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Research Article

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Study on Clinical Assessment of Central Blood Pressure in Healthy Volunteers, and its Relation to Clinical Phenotyping

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Abstract: The Unani system of Medicine is a holistic system of medicine and does not confine to molecular approach but refers to knowledge as a total recognition of the person and stresses on health of body, mind and soul. Unani medicine states that disease is a natural process and that symptoms are the reactions of the body to disease. The individual humoural balance is influenced by lifestyle factors. It employs the humoral theory which presupposes the presence of four akhlaat (humours) in the body – dam (blood), balgham (phlegm), safra (yellow bile) and sauda (black bile). The Unani philosophy has 4 humours under clinical phenotyping such as Sanguine (Damavi), Phlegmatic (Balghami), Bilious (Safravi) and Melancholic (Saudavi). The 400 Healthy volunteers with 100 each from four different temperaments (balghami, saudavi, safravi, damavi) were selected.The present study validates some of the Unani concepts of humours or temperament with central hemodynamic parameters or Pulse Wave Analysis (PWA). A specially designed case record form as per the Unani classical text was designed for assessment of humours and the information obtained were recorded from healthy volunteers as subjects and determination of central hemodynamic parameters was performed by SphygmoCor technology (AtCor Medical, Sydney, Australia). The temperament of the present study showed that the Pulse Wave Analysis in healthy volunteers although showed the results in physiological range but the analysis in safravi (bilious) subjects is found to be significant when compared to other clinical phenotypes.

Keywords: Central hemodynamic parameters, unani temperaments, clinical phenotyping, SphygmoCor technology.

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1.   INTRODUCTION

In the unani system, the temperament of the individual is very important and it is believed to be the result of the interaction of the elements. For maintaining the health of an individual, it is imperative to maintain temperament. It is also very important to keep the temperament in mind while diagnosing a disease.[1] Temperament of a person is given importance for the lifestyle processes promoting health of a particular clinical phenotype. Every person and every organ of the body had a different Mizaj and also differs from person to person.[2-4] Mizaj (Temperament) forms the base of diagnosis and treatment in the Unani System of Medicine. Evaluation and classification of various temperaments are based on the intermixture of four akhlat (humours) in the

blood in different proportions and thus blood plays an important role in the constitution of Mizaj.[5] On the basis of mizaj human beings have been categorized into four qualitative types: sanguinous (damavi), bilious (safravi), phlegmatic (balghami), melancholic (saudavi). They were supposed to result from predominant humor in the body.[6] The fundamentals of unani medicine are mainly based upon the temperament (Mizaj) and Humours (Akhlat).Unani philosophy is of the opinion that every individual has their own unique temperament as per clinical phenotyping which is related to humoral constitution, and other external factors. The interaction between four elements in the body produces various states which determine the temperament (Mizaj) of an individual.[7]

Table 1. Assessment of Temperament (Mizaj)				
Parameter	**Temperament (Mizaj)**			
	Sanguine (Damavi)	**Phlegmatic (Balghami)**	**Bilious (Safravi)**	**Melancholic (Saudavi)**
Complexion	Reddy (Reddish/ Whitish Brown)	Chalky (Whitish)	Pale (Yellowish)	Purple (Blackish)
Built	Muscular & Broad	Fatty & Broad	Muscular & Thin	Skeleton
Touch	Hot & Soft	Cold & Soft	Hot & Dry	Cold & Dry
Hair	Black & lustrous thick, rapid growth	Black & thin slow growth	Brown & thin rapid growth	Brown & thin slow growth
Movement	Active	Dull	Hyperactive	Less Active
Diet (Most Liked)	Cold & Dry	Hot & Dry	Cold & Moist	Hot & Moist
Weather(Most Suitable)	Spring	Summer	Winter	Autumn
Sleep	Normal (6-8 hrs)	In excess	Inadequate	Insomnia
Pulse	Normal in rate (70-80 min) Large in volume	Slow in rate (60-70 min) Normal in volume	Rapid in rate (80-100min) Normal in volume	slow in rate (60-70 min) Less in volume
Emotions	Normal	Calm & Quiet	Angry	Nervous

Cardiovascular system is an important system of the body.[8] Cardiovascular System refers to the Cardio (heart) and vascular (blood vessels). The system has two major functional parts: central circulation system and systemic circulation system. Central circulation includes the pulmonary circulation and the heart from where the pulse wave is generated. Systemic circulation is the path that the blood goes from and to the heart. Functional and structural changes in the arterial wall can be used as early markers for the hypertensive and cardiac diseases.[9] one of the earliest devices in the field for aortic pressure waveform assessment was the SphygmoCor Cardiovascular Management Suite (AtCor Medical, Sydney, Australia). This device relied on applanation tonometry for acquisition of the radial, carotid, and femoral blood pressure waveforms. The SphygmoCor systems integrate pressure pulse wave analysis, developed from the concept that there is hemodynamic information contained in the shape of the arterial pressure pulse that can be used to supplement the conventional measurement of blood pressure.[10] It was therefore of our interest to study the pulse wave analysis in relation to temperament and it is the first kind of study.

2.   MATERIAL AND METHODS

2.1   Selection of Study Subjects

This study was approved by the Institutional Ethics Committee of NRIUMSD IEC Approval No: 38-67/11-

CRIUM/TECH-IEC3/01 dated 28-11-2013. A specially designed Clinical Research Format (CRF) as per the dictums of Unani classics were designed for clinical assessment of phenotypes (Temperament) and the information obtained from healthy volunteers (Subjects) recorded and documented. A total of 400 subjects of age group 21 - 60 yrs were selected on the basis of clinical history by Unani physicians from the OPD of National Research Institute of Unani Medicine for Skin Disorders, Hyderabad. All participants were screened for Central Hemodynamic Parameters by using the SphygmoCor technology. The clinical features, family history, body physiognomy and all the systems were noted in the CRF which is followed by the assessment of the dominant clinical phenotype and the subjects classified as Damavi (Sanguine), Balghami (Phlegmatic), Safravi (Bilious) and Saudavi (Melancholic).The healthy volunteers as subjects have also filled in the willingness form to take part in the research process.

2.2   Pulse Wave Analysis/ Central Hemodynamic Parameter

One of the main attributes of the SphygmoCor systems is the ability to derive the central aortic pressure waveform non-invasively from the pressure pulse recorded at a peripheral site. Two specific things made this possible and contributed to the practical use of the device in both research and clinical situations: (1) the ability to accurately record the peripheral pulse and (2) a common relationship

between the frequency components of the aortic and peripheral pressure waveform shapes across the adult population, quantified as a generalized transfer function.[11] The SphygmoCor systems (AtCor Medical, Sydney, Australia) integrate pressure pulse wave analysis, developed from the concept that there is hemodynamic information contained in the shape of the arterial pressure pulse that can be used to supplement the conventional measurement of

blood pressure. The systolic and diastolic values of blood pressure are the maximum and minimum points of the pressure curve obtained in a peripheral location, usually the upper arm. However, similar values of systolic and diastolic pressures can be associated with many different pulse wave shapes (Fig.1), and these determine the type of interaction between the heart as a pump and the arterial system as the load.
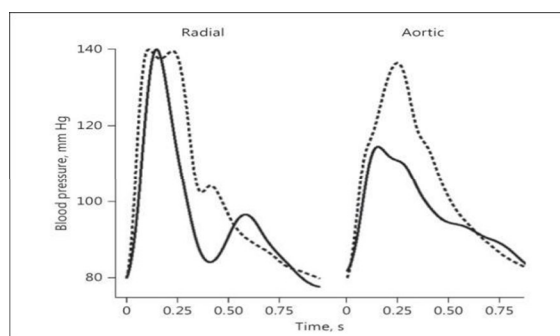

Fig.1: Peripheral (radial) and aortic arterial blood pressure waveforms. This difference in magnitude is relayed in the waveform shape of the peripheral waveform.

The SphygmoCor detects radial arterial pressure through applanation tonometry. A general transfer function is applied to the non-invasively acquired peripheral signal to calculate the aortic waveform. The SphygmoCor systems calculate over 20 different parameters quantifying the aortic waveform. Related to the stiffness of large arteries are the reflection time index, the reflection magnitude, and the aortic augmentation index (AIx). The augmentation of the pressure wave also has implications for the relative pressure during

systole and diastole, summarized in the subendocardial viability ratio (SEVR).The AIx is a measure of the degree to which the peak of a measured pressure wave is over and above the peak of the incident pressure wave due to the addition of the reflected pressure wave. (Fig: 2)The AIx is dependent on the timing and magnitude of the reflected waveform and is influenced by the compliance and structure of vessels distal to the site of measurement.[12]
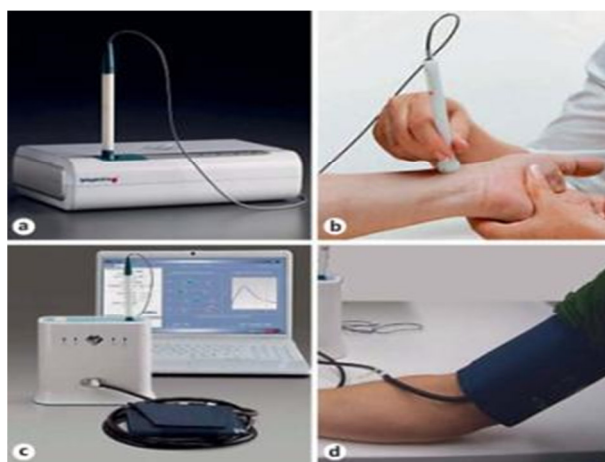

Fig.2 : a, b The SphygmoCor CvMS device, which utilizes tonometry (b) for acquisition of the peripheral vascular waveform. c, d The SphygmoCor XCEL device, which utilizes cuff-based volumetric displacement (d) for acquisition of the peripheral vascular waveform.

Arterial pressure varies continuously over the cardiac cycle, but in clinical practice only systolic and diastolic pressures are routinely reported. These are invariably measured in the brachial artery using cuff sphygmomanometer. However, the shape of the pressure waveform changes continuously throughout the arterial tree. Although diastolic and mean arterial pressures are relatively constant, systolic pressure may be up to 40 mmHg higher in the brachial artery than in

the aorta.[13] This phenomenon of systolic pressure *amplification* arises principally because of an increase in arterial stiffness moving away from the heart (Fig: 3). As the pressure wave travels from the highly elastic central arteries to the stiffer brachial artery, the upper portion of the wave becomes narrower, the systolic peak becomes more prominent, and systolic pressure increases.[14]
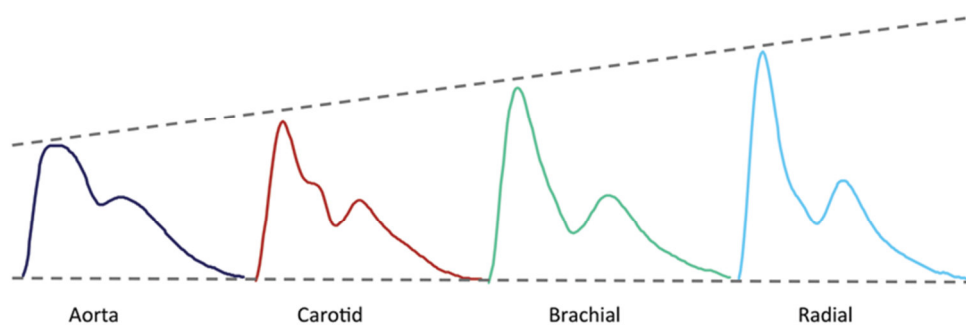
Fig.3: Amplification of the pressure waveform moving from the aorta to the radial artery.

The 400 Healthy subjects each n=100 damavi (sanguine), n=100 balghami (phlegmatic), n=100 safravi (bilious) and n=100 saudavi (melancholic) were selected for the study. Clinical systolic blood pressure (SBP) and diastolic blood pressure (DBP) were obtained by mercury cuff sphygmomanometer on the right brachial artery in a seated position after 15 minutes of rest. Measurements were repeated at least 2 minutes apart, the aortic waveform was recorded and calculated. Pulse wave analysis was performed using the SphygmoCor Technology (AtCor Medical, Sydney, NSW, Australia). The pressure wave in the aortic arch is reflected from sites of impedance mismatch such as arterial branching, changes in arterial diameter, and changes in vessel wall material stiffness. The magnitude of the reflected waveform is therefore dependent upon the geometry and the stiffness of the arterial tree distal to the aortic arch. Therefore, parameters of the aortic pressure waveform that relate to wave reflection are influenced by the stiffness of the distal arterial tree. Non-invasive measurement of the aortic waveform morphology allows these parameters to be quantified in both a clinical environment and in population studies.

3. STATISTICAL ANALYSIS

In the present study results were presented as mean ± standard deviation. Statistical differences were calculated with one way ANNOVA using Open epi software (Version 3.01). $p<0.05$ has been considered as the level of significant.

4. RESULTS

In the present study, the results of 400 healthy volunteers along with clinical phenotyping as per Unani philosophy each n=100 of damavi (sanguine), balghami (phlegmatic), safravi (bilious) and saudavi (melancholic) which served as subjects using the unani criteria for subject selection. The parameter was performed in triplicates. Values were expressed as mean and standard deviation. The results showed that physiology of the Central Hemodynamic parameters in healthy volunteers are found significant in safravi subject when compared to other clinical phenotypes as shown in table2-5 .

Table 2. Showing Anthropometric Parameters (Mean ± S.D) of Healthy volunteers						
Parameter Mean ± S.D (Range)	Damavi (Sanguine) n=100	Balghami (Phlegmatic) n=100	Safravi (Bilious) n=100	Saudavi (Melancholic) n=100	F - Statistics	p - Values
Age (Years)	39 ± 11	38 ± 12	38 ± 11	39 ± 11	0.2629	0.852
Body Height(cm)	158 ± 9	154.2 ±7.2	165 ± 10	160 ± 9.2	25.484	<0.0001
WT (Kg)	68 ± 13	69.7 ±13.4	72 ± 15	65 ± 14	4.516	0.0039
BMI(Kg/m^2)	27 ± 4.9	29.2 ±5.2	26 ± 4.9	25.5 ± 5.39	10.331	<0.0001

Table: 3 Showing Blood Pressure Dynamic Parameters (Mean ± SD) of Healthy Volunteers							
Parameter Mean ± S.D (Range)		Damavi (Sanguine) n=100	Balghami (Phlegmatic) n=100	Safravi (Bilious) n=100	Saudavi (Melancholic) n=100	F Statistics	p – Values
Systolic Pressure (mm/hg)	Aortic	105 ±15.7	105.1 ± 16.4	105 ± 13	109 ± 15.1	1.725	0.161
	Radial	117 ±15.7	115.2 ± 17.2	118 ± 16	119.3 ± 16.49	1.117	0.342
Diastolic Pressure (mm/hg)	Aortic	80 ± 9	79.2 ± 9.2	81 ± 9.6	83.1 ± 8.13	3.510	0.015
	Radial	79.3 ± 8.65	78.4 ± 7.9	80 ± 9.3	81.8 ± 8	2.885	0.035
Mean Pressure (mm/hg)		91.7 ±11.2	91.5 ± 10.8	93 ± 11	95 ± 10.7	2.172	0.091

Table: 4 Showing Blood Pressure Dynamic Parameters (Mean ± SD) of Healthy Volunteers							
Parameter Mean ± S.D (Range)		Damavi (Sanguine) n=100	Balghami (Phlegmatic) n=100	Safravi (Bilious) n=100	Saudavi (Melancholic) n=100	F Statistics	p – Values
Pulse Pressure (mm/hg)	Aortic	26 ±10.1	25.2 ± 11.3	24 ± 7.4	25.4 ± 9.58	0.747	0.524
	Radial	38.6 ±11.9	36.8 ± 12.8	38 ± 10	38 ± 12.9	0.251	0.86
T1	Aortic	101 ±11.6	102.2 ± 14.5	106 ± 14	101 ± 10.6	3.435	0.017

(m/Sec)	Radial	101 ±16.2	104.6 ± 22.0	101 ±14	102 ±13.9	1.017	0.384
T2	Aortic	195 ± 18.5	196.4 ± 17.7	186 ± 20	194 ± 19	6.162	0.004
(m/Sec)	Radial	189 ±19	188.1 ± 20.9	184 ± 21.4	182 ± 32.2	1.931	0.123

Table 5. *Showing Central Hemodynamic Parameters (Mean ± SD) of Healthy Volunteers*

Parameter Mean ± S.D (Range)	Damavi (Sanguine) n=100	Balghami (Phlegmatic) n=100	Safravi (Bilious) n=100	Saudavi (Melancholic) n=100	F Statistics	p – Values
Heart rate (Bpm)	85.8 ± 12.6	88.78 ±13.47	91.9 ± 22.86	88.4 ± 14.15	0.278	0.841
Eject duration (ms %)	273.9 ± 24.5	276.79 ±22.28	264.2 ± 36.3	270.3 ± 34.04	3.2954	0.0205
Augmentation pressure (mmhg)	4.32 ± 4.69	4.86 ±5.63	2.18 ± 3.81	4.70 ± 4.57	6.949	0.00014
Augmentation Index (%)	14.28 ± 13.06	16.32 ±12.73	8.62 ± 12.3	16..07 ± 13.27	7.7907	0.00045
Augmentation Index @ HR 75(%)	8.9 ± 12.37	9.25± 9.04	5.07 ± 12.01	7.38 ± 6.60	3.4401	0.0169
Buckburg Subendothelial Viability Ratio (%)	140.5 ± 29.1	132.66 ±25.03	185.75 ± 238.48	137.73 ± 25.69	4.105	0.0069
Pressure time index(m/hr)	2300.2 ± 446.9	2383.9 ±373.2	2482.3 ± 444.27	2430 ± 392.19	3.455	0.00165
End Systolic Pressure (mmhg)	99.7 ± 14.4	98.66 ±14.13	99.125 ±11.85	102.32 ± 13.21	1.481	0.218
Mean Pressure (Sys & Dia) (mmhg)	98.9 ± 12.9	98.11 ±13.18	99 ± 11.13	101.6 ± 12.69	1.474	0.221

5. DISCUSSION

Central Blood Pressure measured with a cuff and sphygmomanometer in the brachial artery is accepted as an important predictor of future cardiovascular risk. However, systolic pressure varies throughout the arterial tree, such that aortic (central) systolic pressure is actually lower than corresponding brachial values, although this difference is highly variable between individuals. The stiffness of the systemic large arteries more than doubles with age[15] is associated with outcome in many different cardiovascular diseases[16] and is a recommended parameter to measure in the management of hypertension[17]. Stiffening of the large arteries increases the speed of the ejected pulse from the left ventricle through the arteries and results in an earlier return of the reflected pressure. This can occur to an extent that it augments pressure during the period of left ventricular ejection. The early arrival of the reflected pulse during systole increases the afterload on the left ventricle and reduces coronary artery perfusion pressure during diastole. This risk of increased arterial stiffness is seen in measures of large artery stiffness being independently predictive of coronary artery disease, stroke, and cardiovascular events in general.[18] With the help of SphygmoCor Technology (AtCor Medical, Sydney, NSW, Australia) and the new age of information technology it was of our interest to investigate the Central Blood Pressure (pulse wave analysis) of 400 subjects with different clinical phenotypes.[19] In the present study 400 Healthy volunteers with 100 each from four different temperaments (balghami, saudavi, safravi, damavi) were selected by using Unani standard parameters of assessment of Mizaj.[20-21] And pulse wave analysis was carried out according to SphygmoCor Technology. The anthropometric Parameters as per clinical phenotype of all the selected subjects were compared between the temperaments and according to results there was no alteration. This type of study is the first

of its kind in relation to clinical phenotypes based on parameters of unani system of medicine.[23] On Pulse Wave Analysis of all the four clinical phenotypes (balghami, saudavi, safravi, damavi) the heart rate was higher in safravi (bilious subjects) which is in concordance with unani philosophy where they are supposed to possess a narrow, rapid and quick pulse wave.[22] The BMI was higher in phlegmatic clinical phenotype (Table :2). During the course of our investigations it was noted that the systolic pressure in all the four clinical phenotypes (both aortic and radial) did not elicit any significant alterations but all are within the physiological limits probably it may be due to the fact that all are healthy volunteers.[24] This is also evident in case of diastolic pressure (Table:3). In the blood pressure dynamics the time in both T1 and T2 are altered in safravi (bilious) healthy subjects which corroborates with the clinical phenotype based on unani philosophy (Table:4). On assessment of central hemodynamic parameters (Table:5) it was noted that the heart rate was higher in safravi (bilious) phenotypes, the ejection duration , augmentation pressure and index all decreased in safravi (bilious) phenotypes which elicits that it corroborates with the unani philosophy.[25] In Unani philosophy safravi healthy subjects have a very efficient cardiovascular system which reflects in the values as obtained. As per Unani philosophy sanguine represents average physiological hemodynamic parameters, Bilious a little higher, phlegmatic and melancholic on the lower physiological level. Bilious phenotype corroborated with the results. This is the first study of its kind correlating central hemodynamic parameters with clinical phenotypes in healthy subjects. Further studies with more sample size and disease condition may help to a confirmatory approach in future.[26].

6. CONCLUSION

The central hemodynamic parameters by using the

SphygmoCor technology (AtCor Medical, Sydney, NSW, Australia) as observed is in concordance with unani philosophy is a new study of its kind, in anticipation that the study would be helpful in understanding and developing further such studies in traditional unani medicine. The pulse wave analysis corroborated with the unani philosophy, which adds an increment to the scientific validation of unani philosophy.

7.   AUTHORS CONTRIBUTION STATEMENT

Juveria Mahmood - All experimental work, analysis of data and documentation of manuscript. Alokananda Chakraborty-Conceptualisation of the project, experimental work, temperament assessment, data analysis, documentation of manuscript and PI of the project. Ghazala Javed- Nodal officer

9.   CONFLICT OF INTEREST

Conflict of interest declared none.

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