

White Coat Syndrome; A Reality Beyond the Myth. A review of the Literature

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Abstract

Introduction: White coat syndrome is not considered a real syndrome or disease it is phenomenon that occurs to patients when going to the doctor or going through the measurement of blood pressure when in the patient's blood pressure figures are higher than the values taken at home. This event is due to multiple factors which influence the increase in the reading of blood pressure.

Methods: The aim of this search was to identify the most highly cited articles in the Medical literature to provide clinicians an adequate approach to this phenomenon when it is diagnosed. Articles identified were reviewed for first autor, year of publicaton, Article name, Publisher and journal impact factor, article type, and number of citations.

Results: A number of 20 most-cited articles from a list of 167 journals were included in this study by research articles on topics such as Hypertension (cited 1450 times) and White coat (cited 568 times). The oldest paper with most citations was written in 1988. 9 of the 20 top-cited articles were published in Hypertension, followed by Journal of the American College of Cardiology.

Conclusion: This study identified the most frequently cited medical articles in the field of White-Coat Syndrome, published in journals indexed in Web of Science. Providing a resource to clinicians to guide them in the field of White Coat Hypertension and how to handle and treat it.

Keywords: White-Coat Syndrome, Hypertension, blood presure.

INTRODUCTION

White coat syndrome was described by Riva-Rocci¹ more than 100 years ago. This syndrome is not considered a real syndrome or disease but rather a warning reaction or phenomenon that usually occurs to a large number of patients when going to the doctor or going through the measurement of blood pressure. The phenomenon of white coat syndrome occurs when in the doctor's office the patient's blood pressure figures are higher than the values taken at home or on an outpatient basis.

The white coat syndrome, it is influenced not only by the presence or absence of the doctor or nurse, but also the place where the measurement takes place, the doctor's office, or, also, the interaction of both factors. It is likely that the white coat hypertension

is not a specific reaction to the doctor, as the name suggests, but a response induced by the accumulated knowledge of the subject that turns the doctor's office into a threatening environment.

This temporary increase in blood pressure and heart rate, as well as an elevation of catecholamines is only identifiable by continuous monitoring (beat to beat) of the blood pressure and heart rate, by means of invasive methods (intra-arterial blood pressure sensor) or non-invasive (digital plethysmography). Hypertensives patients can also suffer from this phenomenon and this does not mean that their tension is not well controlled with the treatment. A simple taking of vital signs, such as measuring blood pressure, can increase or trigger blood pressure, and this depends on the patient's negative predisposition, which will lead him

to present levels above his “normal” average. However, it is necessary to consider that this is an event that is due to multiple factors which influence the increase in the reading of blood pressure, all of them associated with an increase in the heartbeat. The phenomenon of white coat hypertension is associated more with characteristics such as advanced age, psychosocial (anxiety, depression, hypochondria) and cultural factors, or less common badly calibrated instruments for measuring blood pressure.

It is estimated that between 25% and 35% of hypertensive patients also have a white coat resistance for which they present higher than real measurements in the medical consultation and that could indicate that their disease is not well controlled when this is not the case.

The presence of White coat hypertension does not exclude the existence of hypertension, since a significant percentage of hypertensive patients have it. Since the definition of white coat syndrome requires the existence of normotension out of consultation and the presence of “reaction of white coat”, does not exclude that we are in a hypertensive patient, the confirmation diagnosis of White coat hypertension requires performing outpatient blood pressure registry to all patients in whom this complication is suspected, since the values of the self-measurement of the arterial pressure may not be sufficiently precise in this regard^{24,25}. Even so, the correlation between the values obtained by self-measurement of blood pressure seems good, which makes this technique very useful as a screening test and in the subsequent follow-up of patients with white coat hypertension detected. The criteria for suspecting white coat hypertension have been gathered in table 1²⁶.

Table 1. *Criteria for suspected White Coat Hypertension*

- Discordance between blood pressure figures and target organ damage.
- Differences between blood pressure in consultation and at home or pharmacy.
- Asymptomatic hypertensive crises without response to treatment.
- Repeated hypotension in treated patients.
- Hypertension refractory to treatment.
- Latent hypertension.

METHODS

The objective of this study was to identify the top cited articles and reviews in the Medical literature and report on their characteristics. Citation analysis is an important measurement for assessing the academic significance of a paper². We sought to provide clinicians, and researchers with resources for identifying the highest-impact literature in White coat hypertension, a frequent phenomenon without an adequate approach when it is diagnosed³.

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement⁴.

Exclusion criteria for these review included: prehospital journals and journals with a non-physician focus. Inclusion criteria for each individual article were the following: it had to be primarily White Coat Hypertension-related or include White Coat Hypertension subjects relevant to clinicians; the journal where the article or review was published had to be in Web of Science index.

The aim of this search was to identify the most highly cited articles published about White Coat Hypertension in journals but also the most highly articles related to White Coat Hypertension and its complications. The key words were: “White-Coat” & “Hypertension”. Articles were placed in descending order of number of citations in an Excel spreadsheet.

Articles were assigned for review and recorded the following information: (1) first autor, (2) year of publicaton, (3) Article name, (4) Publisher and journal impact factor, (5) article type, and (6) number of citations.

RESULTS

A list of 167 journals of the type of “White Coat Hypertension” were identified. The 20 most-cited articles were included in this study. (Table 2). The number of citations ranged from 1450 to 7. Articles were listed in descending order with a rank from 1-20 based upon the number of citations, as found in Web of Science at the time of the search. The 20 top-cited articles were published in English (Table 3): Hypertension (9) published the largest number of papers, followed by Journal of the American College of Cardiology (3); Journal of the American Medical Association (1); Journal of Human Hypertension (1); Nature Reviews Cardiology (1); Clinical and Experimental Pharmacology and Physiology (1) American Journal of Hypertension (1); Journal of Hypertension (1); Current Hypertension Report (1) and Swiss Medical Weekly (1).

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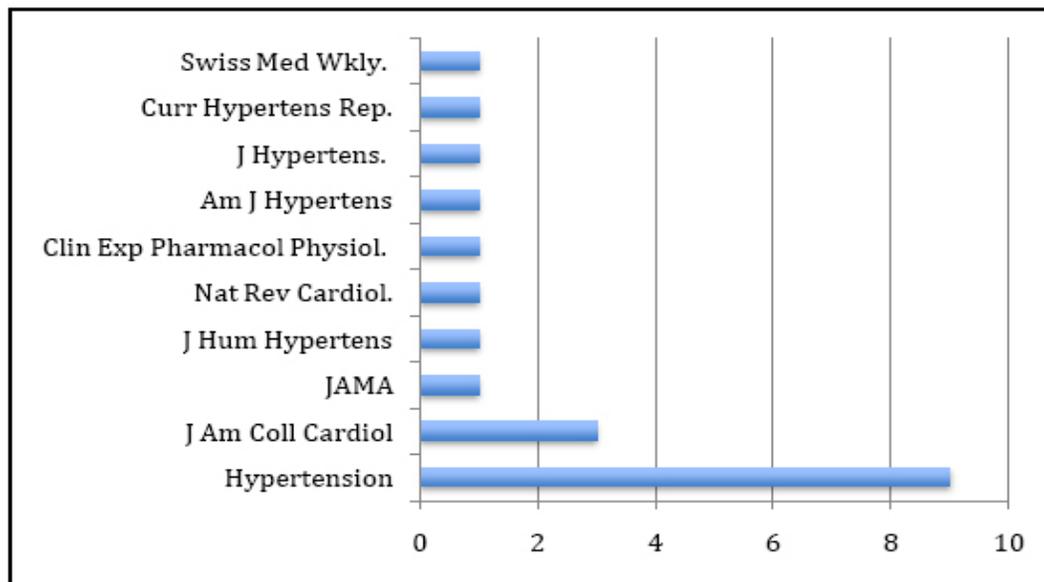
Table 2. Most cited White Coat Hypertension articles

Rank	First Author	Year	Title	Journal; Impact Factor	Category	Number of citations
1	Pickering, TG	1988	How Common Is White Coat Hypertension?	Journal of the American Medical Association; 3.83	Article	1450
2	Ohkubo, T	2005	Prognosis of "Masked" Hypertension and "White-Coat" Hypertension Detected by 24-h Ambulatory Blood Pressure Monitoring	Journal of the American College of Cardiology; 2.08	Article	568
3	Gustavsen, PH	2003	White coat hypertension is a cardiovascular risk factor: a 10-year follow-up study	Journal of Human Hypertension; 2.79	Article	203
4	Franklin, SS	2012	Significance of White-Coat Hypertension in Older Persons With Isolated Systolic Hypertension	Hypertension; 6.69	Article	166
5	Franklin, SS	2013	White-Coat Hypertension New Insights From Recent Studies	Hypertension; 6.69	Review	108
6	Stergiou, GS	2014	Prognosis of White-Coat and Masked Hypertension	Hypertension; 6.69	Article	102
7	Mancia, G	2013	Long-Term Prognostic Value of White Coat Hypertension	Hypertension; 6.69	Article	88
8	Tientcheu, D	2015	Target Organ Complications and Cardiovascular Events Associated With Masked Hypertension and White-Coat Hypertension: Analysis From the Dallas Heart Study.	Journal of the American College of Cardiology; 18.45	Article	70
9	Mancia, G	2011	Diagnosis and management of patients with white-coat and masked hypertension.	Nature Reviews Cardiology; 5.16	Article	61
10	Shih-Hsien, S	2013	White Coat Hypertension Is More Risky Than Prehypertension	Hypertension; 6.69	Article	47
11	Martin, CA	2014	White-coat hypertension.	Clinical and Experimental Pharmacology and Physiology; 2.01	Review	37
12	Franklin, SS	2016	The Cardiovascular Risk of White-Coat Hypertension	Journal of the American College of Cardiology; 19.89	Article	36
13	Cacciolati, C	2013	Blood pressure variability in elderly persons with white-coat and masked hypertension compared to those with normotension and sustained hypertension.	American Journal of Hypertension; 0.59	Article	29
14	Kang, YY	2015	Accuracy of home versus ambulatory blood pressure monitoring in the diagnosis of white-coat and masked hypertension.	Journal of Hypertension; 2.89	Article	24
15	Mancia, G	2014	Effect of Long-Term Antihypertensive Treatment on White-Coat Hypertension	Hypertension; 6.69	Article	23
16	Myers, MG	2012	Pseudoresistant Hypertension Attributed to White-Coat Effect	Hypertension; 6.69	Review	23

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17	Satoh, M	2016	Long-Term Stroke Risk Due to Partial White-Coat or Masked Hypertension Based on Home and Ambulatory Blood Pressure Measurements	Hypertension; 6.85	Article	16
18	Mancia, G	2015	Adverse Prognostic Value of Persistent Office Blood Pressure Elevation in White Coat Hypertension	Hypertension; 6.35	Article	14
19	Cuspidi, C	2016	White Coat Hypertension: to Treat or Not to Treat?	Current Hypertension Report; 2.49	Review	8
20	Sebo, P	2014	White coat in primary care: what do patients think today?	Swiss Medical Weekly; 0.60	Article	7

Table 3. Journals of the 20 top-cited articles



It was calculated the Pearson correlation coefficient (r) to determine if the age of the article was correlated to the number of citations received and it was found that there was a negative correlation between the year of publication and the number of citations ($r = -0,94$), meaning that the more recently published articles were cited less often. The greatest number of articles were classified as articles (16) and reviews (4). Four of these articles were review papers while sixteen were original articles related to White Coat Hypertension Syndrome and its consequences. Six of which included the complications of the syndrome and three articles summarized the best treatment for that syndrome.

The oldest paper, written in 1988, ranked 1st, while the most recent articles, published in 2016, ranked 12th, 17th and 19th. The most frequently cited article was "How Common Is White Coat Hypertension?" by Pickering, published in Journal of the American Medical Association in 1988 and based on a study of

Twenty-one percent of 292 patients with untreated borderline hypertension (clinic diastolic blood pressures persistently between 90 and 104 mm Hg) who were found to have normal daytime ambulatory pressures. This fact defined these patients as having "white coat" hypertension. Most of these patients were younger women, with lower weight and more recently diagnosed than patients whose pressure was elevated both in the clinic and during ambulatory monitoring, these patients did not show a generalized increase of blood pressure lability, nor an exaggerated pressor response while at work; typical phenomenon from "White coat hypertension". This article was cited 1450 times. In contrast, the less cited paper was written in 2014, ranked 20th and titled "White coat in primary care: what do patients think today?", an article where it is described that patient preference for their doctor's attire can influence their assessment of the quality of care²³.

DISCUSSION

The top-cited articles represent the most influential articles in the field^{5,6,7,8,9}. The 20 papers were all published in English, probably because English is the most common language used in medical journals. The top 20 papers were published in 10 journals (table 2). The journal that included the largest number of papers was Hypertension (9), indicating that the high level of articles about White Coat Hypertension were published in this journal because it plays an important role in this field. The impact factor of the Hypertension journal was the most important indicator of the number of citations, and a large proportion of the most-cited papers were published in this journal. However, this was not borne out by our study. The Journal of the American College of Cardiology; which had the highest impact factor (19.89 in 2016, 18.45 in 2015) on the journal list, published fewer articles than Hypertension. This result suggests that citations are not necessarily affected by the journal impact factor because various other factors contributed to the citations for certain journals.

The aim of this study was to identify the 20 most frequently cited articles White Coat Syndrome and to examine their characteristics in order to gain insight into the history and main developments of this syndrome. It is of interest to note that articles published in the journals of medium – lower level of impact factor^{5, 6, 7} attracted more citations than those published in higher levels of impact factor.

The findings from this study show that the in most cited articles^{5, 6, 7, 8, 9}, The significance of white-coat hypertension in older persons with isolated systolic hypertension remains poorly understood, because persons with white-coat and masked hypertension, would not have been diagnosed accurately with exclusive use of conventional clinic or office blood pressure measurements; and in untreated subjects, those with white-coat hypertension the cardiovascular risk was similar in subjects with normal blood pressure. Despite many investigations controversy persists, and extent of increased cardiovascular risk in Isolated systolic hypertension patients as well as in patients with white-coat hypertension as compared with a normotensive population^{17, 18, 19, 20}.

Several studies have attempted to compare the evidence of target organ damage in the patient with White coat hypertension compared to normotensive

and hypertensive patients. Several publications have established that patients with white coat hypertension were more likely to present with microalbuminuria²⁶, functional and or structural cardiac abnormalities and metabolic alterations than normotensive patients⁴. The presence of increased sodium reabsorption in the proximal tubule has also been demonstrated, similar to patients with true hypertension⁷, as well as hemodynamic alterations similar to hypertension^{9,11}.

Other studies^{9,11,12,13}, suggested that the cardiovascular risk of patients suffering from white coat hypertension is very low, practically similar to normotensive patients. It has been suggested that white coat hypertension could be a precursor to sustained hypertension and it seems that the possibility of a patient evolving to clinical hypertension also depends on the blood pressure detected in the outpatient blood pressure record. The study of Mancia¹⁸, in a short follow-up, suggested that it did not improve.

The effect of the pharmacological treatment on the white coat reaction seems to be scarce, if not absolutely absent²⁸. Virtually only central agents such as clonidine and blockers of the alpha adrenergic pathway at the peripheral level are limitedly effective. However, the clinical correspondence of these results is not so clear, although it has been shown that doxazosin could reduce clinical blood pressure in patients with white coat hypertension²⁸.

Thus, a significant number of patients with refractory hypertension will in fact have a white coat hypertension that is truly rebellious to any treatment that is performed.

The clinicians should be aware that untreated subjects with white-coat hypertension may still be at increased cardiovascular risk, which will be dependent on associated factors. For researchers of cardiovascular outcomes the review highlights the necessity to define the risk associated with white-coat hypertension^{5,6,7,12}.

In conclusion, hypertension carries the same risk as sustained hypertension untreated and treated subjects, whereas white-coat hypertension is a risk factor in untreated but not in treated subjects^{13,15,19}.

Limitations

This study has several limitations: the fact that articles were researched in only one database, the Web of Science. It is possible that a search performed in a different database, such as SCOPUS, may have provided

additional articles or slightly different search findings. Self-citation and citations in text books and lectures could not be investigated in this study. In addition, the authors tended to cite papers from the journals to which they submit their own research studies

CONCLUSIONS

This study identified the most frequently cited White Coat Hypertension journals in the field of medicine, published journals indexed in Web of Science. The results identified impactful articles that were collected by the number of citations, providing a resource to others while identifying trends that may be used to guide in the field of White Coat syndrome and how to handle and treat it. These review should be taken into account in the management of hypertension in clinical practice, to identify those patients with White Coat Hypertension.

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Citation: Dr. M. A. Lopez-Ruiz. *White Coat Syndrome; A Reality Beyond the Myth. A review of the Literature. Open Access Journal of Internal Medicine*. 2018; 1(1): 25-31.

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