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COVID19 and Hypertension: Are We Facing a Syndemic?



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Control of High Blood Pressure in Iraq still underestimated

Control of High Blood pressure in Iraq, Still underestimated

In developing countries including Iraq, the high prevalence of hypertension and poor hypertension control are important factors in the rising epidemic of cardiovascular disease. In Iraq, around 39% prevalence of hypertension is reported among the general population.

Iraq has a higher prevalence of hypertension compared to Tunisia (30, 6%) [1], Greece (30, 5%) [2], Turkey (31.8%) [3] and Jordan (15%) [4].

The main challenge about hypertension is the number of patients who are not in control of their BP. If left uncontrolled, hypertension can lead to coronary artery disease, an enlargement of the heart and eventually heart failure [5]. The number of uncontrolled hypertensive patients also varies by countries [6]. Such that, in USA, analysis of data from the National Health and Nutrition Examination Survey (NHANES) 2003-2010 showed that among patients with hypertension in the general population, an estimated 35.8 million (53.5%) did not have their hypertension controlled at the 140/90 mm Hg threshold [7]. Meanwhile, within Europe, rates of BP control among hypertensive treated cases were 40%, 30%, 28%, 19% and 21% respectively in England, Germany, Italy, Spain and Sweden at the 140/90 mm Hg threshold from 1997 to 1990 [6]. Similarly, hypertension was not controlled to the recommended levels of BP in about one-half (50.4%) of patients during the period of June to December 2006 in Jordan. In Iraq, BP control was suboptimal. Effective feasible strategies should be implemented to increase BP control to reduce hypertension-related complications.[11]



Globally, the low BP control rates have been difficult to explain, given the number of apparently well-tolerated medications available for the management of hypertension. Factors related to access to care, medical practice patterns, patient education, poor compliance to prescribed treatment and patient cardio-metabolic profile have all been proposed as barriers to BP control [8–10]. However, BP is also determined by other factors, including age, severity of disease, health habits, and early control and comorbidities [9, 10].

Further identification of patients at risk of poor control can lead to targeted interventions to improve management of hypertension. Besides, in order to improve the BP control rate in the population with hypertension, a more complete understanding of the predictors of BP control is fundamental.



Professor Ghazi F. Haji President of IqSH

References

[1] Jarraya F, Kammoun K, Mahfoudh H, Kammoun K, Hachicha J: Management of arterial hypertension in Tunisia: the challenge of a developing country. Rev Med Suisse. 2012, 8: 1725-1726. 1728–1730. [Article in French]

[2] Sarafidis PA, Lasaridis A, Gousopoulos S, Zebekakis P, Nikolaidis P, Tziolas I, Papoulidou F: Prevalence, awareness, treatment and control of hypertension in employees of factories of northern Greece: the Naoussa Study. J Hum Hypertens. 2004, 18 (9): 623-629. 10.1038/sj.jhh.1001724.

- [3] Altun B, Arici M, Nergizoglu G, Derici U, Karatan O, Turgan C, Sindel S, Erbay B, Hasanoglu E, Caglar S, Turkish Society of Hypertension and Renal Diseases: Prevalence, awareness, treatment and control of hypertension in Turkey (the PatenT study) in 2003. J Hypertens. 2005, 23: 1817-1823. 10.1097/01.hjh.0000176789.89505.59.
- [4] Brown DW, Mokdad AH, Walke H, As'ad M, Al-Nsour M, Zindah M, Arqoob K, Belbeisi A: Projected burden of chronic, noncommunicable diseases in Jordan [letter]. Prev Chronic Dis. 2009, 6 (2): A78-
- [5] World Health Organization: A global brief on Hypertension. Silent killer, global public health crisis. World Health Day 2013. 2013, Geneva, Switzerland: World Health Organization, Available from: http://apps.who.int/iris/bitstream/10665/79059/1/WHO_DCO_WHD_2013.2_eng.pdf. Last access: 8th of July 2013
- [6] Wolf-Maier K, Cooper RS, Kramer H, Banegas JR, Giampaoli S, Joffres MR, Poulter N, Primatesta P, Stegmayr B, Thamm M: Hypertension treatment and control in five European countries, Canada, and the United States. Hypertension. 2004, 43: 10-17. 10.1161/01.HYP.0000103630.72812.10.
- [7] Centers for Disease Control and Prevention (CDC): Vital signs: awareness and treatment of uncontrolled hypertension among adults — United States, 2003–2010. MMWR Morb Mortal Wkly Rep. 2012, 61: 703-709.
- [8] Knight EL, Bohn RL, Wang PS, Glynn RJ, Mogun H, Avorn J: Predictors of uncontrolled hypertension in ambulatory patients. Hypertension. 2001, 38: 809-814. 10.1161/hyo901.091681.
- [9] Cushman WC, Ford CE, Cutler JA, Margolis KL, Davis BR, Grimm RH, Black HR, Hamilton BP, Holland J, Nwachuku C, Papademetriou V, Probstfield J, Wright JT, Alderman MH, Weiss RJ, Piller L, Bettencourt J, Walsh SM, ALLHAT Collaborative Research Group: Success and

predictors of blood pressure control in diverse North American settings: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). J Clin Hypertens (Greenwich). 2002, 4: 393-404. 10.1111/j.1524-6175.2002.02045.x.

[10] Duggirala MK, Cuddihy RM, Cuddihy MT, Naessens JM, Cha SS, Mandrekar JN, Leibson CL: Predictors of blood pressure control in patients with diabetes and hypertension seen in primary care clinics. Am J Hypertens. 2005, 18: 833-838. 10.1016/

j.amjhyper.2004.12.016

[11] Ola Ali Nassr, MSc, BSc (Hons) and Paul Forsyth. Evaluation of Blood Pressure Control and Associated Factors among Patients with Hypertension in Iraq: A Prospective Cross-sectional Study.

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IqHS Scientific Activity Timeline during 2021

After a period of relative withhold the IqHS were back on the line again to resume its scientific activities .here is a timeline of some important activities:

- 1 The most recent one was in Mosul and with the collaboration of Mosul college of medicine and Denk pharmaceutical company we held a scientific symposium entitled "Highlights on Hypertension during Corona pandemic" on twenty third of September 2021.
- **2** On Friday 17 September and with the collaboration of Merck Pharmaceutical company we held a round table virtual symposium with the former ESC president professor Roberto Ferrari, FESC discussing the Role of Beta blockers in Hypertension managements.
- **3** On Friday 10 of September the IqSH represented by its president professor Ghazi F. Haji held a Discussion in Qasr Alkaram Res. about the Antihypertensive drugs sponsored by Awamedica company.
- **4** " Focus on the management of hypertension in pregnant women" was the title of the scientific session with participation of Acino Pharmaceuticals on 13 August in the same place.
- **5** On Friday sixth of August Dr Ghazi discussed a topic entitled highlighted topics in Hypertension",
- **6** With the collaboration of Astra Zeneca Pharmaceutical company a Panel discussion was held in Babylon hotel entitled "A-Z interact Hypertension" on 9 of July 2021.
- **7** A virtual Webinar with distinguished speakers Dr.Elie Chammas cardiology MD, Dr Raed Owaysha cardiology MD from Amman ,Jordan and Prof. Abdulhameed AL-Qaseer IM, MD. , Baghdad entitled "Stable Pressure means healthy Beating heart" arranged by Sanofi pharmaceutical on 11.6. 2021.
- **8** Also the IqHS held a special consolation ceremony for the martyrs souls of the Ibn Al- Khateeb hospital disaster on 25 of April 2021.
- **9** On ninth of April 2021 IqHS also held a scientific symposium "Hypertension in Iraqi people" with Multiple IqHS speakers sponsored by Acino company.











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Hypertension in polycystic ovarian syndrome (PCOS)

Prevalence:

he reported prevalence of hypertension varied around the world, with the lowest prevalence in rural India (3.4% in men and 6.8% in women) and the highst prevalence in Poland (68.9% in men and 72.5% in women). (1)Polycystic ovary syndrome (PCOS), a heterogeneous endocrine and metabolic disorder affecting 6% to 10% of women of reproductive age, is associated with ovulatory dysfunction, abdominal obesity, hyperandrogenism, and in many cases hypertension and profound insulin resistance. (2). Women with polycystic ovarian syndrome (PCOS) showed a higher prevalence of high blood pressure compared to women without PCOS, regardless of race or ethnicity (3).

The prevalence of hypertension in women with PCOS is around 40% [4, 5].

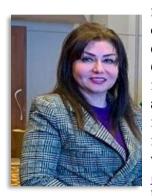
A considerably increased risk (relative risk of 7.4) of developing myocardial infarction was observed for women with PCOS compared to age-matched referents.(6),.Women with PCOS are more likely to be overweight or obese, have diabetes, higher triglyceride levels (4), and more susceptible to get stroke, 19% higher risk of developing cardiovascular disease especially in their 30 and 40 years (5) women with signs and symptoms of metabolic syndrome may have elevated blood pressure, with a systolic blood pressure of 130 mm Hg or higher and a diastolic blood pressure of 85 mm Hg or higher (7). Observed increased risk for hypertension in PCOS women seems to be associ

ated with insulin resistance and hyperinsulinemia. Both conditions interfere with the endothelium-dependent vasodilatation

mechanisms causing vascular muscle wall hypertrophy. Obesity and insulin resistance are considered key factors for the alteration of blood pressure in PCOS women (8). And can add hypertension to their long list of metabolic complications (3, 4), women with PCOS also develop a hyperactive response to stress (8)



The heterogeneity of the disorder suggests that there are subpopulations within the syndrome. Hypertension and insulin resistance are not uniformly present, and hypertension may be absent despite profound insulin resistance and vice versa [9]. It is not clear whether PCOS increases the risk of CVD independently of the metabolic syndrome [10].



Dr Raghdaa Dheyaa Sadeq

Specialist physician Public health directorate MOH

Prevention

To prevent high blood pressure starts with:

- Living a healthy lifestyle.
- Maintaining normal body weight
- Exercising routinely.
- Following a healthy diet.
- Eat Less Salt.
 - Add More Fruits and Vegetables: The DASH (Dietary Approaches to Stop Hypertension) proof that fruits and vegetables help to reduce blood pressure in women with PCOS due to nutrients rich materials such as magnesium, calcium, and potassium, which work to counteract the effects of high sodium in the bodies.
 - Emphasizes Nuts, Seeds, and Legumes: including 4 to 5 servings a week provide a good source of fiber, magnesium and potassium to lower blood pressure.
 - Omega-3 fatty acids that found in fish, nuts, avocados, and olive oil(3)
 - Encouraged young women with PCOS to stay positive: "PCOS can be a distressing condition & may cause anxiety and depression. (5).

Medications:

If diet and lifestyle interventions are not effective, medications can be used including diuretics, calcium channel blockers, ACE inhibitors, or beta-blockers(3). It is hypothesized that spironolactone treatment could ameliorate endothelial dysfunction in PCOS women. Recently it was shown that telmisartan, angiotensin II receptor antagonist poses insulin sensitizing capacity to activate PPAR (peroxisome proliferator-activated receptors) gamma and mediate favorable metabolic and reproductive effects in hypertensive PCOS women(8).

References:

- [1] Kearney, Patricia M^a; Whelton, Megan^a; Reynolds, Kristi^a; Whelton, Paul K^{a,b}; He, Jiang^{a,b}, a systematic review, Journal of Hypertension: January 2004 Volume 22 Issue 1 p 11-19)
- [2] Susan M Sirmans and Kristen A Pate, Epidemiology, diagnosis, and management of polycystic ovary syndrome,

- Clin Epidemiol. 2014; 6: 1–13, Published online 2013 Dec 18. doi: 10.2147/CLEP.S37559, PMCID: PMC3872139, PMID: 24379699, PMC.)
- [3] Angela G., Richard N. F.: High Blood Pressure and PCOS, very well health journal, December 12, 2019).
- [4] Johanna Schmidt Kerstin Landin-Wilhelmsen Mats

 BrännströmEva Dahlgren, *The Journal of Clinical Endo-*crinology & Metabolism, Volume 96, Issue 12, 1 December 2011, Pages 3794–3803, https://doi.org/10.1210/
- jc.2011-1677, Published: 01 December 2011)
 [5] Sophia *Antipolis*, Young women with polycystic ovary syndrome have raised risk of heart disease, *Risk Factors and Prevention*, European society of cardiology, 03 Aug 2020
- [6] E. Dahlgren M.D.,P. O. Janson,S. Johansson,L. Lapidus,A. Odén,, (Polycystic ovary syndrome and risk for myocardial infarction: Evaluated from a risk factor model based on a prospective population study of women, First published: December 1992, Citations: 333, AOGS journal
- [7] Richard Scott Lucidi, What does a finding of high blood pressure suggest in women with polycystic ovarian syndrome (PCOS)?, Sep 19, 2019
- [8] (Macut, Djuro; Mladenović, et al , Hypertension in Polycystic Ovary Syndrome: Novel Insights, Current Hypertension Reviews, Volume 16, Number 1, 2020, pp. 55-60(6)
- [9]. Zimmermann S, Phillips RA, Dunaif A, Finegood DT, Wilkenfeld C, Ardeljan M, Gorlin R, Krakoff LR: Polycystic ovary syndrome: lack of hypertension despite profound insulin resistance. J Clin Endocrinol Metab. 1992, 75: 508-513. 10.1210/jc.75.2.508, PubMed 10. Cattrall FR, Healy DL: Long-term metabolic, cardiovascular and neoplastic risks with polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaccol. 2004, 18: 803-812. 10.1016/j.bpobgyn.2004.05.005.

Reverse dipping and its contribution to hypertension outcome

uring the past 4 decades, combined office and out-of-office blood pressure (BP) measurements (self-measured home BP or 24-hour ambulatory BP monitoring) have been recognized to provide a more accurate assessment of BP status and are increasingly applied in clinical and research settings. Overall, combined office and home or 24-hour ambulatory BP measurements define four different BP phenotypes: (1) sustained normotension (ie, normal office and out-of-Office

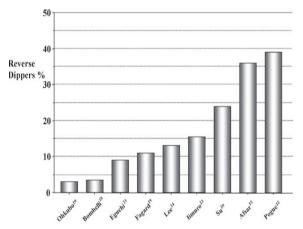
BP); (2) sustained hypertension (elevated in -office and out-of- office BP); (3) white-coat hypertension, alternatively termed isolated clinic hypertension (elevated

office and normal out-of- office BP); and (4) masked hypertension (normal office and elevated out-of-office BP). These BP patterns have been reported to substantially differ in terms of prevalence, demographic and clinical characteristics, and burden of subclinical organ damage as well as risk of cardiovascular morbidity and mortality. Furthermore, by providing a much larger number of BP readings

during 24 hours compared with office and home BP measurements, ambulatory BP monitoring offers the opportunity to evaluate day-night BP variability. A circadian rhythm of BP has been documented in the majority of normotensive and hypertensive individuals, with nighttime BP values being 10% to 20% lower than daytime values due

to the reduction in sympathetic tone and the parallel increase in vagal activity during the sleep period [2]

According to recent hypertension guidelines, assessment of nocturnal BP values and dipping status is enabled by 24-h ambulatory blood pressure monitoring (ABPM), which allows the classification of



patients in four different circadian BP phenotypes: (a) dipping: physiological decrease of 10–20%; (b) non-dipping: reduction of night-time BP less than 10%; (c) reverse dipping RD: a rise of night-time BP; and (d) extreme dipping: a night-time BP decrease higher than 20%[1]

A growing amount of evidence indicates that non dippers have more marked cardiac and extracardiac organ damage compared with patients with preserved nocturnal BP fall and, more importantly, an increased likelihood of cardiovascular events. Reverse or inverted dipping represents an extreme, not rare, alteration in circadian BP rhythm, usually regarded as a particularly harmful BP phenotype.



Dr Samer M. Yousaf Internist & Echocardiographer

Prevalence

Data on the prevalence of RD profile have been reported in population-based samples as well as in several clinical settings including those with hypertension, chronic kidney disease (CKD), diabetes mellitus, and sleep apnea syndrome (Figure 1) range from 3.5 - 39 % and in those studies. RD were more likely to be men and have a longer duration of hypertension and taking a larger number of antihypertensive medications.

Association with subclinical organ damage

A consistent body of evidence supports the view that quantitative markers of organ damage (ie, increased QRS voltage/duration, left ventricular mass index, carotid intima-media thickening, pulse wave velocity, urinary albumin excretion, and reduced glomerular filtration rate) are associated with a higher incidence of cardiovascular events. Ivanovic and colleagues[3] were able to demonstrate that LVH rates increased progressively from extreme dippers (5%) to dippers (9%), non dippers (17%), and reverse dippers (31%, P<.01 vs all groups). Proteinuria in reverse dippers was 66% higher than in dippers and approximately four-fold greater than in extreme dippers.

In patients with RD and non dipper hypertensive patients, common carotid intima-media thickness was significantly higher. In a study including 524 hypertensive patients, RD pattern was the strongest independent variable in predicting the presence of mild carotid plaques. Lee and colleagues [4] demonstrated a significant association between RD and cerebral white matter changes;

Association with cardiovascular disease

A further line of research has investigated the link between RD and overt cardiovascular disease in a variety of clinical settings such as cognitive impairment/vascular dementia, stroke, coronary heart disease, and heart failure ,RD pattern was

found to be the most important predictor of lacunar infarction, cerebral microbleeds, 1.5 fold increase in coronary artery disease risk, an independent correlate of heart failure with preserved systolic function and had an increased risk of renal death and cardiovascular events compared with patients with preserved circadian BP rhythm, independently of 24-hour systolic BP levels. Of note that alteration in BP dipping not only associated with adverse cardiovascular events but also with Many psychological dimensions. For example, high levels of alexithymia, expressed by difficulty identifying and describing feelings, were associated with extreme and nondipping patterns in a sample, including hypertensive and normotensive people[2]

Therapeutic interventions

Although reversal of altered circadian BP profiles is considered a therapeutic target for improving cardiovascular prognosis in hypertensive patients, no studies have addressed this topic in the setting of RD. Nonetheless, data concerning therapeutic interventions in patients with less extreme alterations in BP circadian rhythm (ie, nondippers) show some benefits. Available evidence on bedtime administration of antihypertensive drugs aimed to normalize nocturnal BP supports the view that this approach may be protective against cardiovascular risk associated with a disrupted BP rhythm. In a retrospective analysis including 1279 patients, telmisartan (a long-acting angiotensin II receptor antagonist with a high smoothness index) normalized circadian BP pattern to a dipper profile in a larger proportion of patients compared with ramipril and reduced early-morning nighttime BP control has recently been investigated by the MAPEC study [5].

The investigators evaluated whether bedtime therapy with one or more hypertensive drugs was able to control BP and reduce cardiovascular risk more effectively than conventional therapy administration (ie, all antihypertensive drugs taken in the morning hours). After a follow-up of 5.6 years, participants taking one or more BP-lowering medications at bedtime had a lower nighttime BP as well as a reduced prevalence of non dipping/ RD status than patients taking all drugs upon awakening. Importantly, the tighter control in nocturnal BP was associated with a substantial decrease (–60%) in relative risk of cardiovascular events.

CONCLUSIONS

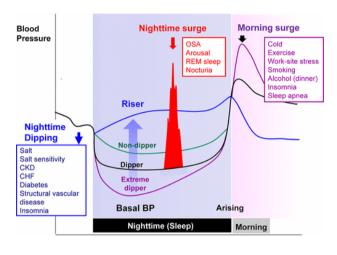
A paradoxical BP increase during sleep has been documented during 24-hour BP monitoring. This impaired circadian BP hythm, although of marginal prevalence in general population samples (<5%), has been reported to be up to 10 times more prevalent in patients with hypertension, type 2 diabetes mellitus, CKD, and sleep apnea syndrome. Because of the high cardiovascular risk associated with RD, an appropriate antihypertensive chronotherapeutic approach to this condition should be performed to improve cardiovascular prevention.

References

- [1] Cesare Cuspidi MD, Carla Sala MD, Marijana Tadic MDet al. Clinical and prognostic significance of a reverse dipping pattern on ambulatory monitoring: An updated review. *J Clin Hypertens*. 2017;19:713–721
- [2] Maria Casagrande 1,*, Francesca Favieri 2, Viviana Langher. The Night Side of Blood Pressure: Nocturnal Blood Pressure Dipping and Emotional (dys)Regulation et al. Int. J. Environ. Res. Public Health 2020, 17, 8892.
- [3] Ivanovic BA, Tadic MV, Celic VP. To dip or not to dip? The unique relationship between different blood pres-

sure patterns and cardiac function and structure. *J Hum Hypertens*. 2013;27:62-70.

- [4] Lee S, Thomas RJ, Kim H, et al. Association between high nocturnal blood pressure and white matter change and its interaction by obstructive sleep apnoea among normotensive adults. *J Hypertens*. 2014;32:2005-2012.
- [5] Hermida RC, Ayala DE, Mojón A, Fernández JR. Influence of circadian time of hypertension treatment on cardiovascular risk: results of the MAPEC study. *Chronobiol Int*. 2010;27:1629-1651



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Nonsteroidal Mineralocorticoid Receptors Antagonists in Cardiorenal Medicine

Ala Ali, MD FASN, FACP, FRCP

fibroblasts, and immune cells. They are involved in studies concluded that finerenone improved urinary fluid and electrolytes homeostasis and, notably, albumin excretion in patients with CKD and type II with tissue remodeling mechanisms. The overactiva- DM compared to placebo. It also induced a 30% or tion of these receptors will lead to more inflamma- more reduction in NT-proBNP levels in a similar protion and fibrosis. Thus, Mineralocorticoid Receptors portion of patients with eplerenone. These positive Antagonists (MRAs) inhibit this overactivation rep- conclusions are supported by less hyperkalemia, resent a potential target for managing heart and mainly if used at low doses. Esaxerenone is apkidney disease. It is now sixty years since the approv-proved for the treatment of essential hypertension al of the first steroidal MRA, spironolactone, for car- in Japan. diovascular protection beyond the diuretic effect. In 2002, the second one, eplerenone added to the group for hypertension management. In addition, finerenone, the nonsteroidal group includes esaxerenone, and apararenone, which were introduced in the last few years.

The steroidal MRAs act on the steroid receptor subfamily. This subfamily also includes receptors for glucocorticoids, estrogen, and progesterone. Conversely, the nonsteroidal antagonists act selectively on the mineralocorticoid receptors. In addition, the steroidal MRAs have a predilection for the kidneys. In contrast, the nonsteroidal MRAs have a balanced heart and kidney distribution. At equal doses, the nonsteroidal MRAs are more potent inhibitors of inflammation and fibrosis. Furthermore, they resulted in good blood pressure lowering effects and more antiproteinuric capability. In addition, steroidal MRAs have relative or absolute contraindications in advanced kidney disease. At the same time, these novel drugs cause less deterioration in renal function and less hyperkalemia. These advantages could permit the use of such agents as an add-on in hypertension, retarding progression of CKD, diabetic renal disease, proteinuric renal disease, and heart failure management.

The classical clinical scenario would be a diabetic patient with the cardiorenal disease. Two study platforms addressed this. The first trial is on kidney outcomes in diabetic patients using finerenone (FIDELIO-DKD; N=5734). The other one is looking for

ineralocorticoid receptors are expressed in the safety and tolerability of finerenone in patients many tissues and cells like the heart, kidney, with heart failure (FINEARTS-HF; N=2000). These

> In conclusion, MRAs could play a key role in retarding the progression of kidney and heart disease. Thus, Nonsteroidal MRAs should establish their role in cardiorenal medicine.

References:

- [1] Gomez-Sanchez E, Gomez-Sanchez CE. The multifaceted mineralocorticoid receptor. Compr Physiol 2014;4:965 -994.
- [2] Kolkhof P, Bärfacker L. 30 YEARS OF THE MINERALO-CORTICOID RECEPTOR: Mineralocorticoid receptor antagonists: 60 years of research and development. J Endocrinol. 2017 Jul;234(1):T125-T140. doi: 10.1530/JOE-16-0600.
- [3] Agarwal R, Kolkhof P, Bakris G, Bauersachs J, Haller H, Wada T, Zannad F. Steroidal and non-steroidal mineralocorticoid receptor antagonists in cardiorenal medicine. Eur Heart J. 2021 Jan 7;42(2):152-161.
- [4] Bakris GL, Agarwal R, Anker SD, Pitt B, Ruilope LM, Rossing P, Kolkhof P, Nowack C, Schloemer P, Joseph A, Filippatos G; FIDELIO-DKD Investigators. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. N Engl J Med. 2020 Dec 3;383 (23):2219-2229.
- [5] Bayer. Study to Evaluate the Efficacy (Effect on Disease) and Safety of Finerenone on Morbidity (Events Indicating Disease Worsening) and Mortality (Death Rate) in Participants with Heart Failure and Left Ventricular Ejection Fraction (Proportion of Blood Expelled per Heart Stroke) Greater or Equal to 40% (FINEARTS-HF); 2020. https://clinicaltrials.gov/ct2/show/NCT04435626 (4 September 2020).

Immunity and Inflammation in Hypertension A Long Way To Go

FRANCISCO J RIOS*

 \P iven the impact of the immune system in cardiovascular diseases and that patients with high blood pressure exhibit increased plasma inflammatory mediators and immune cells infiltration in the cardiovascular and renal tissues, it comes as no surprise that biomedical research is focused on applying these observations to hypertension research, and this has been under intense investigation in the past 15 years 3,4,5 Hypertension is a multifactorial disease, that involves different pressor mediators, oxidative stress, genetic predisposition, and lifestyle. The immune system is educated according to the challenges received over the years, and if individuals with predisposition to hypertension have more pressor mediators and oxidative stress, the low-grade inflammation will be present during life. Therefore, it is expected that the inflammation and immune response observed in these different scenarios are different, at least qualitatively. Current research about the immune system in hypertension models shows the importance of activation of subpopulations of macrophage s, dendritic cells presenting modified endogenous molecules, activation of CD4+ and CD8+ T lymphocytes, including subpopulations of CD4+ T cells, such as regulatory T, and more recently gamma-delta T cells in several hypertensive models5,4. The activation of granulocytes has also been observed, since NET (Neutrophil Extracellular Traps) formation by activated neutrophils are important mediators of vascular injury6,7. Therefore, it is important to determine whether these different arms of the inflammation and immune activation system play an important role according to time and model of hypertension

development and organ damage. All these studies are very exciting and bring new paradigms and concepts to the research in hypertension.

*Institute of Cardiovascular and Medical Sciences, BHF Glasgow Cardiovascular Research Centre, University of Glasgow,

COVID19 and Hypertension: Are We Facing a Syndemic?

NICOLAS F. RENNA ^

he term "syndemic" refers to synergistic health problems that affect the health of a population in its social and economic context. Coronavirus disease 2019 (COVID-19), indiced severe, acute respiratory syndrome Coronavirus 2 (SARSCoV- 2), has become a global pandemic that is responsible for millions of deaths worldwide. High blood pressure is an important risk factor for cardiovascular disease and causes 7.5 million deaths per year (12.8% of all deaths annually). The global burden of disease study suggests that systolic blood pressure is accountable for the highest proportion of premature death, with 212 million years lost1. Early benign case series did not indicate an excess of hypertension in people admitted to hospital with COVID-192. Some later data showed a higher case fatality in patients with hypertension although not related for age3. New evidence from medical records in England, suggests that hypertension is not associated with hospital mortality from COVID -19, hazard ratio (HR) 0.95, (95% CI 0.89-1.01). In sensitivity analyses, selfdiagnosed hypertension was associated with a slightly higher risk (HR 1.07, 95% CI 1.00-1.15)4. Although some studies have concluded that hypertension could be a clinical predictor of severity, the mechanism by which hypertension leads to an increased risk of COVID-19 is undoubtedly complex and may well be related to the underlying comorbidity. The prognosis for people with hypertension is markedly worse when COVID-19 infection is complicated by myocardial injury and in the presence of cardiovascular disease6. Target organ damage and cardiovascular events associated with poor blood pressure control increase with age. Therefore, it seems plausible that they may explain the observed associations between age, hypertension, and severity of COVID-19 infection.

[^] Department of Pathology, Hospital Español de Mendoza, National University of Cuyo, IMBECU-CONICET, Mendoza, Argentina

Are antihypertensive medications a serious risk of COVID-19 disease? From the beginning of the pandemic, many patients wondered whether they should discontinue these treatments, and inevitably some will have. The concern was fueled by the recognition that coronavirus 2 enters cells by binding to a component of the renin- angiotensin system, particularly ACE2. High-quality, large-scale, case-controlled, observational cohort studies reported that chronic treatment with ACEIs or ARBs was not associated with an increased risk of becoming infected with SARS-CoV-2, or of being hospitalized or dying from COVID-198. However, it is well known that observational studies have important limitations. The advent of randomized clinical trials (RCT) was very important. Cohen J et al.9 report the first results of an RCT (the REPLACE COVID trial) examining the impact of continuing or withdrawing chronic ACEI or ARB treatment in 152 hospitalized COVID-19 patients at 20 international centers. This study showed that the results for patients previously treated with ACEIs or ARBs and hospitalized for COVID-19 were similar, regardless of whether treatment with renin-angiotensin system inhibitors was continued or suspended during their hospital admission. Further reassurance comes from the fact that the conclusions of this REPLACE COVID trial are broadly consistent with the results of an RCT previously presented in the BRACE CORONA study. All hypertensive patients can be confident that continuing their current medications is safe and desirable. Hypertension and COVID-19: What controversies remain? The relationship between blood pressure level and SARS-CoV-2 susceptibility or outcome in COVID-19 patients has not been sufficiently investigated, and the potential blood pressure target value in these patients is still unknown. The influence

Salt and Hypertension

CESAR ROMERO*

high-salt intake is a pernicious habit, especially for people with hypertension, heart, and kidney diseases. For many years, epidemiological studies have shown negative outcomes of high

salt intake. More recently, scientific evidence is elucidating the pathophysiological mechanisms associated with this habit. Some of these concepts have been presented at the 2021 ESH-ISH Joint Meeting. The classical view that high-salt diet increases fluid intake, inducing extracellular space expansion, to later eliminate excess sodium and water has been challenged recently. A new mechanism, named natriuretic-ureotelic regulation, has been proposed, where the kidneys optimize the renal concentration mechanisms to excrete more sodium and less free water, preventing sodimassociated osmotic diuresis1. This requires the generation of a massive production of osmolytes (urea) from a catabolic-proteolytic state (mainly in skeletal muscle). The subsequent muscle and liver urea generation ultimately increases plasma urea concentration, expands extracellular space, potentiates the kidney medullary concentration mechanism with less free water excretion, and favors metabolic water generation. Additionally, the muscle's catabolic state is accompanied by a significant energy expenditure of the osmolyte generation. This process has been demonstrated by administering high-salt diets to rodents and a few healthy humans but not in larger population studies. However, during the Glasgow meeting, Giacomo Rossito (Glasgow, UK) presented data exploring the natriuretic-ureotelic regulation hypothesis in a retrospective cohort analysis of essential hypertensive patients. Using metabolomic analysis, he showed that patients with high salt intakes (> 5 gr/day) presented higher urinary sodium excretion with less free water excretion, higher urea levels, and more end products of protein catabolism or the urea cycle than those with low salt intakes. These results support the smaller original studies, proposing a new concept in salt and water homeostasis. It is unclear how much the natriuretic- ureotelic mechanism affects hypertension genesis and hypertensive organ damage. However, this

^{*}Renal Division, School of Medicine, Emory University, Atlanta, Georgia, USA

study obligates physicians and researchers to consider this mechanism in the study of salt and water homeostasis. Additionally, the Rossito's research has confirmed that patients on high-salt diets exhibit higher rates of glomerular filtration and glomerular hyperfiltration. Previous studies in animals have shown that a high salt intake could lead to glomerular hyperfiltration. These results may arise from a positive autoregulatory feedback mechaism on the connecting tubule, mediated by the epithelial sodium channel (ENaC), called connecting tubule-glomerular feedback, that may explain these findings. During the ESH-ISH Meeting, chloride has also been discussed, as problems related to a highsalt diet involve not only sodium but also chloride. Thus, previous studies have shown that replacing chloride with other anions, such as citrate, evokes neither the same extracellular space expansion nor the blood pressure changes associated with high-salt diets. Additionally, specific chloride transports, such as the bicarbonatechloride exchanger Pendrin, are key in sodium reabsorption and blood pressure regulation. In this regard, Dr.Michael Stowasser (Brisbane, Australia) explored the expression of kidney transports through urinary extracellular vesicles (uEVs) analysis coupled with liquid chromatography tandem mass spectrometry. Their results showed for the first time in humans the increased abundance of Pendrin in patients with primary aldosteronism compared with low-renin essential hypertensive patients. However, no changes in the sodiumchloride channel (NCC) or aquaporin 2 (Aqp 2) were observed. Unfortunately, no ENaC subunits were detected in the uEVs. These findings also confirm previous studies in rodents, where Pendrin abundance was observed in aldosteroneinfused animals. Additionally, chloride's role was highlighted during an oral kidney session at the

conference. Dr. Puyol (Buenos Aires, Argentina) presented the effect of the anion chloride on the induction of oxidative stress on a high-salt diet. This revealed the chloride anion was associated with more glutathione peroxidase activity than the sodium cation in the kidney cortex, favoring



a prooxidative state. Outside of the kidney, Dr. Constantino ladecola (NY, USA) revealed the mechanisms associated with high salt intake and cognitive impairment. In animal studies, high salt, independently of blood pressure levels, induces endothelial dysfunction in the brain. This

السيطرة على ضغط الدم المرتفع في العراق مازالت غير مقدرة

البروفيسور غازي الحجي

رئيس الجمعية العراقية لارتفاع ضغط الدم

في البلدان النامية بما في ذلك العراق ، يعد الانتشار المرتفع لارتفاع ضغط الدم وضعف التحكم في ارتفاع ضغط الدم من العوامل المهمة في زيادة وباء أمراض القلب والأوعية الدموية. في العراق ، تبلغ نسبة ارتفاع ضغط الدم حوالي 30.8٪ بين عامة السكان. وان معدل انتشار ارتفاع ضغط الدم في العراق أعلى مقارنة بتونس (% 30.6) ، اليونان (% 30.5) ، تركيا (% 31.8) والأردن (15٪).

التحدي الرئيسي فيما يتعلق بارتفاع ضغط الدم هو ارتفاع عدد المرضى الذين لايزال الضغط غير مسيطر عليه عندهم. وبقاء هذا الضغط المرتفع لديهم قد يؤدي إلى مرض الشريان التاجي وتضخم القلب وفي النهاية فشل القلب. كما يختلف عدد مرضى ارتفاع ضغط الدم غير المسيطر عليه حسب البلدان , ففي الولايات المتحدة الأمريكية ، أظهر تحليل البيانات المأخوذة من المسح الوطني لفحص الصحة والتغذية 2010-2003 (NHANES) أنه من بين المرضى المصابين بارتفاع ضغط الدم في عموم السكان ، لم يتم التحكم في ارتفاع ضغط الدم عند 35.8 مليون (53.5٪) عند عتبة 140/90 مم زئبق , وفي الوقت نفسه ، في أوروبا ، كانت معدلات التحكم في ضغط الدم بين الحالات المعالجة بارتفاع ضغط الدم 40٪ و 30٪ و 20٪ و 10٪ على التوالي في إنجلترا وألمانيا وإيطاليا وإسبانيا والسويد عند عتبة 140/90 ملم زئبق من 1997 إلى 1990. وبالمثل ، لم يتم التحكم في ارتفاع ضغط الدم إلى المستويات الموصى بها من الضغط في حوالي نصف (50.4٪) من المرضى خلال الفترة من حزيران (يونيو) الدم إلى المستويات الموصى بها من الضغط في حوالي نصف (50.4٪) من المرضى خلال الفترة من حزيران (يونيو) إلى كانون الأول (ديسمبر) 2006 في الأردن.

في العراق ، كانت السيطرة على ضغط الدم دون المستوى الأمثل مما يحتم تنفيذ استراتيجيات فعالة وممكنة لزيادة التحكم في ضغط الدم لتقليل المضاعفات المرتبطة به.

على الصعيد العالمي ، كان من الصعب تفسير المعدلات المنخفضة التحكم في ضغط الدم بالرغم من وفرة الأدوية التي تبدو جيدة التحمل وقليلة الاعراض الجانبية لإدارة ارتفاع ضغط الدم . وتعتبر القدرة على الحصول على الرعاية ، وأنماط الممارسة الطبية ، وتثقيف المريض ، وضعف الامتثال للعلاج الموصوف وملف تعريف القلب والأيض للمريض حواجز أمام التحكم في ضغط الدم. ومع ذلك ، يتم تحديد ضغط الدم أيضًا من خلال عوامل أخرى ، بما في ذلك العمر وشدة المرض والعادات الصحية والسيطرة المبكرة على الامراض المصاحبة .

ارتفاع ضغط الدم و متلازمة تكيس المبايض (PCOS)

د رغداء صادق

طبيبة اختصاص / قسم الصحة العامة في وزارة الصحة

انتشار المرض:

أظهرت الدراسات بان النساء المصابات بمتلازمة تكيس المبايض (PCOS) اكثر عرضه للاصابة بارتفاع ضغط الدم مقارنة بالنساء غير المصابات بمتلازمة تكيس المبايض حوالي 40٪ ، كما لوحظ وجود خطر متزايد بشكل كبير (خطر نسبي) لحدوث احتشاء عضلة القلب لدى النساء المصابات بمتلازمة تكيس المبايض مقارنة بالنساء الغير مصابات لنفس الفئة العمرية ، كذلك فان النساء المصابات بمتلازمة تكيس المبايض أكثر رضة لزيادة الوزن أو السمنة ، مرض السكري ، مع ارتفاع مستويات الدهون الثلاثية ، وهم أكثر عرضة للإصابة بالسكتة الدماغية ، وأمراض القلب والأوعية الدموية بنسبة 19٪ خاصة في عمر 30 و 40 و 40 عامًا . وقد يبلغ ضغط الدم الانقباضي 130 ملم زنبق أو اكثر وضغط الدم الانبساطي 85 ملم زنبق أو اكثر وهذه الزيادة في الضغط مرتبطة بمقاومة الانسولين وفرط ألاسولين في الدم وقد تتداخل كلتا الحالتين مع آليات توسع الأوعية نتيجة حدوث خلل في بطانة الاوعية الدموية مسببة تضخم مرتبطة بمقاومة الأنسولين وفرط ألانسولين وفرط ألانسولين في الدم وقد تتداخل كلتا الحالتين مع آليات توسع الأوعية نتيجة حدوث خلل في بطانة الاوعية الدموية مسببة تضخم مرتبطة بمقاومة الأنسولين وفرط ألانسولين في الدم وقد تتداخل كلتا الحالتين مع آليات توسع الأوعية نتيجة حدوث خلل في بطانة الاوعية الدموية الانسولين فهي لاتحدث عند الجميع وانما بشكل متفاوت، فقد لايحدث ارتفاع ضغط الدم على الرغم من وجود مقاومة للانسولين والعكس صحيح . لم يشت لدد الان بان متلازمة تكيس المبايض تزيد من خطر الإصابة بأمراض القلب والأوعية الدموية بشكل مستقل او انها تحدث نتيجة خلل في متلازمة التمثيل الغذاني .

الوقاية:

- 1. اتباع أسلوب حياة صحى.
- المحافظة على وزن جسم مثالي.
- 3. ممارسة النشاط الرياضي بشكل روتيني.
 - 4. اتباع نظام غذائي صحى.
 - 5. الاقلال من تناول الملح
- 6. الاكثار من تناول الفواكه والخضروات: اعتمادا على ((DASH (الأساليب الغذائية لوقف ارتفاع ضغط الدم) أن الفواكه والخضروات تساعد على خفض ضغط الدم لدى النساء المصابات بمتلازمة تكيس المبايض لكونها غنية بالمغذيات مثل المغنيسيوم، الكالسيوم، والبوتاسيوم، والتي تعمل على تحجيم ناثير ارتفاع الصوديوم المتناول في الطعام على الجسم.
- 7. الاكثار من تناول المكسرات والبذور والبقوليات: بحيث لاتقل عن (4 إلى 5 حصص في الأسبوع) كونها تمثل مصدرًا جيدًا للألياف والمغنيسيوم والبوتاسيوم والتي تساعد في خفض ضغط الدم.
 - 8. تناول الأغنية الغنية باحماض (أوميغا 3) الدهنية الموجودة في الأسماك والمكسرات والأفوكادو وزيت الزيتون
- إ. تشجيع النساء المصابات بمتلازمة تكيس المبايض (PCOS) على البقاء إيجابيات وممارسة الحياة بشكل طبيعي كون ان
 المتلازمة تكون مزعجة لمعظم النساء وقد تسبب القلق والاكتناب

العلاج الدوائي:

في حال عدم كفاية التداخلات الاخرى من نمط النظام الغذائي ونمط الحياة وغيرها ، فيمكن استخدام الأدوية المخفضة للضغط بانواعها وحسب الحالة.

كما يمكن استخدام (diuretics, calcium channel blockers, ACE inhibitors, or beta-blockers) مثل (spironolactone) مثل الذي يحدث في بطانة الاوعية عند المصابات بالتكيس.

النكوص العكسى ومساهمته في ارتفاع ضغط الدم

د. سمير مجيد

Reverse dipping and its contribution to hypertension outcome

اختصاص باطنية وايكو

خلال العقود الأربعة الماضية ، تم التعرف على قياسات ضغط الدم المشتركة في المكتب وخارج المكتب (قياس ضغط الدم في المنزل أو مراقبة ضغط الدم المتنقل على مدار 24 ساعة) لتوفير تقييم أكثر دقة لحالة ضغط الدم ويتم تطبيقها بشكل متزايد في الإعدادات السريرية والبحثية. بشكل عام ، تحدد قياسات ضغط الدم المتنقل في المكتب والمنزل أو على مدار 24 ساعة أربعة أنماط ظاهرية مختلفة للضغط ال) ضغط طبيعي مستدام ؛ (2) ارتفاع ضغط الدم المستمر (ضغط الدم المرتفع في العيادة وخارج العيادة) ؛ (3) ارتفاع ضغط الدم ذو الغلاف الأبيض ، ويطلق عليه بدلاً من ذلك ارتفاع ضغط الدم المعزول في العيادة ؛ و (4) ارتفاع ضغط الدم المقنع. تختلف أنماط ضغط الدم هذه اختلافًا كبيرًا من حيث الانتشار والخصائص الديموغرافية والسريرية وعبء تلف الأعضاء تحت الإكلينيكي بالإضافة إلى خطر المراضة القلبية الوعانية والوفيات. علاوة على ذلك ، ومن خلال توفير عدد أكبر بكثير من قراءات الضغط خلال 24 ساعة مقارنة بقياسات الضغط في المكتب والمنزل لذلك توفر مراقبة الضغط المتنقلة فرصة لتقييم تقلب الضغط في النهار والليل.

وفقًا لإرشادات ارتفاع ضغط الدم الحديثة ، يتم تمكين تقييم قيم ضغط الدم الليلية وحالة الغمس من خلال مراقبة ضغط الدم الإسعافية على مدار 24 ساعة (ABPM) ، مما يسمح بتصنيف المرضى في أربعة أنماط ظاهرية مختلفة من الضغط اليومي: (أ) النكوص: انخفاض فسيولوجي بمقدار 10 - 20٪ ؛ (ب) عدم النكوص: تقليل ضغط الدم الليلي بنسبة أقل من 10٪ ؛ (ج) النكوص العكسي (غع): ارتفاع ضغط الدم الليلي بنسبة تزيد عن 20٪.

تشير كمية متزايدة من الأدلة إلى أن مرضى عدم النكوص لديهم تلف ملحوظ في أعضاء القلب وخارج القلب مقارنة بالمرضى الذين يعانون من انخفاض ضغط الدم الليلي المحفوظ، والأهم من ذلك، زيادة احتمالية حدوث أحداث قلبية وعائية. يمثل النكوص العكسي أو المعكوس تغيرًا شديدًا، وليس نادرًا، في إيقاع ضغط الدم اليومي، وعادة ما يُنظر إليه على أنه نمط ظاهري ضار بشكل خاص من الضغط.

كانت نسبة النكوص العكسي وكذلك في العديد من البيئات السريرية بما في ذلك أولئك الذين يعانون من ارتفاع ضغط الدم وأمراض الكلى المزمنة (CKD) ومرض السكري ومتلازمة توقف التنفس أثناء النوم بين 3.5 إلى 39 ٪، وكانت نسبة النكوص العكسي أكثر احتمالا من الرجال الذين لديهم مدة أطول من ارتفاع ضغط الدم، وتناول عدد أكبر من الأدوية الخافضة للضغط.

لقد وجد ان في المرضى الذين يعانون من النكوص العكسي ان سمك بطانة الشريان السباتي الشائع أعلى بشكل ملحوظ من مرضى ارتفاع ضغط الدم الذين لا يعانون من النكوص .

الارتباط بأمراض القلب والأوعية الدموية

قام خط بحث آخر بالتحقيق في الارتباط بين النكوص العكسي وأمراض القلب والأوعية الدموية العلنية في مجموعة متنوعة من الإعدادات السريرية مثل ضعف الإدراك / الخرف الوعائي والسكتة الدماغية وأمراض القلب التاجية وفشل القلب ، ووجد أن نمط النكوص العكسي هو أهم مؤشر على الإصابة بالاحتشاء الجوبي ، نزيف دماغي دقيق ، زيادة في مخاطر الإصابة بأمراض الشريان التاجي بمقدار 1.5 مرة، ارتباط مستقل بين قصور القلب والوظيفة الانقباضية المحفوظة وزيادة خطر الوفاة الكلوية والأحداث القلبية الوعائية مقارنةً بالمرضى الذين يعانون من إيقاع ضغط الدم اليومي المحفوظ ، بصرف النظر عن مستويات ضغط الدم الانقباضي على مدار 24 ساعة .

تجدر الإشارة إلى أن التغيير في انخفاض ضغط الدم لا يرتبط فقط بأحداث قلبية وعانية ضارة ولكن أيضًا مع العديد من الأبعاد النفسية. على سبيل المثال ، ارتبطت المستويات العالية من الألكسيثيميا ، والتي يتم التعبير عنها بصعوبة تحديد ووصف المشاعر ، بأنماط متطرفة وغير منكوصة في عينة ، بما في ذلك الأشخاص الذين يعانون من ارتفاع ضغط الدم وضغط الدم العادي .

لذلك يجب تنفيذ نهج العلاج الزمني المناسب الخافض للضغط لهذه الحالة لتحسين الوقاية من القلب والأوعية الدموية.