eta_i$, which implies that $\theta_i = z_i^T \beta_i$, then the link function is denominated as a canonical link function.

In the presence of dichotomous data, discrete models are usually estimated by logistic or probit regression [9].

Logistic regression is applied widely in models with dichotomous data and/or proportions. It is assumed that the response variable Y verifies $Y_i \cap Bin(1, \pi_i)$, i.e.,

$$f(y_i|x_i) = (\pi_i)^{y_i} (1 - \pi_i)^{1-y_i} \tag{3}$$

and that each individual i has an associated specification vector z_i, which results from p covariates $x = (x_1, x_2, \ldots, x_p)$. Given that

$$E[Y_i] = \pi_i, \qquad \theta_i = \ln\left(\frac{\pi_i}{1 - \pi_i}\right) \quad \text{and} \quad \theta_i = \eta_i = z_i^T \beta_i, \tag{4}$$

we can conclude that the logistic function is the link function g. The probability of success π_i is given by

$$\pi_i = \frac{e^{z_i^T \beta_i}}{1 + e^{z_i^T \beta_i}}. \tag{5}$$

It should be noted that $E[Y_i] = \pi_i = \mu_i \in [0, 1]$, so another distribution function can be a candidate for the inverse of the link function. We may assume that the probability of success π_i and the covariate vector are related by

$$\pi_i = \Phi(\eta_i) = \Phi(z_i^T \beta_i), \tag{6}$$

where $\phi(.)$ is the Gaussian distribution $N(0, 1)$. In this case, we obtain the link function $g(\mu_i) = \Phi^{-1}(\mu_i)$, which is the probit function, and the estimated model is known as the probit model.

The GLM methodology can be summarized in three steps as follows.

1. Model formulation: identify the response variable distribution, select the preliminary covariates and specification matrix, and select the link function, g.
2. Model adjustment: estimate the model parameters and apply suitable measures of the estimates.
3. Selection and validation of models: select the variables, diagnostics, residual analysis, and interpretation.

3. Empirical application

3.1. Data

Between May and December 2014, we performed an observational and prospective study, where all of the participants came from the outpatient Pediatric Department of Santa Maria Hospital, and we obtained approval for this study from the department's director. We provided questionnaires to a random sample of 128 individuals, all of whom were caregivers for children and/or adolescents (first-degree relatives or their legal representatives), users of the National Health System, and they attended external consultations (general pediatrics and/or sub-specialties) for reasons not related to changes in the BP. Only 107 questionnaires were completed correctly.

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where θ and ϕ are parameters, and $a(.)$, $b(.)$, and $c(.)$ are known functions that verify some regularity conditions. The parameters θ and ϕ are the canonical forms of localization and dispersion parameters, respectively. If ϕ is known, then f belongs to an uni-parametric exponential family, whereas if ϕ is unknown, f belongs to a bi-parametric exponential family.

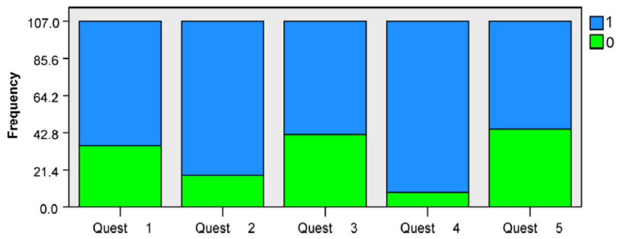

Fig. 1. Response to the questionnaire: questions 1–5. “1” = Yes; “0” = No.

Table 1
Confidence interval (CI) and paired t-test for the mean differences in the questions.

Pair	CI (95%)	p-value
Q1–Q2	(0.056, 0.261)	0.003
Q1–Q3	(−0.17, 0.058)	0.333
Q1–Q4	(0.157, 0.348)	0.000
Q2–Q3	(−0.33, −0.10)	0.000
Q2–Q4	(0.017, 0.170)	0.018
Q3–Q4	(0.202, 0.415)	0.000

3.2. Model estimation

The first step was to organize the data using descriptive statistical techniques. In the preliminary data analysis and considering the non-quantitative nature of the variables, we calculated measures of association, determined the nonparametric Spearman’s correlation coefficient, and performed the nonparametric Friedman test for paired samples [10].

Fig. 1 summarizes the questionnaire answers as percentages for the 107 participants. About 66.6% of participants claimed that they knew that pediatric HT may emerge in children, 82% stated that HT is frequently a silent disease, 61.3% reported that BP measurements should be acquired from three years of age in health surveillance visits, and 91.9% were aware that some risk factors may be associated with HT. Question 5 was used to verify whether regular measurements of the pediatric BP were obtained according to the current recommendations. However, this regular measurement was not made for 40.5% of the subjects. Initially, the statistical analysis of the questionnaire considered questions 1, 2, 3, and 4.

We determined the homogeneity and internal consistency of the questionnaire and its validation. The Cronbach’s alpha coefficient was lower than expected, thereby indicating sufficient, bad, or not good internal consistency. We also performed a paired t-test (Table 1). The t-test suggested the exclusion of question 3. In addition, the nonparametric Spearman’s coefficient of association was significant for the pair of question 1–question 3. Cochran’s Q tests rejected the distributions of question 1, question 2, question 3, and question 4 as the same. In the preliminary stage, we measured the associations between the answers to the questionnaire and the sociodemographic characteristics of the participants. Spearman’s coefficient was significant for the relationships between question 1 and question 3, question 2 and age, and question 2 and profession. The Kruskal–Wallis test was significant between question 4 and age (η-*coefficient* $= 0.561$), and between question 4 and level of education (η-*coefficient* $= 0.224$).

The internal consistency analysis was another key step, where r-tests were performed for paired samples and we calculated the Cronbach’s alpha coefficient. These measures were considered to be indicative due to the qualitative nature of the non-ordinal variables.

The next step in the process involved estimating, validating, and selecting the models for GLM. Different link functions g were used to estimate several models, including log–log, logistic, and probit regressions. Stepwise selection was used to obtain the best explanatory variables in each case.

After obtaining the dichotomous data, discrete models were estimated by logistic and probit regression. Most of the estimated and selected models had validation tests with p-*values* between 0.05 and 0.10. Only question 2 had an adequate model with an associated validation test p-*value* of less than 0.05, which suggested that the questionnaire might need to be restructured.

During the estimation process, we did not consider the residential area and race because there were few individuals in some categories. The descriptions of the variables considered and their codification are shown in Table 2. Next, we describe the estimation of the logistic model in several steps. Initially, the selection of the set of covariates that obtained the “best” model was conducted in a stepwise manner based on the p-values produced by Wilks’ likelihood ratio tests according to the inclusion/exclusion of covariates. The impact of a covariate was measured by the p-*value* obtained, where a small p-*value* indicated a significant influence. The principal effects were selected first, followed by the second order interactions.

Next, we describe the models that associated question 1 with sociodemographic characteristics of the participants because our main aim was to evaluate knowledge of the possibility of pediatric HT occurring, as well as establishing correlations with known individual characteristics.

Table 2
Description of variables and codification.

Variable	Description	Codification
Y_1	Question 1	1 = Yes 0 = No
Y_2	Question 2	1 = Yes 0 = No
Y_3	Question 3	1 = Yes 0 = No
Y_4	Question 4	1 = Yes 0 = No
x_1	Education level	1 = primary 2 = High school 3 = University
x_2	Profession	11 = Other 10 = Without qualification or specialization ⋮ ⋮ 1 = High qualification
x_3	Age	'1' = ([18, 29]) '2' = ([30, 49]) '3' = (≥50)
x_4	Sex	0 = Female 1 = Male

Table 3
Logistic models and parameter estimates for $\hat{\beta}_i$ (7) and $\hat{\alpha}_i$ (8).

Effect	Parameter Model (7)	Estimate Model (7)	Parameter Model (8)	Estimate Model (8)
Intercept	$\hat{\beta}_0$	0.634	$\hat{\alpha}_0$	−9.915
Education level (x_1)	$\hat{\beta}_1$	−0.093	$\hat{\alpha}_1$	3.507
Profession (x_2)	$\hat{\beta}_2$	−0.051	$\hat{\alpha}_2$	0.612
Age (x_3)	$\hat{\beta}_3$	−0.151	$\hat{\alpha}_3$	4.888
Sex (x_4)	$\hat{\beta}_4$	−0.769	$\hat{\alpha}_4$	−0.363
Education level.Age ($x_1.x_3$)			$\hat{\alpha}_5$	−1.764
Profession.Age ($x_2.x_3$)			$\hat{\alpha}_6$	−0.297
Profession.Sex ($x_2.x_4$)			$\hat{\alpha}_7$	−0.091

For question 1 (the main aim of the study), the model obtained considered the principal effects (sex, age, level of education, and profession) in structural form (7),

$$\ln\left[\frac{\pi_i}{1-\pi_i}\right] = \beta_0 + \sum_{j=1}^{4} \beta_j x_{ij}. \tag{7}$$

Considering the principal and secondary effects, the estimated model is summarized by the structural equation (8),

$$\ln\left[\frac{\pi_i}{1-\pi_i}\right] = \alpha_0 + \sum_{j=1}^{4} \alpha_j x_{ij} + \alpha_5 x_{i1} x_{i3} + \alpha_6 x_{i2} x_{i3} + \alpha_7 x_{i2} x_{i4}. \tag{8}$$

The estimated parameters for models (7) and (8) are shown in Table 3. Model (7) had a deviance global test where *p-value* = 0.0995, and model (8) obtained *p-value* = 0.0979. Another evaluation of model A was performed based on residuals analysis by computing the deviance residuals for the 107 individuals. The plot of the deviance residuals is shown in Fig. 2, with the deviance residuals for model (7) on the left and the deviance residuals for model (8) on the right.

After completing all of the validation and selection techniques, we had to choose correctly between different models with similar explanatory performance. The best models with similar estimation performance were combined using a weighted

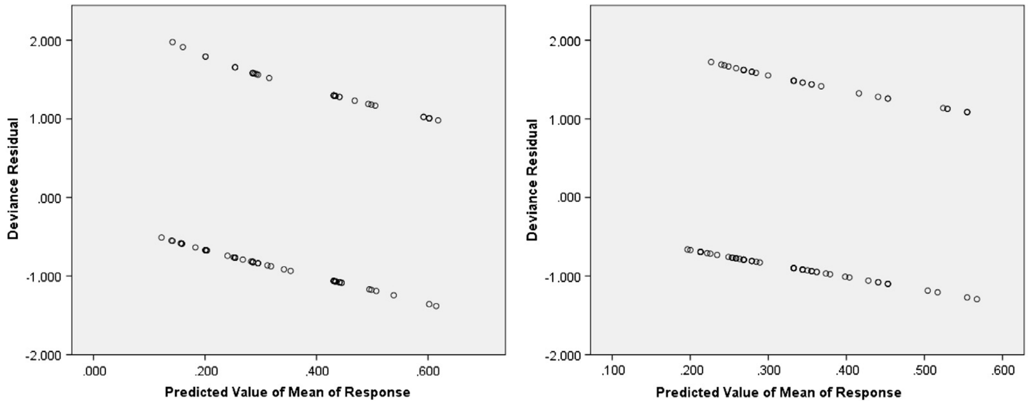

Fig. 2. Deviance residuals versus fitted values. Models (7) and (8) are shown on the left and right, respectively.

mean of the *p-values* from the global test. We aimed to evaluate awareness of the possible occurrence of pediatric HT and to establish associations with the sociodemographic characteristics of the participants. Using models (7) and (8), we estimated the odds ratio for some values of the covariates. For example, we estimated the odds ratio (Yes/No) for men in question 1 relative to women, Ψ_{sex}, assuming that they had a similar profession and level of education. Based on model (7), we obtained $\Psi_{sexA} = e^{-0.769} = 0.4635$ and using model (8), we had $\Psi_{sexB} = e^{-0.363-0.091x_2} = 0.4413$, when we considered a median profession. According to the odds ratio from model (8), we obtained $\Psi_{sexB} \leq 0.6959$ for any profession and it decreased for individuals with lower professional qualifications. We can conclude that the possible awareness of the occurrence of HT in children was lower among men than women with similar age, education, and profession.

We obtained similar results for the other variables, e.g., by varying the profession from the maximum to median qualification or from the median to minimum qualification (from 0 to 5 or 5 to 10), the odds ratio $\Psi_{prof\,B}$ obtained from model (8) was given by $\Psi_{prof\,B} = e^{0.664\times5-0.152\times5x_2-0.298\times5x_3}$. $\Psi_{prof\,B}$ was less than that for older women (age $=$ 3) and greater than that for women with ages at level 1 or 2 (age $=$ 1, 2). For younger men, $\Psi_{prof\,B}$ was greater than one, but the opposite was found for the other age levels (age $=$ 2,3). $\Psi_{prof\,A}$ was always less than one in the same conditions. The level of qualification was important for older individuals because when we decreased the five qualification levels, the odds ratio clearly decreased from values greater than one to values less than one.

We also studied the education level and odds ratio (Yes/No) Ψ_{educ} under several conditions. Using model (8), we obtained $\Psi_{educ\,B} = e^{3.507-1.786x_3}$ when we increased the level of education by one. Only the youngest individuals (men or women) obtained an odds ratio greater than one. Thus, when we increased the level of education by one degree, the youngest individuals were more likely to know about the occurrence of pediatric HT.

4. Discussion

Arterial HT is a global public health problem and a major cause of morbidity and mortality from cardiovascular disease and end stage renal disease at any age. HT was once thought to be rare in children and adolescents, but its estimated current prevalence is between 1% and 5% in the USA [11,12] and 3% to 5% in Europe [2]. The frequency of HT in children can be expected to increase with the occurrence of metabolic syndrome as childhood obesity rates rise [11,12]. HT is a silent disease in most cases, but it evolves with the appearance of lesions in target organs (heart, kidney, eye, and central nervous system). About 50% of hypertensive children may become hypertensive adults. The diagnosis requires regular measurement of the BP values, so it is important that parents are aware of the existence of the condition and the need to consult a doctor for regular assessments of the BP. Most participants in this study (67%) were aware that HT may emerge in children and most (82%) knew that this disease can have a silent evolution in the pediatric population. This awareness may help to increase the likelihood of early diagnosis.

The European Society of Hypertension recommends measuring the arterial pressure during all health surveillance consultations from three years of age [2]. We found that 61% of respondents were aware of this recommendation and 60% of respondents said that the BP was evaluated regularly in their children. A higher percentage would be desirable. Thus, it will necessary to develop awareness campaigns to increase knowledge of these recommendations. Early diagnosis facilitates early and appropriate therapeutic interventions, which are important for changing the natural history of the disease, thereby slowing or preventing its progression.

Recognition of risk factors for the onset of HT was reported by 92% of participants. Age, male sex, black race, family history of HT, premature birth, low birth weight, or delayed intrauterine growth are some of the non-modifiable risk factors [13]. The modifiable risk factors include obesity/overweight, physical inactivity, stress, unhealthy diet (excessive consumption of salt, fat, and consuming small amounts of liquid), sleep deprivation, drug use, alcohol, tobacco, and certain drugs. Controlling these modifiable risk factors and promoting breastfeeding may be important areas for improving prevention [2]. It is necessary to make people aware of the importance of prevention.

Our analyses of the associations with variables showed that participants who were older, with a higher education level, and specific professions had greater awareness of the disease. The internal consistency of the survey showed that the method can be improved to increase the amount of information obtained regarding the awareness of existing recommendations, the risks, and the importance of assessing arterial BP.

4.1. Summary and ongoing research

After constructing a simple questionnaire to obtain quick and easy answers, we found that it was not necessary to reject the questionnaire in terms of its internal consistency, but there was some evidence that it needed improvement, e.g., reformulating some questions. The models estimated by GLM explained the data reasonably well. The use of additional statistical methods [14], e.g., correspondence analysis or other multivariate methods, could help to explain the contributions to the variability in the data.

We found that most caregivers were aware of pediatric HT and the fact that is silent in most cases. An early diagnosis is necessary to improve the survival and quality of life in hypertensive patients by facilitating early and appropriate therapeutic interventions. Prevention is possible by controlling known modifiable risk factors. Prevention requires a higher degree of awareness and possibly the implementation of awareness campaigns to promote regular assessments of arterial pressure in children.

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