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Title:

Systolic and Diastolic Blood Pressure Percentiles by Age and Gender in Northeastern Iran

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Abstract

Background: Hypertension (HTN) is a major risk factor for coronary artery disease (CAD). Its frequency is increasing globally. The aim of our study was to evaluate the reference range of BP in the Iranian population stratified for age and gender.

Methods: A total of 1449 subjects without diabetes, CVD, dyslipidemia, hypertension history and with a normal BMI (18.5≤BMI<25) were recruited in current study. Participants were enrolled from the Mashhad stroke and heart atherosclerotic disorder (MASHAD) study. Anthropometric indices and demographic data were collected by two healthcare specialists. A quantile regression model (QR) was used to estimate the expected SBP and DBP at specific ages. A P-value of <0.05 was considered significant for all analyses. All statistical analyses were performed using R (version 3.4.1) and SPSS software.

Results: The population included more men than women (51.6% vs. 48.4%). The mean and standard deviation of age in men (47.5±8.4) was 2 years higher than women (45.63±7.9), (P<0.001). SBP and DBP were higher in men than women (P<0.001). By using a quantile regression model, we concluded that, the 5th to 90th percentile of SBP, for men aged 30-69 years, ranged from 95 to 148.08 mmHg and in women ranged from 86.66 to 140. The 5th to 90th percentile of DBP, for men aged 30-69 years, ranged from 60 to 91.66 mmHg and in women ranged from 60 to 91.22.

Conclusions: We have, for the first time, established the BP percentiles (1, 5, 10, 50, 90, 95, 99) in an Iranian population stratified by age and gender. These data suggest that a local program for health promotion is necessary for the early identification of hypertension in adults aged ≥30 years.

Introduction

One of the important factors in the evaluation of cardiovascular (CV) risk is blood pressure (BP). A systolic BP (SBP) ≥ 140 mmHg, or a diastolic BP (DBP) ≥ 90 mmHg are the threshold values used to define hypertension (HTN) (1) and this is an important risk factor for cardiovascular disease (2, 3). Global HTN frequencies are high and increasing. The World Health Organization (WHO) has reported that a high blood pressure is projected to be the cause of 7.5 million deaths per annum, about 12.8% of the total of all mortality globally. Hypertension is the cause of 57 million disability adjusted life years (DALYS) or 3.7% of total DALYS (3). The WHO has reported that the prevalence of high blood pressure was highest in Africa (46%) and lowest in the Americas (35%). In South-East Asia, 36% of adults suffer from HTN. In Iran, the total pooled prevalence of HTN is increasing (4-8). Globally, men have a higher prevalence of hypertension than women (9).

A meta-analysis from 61 prospective observational studies comprised one million adults without a history of vascular disease, has reported that in every decade of age at death, the relative difference in the vascular mortality risk associated with a certain difference in normal BP is approximately equal to at least 115 mmHg normal SBP and 75 mmHg normal DBP. In the age range between 40-69 years, a 20 mmHg increase in SBP (or approximately 10 mmHg in DBP) was associated with a doubling in the risk of stroke mortality. These differences in vascular death are reduced by approximately 50% at older ages (80-89 years) compared to younger ages (40-49 years), but the absolute risk is higher in older age range. Whilst great efforts have been made to improve the rates of high blood pressure over the last decade, its prevalence continues to rise in most countries (9).

Few prospective studies have been done in low income countries, such as those in the Middle East, to determine the the risk factors for hypertension. Analysis and evaluation of hypertension risk factors in low income countries could have implications for the global management of this important condition, and may provide insights into the risk of hypertension for ethnic diaspora living in the West (10). A systematic investigation of the genetic and environmental factor interaction has not been undertaken in the Middle East. The Mashhad stroke and heart atherosclerotic disorder (MASHAD) study is a large longitudinal cohort study, aimed to investigate the risk factors for CVD including hypertension in the Iranian population. The participants will continue to be followed-up for a period of at least 10 years (2010-2020) for the development of CVD and hypertension as clinical endpoints. The precise aims of this current study were to:

(1) Define the prevalence of hypertension and its association with age and gender; (2) determine the relationship between several genetic and environmental risk factors and cardiovascular disease

endpoints; (3) determine the characteristics related to the development of hypertension; and (4) track the variations in hypertension risk measures over a period of at least 10 years in this population sample (11).

The reference values for SBP and DBP may be used as a guide the assessment of individuals and to provide effective criteria for assessing cardiovascular risk. The reference intervals for many laboratory tests is defined by threshold values of a specified percentage (usually 95%) for healthy persons. In the Iranian population, due to a lack of assessing the relationship between BP and clinical outcomes, the levels of health-related cut-off values for an increased BP, age and gender distributions of BP (90th and 95th percentiles) were used to define normal BP thresholds.

Methods

Participants were chosen from three areas in Mashhad, situated in north-eastern Iran, using a stratified cluster random sampling method. Households with individuals within the qualifying age range (between 30 and 69 years) were identified and the local population establishments provided a brochure with information of the study for the families. Eighty-two percent of subjects responded and agreed to register in the study. The non-responders (n = 2035) were contacted and information was obtained with respect to their socioeconomic, demographic profile, hypertension state and self-described diabetes (11). The anthropometric, demographic and lifestyle data were taken and registered by two healthcare specialist and a nurse. Our health-associated questionnaires included (a) demographic data, tobacco and alcohol usage, physical exercise, a food frequency questionnaire (FFQ) and 24-h food consumption (b) depression and anxiety tests and (c) anthropometric gauges, cardiovascular risk-associated questionnaire (11).

The blood pressure was measured twice using a standard mercury sphygmomanometer on the left arm, with the participants seated, and were at rest for a duration of 15 minutes before measurement. The average of the two measurements was recorded. If the difference of the first two readings was more than 15 mmHg in DBP or 25 mmHg in SBP, we took a third reading and the average of the two closest readings that was documented as the mean blood pressure (12).

Database characteristics

In total, data on 9847subjects were collected. The subjects who were included in the analysis were apparently healthy, did not have a history of clinical hypertension, or treatment for dyslipidemia (TC ≥ 240 mg/dl or LDL-C ≥ 160 mg/dl or HDL-C≤ 50 mg/dl (female)/40 mg/dl (male), TG ≥ 250 mg/dl), and were free from overt CVD (defined as the presence of cerebrovascular, coronary heart disease, valvular, peripheral artery disease, impaired cardiac ejection fraction, left ventricular hypertrophy, or atherosclerotic plaque) and diabetes (plasma fasting glucose ≥126 mg/dl). Data for all essential variables were available on 1449 subjects without diabetes, CVD, dyslipidemia, hypertension history and have normal BMI (18.5≤BMI<25). Other patients were excluded from the data analysis.

Statistical analyses

Descriptive analyses are reported as mean ± standard deviation (SD) for quantitative variables. The sex differences in means of normally distributed variables: age, weight, height, SBP, DBP were tested using independent t-tests.

In order to obtain a reference range for blood pressure, we calculated the percentiles of each variable; we considered the values between the 5th to 90^{th} percentiles as the reference range and values between the 90th to 95^{th} percentiles as prehypertension, and greater than 95^{th} percentile as hypertension. To achieve this aim, we used quantile regression (QR).

Quantile regression is a nonparametric method that is free from distributional assumptions, and is not influenced by outliers of the dependent variable. To implement these methods, a separate regression is implemented for each quantile. In this study we fitted conditional BP quantiles: 0.01, 0.05, 0.1, 0.5, 0.9, 0.95 and 0.99 by age and gender. In this model, SBP and DBP are the dependent variables, and age as an independent variable, in gender groups separately. We used different categories of age for quantile regression model. Then the mean age of category was used as a representative of that category.

QR models provide a good fit to the data. To assess the goodness-of-fit, observed and expected frequencies of BP in percentile bands <1, 1–4.9, 5–9.9, 10–49.9, 50–89.9, 90–94.9, 95–98.9 and >99 were compared using a chi-square goodness-of fit test. In all statistical analysis the P-values less than 0.05 were considered significant.

All statistical analysis were performed using R (version 3.4.1) Quantreg package and SPSS software.

Results

Population characteristics

The demographic and clinical characteristics of the population sample are shown in Table 1. The population included more men than women (51.6% vs48.4%). All of the characteristics were significantly different between men and women (p-value<0.05). Men were taller (13 cm), heavier (9 kg) and SBP and DBP were higher in men than in women: 5 and 4mm Hg, respectively. Mean age in men was 2 years higher (P<0.001). BMI in men was lower than for women (the difference was 0.24 kg/m^2, P= 0.005).

Table 1 Descriptive data for men and women

	Men(n=747)	Women(n=702)	
variables	Mean±SD	Mean±SD	p-value
Age(years)	47.5±8.40	45.63±7.90	<0.001
SBP(mmHg)	116.19±14.49	111.38±14.06	<0.001
DBP(mmHg)	76.45 ±9.76	72.82±9.92	<0.001
Height(m)	1.69±0.06	1.56±0.06	<0.001
Weight(kg)	65.05±7.24	55.67±5.89	<0.001
BMI(kg /m ^{2})	22.65±1.66	22.89±1.60	0.005

Reference values for systolic blood pressure

We have shown the predicted (1st, 5th, 10th, 25th, 50th, 90th, 95th, 99th) percentiles of BP and its relation with age in Figure 1 and 3. Linear quantile regression for SBP in men and woman indicated in Figure 1. From the non-parallel lines it can be inferred that for increasing age, SBP increases for each quantiles differently. SBP increases with age in men and women at 1st, 5th and 10th, 50^{th}, 90th, 95^{th} percentiles, with almost the same slope, but at 99th percentiles, increases with higher slope in women than men. The full list of the 1st, 5th, 10th, 25th, 50th, 90th, 95th, and 99th percentiles of SBP by age -sex groups is shown in Table 2.

Variation of 5^{th}, 50^{th} and 90^{th} percentiles with age group:

By increasing age, the median quantile for women varied from 107.63to 115.33 and for men varied from 110to 123.33. The 5th percentile of SBP in men varied from 95 to 100 and in women from 86.66 to 97.5. The 90th percentile of SBP in men varied from 125.33 to 148.08 and in women from 121.33 to 140mmHg.

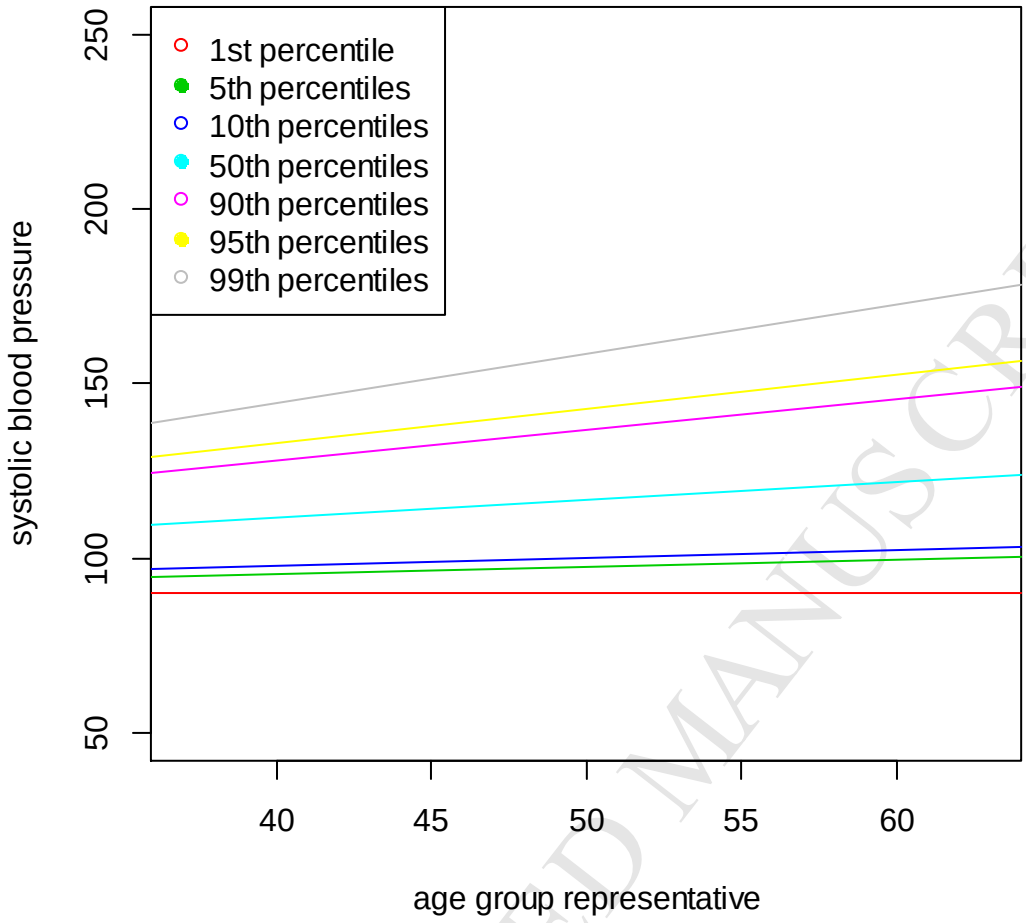
Reference range of SBP for each age group:

In the age range from 30-39 years, the 5th and 90th percentiles of SBP was 95and 125.33and for woman was 86.66 and 121.33mmHg. In men aged 40-49, the 5th and 90th percentiles of SBP was 96.35 and 131.46and for woman was 90 and121.07mmHg. In men aged 50-59, the 5th and 90th percentiles of SBP was 98.08 and 139.33 and for woman was 93.75 and 133.54 mmHg. In men aged 60-69, the 5th and 90th percentiles of SBP was 100and 148.08 and for woman was 97.5 and 140mmHg.

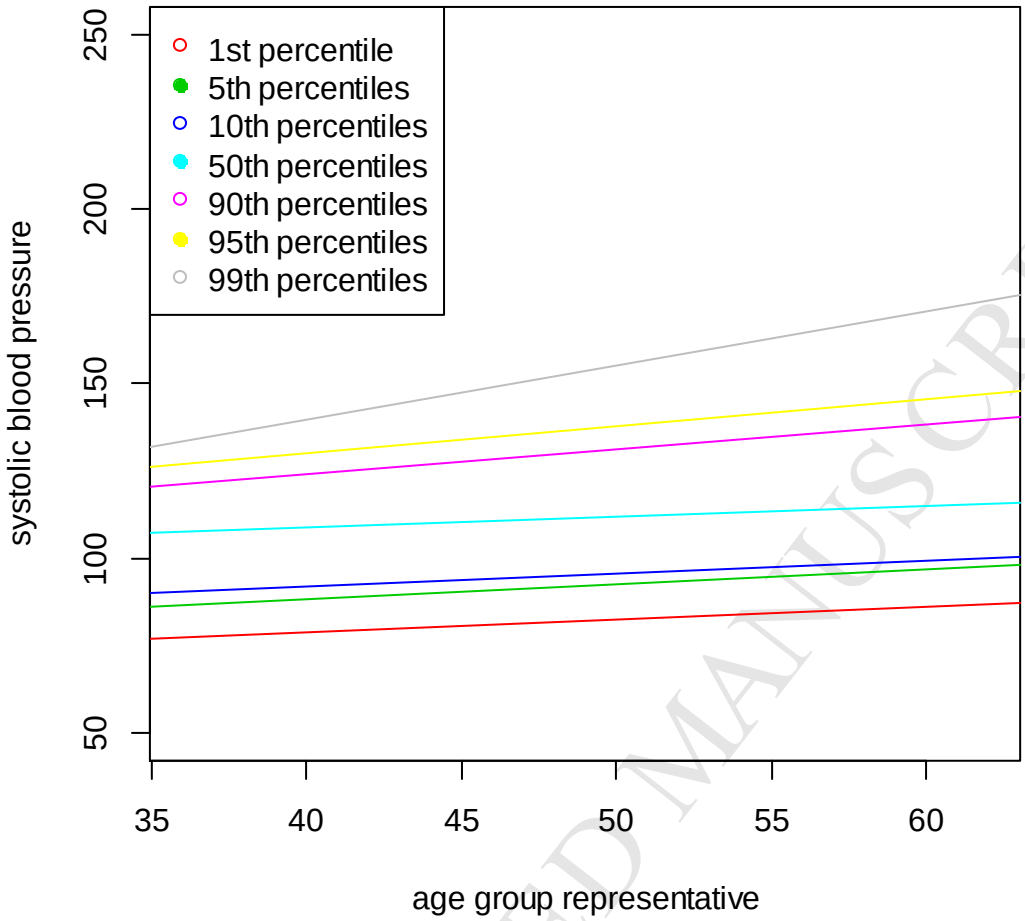
Table 2. Systolic blood pressure percentiles for men and women by age, quantile regression models

men	Percentiles of systolic blood pressure						
Age group	**0.01**	**0.05**	**0.1**	**0.5**	**0.9**	**0.95**	**0.99**
30-39	90.00	95.00	97.11	110.00	125.33	130.00	140.00
40-49	90.00	96.35	98.66	113.59	131.46	136.82	150.00
50-59	90.00	98.08	100.66	118.20	139.33	145.60	162.85
60-69	90.00	100.00	102.88	123.33	148.08	155.33	177.14

women	Percentiles of systolic blood pressure						
Age group	**0.01**	**0.05**	**0.1**	**0.5**	**0.9**	**0.95**	**0.99**
30-39	77.04	86.66	90.37	107.63	121.33	126.66	133.66
40-49	80.00	90.00	93.33	110.00	127.07	132.92	146.05
50-59	83.33	93.75	96.66	112.66	133.54	139.96	160.00
60-69	86.66	97.50	100.00	115.33	140.00	147.00	173.94



(a)



(b)

Figure 1.Comparison of (1st, 5th, 10th, 25th, 50th, 90th, 95th, 99th) systolic blood pressure percentiles by age for men (a) and women (b)

The normal range of systolic blood pressure, including 5th and 90th percentiles for men and women, is shown in Figure2. Both the 5th and 90th percentiles of systolic blood pressure are higher in males than in females. In both sexes, systolic blood pressure percentiles have increased with increasing age group. Details are in table2.

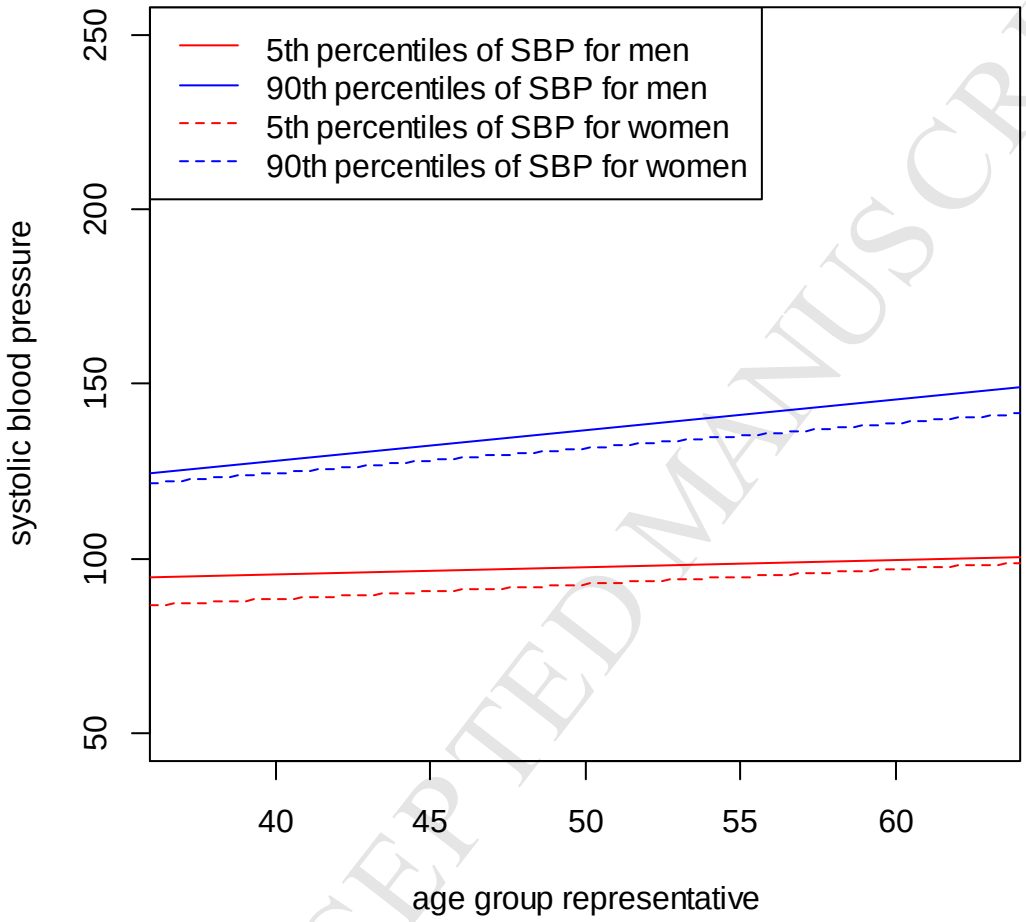


Figure2. Comparison of 5th and 90th systolic blood pressure percentiles for men and women

Reference values for diastolic blood pressure

Linear quantile regression for DBP in men and women is shown in Figure 3. From non-parallel lines can inference that as increase in age, DBP increases for interest our quantiles are different. A complete table of the 1st, 5th, 10th, 25th, 50th, 90th, 95th, and 99th percentiles of DBP by age -sex groups is given in Table 3.

Variation of 5^{th}, 50^{th} and 90^{th} percentiles with age group:

As increase in age the median quantile for woman varied from 70to 74.33 and for men varied from78 to 80. The 5th percentile of DBP in both men and women was fixed in 60.The 90th percentile of DBP in men varied from 87.33 to 91.66 and in woman from 80 to 91.22 mmHg.

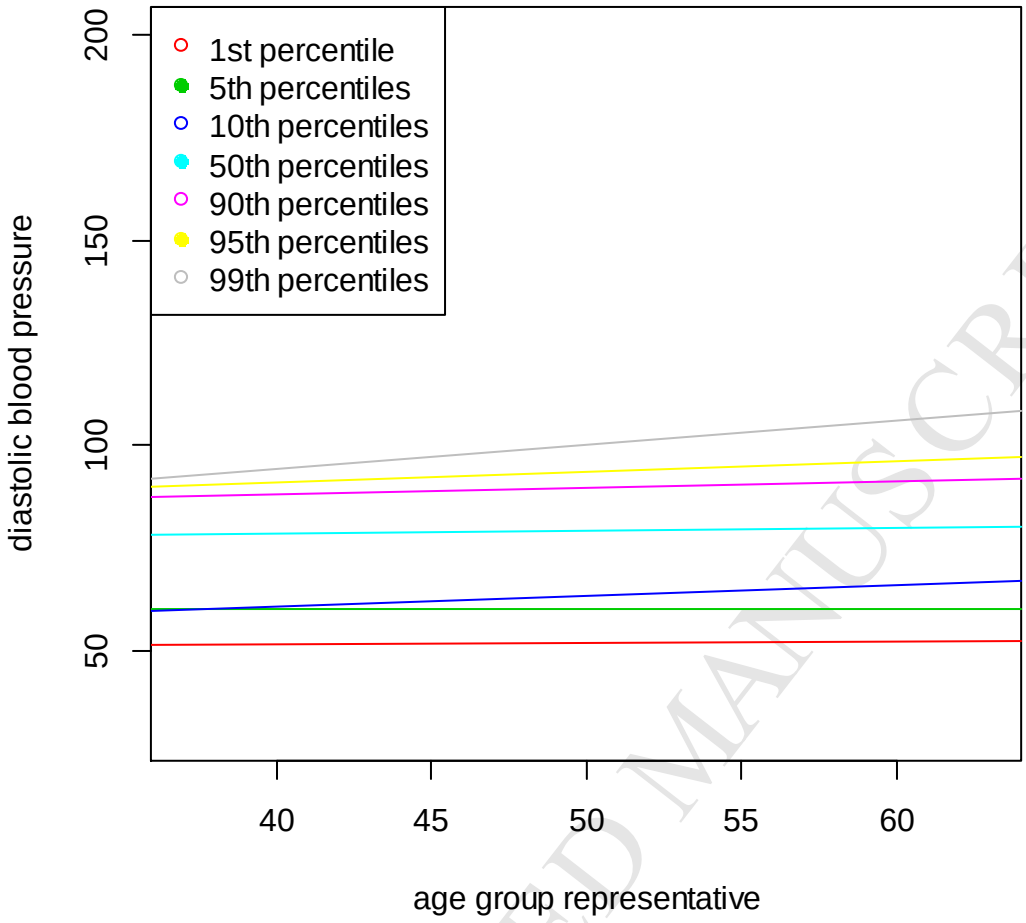
Reference range of SBP for each age group:

In men aged 30-39, the 5th and 90th percentiles of DBP was 60 and 87.33 and for woman was 60 and 80 mmHg. In men aged 40-49, the 5th and 90th percentiles of DBP was 60and 88.5and for woman was 60 and 83.45 mmHg. In men aged 50-59, the 5th and 90th percentiles of DBP was 60 and 90 and for woman was 60 and 87.33 mmHg. In men aged 60-69, the 5th and 90th percentiles of DBP was 60 and 91.66 and for woman was 60 and91.22mmHg.

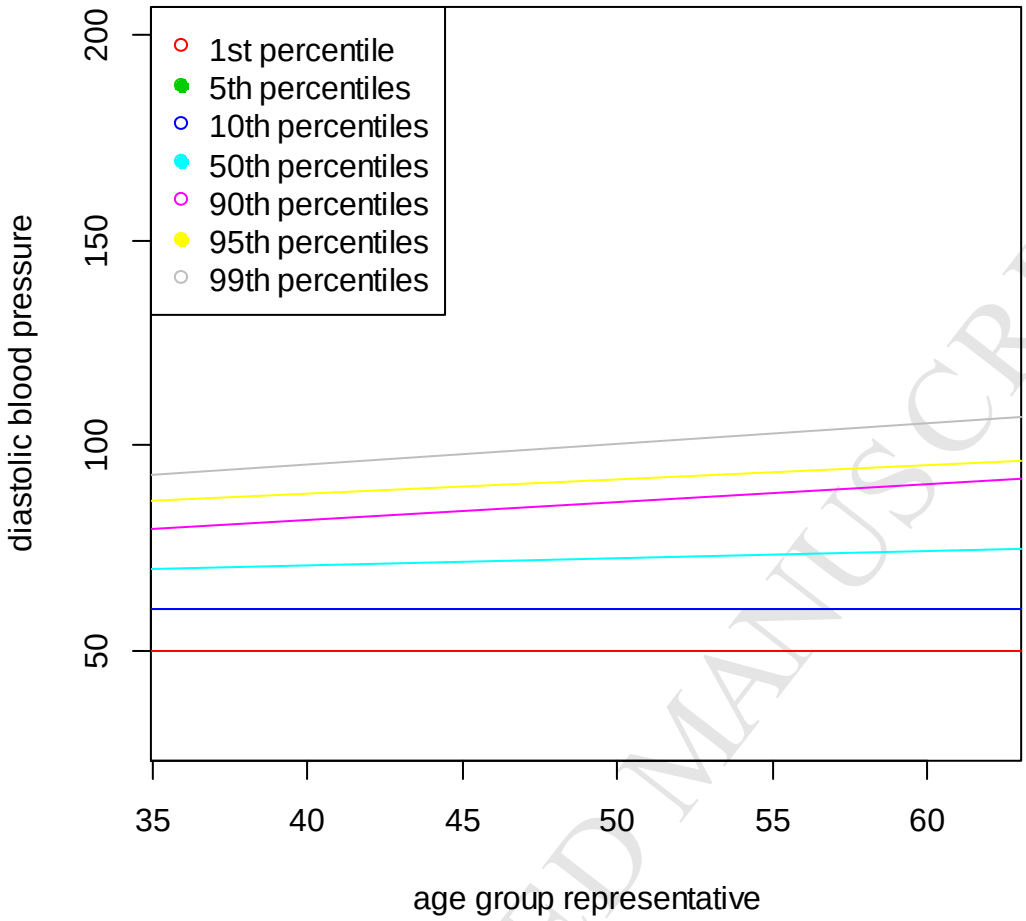
Table 3. Diastolic blood pressure percentiles for men and women by age, quantile regression models

men	percentiles of diastolic blood pressure						
Age group (y)	**0.01**	**0.05**	**0.1**	**0.5**	**0.9**	**0.95**	**0.99**
30-39	51.40	60.00	60.00	78.00	87.33	90.00	92.52
40-49	51.66	60.00	61.79	78.54	88.50	91.79	96.66
50-59	52.00	60.00	64.10	79.23	90.00	94.10	102.00
60-69	52.37	60.00	66.66	80.00	91.66	96.66	107.93

women	percentiles of diastolic blood pressure						
Age group	**0.01**	**0.05**	**0.1**	**0.5**	**0.9**	**0.95**	**0.99**
30-39	50.00	60.00	60.00	70.00	80.00	86.66	93.33
40-49	50.00	60.00	60.00	71.33	83.45	89.50	97.41
50-59	50.00	60.00	60.00	72.83	87.33	92.66	102.00
60-69	50.00	60.00	60.00	74.33	91.22	95.84	106.60



(a)



(b)

Figure 3. Comparison of (1st, 5th, 10th, 25th, 50th, 90th, 95th, 99th) diastolic blood pressure percentiles by age for men (a) and women (b)

The normal range of diastolic blood pressure, including 5th and 90th percentiles for men and women, is shown in Figure4. The 90th percentile of diastolic blood pressure is higher in men than in women but the 5th percentile of diastolic blood pressure is the same in both gender and is consistent with increasing in age group.

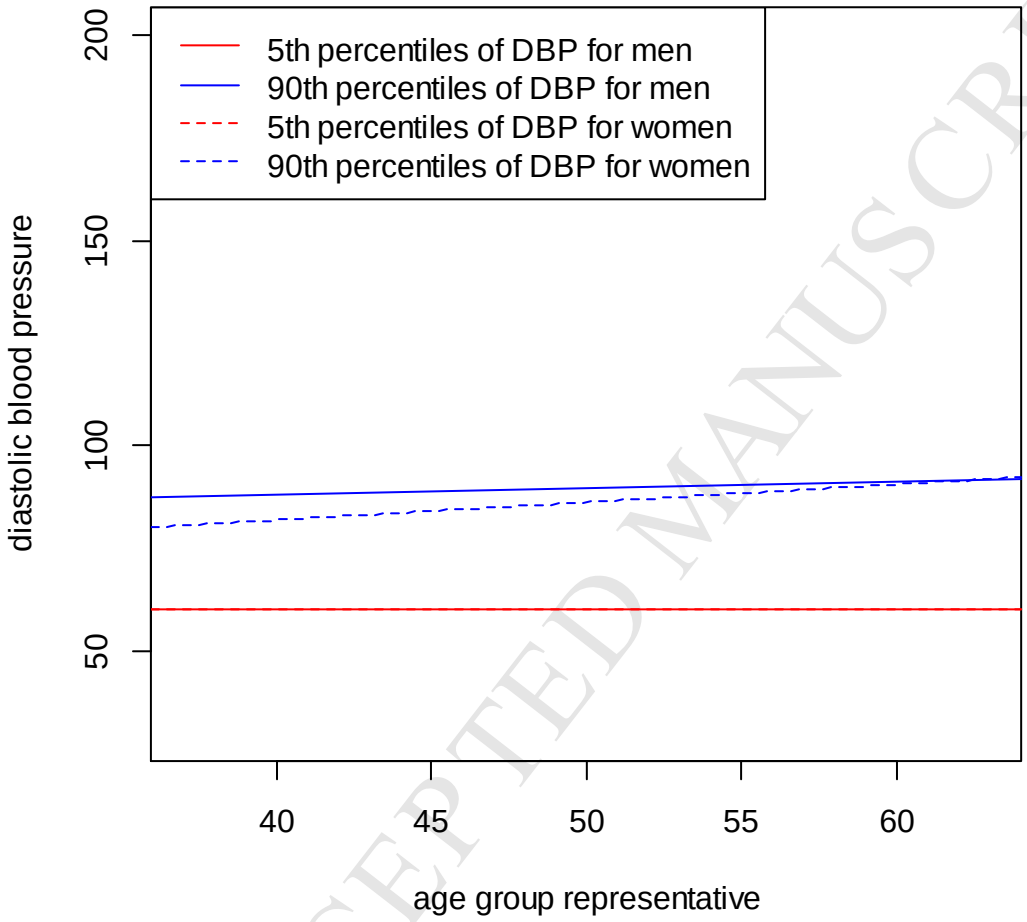


Figure 4. Comparison of 5th and 90th diastolic blood pressure percentiles for men and women

Goodness of fit test for model

The goodness-of-fit of the quantile regression model is excellent, with no significant differences between observed and expected values (Table 4). We subdivided the data for any age, based on the sex-specific predicted BP percentile (1%, 5%, 10%, 50%, 90%, 95%, and 99%) that the cut points were included in the upper segment. For each sex, we compared the observed distribution of subject in these blood pressure percentile groups with the expected distribution and performed a chi-square

goodness-of-fit test for QR method for each of the age-sex groups (Table 4). Comparison of observed (obs.) versus expected (exp.) frequencies (1, 4, 5, 40, 40, 5, 4 and 1%) of blood pressure in the sample relative to QR-fitted percentiles: chi-square goodness-of-fit test results

	BPS			BPD		
Men	N	%obs	%exp	N	%obs	%exp
<1	6	0.8	1	8	1.07	1
1-4.9	29	3.88	4	7	0.94	4
5-9.9	32	4.28	5	59	7.9	5
10-49.9	302	40.43	40	299	40.03	40
50-89.9	302	40.43	40	293	39.22	40
90-94.9	38	5.09	5	37	4.95	5
95-98.9	30	4.02	4	29	3.88	4
>99	8	1.07	1	15	2.008	1
	Chi-sqr= 0.066 p-value=1			Chi-sqr=1.94 p-value=0.96		

	BPS			BPD		
Women	N	%obs	%exp	N	%obs	%exp
<1	2	0. 28	1	1	0.14	1
1-4.9	28	3.99	4	25	3.56	4
5-9.9	38	5.41	5	0	0	5
10-49.9	236	33.62	40	194	27.64	40
50-89.9	326	46.44	40	411	58.55	40
90-94.9	36	5.13	5	26	3.7	5
95-98.9	28	3.99	4	36	5.13	4
>99	8	1.14	1	9	1.28	1
	Chi-sqr= .59 p-value=1			Chi-sqr= 2.24 p-value=0.94		

Discussion

In our population sample SBP increased with age in both males and females. It was lower in women than men for age categories 30-39 years and 40-49 years. It has been documented that an increase in blood pressure with age may be associated with a reduction in β-adrenoreceptor responsiveness (11, 12).

The most important finding of this study was that the threshold values of 140 mmHg for SBP and 90 mmHg for DBP seem to be high in our population. We found that, for the age group ≥50 years old, the 50th SBP percentile for men and women were of 121.66-126.66 and 120–125 mmHg. Moreover, for both genders, the 90th SBP percentile for the all participants, aged 30-69 years, of 126.66–156.66 mmHg, was higher than the threshold 120 mmHg for the identification of prehypertension according to the NCEP-ATPIII guidelines (13). For the males aged ≥50 years old, the 50th DBP percentile was of 80-81.33 mmHg, which was higher than the threshold 80 mmHg for the identification of prehypertension as recommended by NCEP-ATPIII guidelines (13). Moreover, for both genders, the 90th DBP percentile for the participants aged ≥40 years old, of 90–96 mmHg, which was higher than the threshold 80-90 mmHg for the identification of prehypertension as recommended.

SBP and DBP increased by nearly 30 and 10 mmHg with increasing age. This is similar to another study in Iran (13). Although compared with American adults, it seems that increased BP level with aging to be greater in our population. Wright et al., have reported that SBP and DBP increase with age in adults aged ≥18 years old in the United States during 2001-2008. Their results showed there was an increasing trend of SBP with age, whereas DBP increased then decreased with rising age in both men and women. Moreover, there was a higher mean BP in non-Hispanic black compared to non-Hispanic white adults (14).

It has been shown that the development of BP percentiles for different populations is reasonable because there are differences in diet, ethnicity, climate and other impacting factors on the HTN development in a population (13).

The results of current study can alert the healthcare assistants and policy makers regarding the detailed reference of BP in adults aged ≥50 years, where there is a need for early assessment to identify hypertension, as this may be helpful to prevent the related late mortalities.

Conclusions

In this study, for the first time, we established the thresholds BP percentiles (1,5, 10, 50, 90, 95,99)th by age and gender for Iranian population and considered 5 to 95 th percentile of blood pressure as a normal range .These percentiles can suggest that a local program for health promotion in our population.

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- The 5th to 90th percentile of SBP, for men aged 30-69 years, ranged from 95 to 148.08 mmHg and in women ranged from 86.66 to 140.

- The 5th to 90th percentile of DBP, for men aged 30-69 years, ranged from 60 to 91.66 mmHg and in women ranged from 60 to 91.22.

- For the first time, established the BP percentiles (1, 5, 10, 50, 90, 95, 99) in an Iranian large population stratified by age and gender.

- A local program for health promotion is necessary for the early identification of hypertension in adults aged ≥30 years.