

Masked Hypertension in Adolescents with Type 1 Diabetes Mellitus: An Exploratory Study

Bachar Afandi^{a, b} Bassam Bernieh^a Sana Roubi^a Juma Al Kaabi^{a, b}^aDepartment of Internal Medicine, College of Medicine and Health Sciences, United Arab Emirates University, Al-Ain, United Arab Emirates; ^bTawam Diabetes and Endocrine Center, Tawam Hospital, Al-Ain, United Arab Emirates

Keywords

Hypertension · Masked hypertension · Blood pressure measurement · Type 1 diabetes mellitus

Abstract

Introduction: Masked hypertension (MHTN) is the finding of elevated out-of-office blood pressure (BP) measurement. This is a pilot study to evaluate the prevalence of MHTN in adolescents with type 1 diabetes mellitus (T1DM). **Patients and Methods:** Normotensive, adolescents with T1DM were recruited from Tawam Adolescents Diabetes Clinic at Tawam hospital, Al Ain, UAE. They consented to wear the ambulatory BP monitoring (ABPM) device. The heart rate and ambulatory BP were recorded at 15-min intervals for 24 h. Abnormal systolic BP (SBP) and diastolic BP (DBP) were defined as readings above 135 and 85 mm Hg; respectively. **Results:** Thirteen patients (10 females) were recruited from “Tawam Adolescents Diabetes Clinic.” The median age was 17 (15–19) years, median BMI 21.4 (14.8–29), and median diabetes duration 9 (3–12) years. All patients had normal retinal examination within the past 12 months. Family history of hypertension (HTN) was present in 6/13 (46%) patients. Office BP measurements revealed a mean DBP \pm SD of 72 ± 6.9 mm Hg and mean SBP \pm SD 116 ± 5.5 mm Hg. The

median HbA1c was 8.4% (5.6–13.7) and median GFR 125 mL/min/m² (87–134). Two patients had microalbuminuria. Twenty-four hour ABPM revealed elevated SBP and DBP in 12.2 and 5.8% of the values; respectively. Further analysis confirmed MHTN in 4 (30%) patients, nondipping pattern of BP in 5 (38%) patients, and elevated pulse pressure in 8 (61.5%) patients. Only 4 (30%) patients had normal studies. **Conclusions:** ABPM uncovered a very high prevalence of MHTN in our patients. Whenever available, ABPM provides an excellent tool for diagnosis and hence early evaluation and management of HTN in adolescents with T1DM. Well-designed large-scale studies are needed to examine the magnitude of MHTN among adolescents with T1DM.

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Introduction

Conventional blood pressure (BP) categorization is based on the average of 2 or more properly taken BP measurements on 2 or more occasions in a healthcare setting. Normal BP is defined by a systolic BP (SBP) <120 mm Hg

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and a diastolic BP (DBP) <80 mm Hg, whereas hypertension (HTN) is defined as either an SBP \geq 140 mm Hg or DBP \geq 90 mm Hg [1].

The prevalence of masked HTN (MHTN) is estimated to range between 10 and 30% of individuals [2]. MHTN was diagnosed by ambulatory BP monitoring in 14% of individuals and by home BP monitoring in 11% of individuals [3]. Patients with MHTN are at increased target organ damage as it is an indicator for increased risk of atrial fibrillation, stroke, CKD, coronary artery calcification, and even mortality from cardiovascular disease [4, 5]. Identification of patients with MHTN is possible using either (a) home BP monitoring or (b) 24-h ambulatory BP monitoring (ABPM) [6].

ABPM is the gold standard to estimate: the mean BP level, diurnal rhythm of BP and estimation of pulse pressure. In clinical practice, the use of ABPM is indicated in patients suspected to have: white-coat HTN, HTN in pregnancy, MHTN, nocturnal HTN, episodic HTN, non-dipping at night, and poor BP control despite appropriate treatment [6]. The accepted phenotypes of HTN measured by ABPM are shown in Table 1; these BP patterns differ markedly in prevalence, clinical characteristics, burden organ damage as well as risk of cardiovascular morbidity and mortality.

The prevalence of MHTN was reported to be 9.5% in youths with type 1 diabetes mellitus (T1DM) [7]. To the best of our knowledge, there is no previous study in the UAE examining the prevalence of MHTN in adolescents with T1DM. Considering the increasing prevalence of T1DM in the MENA region, the literature review has shown scarce publications addressing this issue [8]. This is a pilot study to evaluate the prevalence of masked HTN in adolescents' patients with T1DM.

Patients and Methods

This is a cross-sectional pilot study. We aimed to evaluate the prevalence of MHTN in a sample of adolescent patients with T1DM regularly attending the outpatient Tawam Adolescents Diabetes Clinic at Tawam hospital, Al Ain, UAE. Inclusion criteria included: adolescents with T1DM for at least 3-year duration, aged 15–20 years, postpubertal, and are known to be normotensive on previous visits. Exclusion criteria were prepubertal patients, outside the specified age range, pregnancy, elevated office BP, receiving antihypertensive medications, having evidence of organ damage such as established diabetic retinopathy, abnormal renal function tests, and having overt proteinuria or hematuria. Following written informed consent, patients wore the ABPM device (MOBIL-O-GRAPH NG Version 12. I.E.M. GmbH, Stolberg, Germany) [9]. Ambulatory BP measurements were taken at 15-min in-

Table 1. Phenotypes of BP measured in the office and by ABPM

	In-office BP	Out-of-office BP
Sustained normotension	Normal	Normal
Sustained HTN	Elevated	Elevated
White coat HTN	Elevated	Normal
MHTN	Normal	Elevated

HTN, hypertension; MHTN, masked hypertension; ABPM, ambulatory BP monitoring; BP, blood pressure.

tervals throughout the subsequent 24-h period, and the device was returned the next day.

The study was conducted during the months of October and November 2018. Sixteen patients screened, 3 excluded (1 delayed puberty, 1 true HTN, and 1 did not consent). A total of 13 Patients, 10 females and 3 males were enrolled into the study. All subjects received verbal and written information about the study and written informed consent was obtained from all the study participants.

We evaluated the rates of masked systolic HTN and masked diastolic HTN. Normotensive, adolescents with T1DM were included in this study. After determining the appropriate cuff size, the device was applied to the nondominant arm and comparing ambulatory readings with an office measurement for correlation. To minimize errors and capture adequate number of readings, instructions and education were delivered to the patients and parents by the treating physician and the nurse educator. A record was kept for the activity and sleep periods. In order to obtain a sufficient number of recordings for interpretation, we programmed the device to record the heart rate and ambulatory BP at 15-min intervals for 24 h. The minimum acceptable ABPM readings of the study to be evaluated was 70% of the possible 1,248 readings. This can be obtained with at least 28 readings per subject during the daytime period and at least 10 readings during the nighttime period.

Definitions

SBP and DBP: SBP and DBP thresholds for daytime, 24 h, and nighttime HTN were based on the USA and international guidelines [6, 10].

Clinic office HTN: It was defined as a mean clinic SBP \geq 140 mm Hg or mean clinic DBP \geq 90 mm Hg.

ABPM: Abnormal ABPM, SBP, or DBP was defined as recording readings with a mean above 135 mm Hg systolic and 85 diastolic mm Hg for any time period, respectively.

Masked HTN: Masked HTN was defined as having an elevated mean BP for any ABPM time (day or night) period [9].

Abnormal nighttime dipping: Abnormal nighttime dipping was defined as the absence of 10% lower BP readings during nighttime.

Reverse/or inverted dipping: Reverse/or inverted dipping was defined as a higher nighttime mean BP compared with daytime BP values.

Abnormal pulse pressure: Abnormal pulse pressure was identified when the difference between SBP and DBPs exceeded 55 mm Hg [10–12].

Results

Thirteen subjects with T1DM (10 females) were recruited from Tawam Adolescents Diabetes Clinic. The median age was 17 (15–19), median BMI 21.4 (14.8–29), and median diabetes duration 9 years (3–12). Four patients (30%) treated with multiple daily insulin injections and 9 patients (70%) with an insulin pump. Family history of HTN was present in 6/13 (46%) patients, 1 patient was an active smoker and 1 was treated with thyroxine treatment for primary hypothyroidism. All patients had a normal retinal examination within 12 months prior to the study. Office BP evaluation revealed a mean DBP \pm SD 72 ± 6.9 mm Hg and mean SBP \pm SD 116 ± 5.5 mm Hg. The median HbA1c was 8.4% (5.6–13.7) and median GFR 125 mL/min/m² (87–134). Two patients (15%) had microalbuminuria (Table 2).

The total reported readings of the 24-h ABPM in the study were 909 (72.5% of the planned readings). The 24-h ABPM revealed elevated BP in 18% out of 909 readings recorded for all patients and elevated SBP and DBP recorded in 12.2 and 5.8%, respectively. Further analysis revealed that 4/13 (30%) patients had normal studies and confirmed MHTN in 4/13 (30%) patients, nondipping pattern of BP in 5/13 (38%) patients, and elevated pulse pressure in 8/13 (61.5%) patients (Fig. 1).

Discussion

In the present study, all our adolescents with T1DM patients were initially classified as normotensive by conventional methods. However, the use of ABPM uncovered a very high prevalence of MHTN, nondipping pattern, and wide pulse pressure. These findings are much higher than anticipated and warrants further studies.

ABPM is superior to clinical BP monitoring in detecting and characterizing changes in BP throughout the observation period [13] and in predicting cardiovascular morbidity and mortality [14, 15]. Although the optimal approach for the detection of MHTN is unknown [16, 17], screening individuals with a high risk is the best approach. MHTN has often been shown to progress to sustained HTN in older people and confers a cardiovascular risk almost similar to sustained HTN [18] in both the general population and in patients with diabetes and CKD.

Masked HTN has recently become a topic of interest in youths. ABPM revealed that one-quarter of the participants with type 1 diabetes had MHTN [19]. Children

Table 2. Baseline characteristics of participants

Characteristic	13 patients
Median age	17 years (15–19)
Median BMI	21.4% (14.8–29)
Median duration of DM	9 years (3–12)
Median HbA1c	8.4% and (5.6–13.7)
Median GFR	125 mL/min/m ² (87–134)
Smoking status	1/13 (7.6%)
Family history of HTN	6/13 (46%)
Insulin pump	9/13 (69%)
Retinal examination	13/13 (100%) normal
Proteinuria	2/13 (15%)

DM, diabetes mellitus; HTN, hypertension.

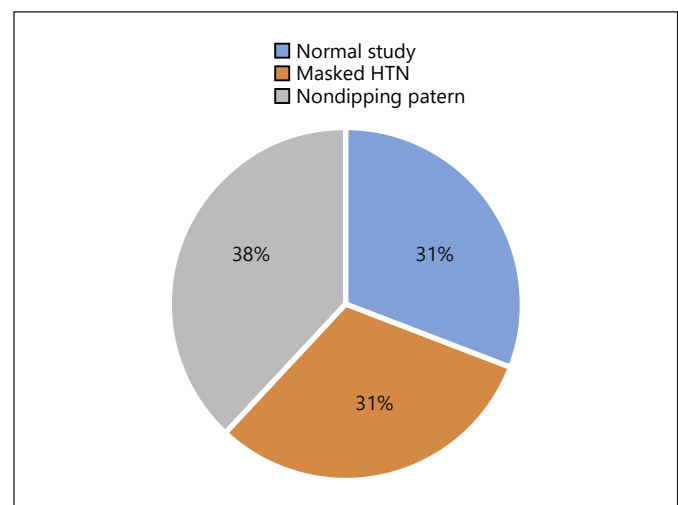


Fig. 1. Ambulatory blood pressure findings. HTN, hypertension.

with MHTN were more likely to be obese, have a positive family history for HTN, and have a higher LV mass index [20–22].

In addition to high MHTN prevalence, our patients had nondipping and/or inverted dipping pattern of BP, a phenomenon that frequently documented in HTN, type 2 diabetes mellitus, CKD, and sleep apnea syndrome. Reverse dipping is considered to be a powerful marker of adverse cardiovascular prognosis [23, 24]. Additionally, increased pulse pressure, an indicator for arterial stiffness, was reported in the majority of our small cohort. Elevated PP in children with T1DM may contribute to the high risk for early development of atherosclerosis [25].

Masked HTN in youth is an entity that is associated with increased prevalence of sustained HTN and in-

creased risk of target organ damage. Therefore, adolescents with T1DM and MHTN should be instructed in lifestyle modifications, monitored closely, and considered for antihypertensive therapy.

The study has a few limitations, including the small sample size, lack of a control group, and lack of normative BP data for regional pediatric populations based on age, gender, BMI, and height. Despite all the taken precautions to obtain accurate readings, technical limitations may be present as the algorithms used in ambulatory oscillometric monitors may vary in children. Saying that, the findings of this study are alarming as possibility of previously unrecognized true hypertensives in the group is high. Considering the high prevalence of genetic predisposition for HTN, presence of overweight or obesity and uncontrolled diabetes, our data warrant future larger, well-structured studies to examine MHTN among young patients with T1DM.

Conclusions

Our cross-sectional pilot study utilizing the ABPM uncovers very high prevalence of masked HTN and cardiac risk indicators in adolescence with T1DM. Whenever available, ABPM provides an excellent tool for diagnosis

and hence early evaluation and management of HTN in adolescents with T1DM. Well-designed large-scale studies are needed to examine the magnitude and determinants of MHTN among adolescents with T1DM.

Statement of Ethics

The study was approved by the Alain Institutional Research Ethics Committee (CR. D 468/16). All subjects have given their written informed consent.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

All authors contributed equally to the conception of the study, data collection and analysis, drafting of the manuscript, and approval of its final version. B.B.: deceased 30 September 2020.

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