Prevalence and Clinical Outcome of Metabolic Syndrome in Acute Non Embolic Ischemic Stroke in Zagazig University Intensive Care Unit, Egypt

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Abstract

Background and aim of the work: Metabolic syndrome (MetS) is a cluster of several inter-related risk factors that carries a great risk for atherothrombotic events leading to significant morbidity and mortality. Few studies evaluated the association between MetS and acute stroke. The aim of this work was to study the prevalence of MetS (defined according to IDF 2006 criteria) and its effect on ICU mortality in acute non embolic ischemic stroke patients admitted to medical ICU in Zagazig university hospital within a period of 9 months.

Patients and Methods: We studied 260 patients presented with acute ischemic stroke diagnosed by CT brain in the medical ICU, Zagazig University hospital for the presence of MetS (according to the International Diabetes Federation 2006 criteria) and its relation to age and sex as well as the number of components of MetS. We studied also the relative risk of MetS with its different components as well as age, sex, Glasgow coma scale (GCS) and APACHE II score on the mortality in those patients.

Results : MetS was found in 53.8% of patients. It was more prevalent in males (55.7%) than females (44.3%). and this prevalence increase progressively in males aged 40-60 years then decrease progressively after that while in females, the prevalence increase progressively with age . Among ischemic stroke patients with MetS, 55.7% of them have 3 components of MetS compared to 44.3% with more than 3 components. The relative risk of mortality was found to be increased with increasing age, male gender, obesity, hyperglycemia, low HDL-C, increased serum triglycerides, lower GCS and higher APACHE II score on admission by 1.2, 1.1,1.2,1.04, 1.2, 2.1, 4.2 and 1.8 folds respectively. Also, there was a significant increase in mortality with the increase in mean arterial pressure (MAP) ($P<0.001$). The presence of MetS Per se increases the relative risk of mortality by 3.4 folds. Furthermore, backward stepwise regression analysis showed that MetS and APACHE II score are good predictors of mortality in those patients

Conclusion: MetS is highly prevalent in acute non embolic ischemic stroke patients especially in the elderly and is associated with poor clinical outcome. MetS and APACHE II score can be used as independent predictors of mortality in those patients.

Key words: Metabolic syndrome, stroke, cerebrovascular disease

INTRODUCTION

Metabolic syndrome (MetS) is defined according to International Diabetes Federation (IDF 2006) as: Central obesity (defined as waist circumference ≥94cm in males and ≥80 cm in females for Arab population) plus two of the following : Triglycerides >150 mg/dl or treatment for elevated triglycerides.

- HDL-C <40 mg/dl for men or <50 mg/dl for women or treatment for low HDL.
- BP >130/85 mmHg or treatment for HTN.
- Fasting plasma glucose >100 mg/dl or previously diagnosed type 2 diabetes **[1]**.

Most MetS patients are at a much greater risk for atheroembolic events than are patients who have impaired glucose tolerance or type 2 Diabetes Mellitus (DM) **[2]**. The components of MetS and their cumulative effect on cardiovascular disease result in significant morbidity and mortality. Abdominal obesity is the most prevalent component and is likely to increase in importance as the epidemic of obesity continues to grow increasing the prevalence of type 2 DM and coronary heart disease **[3]**.

Hypertension (HTN) is also an important component of MetS particularly in older individuals, and is often poorly controlled in the general population **[4]**.

Stroke is the leading cause of disability and the third leading cause of death in the US, with 700.000 incidence of stroke and 160.000 stroke related deaths reported annually. However, little is known about the particular MetS clusters and the risk differences in the development of stroke. Therefore, we performed this study to estimate the prevalence of MetS in acute ischemic stroke patients in the medical Intensive Care Unit (ICU) in Zagazig University Hospital admitted within a period of 9 months and its relation to age and sex as well as to find out the relative risk of MetS with its different components together with the effect of age, sex, GCS and APACHE II score on the mortality in those patients.

PATIENTS AND METHODS

This observational, descriptive and analytic study had been carried out in the stroke subunit in the medical ICU of Internal Medicine Department, Faculty of Medicine, Zagazig University in the period between January 2011 to September 2011.

A total number of 260 patients were included in this work presented with acute ischemic stroke (within 24 hours). All patients had a CT scan of the brain showing evidence of recent ischemic stroke with or without the presence of

neurologic deficit. An informed consent was signed by the patient relatives to participate in the study.

Exclusion criteria:

1. Patients with chronic renal failure, liver cell failure, known cancer, or thyroid illness.
2. Patients with embolic and hemorrhagic stroke.
3. Patients with brain space occupying lesions.
4. Patients with CNS infections (e.g encephalitis).

All patients were subjected to the following :

I- Thorough history taking and full examination as follow :

A- History of the present illness and past history of previous hospital admissions and any medical disorder with particular attention to HTN, DM, cardiovascular disease, dys-lipidemia, smoking, past history of stroke and family history of similar attacks.

B- Full general examination with special attention to :

- BP measurement after patient admission. It was measured by a mercury sphygmomanometer with the patient recumbent in bed with the arm supported and positioned at the level of the heart. Mean arterial blood pressure (MAP) was calculated as follow :

$$MAP = \frac{(2 \times DP) + SP}{3}$$

- Pulse examination and character.
- Temperature and respiratory rate.
- Full cardiac examination including heart sounds and valvular lesions.

C- Full neurologic examination (Mental state, cranial nerves, sensory and motor systems, gait and cerebellar function examination)

(II) Routine investigations including complete blood picture, renal and liver function tests, bleeding profile (PT, PTT, INR), lipid profile (LDL-C, HDL-C, total cholesterol and serum triglycerides), fasting and 2 hours postprandial blood glucose levels, serum uric acid, C-reactive protein, chest x-ray and ECG in addition to Echocardiography and carotid doppler .

(III) Neuroimaging : All patients were subjected to CT scan of the brain. They were examined on admission and after 48 h if the initial scan was normal.

(IV) MetS was diagnosed according to IDF criteria (2006) as central obesity (defined as waist circumference ≥94cm in males and ≥80 cm in females for Arab population) plus two of the following: triglycerides ≥150 mg/dl, HDL-C <40 for men or

<50 for women, Bp ≥130/85 mmHg and fasting plasma glucose ≥100 mg/dl

(V) Severity assessment: That was done by the most commonly used scoring systems in ICU which are Glasgow coma scale (GCS) **[5]** and Acute Physiology and Chronic Health Evaluation (APACHE II) score **[6]**.

All data were coded, checked, entered and analyzed using SPSS software version 17 **[7]**.

A- Glasgow coma scale (Steiner et al. 1997): [5]

	1	2	3	4	5	6
Eyes	Does not open eyes	Opens eyes in response to painful stimuli	Open eyes in response to voice	Open eyes Spontaneou sly	N/A	N/A
Verbal	Makes no sounds	Incomprehensi ble sounds	Utters inappropriat e words	Confused, disoriented	Oriented converses normally	N/A
Motor	Makes no movemen ts	Extension to painful stimuli (decerebrate response)	Abnormal flexion to painful stimuli (decorticate response)	Flexion/ Withdrawal to painful stimuli	Localizes painful stimuli	Obeys commands

Generally, brain injury is classified as : Severe with GCS ≤8, Moderate GCS 9-12, Minor GCS ≥13

B- APACHE II score [6]

Physiologic Variable	High Abnormal Range					Low Abnormal Range				
	+4	+3	+2	+1	0	+1	+2	+3	+4	Points
Temperature - rectal (^{0}C)	≥ 41	39-40.9		38.5-38.9	36-38.4	34-35.9	3233.9	30-31.9	≤ 29.9	
Mean Arterial Pressure - mm Hg	≥160	130-159	110-129		70-109		50-69		≤ 49	
Heart Rate (ventricular response)	≥180	140-179	110-139		70-109		55-69	40-54	≤ 39	
Respiratory Rate (non-ventilated or ventilated)	≥ 50	35-49		25-34	12-24	10-11	6-9		≤ 5	
Oxygenation: A-aDO_2 or PaO_2 (mm Hg) a. FIO_2 ≥0.5 record A-aDO_2 b. FIO_2 <0.5 record PaO_2	≥500	350-499	200-349		< 200 PO_2>70	PO_2 61- 70		PO_2 55-60	PO_2<55	
Arterial pH (preferred) Serum HCO3 (venous mEq/l) (not preferred, but may use if no ABGs)	≥7.7 ≥52	7.6-7.69 41-51.9		7.5-7.59 32-40.9	7.33-7.49 22-31.9		7.25-7.32 18-21.9	7.15-7.24 15-17.9	<7.15 <15	
Serum Sodium (mEq/l)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110	
Serum Potassium (mEq/l)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5	
Serum Creatinine (mg/dl) Double point score for acute renal failure	≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6			
Hematocrit (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20	
White Blood Count (total/ mm^3) (in 1000s)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1	
Glasgow Coma Score (GCS) Score = 15 minus actual GCS										
A. Total Acute Physiology Score (sum of 12 above points)										
B. Age points (years) ≤44 = 0; 45 to 54 = 2; 55 to 64 = 3; 65 to 74 = 5; ≥75 = 6										
C. Chronic Health Points (see below)										
Total APACHE II Score (add together the points from A+B+C)										

Interpretation of the score

0 – 4 = 4% death rate	20 – 24 = 40% death rate
5 – 9 = 8% death rate	29 – 29 = 55% death rate
10 – 14 = 15% death rate	30 – 34 = 75% death rate
15 – 19 = 25% death rate	Over 34 = 85% death rate

RESULTS

Table (1) shows Demographic, clinical and biochemical characteristics of the studied patients.

Table (2) shows the prevalence of MetS among 260 patients with ischemic stroke. 140 patients (53.8%) has MetS while 120 patients (46.2%) do not have MetS.

Table (3) shows the prevalence of MetS in relation to age and sex. It shows the more occurrence of MetS in males (55.7%) than females (44.3%). In males, the prevalence was more in the age group between 61-70 y. and decreasing after that while in females, this prevalence increase steadily from the age of 51 y. (P <0.001).

Table (4) shows the prevalence of the different components of MetS among acute ischemic stroke patients in males and females. It shows the more prevalence of MetS with 3 components than MetS with more than 3 components in acute non embolic ischemic stroke patients. This was more apparent in males while in females, MetS with more than 3 components was more prevalent than MetS with 3 components ($p < 0.0001$).

Table (5) shows the relative risk of increasing age, gender, obesity, hyperglycemia, decreased serum HDL-C, increased serum triglycerides, decreased GCS and increased APACHE II score on the mortality in ischemic stroke patients with MetS. It shows that an age over 60 years increases the relative risk of mortality by 1.2 folds. Male gender increases the relative risk of mortality by 1.1 folds. Also, obesity increases the relative risk of mortality by 1.2 folds. Hyperglycemia increases the relative risk of mortality by 1.04 folds. Decreased serum HDL-C level also increases the relative risk of mortality by 1.2 folds. Increased serum levels of triglycerides is another factor that increases the relative risk of mortality by 2.1 folds. This table also shows that admission GCS lower than 8 increases the relative risk of mortality in ischemic stroke patients with MetS by 4.2 folds. Also, patients with APACHE II score more than 20 on admission have a relative risk of mortality 1.8 folds.

Table (6) shows the effect of stage of HTN on the mortality in ischemic stroke patients with MetS. There was significant increase in mortality rate with the increase of MAP (mortality rate 16.4%, $P<0.001$).

Table (7) shows that MetS Per se increase relative risk of mortality in patients with ischemic stroke by 2.8 fold more than those without MetS.

Table (8) shows the backward stepwise regression analysis of the factors predicting survival among the study group including APACHE II score with cut-of point ≥ 20. It shows that MetS and APACHE II score are independent predictors of mortality.

Table (1) : Demographic, clinical and biochemical characteristics of the studied patients.

Variable	MetS.	Non MetS	t	P
Age	59.3 ± 8.7	57.9 ± 9.7	1.2	0.23
Sex : Male/Female	78/62	70/50	0.18 (x^2)	0.67
Systolic blood pressure	156.2 ± 29.1	135 ±28.1	8.41	0.000
Diastolic blood pressure	94.3 ± 8.9	81.8 ± 13.8	8.79	0.000
MAP	111.0 ± 17.3	98.4 ± 17.6	5.84	0.000
GCS	9.2 ± 3.34	10.17± 3.11	2.39	0.017
Fasting blood sugar	127 ± 90	79 ± 40	73.5	0.000
HDL-C	42.2 ± 8.3	45.9 ± 6.3	2.051	0.294
LDL-C	112.5 ± 14.9	110.6 ± 13.8	1.025	0.078
Uric acid	8.7 ± 3.2	8.4 ± 3.5	0.445	0.657
C-reactive protein	67.2 ± 69.3	55.9 ± 59.8	1.394	0.165
Serum Triglycerides	167.6 ± 39.9	148.1 ± 31.1	4.345	0.000
APACHE II score	18.81 ± 4.81	13.64± 4.4	3.30	0.002
Waist Circumference (meter)	0.985	0.753	9.20	0.000

Table (2) : Prevalence of MetS among acute non embolic ischemic stroke patients.

	MetS	Non MetS	Total
Number	**140**	**120**	**260**
Percent	**53.8**	**46.2**	**100%**

Table (3) : Prevalence of MetS according to age group in male and female patients.

	40-50 y.	51-60 y.	61-70 y.	≥ 70 y.	Total	X^2	OR (95%CI)	P
Male : Number	8	30	34	6	78/140	39.2	0.866-0.937	<0.001
Percent	10.2	38.5	43.6	7.7	55.7			
Female : Number	3	15	19	25	62/140			
Percent	4.8	24.2	30.7	40.3	44.3			

OR= Odds Ratio
CI= Confidence interval

Table (4) : Prevalence of different components of MetS among acute non embolic ischemic stroke patients in both genders.

	MetS with 3	MetS with >3	Total	X^2	P

	components	components			
Total no. (%)	**78 (55.71%)**	**62 (44.28%)**	**140**	**17.017**	**<o.ooo 1**
Males	56 (71.8%)	22 (28.2%)	78		
Females	22 (35.5%)	40 (64.5%)	62		

Table (5) : Relative risk of mortality in relation to increasing age, gender, obesity, hyperglycemia, decreased serum HDL-C, increased serum triglycerides, decreased GCS and increased APACHE II score in acute non embolic ischemic stroke patients with MetS.

		Deceased (n=48)	Survived (n=92)	Total (n=140)	RR
Age :	≥60 years	29	50	79	1.2
	<60 years	19	42	61	
Gender :	Male	28	50	78	1.1
	Female	20	42	62	
Obesity :	Present	45	85	130	1.2
	Absent	3	7	10	
Hyperglycemia :	Present	37	70	107	1.04
	Absent	11	22	33	
Serum HDL-C : mg/dl	≤41	23	37	60	1.2
	>41 mg/dl	25	55	80	
Serum triglyceride : mg/dl	≥170	31	34	65	2.1
	<170 mg/dl	17	58	75	
GCS:	≤8	35	20	55	4.2
	>8	13	72	85	
APACHE II score :	≥20	36	51	87	1.8
	<20	12	41	53	

Table (6) : Effect of stage of HTN on the mortality of acute non embolic ischemic stroke patients with MetS.

MAP (mmHg)	NO	Deceased	Survived	Mortality rate (%)	X^2	P
<100	34	4	30	11.8	76.4	<0.001
100-112	50	7	43	14		
113-133	38	7	31	18.4		
>133	18	5	13	27.8		
Total	**140**	**48**	**92**	**34.3**		

Table (7) : Relative risk of MetS Per se on mortality in patients with acute non embolic ischemic stroke.

	Deceased	Survived	Total	RR
MetS	48	92	140	3.4
Non MetS	12	108	120	
Total	**60**	**200**	**260**	

Table (8) : Backward stepwise regression analysis of the factors predicting survival among the studied patients.

Variable	B-value	St. Er	WALD	Sig.	95.0% C.I for Exp.	
					Lower	Upper
MetS	1.023	0.553	3.686	<0.03	0.979	7.908
APACHE II score	5.870	0.648	81.991	<0.001	99.407	1261.792
Constant	4.430	0.628	49.843	<0.001	-	-

Discussion

Stroke is a major community problem with a high incidence and major neurologic disabilities. MetS is becoming a health risk not only prevalent among US and European populations, but also in many countries. Recent studies demonstrated the prevalence of MetS in the hospitals and ICU settings and how it correlates with acute stroke **[8]**. The components of MetS and their cumulative effect on CVD results in significant morbidity and mortality. Over the past decade, a succession of research findings have produced preliminary clues on the relationship between MetS and stroke. Out of the different proposed criteria for the definition of MetS, the last and most expressive definition was proposed by the IDF **[1]**.

The aim of the present study was to estimate the prevalence of MetS in acute ischemic stroke patients and to evaluate the effect of age, sex, MetS and its components, GCS and APACHE II score on the mortality of acute ischemic stroke patients with this medical problem.

The study included 260 patients admitted in the stroke subunit in Zagazig University Hospital medical ICU in the period from January to September 2011. Ischemic stroke was confirmed by CT scan of the brain.

Among acute ischemic stroke patients, 140 of them had MetS (53.8%) compared to 120 patients without MetS (46.2%). This is in agreement with **Ford** , who stated that the prevalence of MetS is steadily rising with the obesity epidemic **[9]**.

Furthermore, the current study showed that MetS is highly prevalent in males (55.7%) compared to females (44.3%). These results agree with the IDF criteria. A screening program on residents ≥40 years showed that the prevalence of MetS is lower in women **[10]**.

The present study showed that patients with MetS had significantly higher age compared to those without MetS (62.5 $\pm$ 5.8 y. vs 57 $\pm$ 9.5 y. respectively). This finding is compatible with **Thomas et al.** who showed that the prevalence of MetS increases progressively with age especially in older women and this may be due to sedentary life, obesity and physical inactivity **[11]**. However, the prevalence of MetS increase with age in males 51-70 y. than progressively decrease after that while, in females it starts to increase at the age of 51 and continues to increase after that. These results coincide with NHANES Cohorts. These cohorts showed that MetS prevalence continues to increase in males up to 6th decade while in females, it is gradually increasing to and then exceeding that of males after the age of 60y. **[9]**. These results suggest an interaction between age and sex on the prevalence of MetS. Also, **Mokdad et al** stated that MetS increases with age related increase in obesity particularly central obesity **[12]**. In contrast, a higher prevalence of MetS in women was reported in two other large scale Cohorts **[13,14]**. These differences may be due to different ethnicity and the interaction of age and sex stated before.

When we analyzed the different components of MetS, we found that 71.8% of ischemic stroke male patients had 3 components of MetS compared to 28.2% with more than 3 components while in females, 35.5% of ischemic stroke patients had 3 components of MetS compared to 64.5% with more than 3 components of MetS. Indeed, a higher number of components of MetS was found to be associated with increased number of stroke events in both genders **[15]**.

We found an increased risk of mortality with the age of 60 y. and above by 1.2 folds . This is in harmony with **Nakanishi et al** who hypothesized that the aging process may imply changes in brain plasticity, diminishing the strength of the brain tissue that normally acts as a restriction wall to the extension of infarction**[16]**. Also, the incidence of stroke was found to increase with age in diabetic patients **[17]**.

The present study showed also that male gender increase the relative risk of mortality by 1.1 fold which agree with **McNeill et al. [18]**.

Also, the relative risk of mortality was found to be significantly increased in patients with MetS by 3.4 fold than those without MetS. This is in agreement with many different studies **[15,19]**. The current study showed also that increased severity of HTN increases mortality of those patients compared to normotensives ($P<0.001$). In a recent multicenter study, systolic BP >140 mmHg after ischemic stroke doubled the risk of subsequent death or disability **[20]**. In a meta-analysis of 23 randomized trials, antihypertensive treatment reduced the risk of stroke by 32% (95% CI, 24%-39%; $P=0.004$) compared to no treatment **[21]**.

We found also that glucose intolerance increase the relative risk of mortality by 1.04 folds. This finding agree with the finding that hyperglycemia is correlated with greater infarct size and worse functional outcome **[22]**. Also, increased levels of triglycerides was found to increase the relative risk of mortality by 2.1 folds. It has been reported that hypercholesterolemia may be associated with an increased risk of disability after stroke,

independent of comorbidities **[23]**. On the other hand, cholesterol lowering treatment had been shown to produce a beneficial effect on stroke outcome **[24]**.

We found also that low HDL-C level increased the relative risk of mortality by 1.2 folds in those patients. This may be explained by the hypothesis that under certain conditions as DM, MetS or due to diet composition, the HDL molecule may by dysfunctional with impaired anti-oxidant, anti-inflammatory and anti-thrombotic properties **[25]**.

Regarding APACHE II score, we found that it was significantly increased in MetS patients compared to non MetS patients (18±4 vs 13±4). APACHE II score above 20 increased the relative risk of mortality by 1.8 folds. This emphasized the importance of this score in the prediction of outcome of acute illnesses **[26]**.

As regard GCS, we found that patients with MetS had lower GCS than non MetS patients (9± 3 vs 10±3). Patients with GCS less than 8 carried increased relative risk of mortality by 4.2 folds. This is in agreement with the result of **Navarette et al**., that emphasized the importance of GCS in evaluating and predicting the outcome of acute neurologic conditions **[27]**. The GCS and APACHE II scores were found to be able to predict mortality in ICU **[6,28]**. From all of the above, a wide list of factors determine the outcome of acute ischemic stroke patients, backward stepwise regression analysis showed that MetS Per se and APACHE II score are good predictors of mortality.

In conclusion, MetS is highly prevalent in acute non embolic ischemic stroke patients especially in elderly patients and is associated with poor clinical outcome. MetS and APACHE II score can be used as independent predictors of mortality in those patients.

Finally, this study reaffirms the need to design preventive as well as treatment strategies for MetS as part of the general guidelines for stroke prevention and management.

References

1- **International Diabetes Federation (IDF) (2006) :** The international diabetes federation consensus world wide definition of the metabolic syndrome. Available http://www.idf.org/webdata/.docs/IDF-met-def-final.pdf.accessed 28/1/2012.
2- **Martin BC, Warram JH, Krolewski AS et al. (1992) :** Role of glucose and insulin resistance in development of type 2 diabetes mellitus: results from a 25-year follow-up study. Lancet; 340 : 925-929.
3- **Lakka HM, Lakka TA, Tuomilehto J et al. (2002):** Abdominal obesity is associated with increased risk of acute coronary events in men. Eur Heart J; 23 : 706-713.
4- **Tkac I (2005) :** Metabolic syndrome in relationship to type 2 diabetes and athero-sclerosis. Diabetes Res Clin Pract.; 68 (Suppl.) : S2-S9.
5- **Steiner T, Mendoza G, De Georgia M et al. (1997) :** Prognosis of stroke patients requiring mechanical ventilation in a neurological critical care unit. Stroke; 28 : 711-715.
6- **Rordorf G, Koroshetz E, Efird JT et al. (2000) :** Predictors of mortality in stroke patients admitted to an intensive care unit. Crit Care Med; 18 : 1301-1305.

7- **Levesque R (2010) :** SPSS programming and data management : A guide for SPSS and SAS users, Fourth Edition, SPSS Inc., Chicago III.
8- **Refatt S, Sheikh B, Fath-Elbab M et al. (2010):** Metabolic syndrome in acute stroke patients in Al-Madina Al-Munawarah, Kingdom of Saudi Arabia. Journal of Medicine and Biochemical Science, ISSN, 2078-2073.
9- **Ford ES (2004):** Prevalence of the metabolic syndrome in US populations. Endocrinol Metab Clin North Am; 33 : 333-350.
10- **Li W, Ma D, Liu M et al. (2008) :** Association between metabolic syndrome and risk of stroke : a meta-analysis of cohort studies. Cerebrovasc Dis; 25 : 539-547.
11- **Thomas Brott MD, Lewis B, Morgenstern MD et al. (2005) :** Major risk factors for intracerebral hemorrhage in the young are modifiable. Stroke; 36 : 1881.
12- **Mokdad AH, Bowman BA and Ford ES (2001) :** The continuing epidemics of obesity and diabetes in the United States. JAMA; 286 : 1195-1200.
13- **Chien KL, Hsu HC, Sung FC et al. (2007) :** Metabolic syndrome as a risk factor for coronary heart disease and stroke : an 11-year prospective cohort in Taiwan community. Atherosclerosis; 194:214-221.
14- **Chen HJ, Bai CH and Yeh WT (2006):** Influence of metabolic syndrome and general obesity on the risk of ischemic stroke. Stroke; 37 : 1060-1064.
15- **Iso H, Baba S and Mannami T (JPHC Study Group) (2004):** Alcohol consumption and risk of stroke among middle-age men : the JPHC study Cohort I. Stroke; 35 : 1124-1129.
16- **Nakanishi N, Tu S, Shin Y et al. (2009):** Neuroprotection by the NR3A subunit of the NMDA receptor. J Neurosci; 29:5260-5265.
17- **Abbott RD, Wilson PWF, Kannel WB et al. (1998) :** High density lipoprotein cholesterol, total cholesterol screening, and myocardial infarction. Arterioscler; 8: 207-211.
18- **McNeill AM, Katz R and Girman CJ (2006) :** Metabolic syndrome and cardio-vascular disease in older people : The cardiovascular health study. J Am Geriatrics Soc; 54 : 1317-1324.
19- **Najarian RM, Sullivan LM and Kannel WB (2006):** Metabolic syndrome compared with type 2 diabetes mellitus as a risk factor for stroke : the Framingham Offspring Study. Arch Intern Med; 166 : 106-111.
20- **Zhang Y, Galloway JM, Welty TK et al. (2008) :** Incidence and risk factors for stroke in American Indians : The strong heart study. Circulation; 118 : 1577-1584.
21- **Pasternak RC, Smith SC Jr, Bairey-Merz CN et al. (2002):** ACC/AHA/NHLBI clinical advisory on the use and safety of stains. Circulation; 106 : 1024-1028.
22- **Baird TA, Parsons MW, Phanh T et al. (2003):** Persistent post-stroke hyperglycemia is independently associated with infarct expansion and worse clinical outcome. Stroke; 34 : 2208-2214.
23- **Vauthey C, de Freitas GR, van Melle G et al. (2000) :** Outcome after stroke with higher serum cholesterol levels. Neurology; 54 : 1944-1949.
24- **Amarenco P, Bogousslavsky J, Callahan 3rd A, et al. (2006) :** High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med; 355 : 549-559.
25- **Ansell H, Hirsh J and Hylek E (2008):** Pharmacology and management of the vitamin K antagonists. Chest; 133 (Suppl. 6) : 160S-198S.
26- **Knaus WA, Wagner DP, Draper EA et al. (1991) :** "The APACHE II prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults". Chest 100 (6) : 1619-1636.
27- **Navarrete-Navarro P, Rivera-Fernandez R, Lopez-Mutuberria MT et al. (2003) :** Outcome prediction in terms of functional disability and mortality among ICU-admitted severe stroke patients: A prospective epidemiological study in the South of the European Union (Evascan Project, Andalusia, Spain). Intensive Care Med; 29 : 1237-1244.
28- **Teasdale G, Murray G, Parker L (1979):** Adding up the Glasgow coma score. Acta Neurochir Suppl. (Wien) 28(1) : 13-16.