RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 4 | April 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Efficacy of A Novel Risk Score In Prediction of Systemic Hypertension In Young Male Patients; The Role of Laboratory Biomarkers In Primary Prevention

KEYWORDS: systemic hypertension, score, non-invasive, biomarkers, prevention

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ABSTRACT *Backgrounds: There is a growing increase in the appearance of hypertension in young adults. The aim of this study is to analyze the metabolic variables in this group of patients and establishment of a predicting clinical score.*

Methods: 240 young aged male patients presented with accidentally discovered systemic hypertension were selected. Specific risk factors which could be associated with hypertension as BMI, WC, AST, ALT, GGT, FBS, insulin, HOMA-IR, QUICKE, trigycerides, uric acid, ferritin, MPV, plasma viscosity and fatty liver were selected. A control group was taken (n=50). Validation group (100) was used to assess the predictive power of the score.

Results: Diastolic hypertension associated with ALT (P=0.002), QUICKI (P=0.035), Uric acid (P=0.001), MPV (P=0.003), PV (P=0.000), Fatty liver (P=0.019). Systolic hypertension with BMI (P=0.038), GGT (P=0.037), FBS (P=0.008), QUICKI (P=0.01), MPV (P=0.02), Fatty liver (P=0.003). A score composed of BMI>26 K/m2, ALT > 34 IU/L, GGT > 32 IU/L, FBS > 100 mg/dl, QUICKI< 0.33, MPV > 10.5 fl, uric acid > 6mg/dl, PV > 1.8mps/s, severity of fatty liver by USG.

Conclusion: The score was successful in identifying metabolically prone patients at risk of systemic hypertension.

Introduction

There is a growing increase in the appearance of hypertension in young adults in coincidence with metabolic syndrome epidemic, mostly due to behavioral changes such as sedentary lifestyle and excessive consumption of energy-rich diet.

Metabolic syndrome is a state of metabolic derangement characterized by abnormal adipose deposition and function with occurrence of insulin resistance (IR) [1]. It is diagnosed when a patient has at least 3 of the following: Fasting glucose ≥100 mg/dl (or receiving drug therapy for hyperglycemia), Blood pressure ≥130/85 mmHg or receiving drug therapy for hypertension, Triglycerides ≥150 mg/dl (or receiving drug therapy for hypertriglyceridemia), HDL-C < 40 mg/dl in men or < 50 mg/dl in women (or receiving drug therapy for reduced HDL-C),Waist circumference ≥102 cm in men or ≥88 cm in women [2].

The visceral but not the subcutaneous Fat correlates with inflammation as omental fat is more resistant to insulin [3], also enhanced production of cytokines, such as tumor necrosis factor, adiponectin, leptin, resistin, and plasminogen activator inhibitor [4].

Obesity is associated with increased production of toxic free fatty acids which generate long-chain acyl CoA, ceramides and diacylglycerols which alter insulin signaling causing IR [5].

The mechanisms responsible for IR include genetic or primary target cell defects, autoantibodies to insulin, and accelerated insulin degradation [6]. Mitochondrial dysfunction may play a role in IR as glucose and lipid metabolism largely depend on mitochondrial energy generation [7].

Insulin sensitivity can be assessed by Homeostatic model assessment for insulin resistance (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI) [8, 9]. The results of both indices are parallel and correlate with the euglycemic clamp technique [10].

IR and hypertension can present simultaneously in metabolic syndrome. Nearly 50% of hypertensive individuals have hyperinsulinemia, whereas up to 80% of patients with type 2 diabetes have hypertension [11]. Insulin has vasculoprotective effect in normal states via induction of vasodilation, inhibition of vascular smooth muscle cell proliferation and anti-inflammatory effect mediated by stimulating nitric oxide-dependent pathway. In hyperinsulinemia, it has vascular injurious effect through mitogen-activated protein kinase pathway [12]. It increases sodium reabsorption in the kidney and promotes sympathetic activity with elevation of blood pressure [13].

Nonalcoholic fatty liver disease (NAFLD) is an increasingly recognized condition [14]. It is one of risk factors of hypertension, ALT are closely related to the severity of hypertension; this might be due to endothelial dysfunction, vascular smooth muscle cell proliferation and insulin resistance [15].

The possible role of iron in the pathogenesis of NAFLD had been searched. Serum ferritin was independently associated with future development of metabolic syndrome [16]. Central adiposity which is an important risk factor for IR is also correlated with ferritin level [17]. Reduction of iron stores by phlebotomy would improve insulin sensitivity [18]

It was postulated that elevated serum uric acid commonly precedes the development of both IR and DM. It can predict the development of fatty liver, obesity, hypertension [19]. Hyperinsulinemia may contribute to hyperuricemia by blocking uric acid excretion and Hyperuricemia induces hypertension through endothelial dysfunction via inhibition of nitric oxide synthetase, and alteration in renin expression [20]. Urate crystals cause inflammation through complement activation and possibly platelet activation [21].

It was shown that hyper-reactive platelets were larger; Nor-

Volume : 6 | Issue : 4 | April 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

mal or increased numbers of large platelets were observed in diabetes mellitus and cardiovascular diseases. Normal or decreased numbers of platelets and elevated mean platelet volume (MPV) were observed in patients with hypertension [22]. MPV represents an indicator of platelet activation and is elevated in patients with prehypertension [23].

Plasma viscosity (PV) is determined by water-content and macromolecular components. It increases in parallel with erythrocyte sedimentation rate and was recommended to substitute it [24]. A study observed 49 normal subjects and 49 patients with untreated essential hypertension revealed that PV was significantly higher in hypertensive subjects ($p<0.05$) [25]. A Study followed 1,592 randomly selected adults, demonstrated that systolic blood pressure was univariately related to PV in males only ($p<0.001$) and diastolic blood pressure was univariately related to PV in both sexes ($p<0.001$) [26].

The aim of this study is to analyze the metabolic variables in a group of accidentally discovered young aged hypertensive Egyptian male patients, and the establishment of a predicting clinical score for the development of systemic hypertension in metabolically prone patients thus can be applied in high risk populations to guide for preventive measures.

Methods

A- Patient selection

This is a longitudinal, observational study extended from April 2008 to March 2014 which enrolled 240 young aged Egyptian male patients presented with accidentally discovered systemic hypertension as they were referred due to other unrelated symptoms as fatigue, exhaustion, difficult breathing, and daytime somnolence. The evaluation was done at Internal medicine outpatient clinic - Zagazig University. Written informed consent was obtained from patients for interview, anthropometric measurements and blood sampling.

Patients were included if they are young (20-40 years), male, no history of smoking, exclusion of secondary causes of hypertension as diabetes (DM), renal disease, endocrinal causes as cushing syndrome, pheochromocytoma, hyperaldosteronism, thyroid, renovascular hypertension or drugs that induce hypertension as steroids, cocaine, cyclosporine, erythropoietin, migraine medications, nasal decongestants. Drugs which induce steatosis (methotrexate, tamoxifen, steroids, valproate and amiodarone) or insulin resistance (B.blockers, steroids, immunosupressives, thiazides, and antipsychotics as clozapine, olanzapine and risperidone).

A control group (n=50) composed of age and sex matched healthy normotensive subjects recruited from internal medicine outpatient clinic who were evaluated and compared with the study patients.

B- Clinical Evaluation

-Waist circumference (WC) was measured in the horizontal plane at the midpoint between the lowest rib and the iliac crest at the end of normal expiration. The cut off value selected is 94 cm [27].

-Body Mass Index (BMI) was calculated as weight divided by the square of height in meters. Healthy weight 18.5-24.9, Overweight: 25-29.9, Obesity grade I: 30-34.9, Obesity grade II: 35-39.9, Obesity grade III: 40 or more

-Blood pressure was measured by a single observer with a mercury sphygmomanometer on both arms with selection of the higher reading and proper cuff size after determining the forearm circumference using a measuring tape placed midway between the shoulder and the anticubital fossa. A size of 9.5-12 inches (Regular adult cuff); 13-16.5 inches (Large adult cuff); >16.5 inches (Thigh cuff) [28]. The patients were evaluated in the sitting position after a five minute period of rest, with back supported, legs uncrossed, patient's arm were supported at heart level, at least 4 hours from the last meal or cigarette smoking and the patient not in urge of defecation or urination.

C- Laboratory analysis

All patients underwent a 12-hour overnight fast before blood tests which included:

-Fasting blood glucose and triglycerides (TGs) by Cobas Integra 400 chemistry autoanalyzer..

-Liver enzymes as ALT, AST, and GGT were estimated using Cobas Integra 400 chemistry autoanalyzer. The cut off values selected were (30, 26, 29 U/L) as they increase the sensitivity for detection of patients with liver injury, primarily patients with hepatic steatosis [29].

-Serum insulin was measured quantitatively by electrochemiluminescence immunoassay (ECLIA) using Cobas e 411 immunoassay analyzer, cut off value is 8.64µIU/ml

-Insulin resistance was calculated from fasting serum glucose (mg/dl) and fasting serum insulin (µIU/ml) by HOMA-IR using following formula: fasting glucose (mg/dl) X fasting insulin (µU/ml) / 405, a value greater than 2 indicates insulin resistance [8].

-QUICKI measures insulin sensitivity by calculating the inverse of the sum of the logarithmically expressed values of fasting insulin and glucose: = 1 / [log (fasting insulin) + log (fasting glucose)]. A value less than 0.339 indicates reduced insulin sensitivity [9].

-Serum fasting uric acid was estimated by Cobas Integra 400 chemistry autoanalyzer with cut off value 6.3 mg/dl which is optimal to identify the high risk of metabolic syndrome [30].

-Serum ferritin was determined quantitatively by ECLIA using Cobas e 411 immunoassay. Normal level in adult males: 30-300 ng/ml [31]. The cut off value applied is 300 ng/ml.

-MPV was detected by Sysmex KX 21N hematology auto analyzer (Sysmex Corporation, Kobe, Japan) from ethylenediamine tetraacetic acid blood samples which were rapidly processed within 1 hour in order to minimize platelet swelling. Reference range is 7.8–11.0 fl.

-Plasma viscosity was measured at 37°C using a falling ball viscosimeter (Microviscosimeter). Normal value is 1.10-1.30 mPa/s [24].

D-Abdominal ultrasonography

The patients were examined after 6 hours fast. The ultrasonographic steatosis score (USS) was calculated as follows:

-No steatosis (score 0) was defined as normal liver echotexture.

-Mild steatosis (score 1) as slight and diffuse increase in fine parenchymal echoes with normal visualization of diaphragm and portal vein borders.

-Moderate steatosis (score 2) as moderate and diffuse increase in fine echoes with slightly impaired visualization of portal vein borders and diaphragm.

-Severe steatosis (score 3) as fine echoes with poor or no visualization of portal vein borders, diaphragm, and posterior portion of the right lobe [32].

E- Validation

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Aiming to assess the predictive power of the scoring model clinically through evaluation in another cohort composed of 100 male patients with the same age group with no previous history of systemic hypertension presented with obesity, fatigue, difficult breathing and sleep disturbances as sleep apnea. The selected laboratory variables which showed high risk values had triggered their follow up. The methods used were similar to those of the study patients. The blood pressure was evaluated every 4 weeks for 4 years (from May 2011 to March 2014) and hypertensive episodes were recorded (Blood pressure >130/85 mmHg).

F- Statistical Analysis

Data were analyzed using PASW Statistics 18. Continuous variables were summarized as mean ± standard deviation and standard of error (SE) when appropriate. Chi square test was used for categorical variables as frequency and percentage. The Student t test and analysis of variance were appropriately used. To identify risk factors associated with hypertension, the potential risk factors were selected as BMI, abdominal obesity (waist circumference > 90 in men or > 80 cm in women), ALT, AST, GGT, FBS, insulin, HOMA-IR, QUICKI, MPV, uric acid, ferritin, HDL, triglycerides, plasma viscosity, and severity of fatty liver by abdominal USG. Binary logistic regression with forward selection, including all of the variables that were significantly ($P<0.05$) associated with hypertension. Estimation of odds ratios (ORs) and corresponding β coefficients. The goodness of fit was assessed by the Hosmer-Lemeshow test [33].

A scoring system was postulated, and points were assigned to each variable based on the magnitude of its regression coefficient; the one with the smallest β coefficient was given 1 point and others were given points according to their strength when compared to the smallest. The summed points were grouped into predefined categories for the risk of systemic hypertension: low (<15%), intermediate (15%- 49%), high (50%-79%), and very high (>80%) [34].

A receiver operating characteristic (ROC) analysis was carried out to examine the diagnostic utility of the constructed scoring model.

Results

A- Study population

The baseline characteristics of the study patients and controls are shown in **table 1**. The study included 240 male patients presented with accidentally discovered systemic hypertension with mean value 150±13/ 92.4±7 mmHg; their mean BMI 30.7± 3.6 kg/m**2**. They showed elevated transaminases with impaired fasting blood glucose, hyperinsulinemia, obvious insulin resistance (HOMA-IR 2.8 ± 1, QUICKI 0.332 ±0.02), increased uric acid, ferritin, triglycerides, with increased MPV (11.1± 1.2 fl), plasma viscosity (1.9±0.24 mPa.s) and that showed a statistically highly significant different from controls.

Mild steatosis was seen in 49 patients (20.3%), moderate steatosis in 82 patients (34%), and severe steatosis in 62 patients (25.7%), however 47 patients showed normally appearing liver (19.5%) as shown in **table 1.**

The patients were further classified into 3 subgroups: isolated systolic hypertension which included 65 patients, diastolic hypertension which included 72 patients and combined systolic and diastolic hypertension which included 103 patients as shown in **table 2.** There was a statistically significant difference among the three subgroups as regards BMI, W.C, AST, insulin, HOMA-IR and ferritin which were higher in combined systolic and diastolic subgroup. FBS and TGs were significantly higher in isolated systolic hypertension subgroup. QUICKI was significantly lower in combined systolic and diastolic subgroup. Other variables as age, ALT, GGT, uric acid, MPV, plasma viscosity and HDL showed statistically no significant difference among the three subgroups.

Normal hepatic architecture (n=47) was seen mainly in patients with diastolic hypertension (n=36, 76.6%) (p=0.000). Mild hepatic steatosis (n=49) occurred mainly in patients with diastolic hypertension (n=36, 73.5%) (p=0.0001), moderate and severe hepatic steatosis were seen mainly in patients with combined systolic and diastolic hypertension (50%, 71%, p=0.0001, respectively), it appeared that severe steatosis was more linked to systolic hypertension.

The development of systolic hypertension was correlated with BMI (r=0.541, p=0.000), WC (r=0.544, p=0.000), AST (0.476, P=0.000), ALT (r=0.516, p=0.000), GGT (r=0.607, p=0.000), FBS (r=0.333,p=0.001), MPV (r=0.602, p=0.000), HOMA-IR (r=0.605, p=0.000), QUICKI (r= -0.649, p=0.000), TGs (r=0.175, p=0.007), fatty liver (r=0.715, p=0.000).

Development of diastolic hypertension was correlated with: BMI (r=0.327, p=0.000), WC (r=0.328, p=0.000), AST (0.198, P=0.002), ALT (r=0.169, p=0.009), GGT (r=0.256, p=0.000), FBS (r=0.212,p=0.001), PV (r=0.235, p=0.001), HOMA-IR (r=0.301, p=0.000), QUICKI (r=0.-261, p=0.000), Uric acid (r=0.143, p=0.026), ferritin (r= 0.146, p=0.024).

Binary logistic regression was done to predict variables mostly associated with development of hypertension. While performing the logistic regression for systolic hypertension, 9 steps were performed to reach the final model, the goodness of fit was highly accepted as the value of Hosmer-Lemeshow test was non-significant (p=1.0). The sensitivity of the model was 97% and specificity 96% with overall percent correct 98%.

For diastolic hypertension, 4 steps were performed to reach the final model, the goodness of fit was highly accepted as the value of Hosmer-Lemeshow test was non significant (p=0.96). The sensitivity of the model was 92%, specificity 54% with overall percent correct 69%.

A proposed scoring system was postulated for early prediction of hypertension in young aged male patients as shown in **table 3**. The cut off point for each variable was determined by the value with the highest sensitivity and specificity. Results of multivariate analysis showed the independent Predictors of systolic and diastolic hypertension with their assigned Score Values according to regression coefficient value; the smallest was given 1 and others given 2 or 3 according to the strength of their coefficients relative to the smallest one shown in **table 3**.

A collective score was formulated as shown in **table 4.** Total score **17; 0-3** β low risk, **4-8** β intermediate risk, **9-13** β high risk, **14-17** β very high risk

Prevalence of hypertension in study population according to summed scoring system points was shown in **table 5**

The predictive power of the scoring system was evaluated in the study population by using Receiver Operating Characteristic (ROC) curve analysis as shown in **figure 1**.

Volume : 6 | Issue : 4 | April 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

The area under the curve 0.836, standard error (SE) 0.028, p=0.000, 95%CI: 0.781 - 0.891.

B- Validation

From 250 obese young male subjects; 100 patients were selected according to parameters of the risk score when their values are high or risky i.e. exceeding proposed corresponding cut off values but still they are not hypertensive. They were followed up closely for 4 years by a 4 weekly visit to evaluate their blood pressure for the occurrence of hypertensive episodes (rise of the blood pressure > 130/85 mmHg). Their main age 35.1± 4.4 year, mean BMI was 30.5 ± 2.1 kg/m2. The main blood pressure at initial evaluation 120±8/ 70±10 mmHg, they showed elevated transaminases, impaired fasting blood glucose, hyperinsulinemia, with insulin resistance (HOMA-IR 2.6 ± 0.4, QUICKI 0.339 ±0.03), increased metabolic biomarkers as uric acid, ferritin, TGs, HDL plasma with increased MPV 10.5 ± 1.9fl and plasma viscosity 1.83 ± 0.14 mPa.s, mg/dl as shown in **table 1.**

54 patients showed hypertensive episodes on regular visits every 4 weeks (54%), minimum number of episodes was 2 and the maximum was 15 times of blood pressure > 130/85 mmHg in 4 years of follow up, with mean value 3.76 ± 1.9 times.

During evaluation by USG, 24 patients showed normal liver echopattern of them 4 patients were hypertensive (16.7%), 33 patients showed mild steatosis (33%) with 15 patients were hypertensive (45.5%), 29 patients showed moderate steatosis (29%) and 25 of them were hypertensive (86.2%), Severe fatty changes in 14 patients (14%), 10 of them were hypertensive (71.4%). It seems that with progression of steatosis, the more prevalent hypertension is (P=0.04), as shown in **table 1**.

The risk score was applied on the validation group as shown in **table 6**. 6 patients achieved a score of (0-3) (6%), and none of them experienced any hypertensive episode. 28 patients showed intermediate risk for hypertension and got a score of 4-8 (28%), 7 patients of them developed episodes of hypertension (25%). 30 patients (30%) showed a high risk (9-13) and 17 patients of them (57%) showed hypertensive episodes, 36 patients were at very high risk as they got a score of 14-17; 30 patients were hypertensive (83%).

The accuracy of the scoring system to predict hypertensive cases from validation group was evaluated using ROC curve analysis. The area under the curve 0.794, SE 0.032, p=0.000, 95% CI: 0.733 - 0.856 as shown in **figure 1**

Discussion

The goal for the proposed scoring System is to identify persons at the risk for systemic hypertension which can be avoided or ameliorated by modifying risk factors or life style. We evaluated specific risk factors of hypertension in this age group which could be associated with high blood pressure as BMI, WC, AST, ALT, GGT, FBS, insulin, HOMA-IR, QUICKI, TGs, uric acid, ferritin, MPV, PV and severity of fatty liver. All of them were correlated with the development of systolic and diastolic hypertension, but logistic regression analysis showed that variables mostly associated with development of diastolic hypertension were ALT (P=0.002), QUICKI (P=0.035), Uric acid (P=0.001), MPV (P=0.003), PV (P=0.000), Fatty liver (P=0.019).

Systolic hypertension was mostly associated with BMI (P=0.038), GGT (P=0.037), FBS (P=0.008), QUICKE (P=0.01), MPV (P=0.02), Fatty liver (P=0.003).

We postulated a clinic-laboratory score which can predict the risk of developing hypertension composed of BMI>26 K/m2, ALT > 34 IU/L, GGT > 32 IU/L, FBS > 100 mg/dl, QUICKI< 0.33, MPV > 10.5 fl, uric acid > 6mg/dl, PV > 1.8 mp.s, severity of fatty liver by USG. The AUC for the score in the study group was 0.836 (95% CI 0.781 to 0.891), whereas it was 0.794 (95% CI 0.733 to 0.856) in the validation group; the area under the ROC curves was not significantly different between the two groups (P = 0.40).

BMI cut off value above which the risk of health hazards are increased is 23 Kg/m2, in our study 26 Kg/m2 is selected. It was shown that elevated ALT (≥29 units/l) predicted incident diabetes and metabolic syndrome [35]. Elevated ALT was associated with insulin resistance and cardiovascular disease in fatty Liver Disease [36].

GGT level as a marker of oxidative stress and hepatic steatosis is positively associated with the development of hypertension, metabolic syndrome and type 2 diabetes [37]. A study confirmed significant and independent associations of GGT and ALT with metabolic syndrome in adult Chinese people [38]. GGT is an inexpensive and readily available marker, the best prognostic cut-off value is 25 U/L [39]. A study showed that the optimal cut-off value of GGT to predict metabolic syndrome for men is 31 U/L, demonstrating a sensitivity of 74.00% and specificity of 62.00% [40], in our study, GGT cut off > 32 IU/L.

QUICKI when used instead of HOMA-IR, a significant contribution to the risk of metabolic syndrome and hypertension were predicted with OR 2.5 (1.7 - 3.6) [41, 42].

Uric acid level even within the normal range is associated with an increase in arterial stiffness in healthy men [43] and a strong and independent risk factor for diabetes [44].

The correlation between MPV and office blood pressure was assessed and confirmed a strong positive correlation with hypertension and metabolic syndrome [45]. There were similar observations in gestational hypertension [46]. MPV was significantly higher in patients with essential hypertension and those suffering 'white coat' hypertension than in normotensive subjects [47].

Plasma viscosity is an important hemorheologic factor that determines the blood flow at the microcirculatory level. It significantly increases the shear stress in the blood-endothelial surface, leads to endothelial dysfunction, rise of blood pressure, and atherothrombotic vascular diseases [48].

In summary, we developed a clinic-laboratory score to identify patients with increased risk of developing systemic hypertension, thus steps can be taken to limit or prevent its occurrence with associated increase in morbidity and mortality.

Acknowledgement

Special thanks to clinical pathologists in Zagazig University Hospital main lab who were kind and provide us with great help in performing laboratory parameters of interest with high efficiency and to physicians in diagnostic radiology department- Zagazig University for their efforts.

Volume : 6 | Issue : 4 | April 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Sources of Funding
The research is self funded.

Disclosure of the potential conflict of interest
The authors declare that they have no conflict of interest.

	Patients (240)	Controls (50)	Validation (100)	p
Age	35.7 ± 3.7	33 ± 2.1	35.1± 4.4	0.008
Systolic blood pressure	150 ± 13 mmHg	110 ± 8 mmHg	120 ± 8 mmHg	0.000
Diastolic blood pressure	92.6 ± 7 mmHg	70.4 ± 7 mmHg	70 ± 10 mmHg	0.000
BMI	30.7± 3.6 kg/m2	20.7± 1.2 kg/m2	30.5 ± 2.1 kg/m2	0.000
W.C	102.4 ± 8.5cm	76.4 ± 6.5cm	105.3 ± 10.4 cm	0.000
ALT	64.2 ± 10.2 IU/L	24.3 ± 8.4 IU/L	58.2 ± 16.7 IU/L	0.000
AST	46.8 ± 13.6 IU/L	18.5 ± 6.6 IU/L	48.5 ± 10.4 IU/L	0.000
GGT	45 ± 10.6 IU/L	25 ± 4.6 IU/L	40.5 ± 10.5 IU/L	0.000
FBS	112.2 ± 17.8 mg/dl	78.2 ± 7.4 mg/dl	115.2 ± 11.8 mg/dl	0.000
Serum insulin	9.9 ± 2.9 µIU/ml	3.9 ± 1.2 µIU/ml	8.8 ± 2.4 µIU/ml	0.000
HOMA IR	2.6 ± 1	0.75 ± 0.02	2.6 ± 0.4	0.000
QUICKI	0.332 ±0.02	0.4 ±0.2	0.339 ±0.03	0.000
UA	8 ± 1.5 mg/dl	4± 0.5 mg/dl	8.4 ± 1.4 mg/dl	0.000
FRT	419 ± 173.7 ng/ml	214 ± 76 ng/ml	309 ± 76.4 ng/ml	0.000
MPV	11.1± 1.2 fl	8.5 ± 0.68	10.5 ± 1.98	0.000
TGs	180 ± 39.6 mg/dl	95 ± 18.2mg/dl	160 ± 45.2 mg/dl	0.000
plasma viscosity	1.9 ± 0.24 mPa / s	1.1± 0.06 mPa / s	1.83 ± 0.14 mPa s	0.000
HDL	38.5 ± 5.7 mg/dl	48.5 ± 3.7 mg/dl	43.5 ± 6.3 mg/dl	0.000
Fatty liver grade by USG				
G0	47 (20%)	Normal USG	24 (4 HTN, 24%)	0.6
G1	49 (20.5%)		33 (15 HTN, 33%)	0.01
G2	82 (34%)		29 (25 HTN, 29%)	0.4
G3	62 (25.7%)		14 (10 HTN, 14%)	0.02

Table (1): Baseline demographic, laboratory and ultrasonographic characteristics of the study and validation groups

	Systolic, diastolic HTN (103)	Isolated systolic HTN (65)	Isolated diastolic HTN (72)	P value
Age	33.4±3.8	33.8 ± 3.3	34.7 ± 3.5	0.1
26-29y	17(16.5%)	19(29.2%)	12(16.6%)	0.001
30-34y	35(34%)	21(32.3%)	30(41.7%)	0.001
35-39y	51(49.5%)	25(38.5%)	30(41.7%)	0.000
BMI	29.7±3	28.2 ± 1.85	27.2 ± 2	0.000
25-27.9	6 (6%)	8 (12.3%)	48(67%)	0.000
28-30.9	63 (61%)	27(41.5%)	24(33%)	0.000
31-33.9	18 (17%)	16(24.7%)	0	0.000
34-37	16 (16%)	14(21.5%)	0	0.000
WC	102.3 ±7.2	97.9 ± 6	95.2 ± 4.8	0.000
ALT	70.7 ± 15.4	68 ± 15	67.1 ± 13.6	0.48
AST	53 ± 12.8	46.2 ± 10.2	44.8 ± 8.8	0. 03
GGT	48.3 ± 8.1	47 ± 6.7	47.5 ± 9.4	0.78
FBS	111.9±18.3	114 ± 15	99.8 ± 14.4	0.001
Insulin	10.1 ± 2.9	8.84 ± 2.6	6 ± 2.2	0.000
HOMA	2.85 ± 0.97	2.5 ± 0.86	1.4 ± 0.7	0.000
QUICKI	0.331 ± 0.02	0.337 ± 0.02	0.372 ± 0.03	0.000
UA	7.7 ± 1.6	7.9 ± 1.2	7 ± 1.14	0.7
FRT	437.1±187	316.5 ±160 (30.1 SE)	196.2 ± 112 (21 SE)	0.000
MPV	13.2 ±1.6	10.9 ± 1.5	11 ± 0.9	0.09
TGs	168.4 ± 44.6	168.8 ± 48.6	136 ± 40	0.043
PV	1.81 ± 0.29	1.81 ± 0.31	1.72 ± 0.17	0.6
HDL	40.4 ± 6.5	39.2 ± 7.2	44 ± 4.9	0.08

Table (2): Characterization of the study population into 3 subgroups according to blood pressure elevation.

Steatosis	Systolic, diastolic HTN (n= 103)	Isolated systolic HTN (n= 65)	Isolated diastolic HTN (n= 72)	P
Absent (n= 47)	11	0	36	0.000
Mild (n= 49)	7	6	36	0.0001
Moderate (n=82)	41	41	0	0.0001
Severe (n= 62)	44	18	0	0.0001

Table (3): Distribution of hepatic steatosis among study population.

Independent predictor	Odds ratio	P	Regression coefficient	score
1-Diastolic hypertension				
ALT	2.9	0.002	1.05	2
QUICKE	1.4	0.035	0.53	1
Uric acid	3.5	0.001	1.29	2
MPV	2.63	0.003	0.968	2
PV	4.9	0.000	1.79	3
Fatty liver	1.6	0.019	0.575	1
2- Systolic hypertension				
BMI	1.2	0.038	0.451	1
GGT	1.3	0.037	0.467	1
FBS	2.4	0.008	0.899	2
QUICKE	2.3	0.01	0.847	2
MPV	1.85	0.021	0.682	1
Fatty liver	2.9	0.003	1.079	0-3

Table (4): Clinical Scoring System for hypertension, results of Multivariate Analysis: Independent Predictors and their assigned Score Values.

Independent predictor	Score
1- BMI > 26 K/m2	1
2- ALT > 34 IU/L	2
3- GGT > 32 IU/L	1
4- FBS > 100 mg/dl	2
5- QUICKE< 0.3	2
6- MPV > 10.5 fl	1
7- Uric acid > 6 mg/dl	2
8- PV > 1.8 mpa/s	3
9- Fatty liver grade	0-3
Total score	17
Low	≤ 3
Intermediate	4-8
High	9-13
Very high	14-17

Table (5): A clinical risk score to predict the risk of development of hypertension in young male patients.

Score	Systolic, diastolic HTN (103)	Isolated systolic HTN (65)	Isolated diastolic HTN (72)
0-3(n=7)	1	2	4
4-8 (n=38)	8(7.8%)	1(1.5%)	29(40.3%)
9-13 (n=96)	49(47.6%)	12(18.5%)	35(48.6%)
14-17(99)	42(40.8%)	52(80%)	5(6.9%)

Table (6): Prevalence of hypertension in study population according to summed scoring system points

The score	number	hypertension
Low (0-3)	6	0/6 (0%)
Intermediate (4-8)	28	7/28 (25%)
High (9-13)	30	17/30 (57%)
Very high (14-17)	36	30/36 (83%)

Table (7): Prevalence of hypertension in Validation group after risk classification by the score.

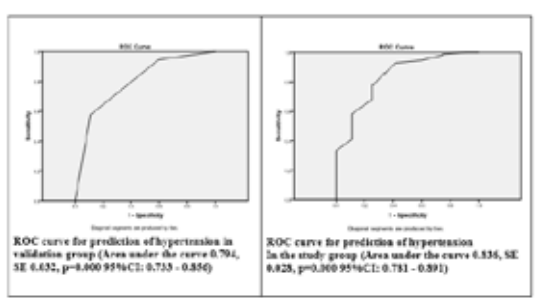

Figure 1: ROC curve for prediction of hypertension in study and validation groups.

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