Associated factors to non-adherence to blood pressure lowering drugs: Results from an urban Tunisian population 2017.

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Abstract

Background: Patients' poor or non-adherence to Blood Pressure (BP) lowering drugs is one of the main factors of suboptimal BP. We aimed to determine the prevalence of non-adherence to BP lowering drugs in hypertensive outpatients followed in our department, and assess associated factors.

Methods: Descriptive observational study conducted between July 24th and November 24th, 2017 at the Rabta hospital in Tunis. According to the recommendations of the European Society of Cardiology (2013), outpatients over the age of 18, followed for High Blood Pressure (HBP) at high (or very high) risk of cardiovascular diseases, were included in this study. The sample was randomly selected among the list of outpatients followed for HBP. The adherence assessment test (TEO) developed by the French HBP control committee, was adopted to assess adherence level. Health-Related Quality Of Life (HRQL) was assessed by MINICHAL questionnaire. Data on socio-demographic and clinical characteristics were collected using a structured questionnaire. Socio-demographic and clinical characteristics and HRQL data were further tested as independent variables to non-adherence. Data entry and analysis were performed by SPSS software version 20.0. A two-sided p-value test was considered to be significant.

Results: A total of 170 patients were included in this survey. The mean age of our study population was 63 ± 0.7 years, (52.9%) were men and (74.2%) had a low educational level. More than half of included patients were classified as hypertensive at very high risk of cardiovascular diseases (58.3%). The prevalence of non-adherence was (59.4%, 95% CI (52.3-67.1)). In multivariable analysis, factors associated with non-adherence were low educational level and having no family support to get treatment. HRQL scores were not significantly associated with non-adherence.

Conclusion: Our study has highlighted a high prevalence of non-adherence to BP lowering drugs in a vulnerable population. Actions focused on three levels (patient, drug-treatment and healthcare system), should be undertaken to enhance adherence.

Keywords: High blood pressure, Adherence, HRQL, Confidence intervals, Cardiovascular.

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Introduction

HBP is a well-known cardiovascular risk factor associated with increased cardiovascular events and hospitalizations with subsequently higher morbidity and mortality rates, and higher costs of care [1]. Although Blood Pressure (BP) lowering drugs have been shown to reduce premature mortality related to cardiovascular complications, suboptimal control level of BP has been consistently reported in population-based studies worldwide, mainly in developing countries [2,3]. In fact, patients poor or non-adherence to BP lowering drugs is a growing concern to clinicians, healthcare systems and other stakeholders, which is admitted to be one of the key contributing factors to suboptimal BP control [2,4].

The definition of HRQL includes the physical, psychological, and social aspects of positive well-being as well as the negative effects of illness, treatment, and infirmity, which is admitted to be affected by HBP as a chronic disease and long-term medication prescription [5].

In Tunisia, following the epidemiological, socio-economic and nutritional transition, cardiovascular diseases become the leading cause of death accounting for almost 30% of deaths in 2013 with an estimated annual incidence of ischemic heart diseases equal to 124.3 per 100 000 inhabitants [6,7]. HBP is a major public health concern and a highly prevalent condition in adult Tunisian population aged between 35 and 70 years, with an estimated prevalence of 30% [6]. Several publications reported the difficulty of HBP management and control among hypertensive outpatients, however, no published data have taken into consideration the association between HRQL and adherence level to BP lowering drugs [8-10]. We, therefore, conducted this study in a teaching hospital of Tunis, the capital city, in order to estimate the prevalence of non-adherence to BP

lowering drugs and assess associated factors taking into account the impact of HRQL on adherence level.

Methods

Study design and population

Our study is a descriptive observational survey, conducted in the cardiology department in the Rabta university hospital of Tunis (Tunisia), between July 24th and November 24th, 2017. We included all hypertensive outpatients at high (or very high) risk of cardiovascular disease aged more than 18 years, followed for at least one year in our department and who had received at least one BP lowering drug. The definition of the European Society of Cardiology (2013) was adopted to define hypertension at high/very high risk of cardiovascular disease [11]. Patients with a mental disorder and/or communication problems were not included. The sample was selected randomly from the list of hypertensive outpatients followed in our department, taking into consideration an estimated prevalence of non-adherence equal to 60% and an alpha risk error of 5%.

Adherence level assessment

Adherence level to BP lowering drugs was measured based on the adherence assessment test (TEO) developed by the French Committee for the Control of Hypertension (CFLHTA) [12]. TEO is a 6-question questionnaire to which patient should answer yes or no (Appendix 1). A TEO scores less than 3 defines the group of adherent patients to BP lowering drugs, and a TEO score greater than or equal to 3 defines the group of non-adherent patients to treatment.

Health-related quality of life assessment

Health-Related Quality of Life (HRQL) was evaluated based on the short form of the Spanish Hypertension Quality of Life Questionnaire (MINICHAL) which has been validated into Brazilian Portuguese (MINICHAL-Brazil) [13,14]. MINICHAL Brazil is a multiple choice 17-items questionnaire organized in 2 main factors: Mental Status (10 questions) and Somatic manifestations (6 questions), and 1 question to assess the patient's perception of how hypertension and its treatment have affected his quality of life (Appendix 2). Considering the 7 preceding days, patients' answers were distributed on a Likert type frequency scale, with 4-answer options from 0 (No, not at all) to 3 (Yes, very much). The maximum score for the somatic manifestations domain is 18 while for the mental status domain it is 30. With this scale, the closer the result is to zero, the better the quality of life [14].

Data collection

Data related to adherence level and health-related quality of life assessment were collected by an external investigator, after the medical consultation. We also collected data on socio-demographic characteristics, baseline clinical characteristics and potentially associated factors to non-adherence that have been reported in the literature. These data were collected by asking outpatients face to face and using a developed structured questionnaire containing 20 items (Appendix 3).

Data entry and statistical analysis

Data entry and all statistical analyses were performed using the statistical software SPSS Inc. (version 20.0). Percentages were used to describe categorical variables whereas mean values and standard deviations were used to describe continuous variables. Student's t-test and Kruskal wall tests were used for comparison of means and medians between groups, respectively. Pearson chi-square test (χ^2) was used for comparison of proportions between groups. A multivariable analysis using logistic regression was carried out taking into account variables that had a p-value less than 20% in univariable analysis. The dependent variable in all analyses was "non-adherence to BP lowering drugs" and was binary (YES or NO). The independent variables were socio-demographic data, clinical baseline characteristics, and HRQL scores. Adjusted Odds Ratios (AORs) and their 95% confidence intervals (CIs) were reported. Hosmer and Lemeshow test was used to assess the goodness-of-fit of the logistic regression model. A two-sided p-value less than 5% was considered significant in all statistical analyses.

Ethical considerations

Since it was not an interventional study; no approval from the ethical committee of our hospital was required. However, oral consent was obtained from each patient after explaining briefly the study aims.

Findings

Study population characteristics

A total of 170 outpatients diagnosed with high BP at high risk of cardiovascular diseases were included. The mean age of patients was 63 ± 0.7 years, 52.9% were male and 74.2% have a low educational level. Almost half of the study population had a history of coronary heart disease or stroke. Six different BP lowering drug classes were used. Most of the patients (80%) were receiving Angiotensin Converting Enzyme Inhibitors (ACEIs), (64.1%) were receiving Beta-Blockers (BBs), and (44.7%) were receiving Calcium Channel Blockers (CCBs). Patient's characteristics and drug use were detailed in Tables 1 and 2.

The prevalence of non-adherent patients to BP lowering drugs was equal to (59.8%; 95% CI (52.3, 67.1)) and (12.6 %; 95% CI (8.2, 18.3)) of patients had a TEO score greater or equal to 5. The prevalence of non-adherence to a low sodium diet was equal to (49.1%; 95% CI (41.2, 56.7)).

***Table 1**. Study population characteristics.*

Variable	Value
Age (years) ± sd†	63 ± 0.7
Male gender (n, %)	90 (52.9)
Educational level (n, %) Secondary school/university degree 126 (74.2) Profession (Yes) 44 (25.8)	
	33 (19.4)
Marital status Married (n, %)	141 (82.9)
Social insurance Yes (n, %)	148 (87.1)
Diabetes (n, %)	105 (61.8)
Dyslipidemia (n, %)	118 (69.4)
Smoking (n, %)	138 (81.2)
Comorbidity (n, %)	149 (87.6)
History of coronary heart disease or stroke (n, %)	86 (50.5)
CVD1 risk High (n, %) Very high (n, %)	71 (41.7) 99 (58.3)
HBP2 for more than 5 years (n, %)	117(68.8)
Mean number of CVRF3 (other than HBP2) ± sd†	2.6 ± 0.09
Mean number of antihypertensive drugs ± sd†	2.5 ± 0.08
Mean number of total prescribed drugs ± sd†	5.4 ± 0.1
1: Cardiovascular disease; 2: High blood pressure; 3: Cardiovascular risk factors; †: Standard deviation	

***Table 2.** Blood pressure lowering drug classes prescribed.*

Blood pressure lowering drug	Number of patients under this treatment n (%)
Angiotensin-converting enzyme inhibitors	136 (80.0)
Beta-blockers	109 (64.1)
Calcium-channel blockers	76 (44.7)
Loop Diuretics	41 (24.1)
Hydrochlorothiazide	34 (20.0)
Valsartan	7 (5.1)

Description of Health-Related Quality of Life (HRQL)

The mean HRQL global score was 12.3 ± 0.6, significantly higher (in univariable analysis) among non-adherent patients to BP lowering drugs (p=0.04) (Figure 1). The mean score for somatic manifestations was significantly higher among non-adherent patients (p=0.01). However, it wasn't significantly different across adherence level categories regarding the mental status score (Figures 2 and 3). The description of HRQL by item was detailed in Table 3.

In univariable analysis, factors significantly associated to non-adherence to BP lowering drugs were: low educational level (p=0.01), no adherence to low sodium diet (p=0.01), having no family support to get treatment (p=0.05) and relatively bad quality of life (p=0.04 for the HRQL global score). Details of the univariable analysis are depicted in Table 4.

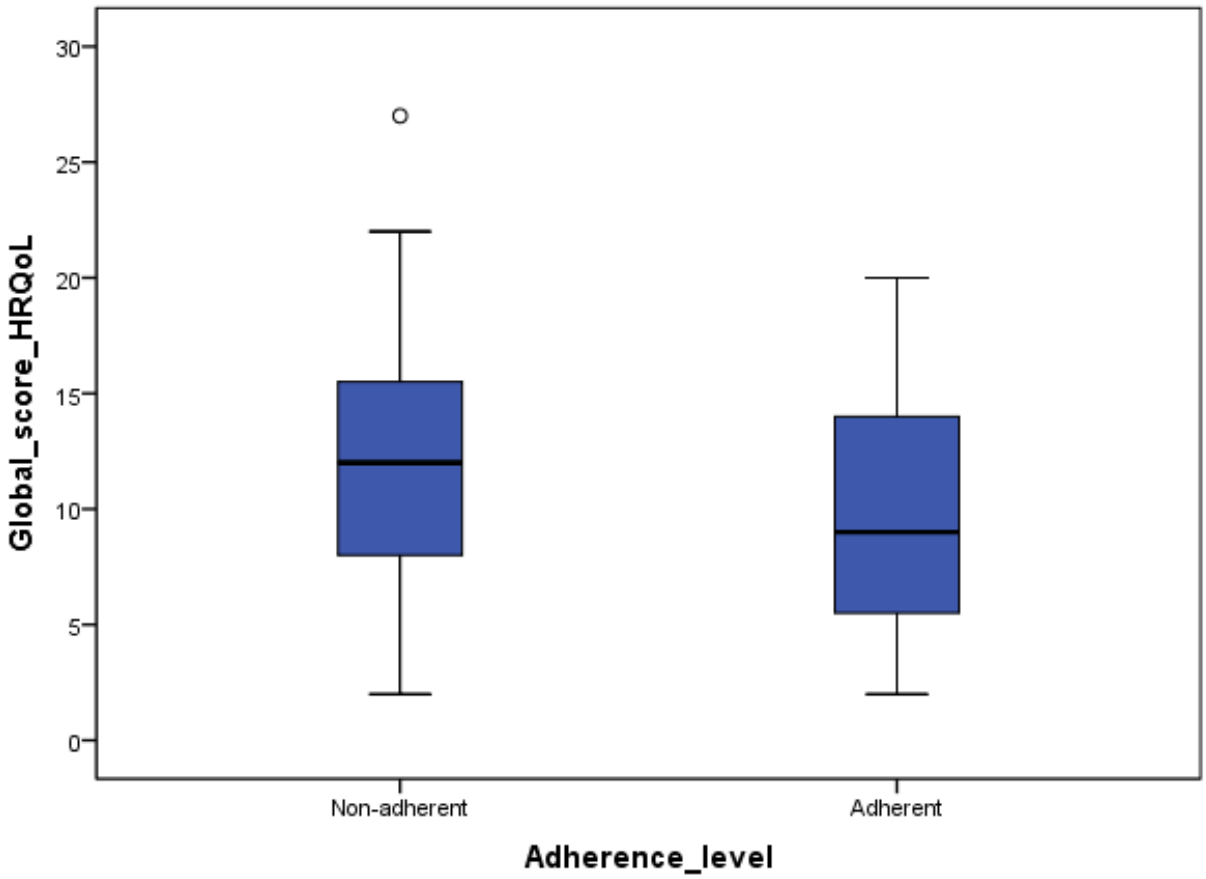

Figure 1. *Box-plot of a global score of HRQL by adherence level category.*

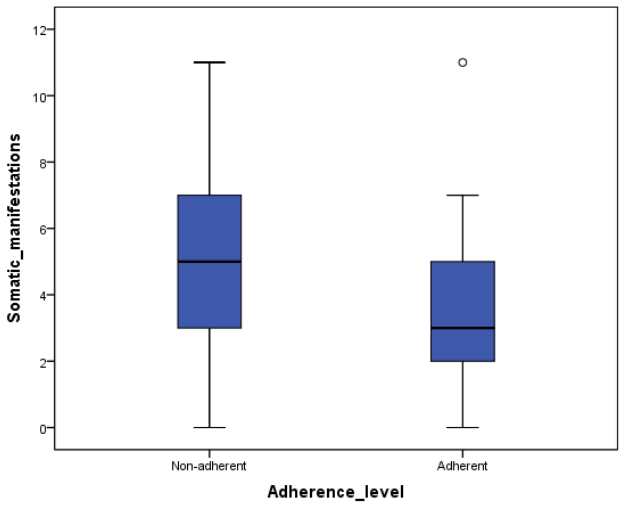

Figure 2. *Box-plot of somatic manifestations scores by adherence level category associated factors to non-adherence in univariable analysis.*

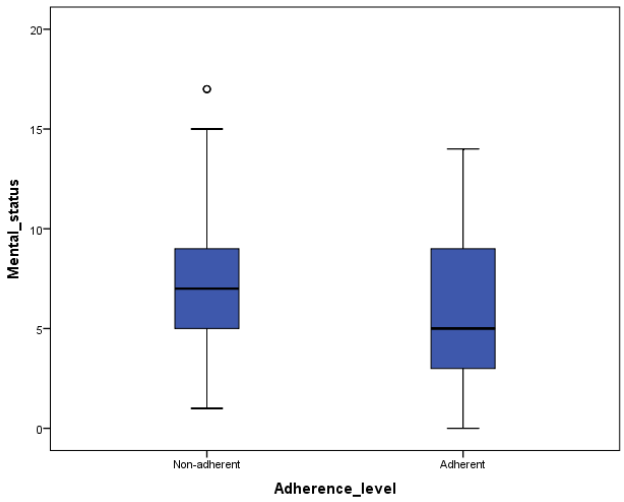

Figure 3. *Box-plot of the mental status score by adherence level category.*

Associated factors to non-adherence in multivariable analysis

In multivariable analysis, only two factors were significantly associated to non-adherence which are: low educational level with an Adjusted Odds Ratio (AOR) equal to 3.5 (p=0.02) and having no family support to get treatment (AOR=2.9, p=0.04). In this level of analysis, relatively bad HRQL was not

significantly associated with non-adherence. Details of the multivariable analysis are depicted in Table 5.

***Table 3**. The description of Health-Related Quality Of Life (HRQL) by item.*

Item	Mean score	Standard deviation	Min-Max
Mental Status Related Items (MsRI)			
Sleeping poorly	0.82	0.1	0-3
Difficulty maintaining usual social relationships	0.42	0.06	0-3
Difficulty interacting with others	0.45	0.06	0-3
Feeling useless	0.26	0.05	0-2
Feeling unable to make decisions and			
Start new things/projects	0.29	0.05	0-3
Feeling continuously distressed and tense	0.96	0.06	0-2
Feeling that life is a constant struggle	0.72	0.07	0-3
Feeling incapable of enjoying your daily activities	0.86	0.06	0-3
Feeling worn-out and powerless	1.34	0.06	0-3
Feeling sick	1.12	0.07	0-3
Total status related items	7.2	0.04	0-20
Somatic Manifestations Related Items (SmRI)			
Difficulty breathing for no apparent reason	0.7	0.06	0-3
Ankles swollen	0.75	0.05	0-2
Urinating more frequently	0.79	0.07	0-2
Mouth dry	0.96	0.07	0-3
Pain in the chest without doing any physical exertion	0.51	0.05	0-2
Numbness or a tingling sensation in any part of the body	0.69	0.06	0-2
Total somatic manifestations related items	4.4	0.25	0-11
Global question			
Hypertension and its treatment have affected your quality of life	0.67	0.07	0-2
Global score (MsRI+SmRI+global score)	12.3	0.6	Feb-30

***Table 4.** Associated factors to poor adherence in univariable analysis.*

Variable	Good adherence (group 1)	Non- adherence (group 2)	p-value
Age (years ± sd†)	63.1 ± 1.2	64.2 ± 0.8	0.2
Male gender (%)	43.7	56.3	0.3
Educational level: Illeterate or primary school (%)	34.1	65.9	0.01
Married (%)	38.8	61.2	0.5
Social insurance (%)	40.7	59.3	0.3
CVD[1] risk-Very high (%)	43.4	56.6	0.3
Dyslipidemia (%)	33.6	66.4	0.1

Diabetes (%)	37.3	62.7	0.2
Smoking (%)	37.5	62.5	0.3
History of coronary artery disease or stroke (%)	44.4	55.6	0.3
No family support for appointment reminder (%)	44.9	55.1	0.1
No family support to get antihypertensive drugs (%)	67.8	32.2	0.05
No adherence to low sodium diet (%)	69.5	30.5	0.01
HBP2 for more than 5 years (%)	37.4	62.6	0.3
Mean number of CVRF (other than HBP[2]) ± sd†	2.3 ± 0.1	2.7 ± 0.1	0.07
Mean number of antihypertensive drugs ± sd†	2.5 ± 0.1	2.6 ± 0.1	0.9
Mean number of total prescribed drugs ± sd†	5.2 ± 0.2	5.4 ± 0.2	0.5
Mean score for somatic manifestations ± sd†	3.6 ± 0.3	4.9 ± 0.3	0.01
Mean score for mental status ± sd†	6.1 ± 0.6	7.8 ± 0.6	0.07
Mean global score for HRQL[3] ± sd†	9.8 ± 0.8	12.7 ± 0.8	0.04
1: Cardiovascular diseases; 2: High blood pressure; †: Standard deviation; 3: Health-related quality of life			

Table 5. *Associated factors to poor adherence in multivariable analysis.*

Variable	**p-value**	**Adjusted OR***	**OR* 95% CI****
Educational level-Illiterate or primary school	0.02	3.5	(1.2-10.1)
No family support to get antihypertensive drugs	0.04	2.9	(1.1- 8.2)
No adherence to low sodium diet	0.1	1.9	(0.8-5.1)
No family support for appointment reminder	0.3	1.6	(0.6-5)
Mean number of CVRF[1] (other than HBP[2]) ± sd†	0.1	1.4	(0.8-2.5)
Mean score for somatic manifestations ± sd†	0.5	1.1	(0.9-1.2)
Mean score for mental status ± sd†	0.4	1.1	(0.8-1.4)
1: Cardiovascular diseases; 2: High blood pressure; †: Standard deviation; *Odds-ratio; **Confidence interval			

Discussion

To our knowledge, this study is the first Tunisian study assessing the adherence level to BP lowering drugs and its associated factors, taking into consideration the impact of HRQL in medication adherence. Our study showed poor adherence to BP lowering drugs in a vulnerable population of hypertensive patients at high risk of cardiovascular diseases, with an estimated prevalence of non-adherence equal to 59.8%. After multivariable adjustment, HRQL was not an associated factor to non-adherence and factors associated significantly were low educational level and having no family support to get BP lowering drugs.

The sample was randomly selected from an exhaustive list of patients followed for HBP in our department, after verifying the inclusion criteria. This way of sampling guarantees good representativeness and allows results extrapolation to other Tunisian public health care facilities [15]. The sample size was calculated using the formula of simple random sampling taking into consideration an estimated prevalence of non-adherence to BP lowering drugs equal to 60% [16]. This proportion was used based on the results of previous similar Tunisian studies [8,10].

The HRQL was assessed based on the MINICHAL questionnaire which is a specific questionnaire to assess HRQL in hypertensive patients. This questionnaire is, however, not validated in Tunisian population but validated in several developing countries and in some countries having the same socio-cultural context as the Tunisian population, such as Middle Eastern countries [17-19]. Alhaddad et al. in a similar study conducted in Middle Eastern countries (Lebanon/ Jordan), showed that the mean score of global HRQL was 15.1(VS 12.3 in our study) [17]. Literature review shows that HRQL scores were lower (better QL) in developed countries where median scores of somatic manifestations and mental status do not exceed 4 and 8, respectively [20,21]. The difference compared to developing countries may be explained by better socioeconomic level and better healthcare systems.

In our study, adherence level assessment was performed based on the French TEO questionnaire [12]. The choice of this assessment tool was adopted in the perspective of being able to compare our results to a similar Tunisian study conducted in Sfax region (Tunisia) [10]. Cramer et al. showed that several assessment tools to measure adherence level to BP lowering drugs exist, which make it difficult to make a comparison between studies [22]. Most authors have used the 8-items Morisky medication adherence scale (MMAS-8), not validated yet in the Tunisian context [23]. Ghozzi et al. in the previous Tunisian study using the TEO assessment tool, reported that the estimated non-adherence prevalence was 63.4% [10]. Taking into consideration differences in study designs and lack of a standardized adherence assessment tool, reported adherence level to BP lowering drugs varies from 28 to 78% in literature [24]; A meta-analysis including 22 studies from low and middle-income countries, showed that the pooled percentage of non-adherence was (63.35%, 95% CI: 38.78-87.91) [25]. Abegaz et al. in another meta-analysis including 28 studies from 15 different countries, showed that the percentage of non-adherence was 62.5% (95% CI=39.9-85.0) in Africa and 43.5% (95% CI=35.0-53.0) in Asia [26]. Better adherence level to BP lowering drugs was reported in European and American studies, where the pooled percentage of non-adherence was 37.1% (95% CI=32.7-41.6) and 36.6% (95% CI=24.4-48.8), respectively [26,27].

This study shows that factors associated with non-adherence in multivariable analysis were low educational level and having no family support. Taking into account the study design (cross-sectional survey) and the sample size limitations, our results can fit with literature reviews data. In fact, several systematic reviews reported that non-adherence to BP lowering drugs and long-term medication generally, may be explained by disease-related factors (disease chronicity and long-term medication), therapy-related factors (type of prescribed BP drugs and side effects), health-system related factors (physician-patient relation, drugs availability), socio-economic related factors (family preparedness, affordable prices) and patient-centered factors (cultural factors, forgetfulness, knowledge, lack of awareness, etc.) [24-26,28].

In the limit of this study, HRQL was a patient-related factor significantly associated with non-adherence in the univariable analysis but not in multivariable analysis, which may be explained by low statistical power related to low sample size. Alhaddad et al. in a similar study conducted in Middle Eastern countries showed that there was a significant association between lower scores of HRQL (better QL) and adherence level improvement ($p<0.001$) [17]. This association has been reported also by Zyoud et al. and by Holt et al., that have shown the significant association between better QL scores and better adherence level to BP lowering drugs with an adjusted Odds Ratio (OR) equal to 2.26 (95% CI 1.74, 2.97) compared to patients with poor adherence level [29,30].

This association between poor QL (mainly poor mental health status) and poor adherence level to antihypertensive medication may be explained by the fact that mood disorders could impair the patient's ability to follow prescribed treatment. In fact, Leonelo et al. have shown that patients with at least mild depression symptoms were 2.5 times more likely to become non-adherent to prescribed blood pressure lowering drugs in the following 3 months, compared to patients with minimal symptoms [31]. Kretchy et al. have also reported that stress among hypertensive patients increased their likelihood of medication non-adherence by 2.42 (OR=2.42 (95% CI 1.06-5.5)) [32].

On the other hand, non-adherence to hypertension management medication tends to add on social-psychological stress on patients and makes them exposed to persistent "negative emotions" thus worsening the BP balance and creating a vicious circle [32].

At the molecular level, the persistent social-psychological stress leads to vascular wall nocuous remodelling by releasing oxidative stress mediators such as reactive oxygen species, leading to augmented vasoconstriction, reduced vasodilation, and increased vascular stiffness [33,34]. The stress impact on the development and maintenance of other cardiac chronic diseases (such as atrial fibrillation), has been also reported in the literature [35-40].

Conclusion and Recommendation

Poor adherence to long-term therapies such as BP lowering drugs compromises severely the effectiveness of treatment and makes it a critical issue to population health. Our study has shown poor adherence level to BP lowering drugs in a vulnerable population, occurring more likely in patients with low educational level and with no family support. Taking as references the guidelines of the European Society of Cardiology and some literature reviews, interventions that need to be to undertaken to enhance adherence level, must be focused on three levels of action:

Patient-level: structured pre-treatment counselling, intensive education, and behaviour change techniques in small group sessions, improve family-members support, improve self-monitoring of blood pressure, etc.

Therapy level: simplification of drug regimen, direct observation of therapy by health workers, dealing with adverse effects, etc.

Health-system level: reduce out-of-pocket expenses; improve the patient-physician relationship, patient involvement in evaluation and treatment, patient reminders, patient health insurance, uninterrupted supply of BP lowering drugs, on-going professional support, etc.

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