



# Non-Dipping Blood Pressure Variations in Juvenile Kazakhs are Derived from Increased Sympathetic Activity and Decreased Parasympathetic Activity Particularly Decreased Daytime Physical Activity

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## ABSTRACT

A large number of adult Kazakhs are reported to have hypertension and to exhibit non-dipping blood pressure variations (BPV). The purpose of this study was to determine whether such non-dipping variations also exist in juvenile Kazakhs. This study aimed to clarify the mechanisms responsible for these non-dipping type BPV by examining the autonomic function and physical activity of juvenile Kazakhs. Briefly, we selected clinically healthy Kazakhs who were aged between 9 and 10 years old from the Xinjiang Autonomous Region of the People's Republic of China. All subjects were active and underwent routine physical, blood, and urine examinations. We also performed ambulatory blood pressure monitoring. We assessed the subjects' autonomic function by performing a frequency domain analysis of their heart rate variability (HRV) and monitored the subjects' physical activity with accelerometry. We analysed systolic blood pressure (SBP) variations with the maximum entropy method (MEM). MEM analysis revealed that the SBP variations of the non-dipping juvenile Kazakhs exhibited a 24-hr periodicity (0.04 1/hr) with a very weak power spectral density. The non-dippers had higher low-frequency/high-frequency (LF/HF) ratios and lower HF/(LF+HF) ratios than the dippers. Neither the 24-hr physical activity scores nor the night-time physical activity scores of the non-dippers and dippers differed significantly. However, the daytime physical activity scores of the non-dippers were lower than those of the dippers. These differences in autonomic function and physical activity might contribute to the generation of weak circadian variations in SBP in juvenile Kazakhs. Thus, these alterations might ultimately lead to the non-dipping SBP variations observed in non-dipping juvenile Kazakhs.

**KEYWORDS:** Blood pressure variation; Non-dipper; Sympathetic; Parasympathetic; Physical activity; Ethnicity; Kazakh; Juvenile

**ABBREVIATIONS:** ABPM: Ambulatory Blood Pressure Monitoring; BPV: Blood Pressure Variations; BL: Body Length; DBP: Diastolic Blood Pressure; ECG: Electrocardiography; FFT: Fast Fourier Transform; HRV: Heart Rate Variability; HF: High-Frequency; LF: Low-Frequency; MEM: Maximum Entropy Method; PSD: Power Spectral Density; PR: Pulse Rate; PRC: Peoples' Republic of China; SD: Standard Deviation; SBP: Systolic Blood Pressure

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## INTRODUCTION

The prevalence of hypertension is high in the northern territory of the Peoples' Republic of China (PRC), where a large number of Kazakhs have been found to display higher blood pressure levels than other minorities [1-4]. We reported that elderly and middle-aged Kazakhs in the Balikun area exhibited an increased prevalence of hypertension [2,3]. We also found that many of them displayed non-dipping systolic blood pressure (SBP) variations [5,6]. Kazakhs have been reported to exhibit reduced cardiac autonomic function-related parasympathetic activity [5,6]. Growing evidence suggests that individuals that exhibit non-dipping blood pressure variations (BPV) are more likely to be older; non-Caucasian; smokers; diabetic; and have target organ damage, such as left ventricular hypertrophy, than those with dipping BPV [7-9]. A few reports have suggested that physical activity plays a role in the mechanisms responsible for non-dipping BPV [10,11]. It has been reported that non-dippers exhibit less physical activity in the daytime and greater physical activity in the night-time [12]. The present study focused on whether non-dipping BPV are also seen in juvenile Kazakhs. We hypothesize that non-dipping BPV in juvenile Kazakhs are caused by the same mechanisms as the non-dipping BPV seen in elderly and middle-aged Kazakhs and that the causative mechanism involves autonomic nervous activity and physical activity [5,6]. However, no information about the prevalence of non-dipping BPV in juvenile Kazakhs or the mechanism responsible for such variations is available at present. Therefore, we decided to perform ambulatory blood pressure monitoring (ABPM) and a frequency domain analysis of heart rate variability (HRV) and to monitor the physical activity of juvenile Kazakhs. In this report, we present BPV, HRV, and physical activity data collected from two groups of juvenile Kazakhs, those that exhibited dipping-type BPV and those that displayed non-dipping-type BPV.

## METHODS AND ETHICS

This study complied with the ethical principles of the Helsinki Declaration and the guidelines for good clinical practice. Each participating institution received approval for the study from their institutional review board. Written informed consent was obtained from all enrolled subjects.

## STUDY POPULATION

We performed cross-sectional surveillance using a previously described procedure [3,5,6]. Briefly, we selected clinically healthy Kazakhs that were aged between 9 and 10 years old from the Balikun region of the Xinjiang Autonomous Region of the People's Republic of China. A total of 40 clinically healthy and active juvenile Kazakhs (males: 21, females: 19) were recruited. All subjects underwent routine physical, blood, and urine examinations as well as chest X-rays. The body mass index was calculated as weight (kg) divided by height. The subjects provided informed consent and were chosen at random based on residence cards from the local government office. All subjects were required to perform their daily physical activities and rest at set times.

### 24-hr BP Monitoring

We defined non-dippers as subjects who exhibited a night-time SBP reduction of less than 10% compared with their daytime SBP. Based on this definition, the juvenile Kazakh subjects were classified into two groups: 1. juvenile Kazakhs that exhibited dipping BPV (9-10 years old,  $n=29$ ) and 2. juvenile Kazakhs that displayed non-dipping BPV (9-10 years old,  $n=11$ ). We used 14

automatic sociometric devices to record the subjects' SBP, diastolic blood pressure (DBP), and pulse rate (PR), as described previously [3]. Meals were taken between the hours of 06:30 and 07:30, 11:00 and 12:00, and 17:30 and 18:30. Each subject was given a diary to record their daily physical activity, including the times at which they ate meals, slept, and micturated. All of the 24-hr measurements, as well as the subjects' daytime and night-time BP levels, are shown as mean values. The 24-hr measurements were averaged at 30-min intervals in order to obtain mean and standard deviation (SD) values. Abnormal SBP values were excluded based on previously reported criteria [3].

### 24-hr Holter ECG Recording

The subjects were monitored for 24 hr with a Holter electrocardiography (ECG) recording system, with the data collection starting 2 hr after the initiation of the ABPM. The ECG data were recorded at a sampling frequency of 256 Hz and stored on a tape recorder, as described previously [5,6]. We performed fast Fourier transform (FFT) analysis every 60 s. We selected ECG recordings with consistent sinus rhythms for analysis, as described previously [5,6].

### Frequency Domain Analysis

We monitored the subjects' autonomic nervous system activity by performing a frequency domain analysis of their HRV, which was recorded using ECG, over 24 hr. The subjects' HRV was calculated using the FFT for each segment, and the following frequency domain variables were calculated: low-frequency (LF) (0.04-0.15 Hz) power ( $\text{ms}^2/\text{Hz}$ ), high-frequency (HF) (0.15-0.40 Hz) power ( $\text{ms}^2/\text{Hz}$ ), the LF/HF ratio, and the HF/(HF+LF) ratio. We analysed the data every minute.

### Spectral Analysis of SBP Variation

After averaging the observed data (every 30 min), the variation in the subjects' SBP was analysed using the maximum entropy method (MEM), as described previously [6]. The main analysis was based on the MEM and the non-linear least squares method.

### Physical Activity

We monitored the subjects' physical activity (physical activity scores) with accelerometry (Life-Corder, Suzuken Co., Tokyo, Japan); i.e., the intensity of the subjects' physical activity was graded on a 10-point scale every 5 min.

## STATISTICAL ANALYSIS

Data obtained using parametric analyses are expressed as mean  $\pm$  SD values, and those obtained using non-parametric analyses are shown as median (Q1, Q3) values. All conventional statistical calculations were performed using the Statistical Analysis System (SAS Institute Inc., SAS Campus Drive, Cary, NC). Inter-group comparisons were carried using two-way analysis of variance (ANOVA) or non-parametric analyses, such as the Mann-Whitney U-test or F-test.  $P$ -values of  $<0.05$  were statistically significant.

## RESULTS

### Physiological Characteristics of Juvenile Kazakhs

As shown in Table 1, the dippers and non-dippers accounted for 72% ( $n=29$ ) and 28% ( $n=11$ ) of the subjects, respectively. The physiological characteristics and mean 24-hr SBP, DBP, and PR values of the dippers and non-dippers did not differ significantly (*n.s.*, Table 1). However, the SBP of the non-dippers was lower

during the daytime and higher during the night-time than those of the dippers (Table 1). The DBP of the non-dippers was lower during the daytime and higher during the night-time than those of

the dippers. The PR of the dippers and non-dippers did not differ significantly at any timepoint.

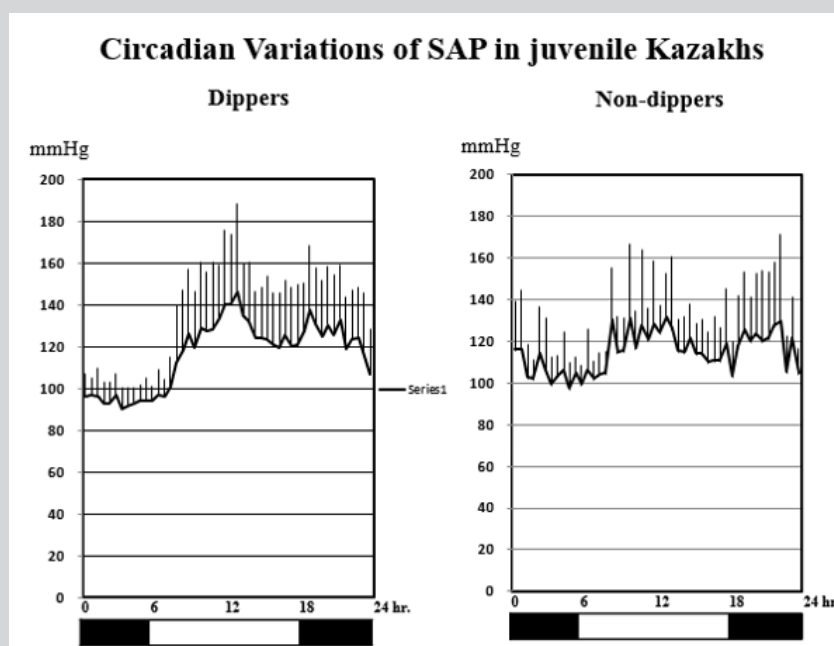
**Table 1:** Physiological characteristics: H: Height; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; PR: Pulse Rate; Mean (SD); n.a: Not Applicable; P-values were calculated using the Kruskal-Wallis test.

Number	Dippers	Non-dippers	p-value
%	29	11	n.a.
Sex ratio	72	28	n.a.
Age (Y/O)	1.5±0.5	1.5±0.5	0.87961
BL (cm)	9.7±0.5	9.8±0.4	0.53325
24hr SBP (mmHg)	139±7	140±7	0.11624
24hr DBP (mmHg)	116 ±8	115±5	0.545567
24hr PR (beats/min)	69±5	69±3	0.60923
Daytime SBP (mmHg)	79±6	79±9	0.86882
Daytime DBP (mmHg)	123±10	117±5	0.02172
Daytime PR (beats/min)	75±7	72±3	0.02663
Night-time SBP (mmHg)	81±7	79±9	0.76261
Night-time DBP (mmHg)	98±7	107±7	0.00041
Night-time PR (beats/min)	56±6	63±7	0.00599

### SBP Variations of the Dipping and Non-Dipping Juvenile Kazakhs

The SBP variations of the dippers exhibited clear circadian variations, with their SBP rising during the daytime and falling at night-time (left and right panels, Figure 1). As expected, the non-dippers demonstrated less marked circadian variations in their SBP than the dippers (left and right panels, Figure 1). The SBP

levels of the dippers and non-dippers differed significantly at many timepoints (dippers vs. non-dippers:  $96 \pm 11$  vs.  $116 \pm 23$  at 0:00;  $97 \pm 8$  vs.  $117 \pm 28$  at 00:30;  $93 \pm 10$  vs.  $102 \pm 9$  at 01:30;  $93 \pm 10$  vs.  $114 \pm 23$  at 02:00;  $92 \pm 9$  vs.  $103 \pm 10$  at 03:30;  $93 \pm 7$  vs.  $106 \pm 19$  at 4:00;  $94 \pm 11$  vs.  $105 \pm 8$  at 05:00;  $96 \pm 9$  vs.  $102 \pm 8$  at 06:30;  $141 \pm 33$  vs.  $125 \pm 13$  at 12:00;  $132 \pm 28$  vs.  $115 \pm 15$  at 13:30;  $127 \pm 23$  vs.  $103 \pm 17$  at 18:00;  $137 \pm 31$  vs.  $117 \pm 25$  at 18:30;  $124 \pm 24$  vs.  $106 \pm 17$  at 22:30; all  $P < 0.05$ ).

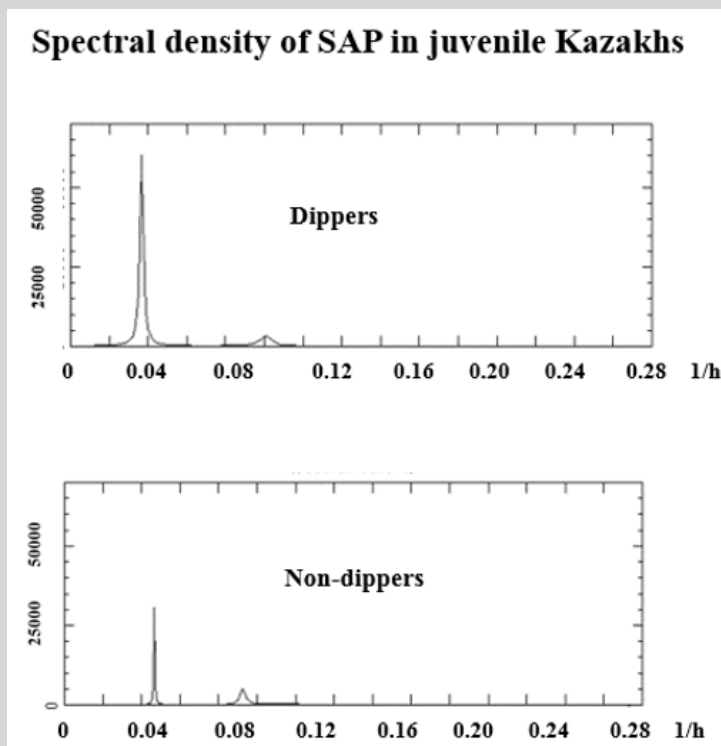


**Figure 1:** Juvenile Kazakhs exhibited clear circadian variations in their SBP, with their SBP rising during the daytime and falling at night-time (left and right panels). However, these circadian variations were less clear in the non-dipping juvenile Kazakhs, as shown in the right panel.

## Spectral Analysis of SBP Variations in Juvenile Kazakhs

We analysed the variations in the mean SBP values of the juvenile Kazakhs using MEM, which revealed that the SBP variations of the dippers and non-dippers displayed a 24-hr

periodicity (approximately 0.04 1/hr) and ultradian variations. The 24-hr periodicity of the dippers' SBP values demonstrated a greater power spectral density (PSD) than that of the non-dippers (upper panel, Figure 2). In fact, the SBP variations of the non-dippers exhibited a 24-hr periodicity with a very weak PSD (lower panel, Figure 2).



**Figure 2:** The SBP variations of the dipping juvenile Kazakhs displayed a 24-hr periodicity (close to 0.04 1/h, and ultradian variations, upper panel) and a greater PSD than that of non-dippers (lower panel). In contrast to those of the dippers, the SBP variations of the non-dippers exhibited a 24-hr periodicity with a very weak PSD and ultradian variations (lower panel).

## Circadian Variations in the LF/HF Ratios of Juvenile Kazakhs

We detected circadian variations in the LF/HF ratios of the juvenile Kazakhs (Figure 3). The LF/HF ratio rose during the daytime (white bar, Figure 3) and fell during the night-time (black bar, Figure 3) in both the dippers and non-dippers (left and right panels, Figure 3). The non-dipping juvenile Kazakhs exhibited higher LF/HF ratios than the dipping juvenile Kazakhs at 36 timepoints (1:05, 1:10, 1:45, 2:30, 3:35, 3:45, 4:15, 4:20, 6:10, 6:45, 6:55, 7:05, 7:55, 8:20, 8:30, 8:35, 8:55, 9:00, 9:15, 9:30, 10:10, 10:20, 13:10, 13:25, 13:30, 14:15, 14:50, 15:25, 15:45, 16:10, 16:30, 19:25, 19:45, 21:45, 22:00, 22:40; all  $P < 0.0497$ ).

## Circadian Variations in the HF/(LF+HF) Ratios of Juvenile Kazakhs

We also detected circadian variations in the HF/(LF+HF) ratios of the juvenile Kazakhs (Figure 4). In contrast to the LF/HF ratio, the HF/(LF+HF) ratio fell during the daytime (white bar, Figure 4) and rose during the night-time (black bar, Figure 4) in both the dippers and non-dippers. The HF/(LF+HF) ratios of the non-dipping juvenile Kazakhs were lower than those of the dipping juvenile Kazakhs at 35 timepoints (1:10, 1:45, 2:30, 3:35, 3:45, 4:15, 4:20, 6:10, 6:45, 6:55, 7:05, 7:55, 8:20, 8:30, 8:35, 8:55, 9:00, 9:15, 9:30, 10:10, 10:20, 13:10, 13:25, 13:30, 14:15, 14:50, 15:25, 15:45,

16:10, 16:30, 19:25, 19:45, 21:45, 22:00, 22:40; all  $P < 0.0497$ ).

## Circadian Variations in the Physical Activity Scores of Juvenile Kazakhs

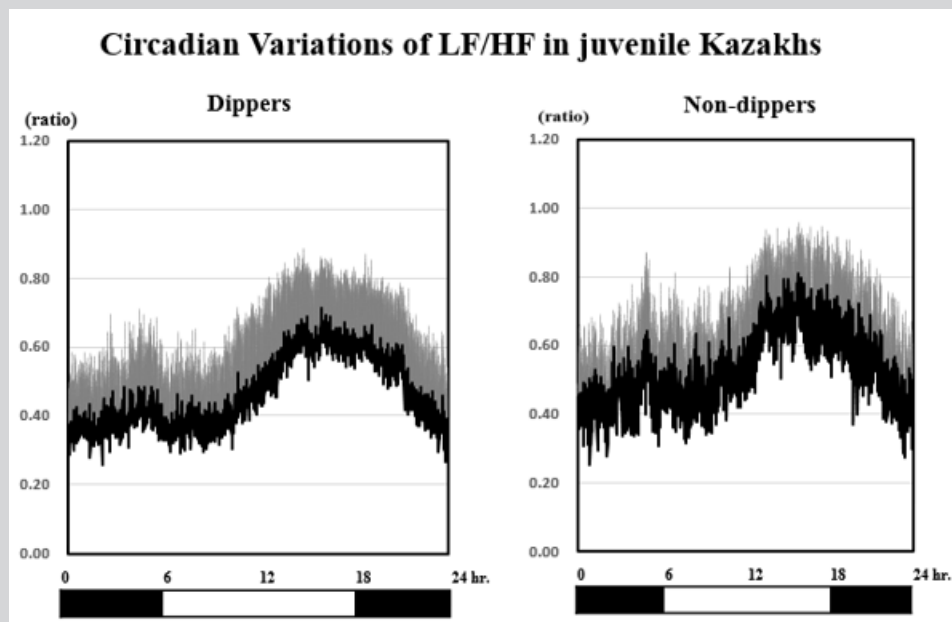
We found that the physical activity scores of the juvenile Kazakhs, which reflected the intensity of their daily physical activity, displayed circadian variations (Figure 5). The physical activity scores of both the dippers and non-dippers rose during the daytime (white bar, Figure 5) and fell during the night-time (black bar, Figure 5). The physical activity scores of the dippers and non-dippers differed significantly at many timepoints (dippers vs. non-dippers:  $1.5 \pm 0.8$  vs.  $1.0 \pm 0.5$  at 9:00;  $1.7 \pm 1.3$  vs.  $1.1 \pm 0.6$  at 10:00;  $1.9 \pm 0.9$  vs.  $0.9 \pm 0.4$  at 13:10;  $1.7 \pm 0.9$  vs.  $0.9 \pm 0.5$  at 13:50;  $1.9 \pm 1.1$  vs.  $1.0 \pm 0.5$  at 14:10;  $1.5 \pm 1.2$  vs.  $0.7 \pm 0.4$  at 15:00;  $1.2 \pm 1.0$  vs.  $0.5 \pm 0.4$  at 15:10;  $1.9 \pm 1.1$  vs.  $0.8 \pm 0.5$  at 17:50;  $1.7 \pm 0.8$  vs.  $1.2 \pm 0.7$  at 18:50;  $1.0 \pm 0.7$  vs.  $0.7 \pm 0.4$  at 21:40, all  $P < 0.05$ ).

## Median LF/HF Ratios, HF/(LF+HF) Ratios and Physical Activity Scores

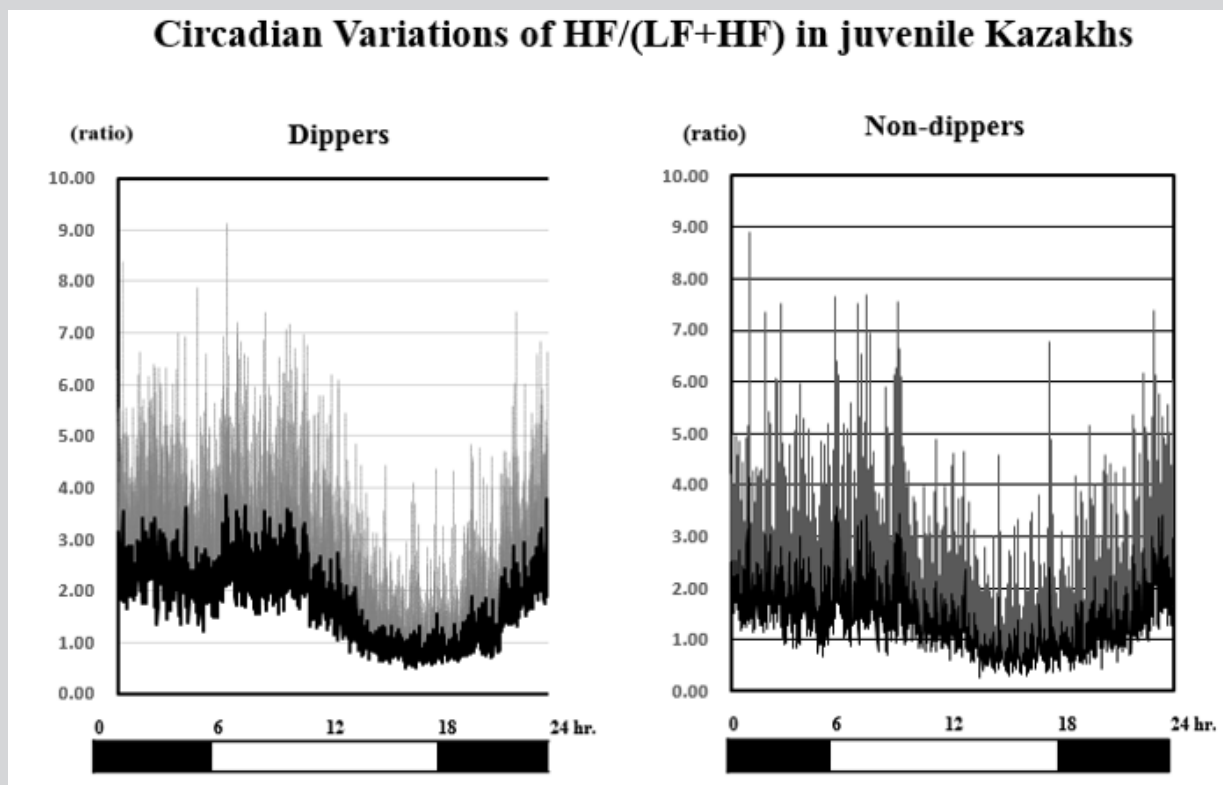
As shown in Figure 6, the non-dippers' LF/HF ratios (24-hr, daytime, and night-time) were higher than those of the dippers (dippers vs. non-dippers: 24-hr: median: 0.43, Q1: 0.37, Q3: 0.57 vs. median: 0.51, Q1: 0.44, Q3: 0.61, Mann-Whitney U-test:  $P = 0.0001$ ,  $F$ -test:  $P = 0.00860$  [left panel, Figure 6]; daytime: median: 0.52, Q1: 0.39, Q3: 0.59 vs. median: 0.56, Q1: 0.48, Q3: 0.66, Mann-Whitney

U-test:  $P=0.0001$ , F-test:  $P=0.0001$  [middle panel, Figure 6]; night-time: median: 0.37, Q1: 0.34, Q3: 0.39 vs. median: 0.42, Q1: 0.38,

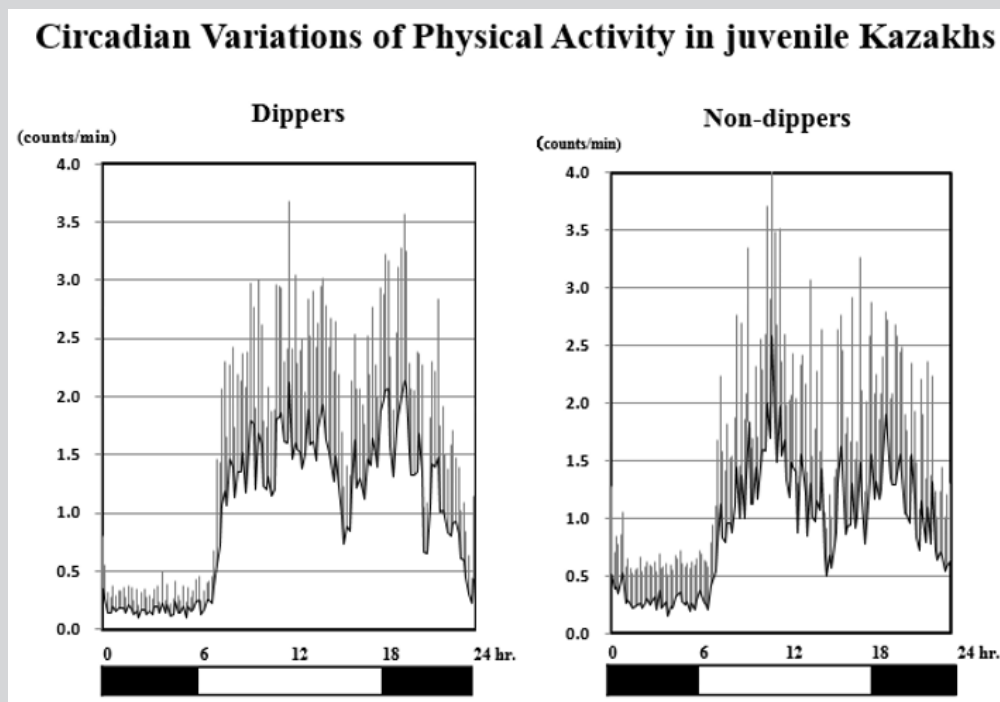
Q3: 0.46, F-test:  $P=0.0001$ , Mann-Whitney U-test:  $P=0.0001$  [right panel, Figure 6].



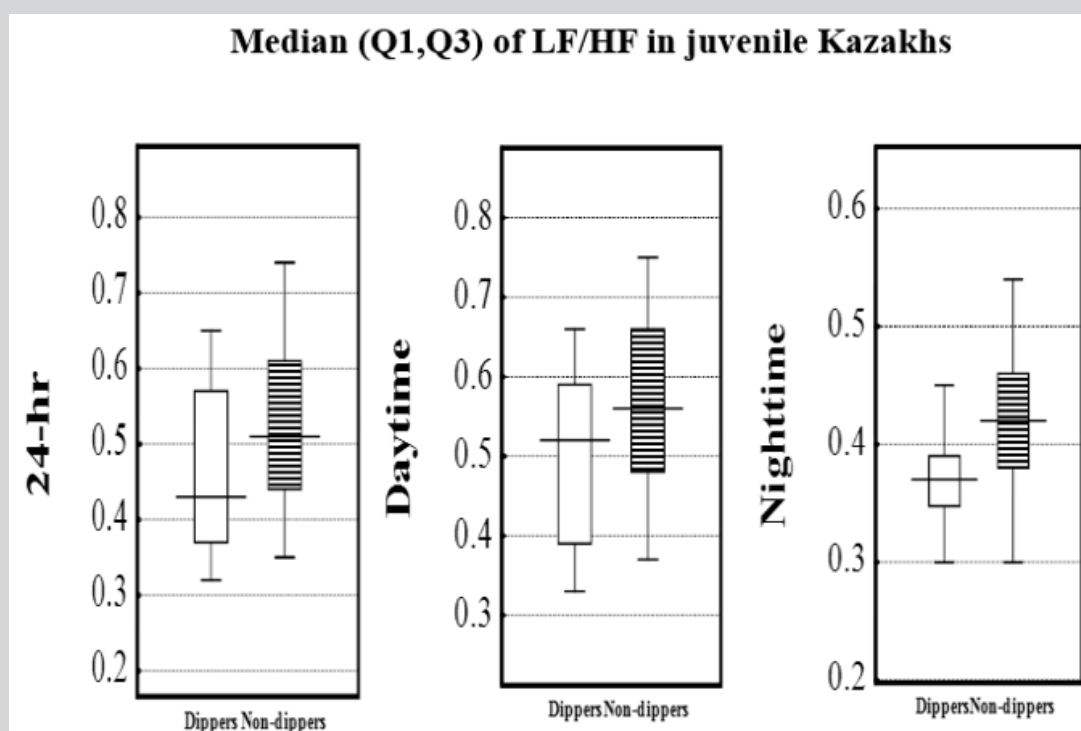
**Figure 3:** The LF/HF ratio rose during the daytime (light bar) and fell during the night-time (dark bar) in both the dipping and non-dipping juvenile Kazakhs.



**Figure 4:** The HF/(LF+HF) ratios fell during the daytime (light bar) and rose during the night-time (dark bar) in both the dippers and non-dippers.



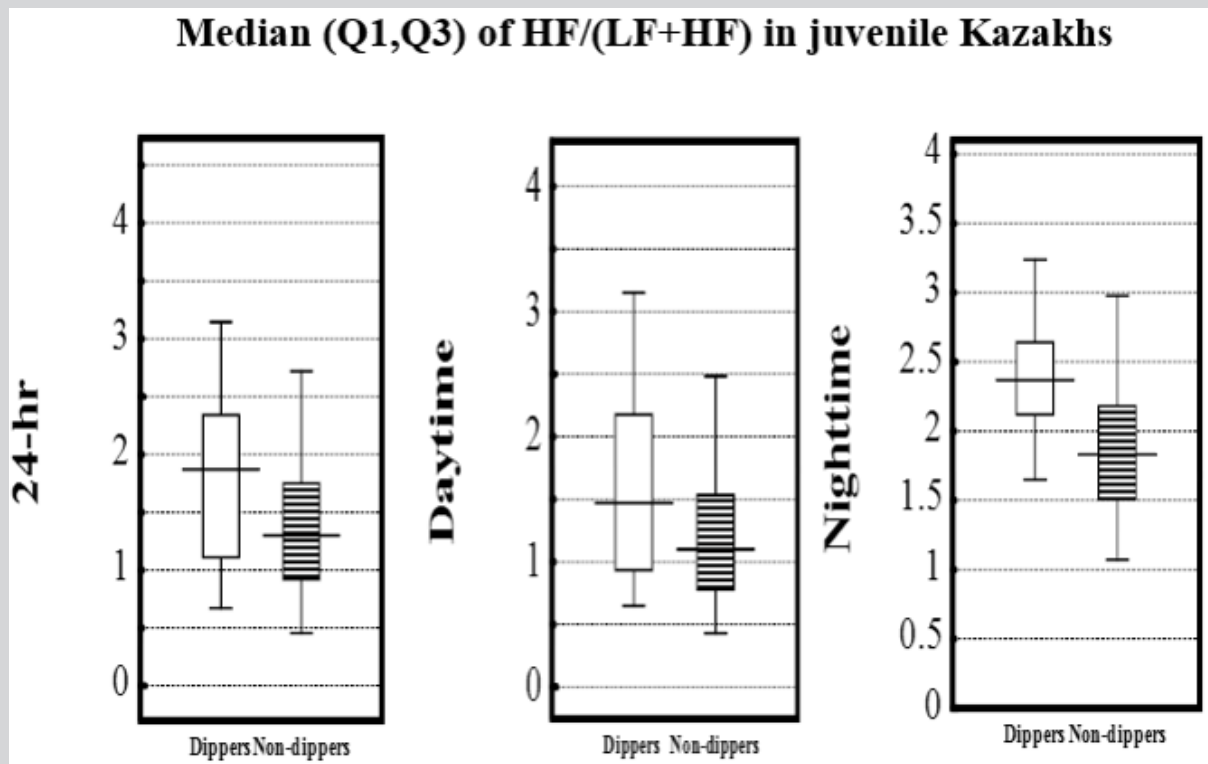
**Figure 5:** The physical activity scores of both the dippers and non-dippers rose during the daytime (light bar) and fell during the night-time (dark bar).



**Figure 6:** Significant differences between the LF/HF ratios of the dippers and non-dippers were observed over 24 hr and during the daytime and night-time (dippers vs. non-dippers; 24 hr, daytime, and night-time, all *F*-test,  $P < 0.00001$ ).

As shown in Figure 7, the non-dippers' HF/(LF+HF) ratios were lower than those of the dippers (dippers vs. non-dippers: 24-hr: median: 1.87, Q1: 1.11, Q3: 2.34 vs. median: 1.30, Q1: 0.92, Q3: 1.75, *F*-test:  $P = 0.0001$ , Mann-Whitney U-test:  $P = 0.0001$  [left panel, Figure 7]; daytime: median: 1.47, Q1: 0.93, Q3: 2.18 vs. median:

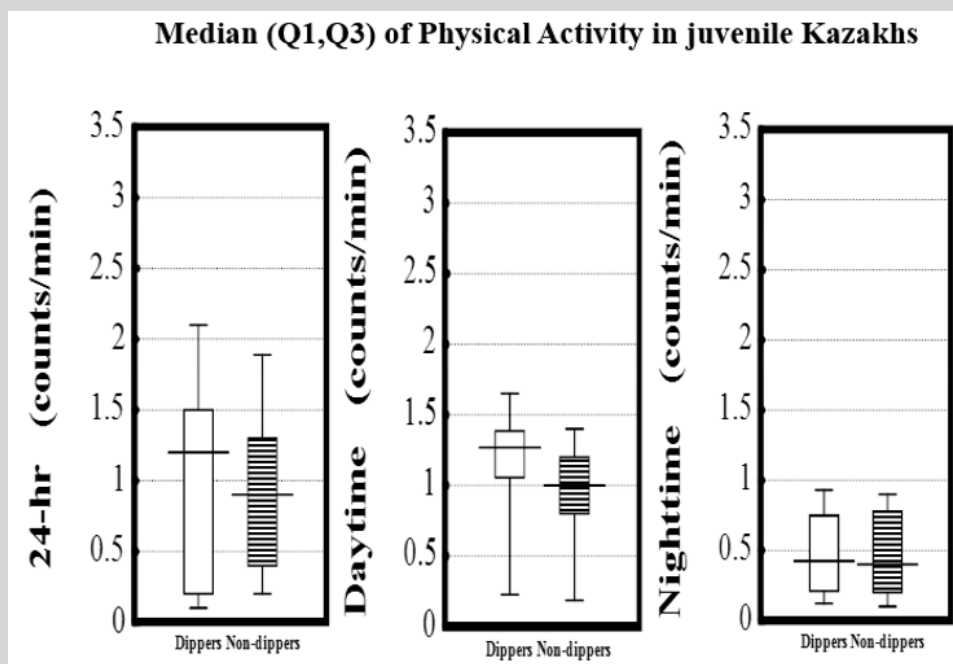
1.10, Q1: 0.78, Q3: 1.53, *F*-test:  $P = 0.0001$ , Mann-Whitney U-test:  $P = 0.0001$  [middle panel, Figure 7]; night-time: median: 2.37, Q1: 2.12, Q3: 2.64 vs. median: 1.83, Q1: 1.51, Q3: 2.18, *F*-test:  $P = 0.0009$ , Mann-Whitney U-test:  $P = 0.0001$  [right panel, Figure 7]).



**Figure 7:** Significant differences between the HF/(LF+HF) ratios of the dippers and non-dippers were observed over 24 hr and during the daytime and night-time (dippers vs. non-dippers; 24 hr, daytime, and night-time, all  $P < 0.00001$ ).

As shown in Figure 8, the 24-hr and night-time physical activity scores of the dippers and non-dippers did not differ significantly (dippers vs. non-dippers: 24-hr: median: 1.20, Q1: 0.20, Q3: 1.50 vs. median: 0.90, Q1: 0.10, Q3: 1.30,  $F$ -test:  $P = 0.0050$ , Mann-Whitney U-test  $P = 0.4368$  [left panel, Figure 8]; night-time: median: 0.42, Q1: 0.21, Q3: 0.75 vs. median: 0.40, Q1: 0.20, Q3: 0.78,  $F$ -test:  $P = 0.4850$ ,

Mann-Whitney U-test:  $P = 0.8270$  [right panel, Figure 8]). However, the daytime physical activity scores of the non-dippers were lower than those of the dippers (dippers vs. non-dippers: median: 1.27, Q1: 1.06, Q3: 1.38 vs. median: 1.00, Q1: 0.80, Q3: 1.20,  $F$ -test:  $P = 0.0733$ , Mann-Whitney U-test:  $P = 0.0001$  [middle panel Figure 8]).



**Figure 8:** The physical activity scores of the dipping and non-dipping juvenile Kazakhs only differed during the daytime (dippers vs. non-dippers; daytime,  $P < 0.0001$ ).

## DISCUSSION

Previously, we reported that many middle-aged and elderly Kazaks were hypertensive and non-dippers [2,3,5,6]. As shown in Table 1, in the present study dippers and non-dippers accounted for 72% and 28% of the subjects, respectively. A previous study reported that SBP was related to height in both males and females [13]. However, our study did not detect any difference in height between the dippers and non-dippers, which also agrees with the findings of another study [14]. Therefore, the differences between the BP patterns of the dippers and non-dippers might not have resulted from differences in physiological characteristics.

### Circadian Variations in SBP in Juvenile Kazakhs

Our previous results suggested that 52% of middle-aged Kazakhs are non-dippers, but also that such individuals exhibit similar physiological characteristics to dippers. In the current study, the SBP of both the dippers and non-dippers exhibited daytime peaks and midnight troughs (left panel, Figure 1), and their SBP variations displayed circadian rhythms. However, the SBP variations of the non-dippers exhibited weaker circadian rhythms (right panel, Figure 2). It was previously demonstrated that the likelihood of becoming a non-dipper increases with age [15,16]. However, in the present study, the living conditions of the dippers and non-dippers were similar, and the timing of physical activities, such as eating, rising, and sleeping, was also standardized. To confirm when physical activities occurred, we examined the diaries of all the subjects.

### Circadian Variations in the LF/HF ratios, HF/(HF+LF) Ratios and Physical Activity Scores of Juvenile Kazakhs

We consider that frequency domain analysis of HRV is the most useful technique for comparing dippers and non-dippers. In the present study, the subjects' LF/HF ratios displayed daytime peaks and midnight troughs (Figure 3), while their HF/(HF+LF) ratios exhibited a midnight peak and a daytime trough (Figure 4). Thus, the subjects' LF/HF and HF/(HF+LF) ratios both displayed circadian variations. The SBP variations of the non-dippers exhibited a circadian rhythm with a weak PSD (Figure 2); thus, the cardiac autonomic nervous system might be at least partially responsible for generating LF/HF and HF/(HF+LF) ratio variations. It has been reported that non-dippers demonstrate relatively high sympathetic nervous system activity during the night-time [18]. Our findings of high sympathetic activity and low parasympathetic and physical activity in the non-dippers agree with these reports. They could also explain the high night-time SBP of the non-dippers. In contrast, another study detected low LF values in non-dippers [19]. However, the latter study examined 24-hr LF/HF ratios instead of separately analysing daytime and night-time LF/HF ratios. If they had measured LF/HF separately during the daytime and night-time, their results might have been different due to the effects of differences in physical activity. Therefore, we consider that this might explain the discrepancy between their results and ours. Furthermore, we postulate that the non-dipping pattern results from the generation of weak circadian variations caused by disturbances of cardiac autonomic function.

Similar to the subjects' LF/HF ratios, their physical activity scores displayed daytime peaks and midnight troughs (Figure 5). No marked differences in circadian rhythms were detected between the dippers and non-dippers. However, the non-dippers exhibited lower daytime physical activity scores than the dippers (middle panel, Figure 8). On the other hand, no differences were

noted between the 24-hr or night-time physical activity scores of the dippers and non-dippers (left and right panels, Figure 8). This indicates that the non-dippers performed less physical activity during the daytime than the dippers. Non-dippers were reported to exhibit smaller increases in their plasma norepinephrine levels than dippers during exercise [10]. This finding would also explain the lower SBP values seen in the non-dippers during the daytime (Figure 1). Nocturnal behavioural activity, such as moving, walking, micturition, wakefulness, and so forth, might lead to the development of a non-dipping status. Based on the entries in the subjects' diaries, no differences were noted between the nocturnal behaviour or quality of sleep of the dippers and non-dippers. Therefore, neither nocturnal urination nor sleep quality appear to be involved in the appearance of non-dipping BPV in this group of juvenile Kazakhs. In field surveillance studies, similar to the current study, it is difficult to assess sleep quality using polysomnography alone. However, our findings suggest that the development of a non-dipping BPV pattern could be caused, at least in part, by the generation of weak circadian rhythms due to insufficient cardiac autonomic function and decreased physical activity during the daytime. Among juvenile Kazakhs, the number of non-dippers was smaller than the number of dippers. This difference might have been age-related, as we reported in our previous studies [2,3,5,6]. Based on the findings of the latter studies and the present study, the number of non-dippers seems to increase with age.

In summary, among juvenile Kazakhs the number of non-dippers was smaller than the number of dippers. The non-dipping juvenile Kazakhs exhibited higher LF/HF and lower HF/(HF+LF) ratios than the dippers. Furthermore, the non-dipping juvenile Kazakhs also performed less physical activity than the dippers during the daytime. These differences in cardiac autonomic functions and physical activity might contribute to the generation of weak circadian rhythms in SBP, and thus, lead to the non-dipping SBP variations observed in non-dipping juvenile Kazakhs.

## STUDY LIMITATIONS

Kazakhs are nomadic. For this reason, it was not possible to obtain a sample size that was large enough to enable separate statistical analyses of normotensives and hypertensives, particularly as most of the juvenile Kazakhs were normotensive. Therefore, we did not divide the juvenile Kazakhs into hypertensives and normotensives. Another limitation of our study was that the numbers of dippers (n=29) and non-dippers (n=11) were not identical because most of the juveniles were dippers. While this might have reduced the statistical power of the study, small inter-group variations were seen in the mean and median values of the majority of the examined parameters. Therefore, we consider that the study had sufficient statistical power to detect significant differences in most of the variables. Furthermore, as the study population was not large enough to allow it to be divided into normotensives and hypertensives, we could not examine the mechanisms responsible for non-dipping BPV separately in these groups. We speculate that the mechanism responsible for non-dipping is the same in normotensives and hypertensives since blood pressure gradually increases with age. Another limitation of this particular type of study is the necessity to assign subjects to a group based on their physical activity (dipper pattern) rather than at random. While the self-selecting nature of this cross-sectional study was unavoidable, it proved to be the study's main limitation, as unknown and unstudied variables could have been responsible for differences in the subjects' BPV patterns instead of the mechanisms we specifically explored and discussed. Therefore, future prospective studies with predefined endpoints



will need to be undertaken. The final limitation of the current study is that the period of BP monitoring was only 24 hr. This might have been too brief to allow a thorough and reliable evaluation of BPV or the elimination of extraneous influences, such as the novelty of the study setting. However, conducting a large-scale ABPM field study over a period longer than 24 hr in such a remote location is not practical. In any case, we consider that none of the abovementioned limitations significantly influenced any of the conclusions of the present study.

## PERSPECTIVE

In future, we hope to conduct prospective studies that will enable us to compare the survival rates of juvenile dippers and non-dippers after they reach adulthood. We hypothesize that in the Kazakh population, dippers will have longer lifespans than non-dippers. In addition, further chronobiological studies of this minority population in the PRC might be a valuable way of identifying physical activity lifestyle patterns that are associated with higher overall survival rates.

## CONCLUSION

Non-dipping BPV are seen in juvenile Kazakhs. However, the number of non-dippers was smaller than the number of dippers. Non-dipping juvenile Kazakhs demonstrated SBP variations that exhibited a 24-hr periodicity with a weak PSD. Their cardiac sympathetic nerve activity was increased, and their cardiac parasympathetic nerve activity was decreased. Furthermore, the non-dipping juvenile Kazakhs performed less physical activity than the dipping juvenile Kazakhs during the daytime.

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