CENTILE ESTIMATION OF BLOOD PRESSURE BY AGE AND SEX FOR ADULTS AGED 35- 64 IN NAMIBIA

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Abstract

Recently, the need to monitor blood pressure in the adult population has been emphasized in efforts to mitigate the expansion and pattern of hypertension in different communities. The development of blood pressure nomograms aids the early detection of hypertension, and it nuances the investigation of population subgroups at the risk of succumbing to high blood pressure implications. This study estimated centiles by age and sex to establish reference data for blood pressure in Namibia. Data analysis was based on a sample size of 3095 adults aged 35-64 years, obtained from the 2013 Namibian Demographic Health survey. The analysis was based on the Generalised Additive Model for Location, Scale and Shape (GAMLSS) approach, where six families of distributions were compared to select the most ideal model to measure the Systolic Blood Pressure (SBP) and the Diastolic Blood Pressure (DBP). The results confirmed that both SBP and DBP levels elevated steadily with increasing age, with 25% of the population estimated as hypertensive, but varied by sex. Findings show that 10 % of males aged 35–41years and females aged 35- 46 years were hypertensive. Additionally, 25% of males aged between 42 – 64 years and 25% of females aged between 47 – 64 years were hypertensive. The study revealed that Namibian population were at higher risk of hypertension; therefore the Ministry of Health and Social Service need to take corrective measures to minimize the increasing rate of hypertension.

Keywords: Centile Estimation, Hypertension, Generalised Additive Model for Location, Scale and Shape (GAMLSS), Blood pressure, nomograms

1. Introduction

The 'centile estimation' tool gained its popularity in the medical science field as a way of estimating age specific values to evaluate the growth of children, especially in obstetrics and pediatrics (Cole, 2021; Indrayan, 2014; Zhan et al., 2021). This statistical tool has been applied in epidemiological studies to develop blood pressure nomograms and much attention was given to children and adolescent rather than to adults. Lately, the need to monitor blood pressure in the adult population has been emphasized in efforts to mitigate the expansion and pattern of hypertension in different communities. Hypertension, referred to as SBP of \geq 140 mm Hg or DBP of \geq 90 mm Hg by Zhou et al. (2017) is a serious medical condition that triggers the risk of vital organ diseases, targeting the heart, kidneys, and brain, among other organs (World Health Organization, 2020). Furthermore, hypertension has been found to exacerbate the impact of the Corona virus pandemic (COVID 19) on general immunity (Rodilla et al., 2020; Tadic, Saeed, Grassi, Taddei, & Mancia, 2021; Xu et al., 2020). The development of centiles aids the early detection of hypertension, and it nuances the investigation of population subgroups at the risk of succumbing to high blood pressure implications. Therefore, more comprehensive studies of this nature are needed across countries to establish national blood pressure centiles, and to aid monitoring blood pressure. Due to the blood pressure distribution which may differ from country to country, studies need to be conducted especially across demographic components, such as ethnicity and race (Hosseini et al., 2015). Spatially targeting affected population segments and clusters will help governments to better target interventions and assistance to the right segments in need. The prevalence of hypertension is known to be high among adults aged 35 – 64 years in Namibia (Craig, Gage, & Thomas, 2018), therefore monitoring adults' blood pressure needs to be maintained.

This study developed age and sex-specific centiles to establish reference data for blood pressure in Namibia. Mean and standard deviations, quantile regression (Koenker & Bilias, 2001), Lambda-Mu-Sigma (LMS) (Cole & Green, 1992) were used in developing the centiles. Some of these measures have however been noted to be unreliable and limited in producing quality results. For instance, the mean and standard deviation approach is restricted to model data that comes from a normal distribution (Cole, 2012). Quantile regression does not assume the distribution of response variables, yet it has limitations, such as the different quantile curves for different values of *p* which may cross each other resulting in negative probability (Rigby & Stasinopoulos, 2014). In addition, the model lacks explicit formula to allow the calculations of quantiles (Buuren, 2007). Burren (2007) does not recommend centiles curves that are constructed by quantile model given their irregularity near extreme and are generally not aesthetically pleasing. The LMS on the other hand is suitable in modeling mu, sigma and positively or negatively skewness, however, is limited in modeling the kurtosis of the distribution. The distribution of blood pressure level may be altered by modifiable factors such as alcohol consumption, obesity, healthy diet and exercise. For instance, the use of antihypertensive medication and exercise can lower the blood pressure, and the opposite effect may transpire with alcohol consumption. These differences can influence the mean and tail of the distribution. Hence, there is a need to model the kurtosis to capture its effect on blood pressure.

This study therefore adopted the GAMLSS model to generate smooth centiles, given its flexibility and recommendation by the World Health Organization (2006) among other competing models. The GAMLSS (Rigby & Stasinopoulos, 2005) is an extension of the LMS that incorporate skewness and kurtosis and suitable for cross sectional data, and is applied for centile estimation of hypertension in Namibian adults aged 35-64 years of age.

2. Methods and Materials

2.1. Data

Data for a total of 3095 adults aged between 35 -64 years was obtained from the 2013 Namibia Demographic Health survey; a cross sectional study intended to provide demographic, socioeconomic, and health data at national and regional levels. Blood pressure measurements (systolic and diastolic) for women and men were assessed by the Life Source UA-767 Plus - a fully automatic, digital upper-arm device. Interviewers were trained to use the device as recommended by the manufacturer's protocol. Three measurements of systolic and diastolic measurements of millimeters of mercury (mmHG) were carried out at an interval at least 10 minutes between the measurements. The average of the second and third measurements was used to classify individuals with respect to hypertension, following internationally recommended categories.

2.2. Construction of Blood Pressure nomograms according to age and sex

Centiles were estimated using a semi-parametric GAMLSS framework. This framework allowed to fit non-normal distribution and normal distribution data. The approach incorporated modelling of location, scale, skewness and kurtosis. Models were fitted separately for both male and female. The process for constructing centile curves involved selecting the best distribution, smoothing function and degree of freedom for modelling parameters of the distribution. Six families of distributions that were tested to construct the centiles were the Box-Cox Cole Green (BCCG) (Cole & Green, 1992), Box Cox Power Exponential (BCPE) (Rigby & Stasinopoulos, 2004), Box Cox t (BCT) (Rigby & Stasinopoulos, 2006), Power Exponential (PE) (Nelson, 1991), skew power exponential type 3 (SEP3) (Fernández, Osiewalski, & Steel, 1995), and the skew t type 3 (ST3) (Azzalini & Capitanio, 2003). Three smoothing functions (penalized splines, cubic splines and fractional polynomials) were tested using the GAIC values, and the function with the smallest values was the better fit for the data. According to the GAIC values, SEP3 was best fit for males SBP, while the BCPE was regarded as the best fit for females SBP and males DBP. The BCT was selected for female DBP. The nonparametric smoothing (penalized spline) was the best smoothing function than the parametric method (fractional polynomial). The penalized spline used the local maximum penalized likelihood estimation method (Rigby & Stasinopoulos, 2014). The automatic procedure in GAMLSS was used to select the appropriate degrees of freedom for distribution parameters and power parameter λ (Rigby & Stasinopoulos, 2004).

2.3. Diagnostics of Residuals

Examining the residuals of the fitted models is an important aspect for the creation of percentile curves. The Z, Q statistics and worm plot were used to diagnose the adequacy of smoothing curves. Both Q and Z stats are useful to verify whether the residuals are normally distributed (Royston & Wright, 2000). If a model fits the data well, the true residuals have a standard distribution. The statistics Z_{gi} where $i = 1,2,3,4$ inspect if the residuals have population mean 0, variance 1, skewness 0 and kurtosis 3. Royston and Wright (2000) computed the Q test statistics as:

$$
Q_i = \sum_{g=1}^G Z_{gi}^2,
$$

The statistics Q_1 , Q_2 , Q_3 and Q_4 were tested under the null hypothesis that the true residuals are normally distributed and suggest a Chi-squared distribution with adjusted degrees of freedom of $G - df_{\mu} (Q_1)$, $G - [df_{\sigma} + 1] (Q_2)$, and $G - df_{\nu} (Q_3)$. The adjusted degree of freedom of Q_4 , was suggested by Rigby and Stasinopoulos (2004) to be equal to $G - df_{\tau}$.

 Figure 1: Z statistics for the fitted models

Table 1: Comparison Q statistics of fitted models

 Figure 2: Worm plot of the fitted models

Any significant among the p-values of the Q statistic suggested the inadequacy in the model. Figure 1 indicated the visual display of Z scores indicating adequacy in the four models because ther[e were no](#page-4-0) squares spotted in the middle of the circle and indicated that all |Z| values are less than 2. All p-values for Q statistics as presented i[n Table](#page-5-0) 1 were greater than significant level of 0.05 indicating the residuals were normally distributed with mean 0, variance 1, skewness closer to 0 and kurtosis closer to 3. For more interpretation details of Z and Q statistics refer to Rigby et al. (2017) and Royston and Wright (2000). In addition, worm plots were used to check the goodness of fit. The shape of worm plots in [Figure 2](#page-5-1) deviates slightly from flat but the points remained in the 95% confidence interval of the two elliptical confidence bands revealing that all models which were selected were reasonable. For interpretation of worm plots, refer to Van Buuren and Fredriks (2001).

3. Results

[Table 2](#page-6-0) presents the demographic characteristic of the study. A total of 3095 adults (1272 males and 1823 females) aged between 35-64 were used to construct centiles. The median SBP for males ranged from 123 mm Hg to 136mm Hg, while females from 119 mm Hg to 135. The mean SBP was high in males aged 60-64 (139.5 mm Hg) and low in females aged 35-39 years (119.9 mm Hg). The mean DBP was low among females aged 60-64 years (81.1 mm Hg). As seen in [Table 2,](#page-6-0) the SBP increased with age.

3.1. Percentile Estimation

Centile estimates by age for SBP and DBP were presented in [Table 3](#page-8-0) an[d Table 4](#page-9-0) for each sex with respect to 25th, 50th, 75th, 90th, 95th and 99th centiles. Centiles curves were portrayed in [Figure 3](#page-11-0) for better interpretation of data. [Figure 3](#page-11-0) shows a rose in SBP level with respect to age for both sexes. Females had a lower median SBP ranging from 116 mm Hg to 132 mm Hg, while the median SBP for males ranged from 123mm Hg to 136 mm Hg. At age 60, males had a median SBP of 134 mm Hg and females had 132 mm Hg. In addition, there was a drastic increase in SBP for the 99th centile for both sexes. The median DBP for females ranged from 80mm Hg to 84mm Hg, while for males from 81mm Hg to 84 mm Hg. For the 99th centile there was a decreased in males DBP for aged 54 to 61 years. A drop down in DBP levels in the $25th$ centile of females was noted in $57 - 64$ years adults. A downward trend in the $50th$ centile of females DBP was seen in adults aged between 59 to 64 years. The 75th age DBP reference range from 89 mm Hg to 94 mm Hg. Hypertension SBP of \geq 140 mm Hg and DBP of \geq 90 mm Hg started from the 75th centile of the reference values. Blood pressure centiles $(25th$ to 99th) steadily increased with an increasing age: the SBP of the men aged 35 ranged $114 - 151$ mm Hg ($\Delta + 51$ mm Hg) and rose to $119 - 202$ mm Hg (∆ +83 mm Hg) in men aged 64. Similar observation was noted in the female, the difference in the lowest centile (25th) and 50th percentile between 35 aged to 64 years was + 9 mm Hg (107 – 116 mm Hg), +13 mm Hg (116 – 127 mm Hg) for the 75th centile and increased to $+$ 40mm Hg (167 -198) in the 99th centile. The trend for male DBP was similar to the SBP. There was an upward trend in the 25th to 99th centile in the male group. DBP rose from $73 - 111$ mm Hg ($\Delta + 38$ mm Hg) in the youngest male aged 35 to 84 – 112 mm Hg (Δ +28mm Hg) males aged 64. In case of females, the difference of DBP between centiles (25th) and 99th) escalated with increasing age; the lowest centile with + 39 mm Hg (72 – 111 mm Hg) in female adults aged 35 to $+ 47$ mm Hg (72 – 119 mmHg) females aged 64.

Table 4: BP Levels for female with respect to age

SBP Percentile of Males

SBP Percentile of Females

DBP Percentile of Males

Figure 3: Centile curves of blood pressure with respect to age for males and females of adults aged 35- 64

Using the definition of hypertension ≥ 140 SBP, the trend of hypertension was as follows; 10% of males aged $35 - 41$ years had high blood pressure and $25%$ of males aged $42 - 64$ were at risk of hypertension. 25% of females aged 47 – 64 years were hypertensive in Namibia. Generally, males were associated with higher SBP mm Hg, while females with high DBP.

4. Discussion

This study constructed a blood pressure reference for Namibia. The study revealed that SBP and DBP elevated steadily with increasing age. This finding is in agreement with the study findings conducted by Hosseini et al. (2015) in Iran and Wong et al. (2020) in the United States of America. The study found a curvilinear trend portrayed in female DBP, suggesting that the DBP in females escalated and decreased with increasing age. This was in contrast with Hosseini et al. (2015)'s finding, who found that the DBP was steadily rising with increasing age. As shown in [Table 3](#page-8-0) and [Table 4,](#page-9-0) the study found that males were associated with high SBP and female with high DBP. Besides that, hypertension for this study was defined in the 75th percentile while the study by Hosseini et al. (2015) for Iranian adults aged 25 to 69 years was defined in the 80th percentile. Indicating that Namibia was at a higher risk of hypertension, compared to Iran. This difference may be the results of geographical area, race, ethnicity, lifestyle behavior, and other factors. A more comprehensive study is needed in Namibia to redefine hypertension based on the population characteristics and comparison of other countries. One needs to determine the correct cut off point for hypertension involving the undergone clinical trials to ensure that bias avoided in the data. The current definition may not be appropriate for Namibia. Henceforth, it is important for countries to produce their blood pressure reference values because it may differ from country-to-country, due to different factors as lifestyle choices and climates. High prevalence of hypertension is noted in this study; hence the Ministry of Health and Social Service need to take action to prevent the increasing rate of hypertension.

5. Conclusion

The study shows that blood percentile elevated with increasing age and varies with sex. There is disparity in blood pressure for different countries therefore, there is a need of countries to develop their references. Therefore, more comprehensive research needs to be conducted for each country in establishing national blood pressure centiles. Due to the blood pressure distribution which may differ from country to country, these studies need to be conducted especially across demographic components and lifestyles. Spatially targeting largely affected population segments and clusters help governments to better target interventions and assistance to the right segments in need.

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7. Appendix A

Probability density function of Box-Cox Cole and Green (BCCG)

Let a positive random variable $Y > 0$ follow a Box-Cox Cole and Green distribution defined through the transformation of a random variable Z defined by:

$$
Z = \begin{cases} \frac{1}{\sigma v} \left[\left(\frac{Y}{\mu} \right)^{v} - 1 \right], & \text{if } v \neq 0 \\ \frac{1}{\sigma} \log \left(\frac{Y}{\mu} \right), & \text{if } v = 0 \end{cases}
$$
(1)

for $0 < Y < \infty$, where $\mu > 0$, $\sigma > 0$ and $-\infty < y < \infty$ such that a random variable Z assumed to follow a truncated standard normal distribution. The probability density function of BCCG/BCCGo (μ, σ, ν) is given by:

$$
f_Y(y|\mu, \sigma, v) = \begin{cases} \mu(1 + \sigma v Z)^{1/v}, & \text{if } v \neq 0 \\ \mu \exp(\sigma Z), & \text{if } v = 0 \end{cases},
$$

where $-1/(\sigma v) < Z < \infty$ if $v > 0$ and $-\infty < Z < 1/(\sigma v)$ if $v < 0$.

Probability density function of Box-Cox power exponential (BCPE)

Assuming a random variable Y come from a Box Cox Power Exponential distribution denoted by BCPE(μ , σ , ν , τ) defined via the transformation of a random variable Z defined by equation (1), such that a random variable Z assumed to follow a standard power exponential distribution with power(kurtosis) parameter $\tau > 0$.

The probability density function of BCPE is given by:

$$
f_Y(y|\mu, \sigma, v, \tau) = \frac{y^{v-1}f_T(z)}{\mu^v \sigma F_T\left(\frac{1}{\sigma|v|}\right)} \qquad , \qquad (2)
$$

For y > 0 where μ > 0 and σ > 0 and $-\infty < v < \infty$, where f_T(t) probability density function and F_T(t) cumulative probability density function of a variable T having a standard power exponential distribution, T~PE $(0,1, \tau)$ defined as:

$$
f_{T}(z) = \frac{\tau}{2c\Gamma(\frac{1}{\tau})} \exp\left\{-0.5 \left|\frac{z}{c}\right|^{\tau}\right\},\,
$$

where $c^2 = \Gamma(1/\tau) [\Gamma(3/\tau)]^{-1}$.

Probability density function of Box-Cox *t* distributions (BCT)

Let a positive random variable $Y > 0$ have a Box-Cox *t* distribution defined through the transformation of a random variable Z in (1), such that a random variable Z assumed to follow a truncated *t* distribution with degrees of freedom, $\tau > 0$. The probability density function of a BCT is defined in equation (2), where $f_T(t)$ probability density function and $F_T(t)$ cumulative probability density function of a variable T having a standard *t* distribution, $T \sim t_\tau(0,1,\tau)$ given by:

$$
f_T(z) = \frac{1}{B\left(\frac{1}{2}, \frac{\tau}{2}\right)^{\tau^{1/2}}}\left[1 + \frac{z^2}{\tau}\right]^{(\tau+1)/2}
$$

,

,

Probability density function Skew Exponential Power type 3 distribution, (SEP3)

Assume Y come from a spliced –scale distribution with a probability density function denoted by SEP3, defined by:

$$
f_Y(y|\mu, \sigma, v, \tau) = \begin{cases} \frac{c}{\sigma} \exp\left[-\frac{1}{2}|vz|^\tau\right], & \text{if } y < \mu\\ \frac{c}{\sigma} \exp\left[-\frac{1}{2}\left|\frac{z}{v}\right|^\tau\right], & \text{if } y \ge \mu \end{cases}
$$

for $-\infty < y < \infty$, where $-\infty < \mu < \infty$, $\sigma > 0$, $v > 0$ and $\tau > 0$ and where $z = (y-\mu)/\sigma$ and $c =$ $v\tau/[(1+v^2)2^{1/\tau}\Gamma(1/\tau)]^{-1}$.

Probability density function Skew *t* type 3 distribution, (ST3)

Suppose Y come from a spliced –scale distribution with a probability density function denoted by ST3, defined by:

$$
f_Y(y|\mu, \sigma, v, \tau) = \begin{cases} \frac{c}{\sigma} \left[1 + \frac{v^2 z^2}{\tau} \right]^{-(\tau + 1)/2}, & \text{if } y < \mu \\ \frac{c}{\sigma} \left[1 + \frac{z^2}{v^2 \tau} \right]^{-(\tau + 1)/2}, & \text{if } y \ge \mu \end{cases},
$$

for $-\infty < y < \infty$, where $-\infty < \mu < \infty$, $\sigma > 0$, $v > 0$ and $\tau > 0$ and where $z = (y-\mu)/\sigma$ and $c =$ $2v/[(1 + v^2)B(1/2, 1/2)\tau^{1/2}]^{-1}$.