Predictors of Poor Adherence to Hypertension Treatment

Les facteurs prédictifs de la mauvaise observance au traitement de l'hypertension artérielle

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RÉSUMÉ

Introduction: L'hypertension artérielle, facteur de risque cardiovasculaire, expose à des nombreuses complications.

Objectifs: Les objectifs de ce travail étaient d'analyser l'observance thérapeutique et d'identifier les facteurs associés à la mauvaise observance au traitement chez les sujets hypertendus.

Méthodes: Il s'agit d'une étude transversale descriptive, auprès de 276 patients hypertendus, suivis au CSB « Riadh1 » de Ksar Helal de la région de Monastir, sur une période de six mois allant de juillet 2016 à janvier 2017.

Résultats: L'âge moyen de nos patients était de 64,9 ans ±10,2 avec une prédominance féminine (69,9%). Les sujets âgés de 65ans et plus représentaient 48,5%. La durée moyenne d'évolution de l'hypertension artérielle était de 10,2 ans (± 7,3). Elle a été associée à un diabète chez 63% des patients. 16,7% des hypertendus avaient une mauvaise observance; la principale cause était l'oubli (51,4%). Les bons observants avaient des chiffres de tension artérielle équilibrés (p<0,001), un nombre réduit de prise médicamenteuse (p=0,001), un nombre réduit de comprimé (p=0,02) et un bon niveau socio-économique (p=0,006). Les femmes avaient 2,37 fois plus de risque d'être mal observantes au traitement que les hommes (p<0,05). Avoir plus de trois comprimés par jour augmente le risque d'être mauvais observant de 4,24 (p<0,05). Les malades ayant un niveau socio-économique bas avaient 7 fois plus de risque d'être mal observant que ceux ayant un haut niveau socio-économique (p<0,05).

Conclusion: L'observance thérapeutique était insatisfaisante dans notre population d'hypertendus. Le médecin de famille doit agir à travers le renforcement de l'éducation thérapeutique du patient hypertendu, son implication active dans sa prise en charge et le bon choix du traitement antihypertenseur bien toléré avec le minimum de prises par jour.

Mots-clés

Hypertension artérielle ; Observance ; Facteurs prédictifs

SUMMARY

Introduction: Hypertension, a cardiovascular risk factor, is likely to lead to many complications.

Aim: To describe the therapeutic adherence and to identify the factors associated with poor adherence among hypertensive patients.

Methods: This is a descriptive cross-sectional study of 276 hypertensive patients, followed at « Riadh1 » Ksar Helal primary health center in the Monastir region over a six-month period from July 2016 to January 2017.

Results: The mean age of our patients was $64.9 \text{ years} \pm 10.2 \text{ with a female predominance } (69.9\%)$. The subjects aged 65 and over accounted for 48.5% of the total number. The average duration of hypertension was $10.2 \text{ years} (\pm 7.3)$. It was associated with diabetes in 174 (63%) patients. Compliant patients had a balanced blood pressure (p <0.001), a reduced drug intake (p = 0.001), a reduced tablet number (p = 0.02), and a good socioeconomic status (p = 0.006). Poor compliance is 2.3 times more likely to occur in women than men (<0.05). Having more than three tablets a day increases the risk of poor compliance by 4.2 (p<0.05). Patients with a low socio-economic level were 7 times more likely to be poor-compliant than those with a high socio-economic level (p<0.05).

Conclusion: Compliance to treatment was unsatisfactory in our hypertensive population, despite its important role in the balance of blood pressure. The family doctor should strengthen the therapeutic education of the hypertensive patient, its active involvement in the management of hypertension and the right choice of well tolerated antihypertensive molecules with the minimum daily intake.

Key-words

Hypertension; Compliance; Predictive factors

INTRODUCTION

Hypertension (HTN) is a worldwide health problem with high cardiovascular morbidity and mortality (1). It has critical long-term consequences for both the patient and the national health service budget, especially as it is estimated that the number of hypertensive patients will increase 60% by 2025 (2). In Tunisia, the surveys carried out recorded hypertension in 30.6% of the adult population (3). Blood pressure (BP) control is a significant goal in the management of hypertension to reduce the major risk of cardiovascular events. Poor control of blood pressure increases the risk of stroke by 9%, heart failure by 5%, coronary insufficiency by 3% and renal failure by 2% (1). Good hypertension management involves the application of dietary and lifestyle guidelines and often the use of antihypertensive drugs to reduce BP values to below 140 / 90 mmHg in the general population. In one out of two cases, despite the indication of drug therapy, the family physician fails to achieve the desired blood pressure goals (4). This can be due to many factors including the choice of the anti- hypertensive drug and withdrawal following the side effects, or the non- adherence of the hypertensive patient to the proposed instructions. This can also be down to the non-compliance with the prescribed drugs (5). The family doctor has an important role in informing hypertensive patients of the benefits and risks of antihypertensive treatment. He is also responsible for their therapeutic education to ensure proper compliance with treatment, and control risk factors to prevent cardiovascular problems. Our study is aimed to describe the therapeutic adherence and to identify the factors associated with poor adherence among hypertensive patients.

METHODS

Study Design

This is a descriptive cross-sectional study, conducted over a six-month period from July 2016 to January 2017 and involving 276 hypertensive patients attending « Riadh1 » Ksar Helal PHC (primary health center), in Monastir region.

Study Population

Inclusion criteria: All hypertensive patients followed and treated at the first-line chronic disease clinic at the « Riadh1 » Ksar Helal PHC, in Monastir region for at least six months.

Exclusion criteria: Hypertensive patients from Ksar Helal PHC who were followed by specialized consultation in cardiology, nephrology and endocrinology Departments in different hospitals in Monastir region. Consultation in the private sector was not included in the study.

Study sitting

The « Riadh1 » Ksar Helal PHC is a health facility, which is part of Ksar Helal health unit serving a population of approximately 6,204 inhabitants. This center offers curative, preventive and promotional care divided into general medical consultations 5 days a week, performed by a single doctor and an individualized consultation twice a week for chronic, diabetic and hypertensive patients performed by a single doctor. During these 2 days, hypertensive patients benefit an individual or a group health education sessions conducted by the doctor. The proposed themes are delivered in Tunisian dialect, including hypertension, its complications as well as associated Cardiovascular Risk Factors (CVRF) and the importance of screening and early management.

Data collection

The collection of data was done prospectively from the patient records and a directed interview. Several parameters have been studied and divided into:

Socio-demographic parameters: age, gender, socio-economic level, type of social security.

History of hypertensive disease: importance, stability, current treatments (number of tablets and doses per day) and complications.

Unmodifiable CVRF associated with hypertension: age, gender, and family history of Ischemic Heart Disease (IHD).

Modifiable CVRF associated with hypertension: smoking, hypertension, dyslipidemia, and Body Mass Index (BMI).

Family history: diabetes and hypertension.

Therapeutic compliance: level of compliance and causes of poor compliance

Operational Definitions

- The definition of hypertension is based on the recommendations of the French Hypertension Society (SFHTA) (6). A HTN is considered to be controlled, or to have achieved objectives, for figures of BP <140 / 90mmHg in the general population and ≤130 / 80mmHg in diabetics.

- Diabetes is defined as fasting blood glucose ≥ 1.26g / I (7.0 mmol / I) after an 8-hour fasting and checked twice by the World Health Organization (WHO) (7).
- BMI is calculated by the following formula: BMI = Weight (Kg) / Height2 (m2). Obesity is defined with a BMI ≥ 30kg / m2.
- Complications of hypertension:
 - * Neuropathy has been retained in the presence of subjective symptom (pain, paresthesia) and objective sensory disturbances (hypoesthesia/anesthesia, numbness ...), elimination of osteotendinous reflexes, or in case of autonomic disorders.
 - * Proliferative retinopathy or non-proliferative has been maintained according to the last fundus data.
 - * Nephropathy has been defined as urinary excretion of albumin greater than 30 mg / 24h.
 - * Arteritis of the lower limbs was retained in the presence of intermittent claudication, elimination of one or more pulse or trophic disorders.
- Importance was given for low socio-economic levels with a monthly income below the Guaranteed Minimum Industrial Wage (SMIG) <300 Tunisian dinar.
- Dyslipidemia is defined by a value of lipids (e.g. cholesterol, triglycerides) higher than the maximum normal value according to our Haj Ali Souaa Hospitol Laboratory (Ksar Helal), (6mmol / I) and (2mmol / I) respectively.
- Adherence to treatment adherence was assessed using the Girerd test (8), consisting of six questions to which the patient answered yes or no by asking questions at the start of the consultation (Table 1).

To study the predictors of poor compliance, patients were divided into three groups: poor observers (total of yes \geq 3), good observers (total of yes = 0) and patients with a minimal adherence problem (total of yes = 1 or 2).

Data analysis

Data entry and analysis were performed on statistical package for the social sciences (SPSS) 21 computer software. For qualitative variables, the results were expressed in terms of numbers and percentage. For comparisons we used the chi- square test. The search for the factors of poor compliance was conducted using a logistic regression. The threshold of significance was set at p <0.05.

Table 1: Adherence Evaluation Test

	TES	NO
1. This morning did you forget to take your		
medicine?		

VEC

- 2. Have you had any medication breakdown since the last consultation?
- 3. Have you had to take your treatment late compared to the usual time?
- 4. Have you ever been away from your treatment because some days your memory is not good?
- 5. Have you ever missed your treatment because some days you feel that your treatment is doing you more harm than good?
- 6. Do you think you have too many tablets to take?

Total YES

RESULTS

Demographic characteristics of the study population:

The study included a cohort of 276 hypertensive patients, followed at « Riadh1 » Ksar Helal PHC, over a six-month period from July 2016 to January 2017. The mean age of our study population was 64.9 years (SD: 10.2), with extremes ranging from 32 to 99 years. Subjects aged 65 and over accounted for 48.5% of the study population. The findings revealed a female predominance (69.9%). Family history was dominated by hypertension and diabetes with rates of 69.2% and 53.6% respectively (Table 2).

Table 2: Characteristics of the study population

Characteristics	N	%
Gender		70
Male	83	30.1
Female	193	69.9
Age classes (years)		
30 - 64 years	142	51.4
65 - 74 years	87	31.5
≥ 75years	47	17.0
Family history		
HTN	191	69.2
Diabetes	148	53.6
Socioeconomic level		
Low	51	18.5
Middle	155	56.2
High	70	25.4

Description of the hypertensive disease

The average duration of hypertension was 10.2 years (SD: 7.3) with extremes ranging from 1 to 37 years. 77.2% of the patients were hypertensive for a period of 1 to 14 years and 22.8% for 15 years or more. HTN was associated with diabetes in 174 patients (63%). The mean duration of diabetes progression was 7.65 years (SD: 8.9).

The therapeutic protocols used were monotherapy in 33%, dual therapy in 45.7%, triple therapy in 18.5% and quadra therapy in 2.9%. The average number of tablets taken per day was 6.3 tablets with extremes of 1 to 17. Among 276 patients, 113 reached the blood pressure goal of 40.9% (Table 3).

Description of the therapeutic adherence

Of 276 patients, 36.6% had good adherence. The main cause of poor compliance, noted in 16.7%, was due to forget fullness (51.4%) (Table 4).

Quantification of the risk of poor compliance

Good observant patients had a balanced BP (p <0.001), a reduced drug intake (p = 0.001), a reduced tablet number (p = 0.02), and a good socioeconomic status (p = 0.006) (Table 5).

Multi-Varied analysis of factors influencing therapeutic adherence

Women were 2.37 times more likely to be poorly observant than men. Having more than 3 tablets a day increases the risk of poor adherence by 4.24. Patients with a low socio-economic level were 7 times more likely to be poorly observant than those with a high socioeconomic level (Table 6).

DISCUSSION

Methodological discussion

- Strengths

The originality of the work stems from the fact that, there are no recent studies on therapeutic compliance on the front line in Tunisia. The strong point of this study was its comprehensive nature, using a large amount of data available on hypertensive disease, emanating from the medical practice of Family Physician. On the other hand, the study involved a population of all ages, different health conditions and varying social conditions.

Table 3: Characteristics of Hypertension Disease

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Characteristics	N	%	
Duration of HTN (years)			
<5	90	32.6	
5 - 9	54	19.6	
10 - 14	69	25.0	
≥ 15	63	22.8	
The BP reading			
BP<140/90	113	40.9	
BP ≥ 140 and / or 90	45	16.3	
Type of HTN			
Systolic-Diastolic	231	83.7	
Systolic	42	15.2	
Diastolic	3	1.1	
CVRF associated with HTN			
Non-modifiable	00	20.4	
Age ≥ 50 for Male Age≥ 60 for Female	83 123	30.1	
Modifiable	123	44.6	
Smoking	26	9.4	
Diabetes	174	63.0	
Dyslipidemia	153	55.4	
Obesity	144	52.2	
overweight	93	33.7	
Duration of Diabetes (years)		00	
<5	147	53.3	
5 - 9	27	9.8	
10 - 14	46	16.7	
≥ 15	55	19.9	
Type of treatment			
monotherapy	91	33	
Dual Therapy	126	45.7	
Triple Therapy	51	18.5	
Quadritherapy	8	2.9	
Micro-angiopathic complications			
Hypertensive retinopathy	28	10.1	
Diabetic retinopathy	47	17.0	
Nephropathy	26	9.4	
Neuropathy	41	14.9	
Macro-angiopathic complications			
Ischemic heart disease	59	21.4	
Arteriopathy of lower limbs	32	11.6	
Stroke	13	4.7	

Table 4: Therapeutic compliance in the study population

	N	%
Adherence to treatment		
Good	101	36.6
Minimal	129	46.7
Poor	46	16.7
Causes of poor adherence		
Oversight	142	51.4
Lack of medication	34	12.3
Side effects of treatment	31	11.2
Polymedication	29	10.5
Negligence	18	6.5

- Limitations of the study:

Our descriptive study did have some shortcomings related to the selection bias of patients. Indeed our study population consisted of hypertensive consultants followed in a single PHC, by the same doctor of the center, without taking into consideration those consulting family doctors of

the private sector or specialists of the region. In addition, during the discussion, we faced a difficulty related to a ranking problem. Indeed, several methods were used in the literature to establish the diagnosis of hypertension.

Discussion of the results

Characteristics of the population studied

The mean age of our population was 64.9 ± 10.2 years, which was close to the data reported by Lkama in Congo (9) and by Andrea Berni (10), with respectively 58.3 ± 10.6 and 70 ± 10 years. The advanced age of patients with hypertension may be explained by the fact that the prevalence of hypertension increases with age (11). The population was predominantly female (69.9%) and the results were consistent with those reported in Douala (64.4%) (12), Burkina Faso (60.4%) (13) and Ivory Coast

Table 5: Factors influencing adherence

	Good adherence	Minimal adherence	Poor adherence	р
BP in the non-diabetics				
<14/9	30 (54.5%)	23 (41.8%)	2 (3.6%)	< 0.001
≥14 / 9	6 (12.8%)	28 (59.6%)	13 (27.7%)	
BP in the diabetics	, ,	,	,	
≤13 / 8	27 (57.4%)	16 (34%)	4 (8.5%)	0.003
> 13/8	38 (29.9%)	62 (48.8%)	27 (21.3%)	
Number of sockets	,	, ,	, ,	
1	13 (52%)	11(44%)	1(4%)	0.001
2	52 (45.2%)	51(44.3%)	12(10.4%)	
3	36 (26.5%)	67(49.3%)	33(24.3%)	
Socioeconomic level	,	` ,	, ,	
Low	13 (25.5%)	23 (45.1%)	15 (29.4%)	0.006
Middle	53 (34.2%)	76 (49%)	26 (16.8%)	
High	35 (50%)	30 (42.9%)	5 (7.1%)	
Number of tablets	,	, ,	, ,	
≤ 3	26 (48.1%)	25 (46.3%)	3 (5.6%)	0.02
> 3	75 (33.8%)	104 (46.8%)	43 (19.4%)	

Table 6: Factors Influencing Therapeutic Adherence

	Good adherence OR (IC 95%)					
Sender						
Male	1		1			1
Female	1	1.438(0.82-2.50)		2.37 (1.03-5.46)*	
ocioeconomic level			·	•	•	,
Low	1		1			1
Middle	1	1.572	572 (0.85-2.89) 2.99 (1.023		2.99 (1.023-8.762)*	
High	1	1,97 (0.85-4.60)			6.93 (2.02-23.80)*	
umber of tablets				,		, ,
≤ 3	1		1			1
> 3	1	1.343	(0.71-	2.53)		4.244 (1.16-15.46)*

^{*}p<0.05

(59.5%) (14). It has become indisputable that women pay more attention to their health than men (15).

The characteristics of HTN

In the present study findings about 40.9% had a good blood pressure control, which is similar to the study conducted in France: 44.9% (16). In contrast, in the United States, according to the NHANES study (17), less than a quarter of hypertensive patients had well-controlled hypertension. A study conducted by Essomba N.E (12) reported that only 25.3% of patients on antihypertensive treatment had well-controlled blood pressure. These differences may be related to the discordant definitions of hypertension according to the authors. The white coat effect was also incriminated to explain the lack of control of blood pressure, which has not been evaluated in our work. Raiiv et al found in their study that the prevalence of the white coat effect increased three-fold with treatment (18), which could also lead to a bias in the assessment of BP control. The mean duration of diabetes progression was 7.6 years with extremes ranging from 0 to 43 years. Our work suggests that diabetes appears to be secondary to hypertension in most patients, as reported by F.Ben Mami and al (19). Khadija Diane and al have demonstrated that hypertension is secondary to diabetes in the elderly 65 years of age and older (20).

Evaluation of the therapeutic adherence

In treated hypertensive patients, rates of poor adherence were highly variable, ranging from 30 to 80% according to the studies (21,22). This variability in the data was related, among other things, to the difference in measurement, sampling and duration of monitoring methods. The 16.7% rate of poor compliance reported in our study was lower than those reported by Ghozzi (23) and Mzoughi (24) in Tunisia, Konin in Ivory Coast (14), Machihude Pio (25), Lkama in Congo (9) and Essomba in Douala (12), with rates of 63.4%, 55%, 52.3%, 32.5% and 25.7%. However Girerd and al in France (26) reported a better result: 8% in a population of hypertensive followed in a specialized environment. Thus the rate of good compliance found in our work was close to that found by Girerd: 39% (26).

Factors of adherence

The study showed that the level of adherence was influenced by gender, which is consistent with the results of Adoubi who found that poor adherence was associated

with female sex and young age (27). Essomba NE reported that poor adherence was related to advanced age and male gender (12).

The low socioeconomic status of our patients was a factor of low therapeutic compliance, which is consistent with the results of several studies (13,14,23-25,28-30). Most authors explained their results by economic difficulties and lack of medical coverage and that the majority of their patients considered their treatment too expensive (25). The present study findings reveals that having three tablets and more to take daily, increases the risk of bad adherence by 4.2 times, this is consistent with the results of Machihude Pio (25) who found that, 94.12% and 67.39% of patients taking respectively three tablets and more than three tablets a day, were poor observers. Konin C. (14) found that 77.3% of patients taking more than three tablets a day were poor observers, as was Ghozzi H (23), who reported that a reduced daily number of tablets was associated with good compliance. We found an inverse correlation between the number of doses per day and adherence to treatment. Having a daily number of catches of three or more increases the risk of being a bad observer (p = 0.001). This is in accordance with the results of some studies (25,31). However, the results of Grant RW were discordant. He noted that adherence was better when the number of drugs to be taken each day was high (32).

Influence of therapeutic adherence on hypertension balance

Tension control depends on several factors namely therapeutic adherence (10). In our study, observant patients had balanced BP counts. In fact, 54.5% of good observers had a balanced BP (p <0.001). Konin reported that the therapeutic nonobservance results in poor blood pressure control. Only 12% and 20% of their patients had normal BP counts for two consecutive visits (14). Lkama M.S. reported that high levels of systolic and diastolic blood pressure were related to poor adherence (9).

Recommendations:

For a better management of hypertensive patients we recommend the family doctor should insert some therapeutic education programs with active involvement of patients in their therapeutic management, with good information on the benefits and risks of treatment. Self-measurement of blood pressure is also an effective way to improve adherence in these hypertensive patients. The

increase in adherence would result partly from the good choice of molecules, adapted to the state of health of the patient with the minimum side effects, and a reduced daily number of tablets.

CONCLUSION

The prevalence of uncontrolled hypertension is still high worldwide. Compliance to treatment was unsatisfactory in our hypertensive population, despite its important role in the balance of blood pressure. The family doctor (general practitioner) must reinforce the therapeutic education of the hypertensive patient, choose antihypertensive molecules that are well tolerated with the minimum of daily doses and actively involve patients in their care.

While the study has highlighted some of the factors that influence treatment adherence, a larger, multicenter, long term cohort study will provide more reliable information on the determinants of poor control of hypertension to provide solutions to achieve the blood pressure goals and avoid the dreadful complications of this pathology.

REFERENCES

- Aroner SA, Jules DE, Mukamol KJ et al. Glycemic status and risk of cardiovascular disease: the multi-ethnic study of atherosclérosis. Atherosclerosis. 2016 May; 248:224-9.
- Kearney P, Whelton M, Reynolds K et al. Global burden of hypertension: analysis of worldwide date. Lancet 2005; 365: 217-23.
- Jarraya F, Mahfoudh H, Kammoun K, Hachicha J, Kammoun K. Prise en charge de l'hypertension artérielle en Tunisie : le défi d'un pays en voie de développement. Rev Med Suisse 2012; 8:1725-30.
- Godet-Thobie H, Vernay M, Noukpoape N et al. Niveau tensionnel moyen et prévalence de l'hypertension artérielle chez les adultes de 18 à 74 ans. ENNS 2006-2007. BEH Thématique 2008.
- Krzesinski J.M, Krzesinski F. Importance de la mauvaise adhésion au traitement antihypertenseur dans la population hypertendue: comment l'améliorer? Rev Med Liège 2010; 65: 278-84.
- Blacher J., Halimi JM., Hanon O, Mourad JJ.et al. Prise en charge de l'hypertension artérielle de l'adulte. Recommandation-SFHTA-2013-Prise-encharge-HTA-de-IAdulte.pdf.
- World Health Organisation, International Diabetes Federation. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia. Report of a WHO/IDF consultation. Gneva:WHO; 2006.
- 8. Girerd X, Hanon O, Anangnostopoulos K et al. Evaluation

- de l'observance du traitement antihypertenseur par un questionnaire: Mise au point et utilisation dans un service spécialisé. Presse Med. 2001; 30(21): 1044-8.
- Ikama Méo S, Nsitou BM et al. L'observance médicamenteuse et ses facteurs dans un groupe d'hypertendus congolais. The Pan African Medical Journal 2013; 15: 121.
- Berni A, Ciani E, Cecioni I, Poggesi L, Abbate R, Boddi M. Adherence to antihypertensive therapy affects Ambulatory Arterial Stiffness Index. Eur J Intern Med. 2011; 22(1):93-8.
- Girndt M., Trocchi P., scheidt-Nave C. et al. The Prevalence of Renal Failure. Dtsch Arztebl Int. 2016; 113(6):85-91.
- Essomba NE, Hamadou Ba, Kedy Koum DC, Atemkeng A, Coppieters Y. Facteurs de non observance au traitement antihypertenseur chez les adultes à Douala. Health Sci.Dis 2017; 18(3) p51-57.
- Heise T, Jennen E et al. Results of a structured hypertension teaching and treatment programme. Z.Gastroenterol.2002; 40: 527-32
- 14. Konin C, Adoh M, Coulibaly I et al. L'observance thérapeutique et ses facteurs chez l'hypertendu. Arch maladies du coeur et des vaisseaux 2007; 100(8):630-4.
- Mabuchi A, Yamamoto R, Ishii K et al. Significance of highnormal blood pressure during early second trimester for predicting the onset of hypertensive disorders in pregnancy. Hypertens Pregnancy 2016; 3:1-8.
- Tilly B, Salanave B, Ricordeau Ph et al. Hypertension artérielle sévère en France: traitement et contrôle tensionnel en 1999 et 2003. Rev Med Ass Maladie 2004; 35 (3): 167-80.
- Hyman DJ, Pavlik VN. Uncontrolled Hypertension as a risk for coronary artery disease: Patient characteristics and the role of physician intervention Curr A theroscler Rep 2003; 5(2):131-8.
- 18. Steiner S, Dorner TE, Fodor JG, Kunze M, Rieder A. Blood pressure awareness in Austria: lessons from a 30 years horizon. Am J Hypertens. 2011; 24 (4): 408-14.
- Ben Mami F, Ben Ahmed I, Ben Romdhane S et al. Caractéristiques de l'hypertension arterielle (HTA) chez un groupe de diabétiques de type 2 tunisiens. Diabetes & Metabolism 2007; 33: 82.
- Diyane K, El Ansari N, El Mghari Gh, Anzid K, et Cherkaoui M. Caractéristiques de l'association diabète type 2 et hypertension artérielle chez le sujets âgé de 65ans et plus. Pan Afr Med J. 2013; 14: 100.
- Claxton AJ, Cramer J, Pierce C. A Systematic Review of the association between dose regimens and medication compliance. clin ther.2001; 23 (8):1296310.
- Iskedjian M, Einarson TR, Mackeigan LD, Shear N. et al. relationship between daily dose frequency and adherence to antihypertensive pharmacotherapy evidence from a metaanalysis. Clin Ther 2002; 24(2):30216.
- 23. Ghozzi H, Kassis M, Hakim A, et al. Observance

- médicamenteuse chez un échantillon d'hypertendus dans la région de Sfax (Tunisie). Ann Cardiol Angeiol. 2010; 59(3): 131-7.
- Mzoughi K, Zairi I, Jemai A, Ben MK, Ben HD, Ben EG, Kraiem S. Factors associated with poor medication compliance in hypertensive patients. La Tunisie medicale. 2018 Jun: 96(6):385-90.
- Pio M, Baragou S, Afassinou Y et al. Observance thérapeutique de l'hypertension artérielle et ses facteurs dans le service de cardiologie du CHU Tokoin de Lomé. PAMJ 2013: 14:48.
- Girerd X, Radauceanu A, Achard JM et al. Evaluation de l'observance par l'interrogatoire au cours du suivi des hypertendus dans des consultations spécialisées. Arch Mal Coeur Vaiss. 2011; 94(8): 839-42.
- Adoubi KA, Diby KF Nguetta R, Yangni-Angate KH, Adoh AM. Facteurs de la mauvaise observance thérapeutique de l'hypertendu en Cote d'Ivoire. Rev Int Sc Med 2006; 8 (2): 18-22.
- Dion Koundar AA. Evaluation du coût de la prise en charge ambulatoire de l'HTA à Abidjan. Thèse Médecine 2004-2005. UFR sciences médicales Abidjan.
- 29. Yaméogo N.V., Kagambège L.J. et al. Facteurs associés à un mauvais contrôle de la pression artérielle chez les hypertendus noir africain : étude transversale de 456 hypertendus burkinabé. Annales de cardiologie et d'angiologie 2013; 62: 38-42.
- 30. Othene Buabeng K, Matowe L, Plange-Rhule J. Unaffordable drug prices: the major cause of non-compliance with hypertension medication in Ghana. J Pharm sci 2004; 7:350-2.
- 31. Kamran A, Sadeghieh A, Biria M, Malepour A, Heydari H. Determinants of Patient's Adherence to Hypertension Medications: Application of Health Belief Model Among Rural Patients. Ann Med Health Sci Res. 2014; 4(6): 922-7.
- Grant RW, O'Leary KM, Weilburg JB et al. Impact of concurrent medication use on statin adherense and refill persistance. Arch Intern Med 2004; 164: 23438.