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A Review on the Role of Hypertension in the Metabolic Syndrome

Abdoljalal Marjani
Department of Biochemistry and Biophysics, Metabolic Disorders Research Center,
Gorgan Faculty of Medicine, Golestan University of Medical Sciences,
Gorgan, Golestan Province, Iran

Abstract: The metabolic syndrome significantly elevates the risk of cardiovascular disease and renal damage. Because of the relationships among different components of metabolic syndrome, it is difficult to understand the cause of these diseases. Blood pressure is one of the most factors of cardiovascular risk and disease. Hypertension is in many cases underrated and undiagnosed. It is suggested that there are different mechanisms to play a role in the blood pressure elevation in different subjects. Elevated blood pressure is believed a significant component of metabolic syndrome. Individuals with metabolic syndrome have been shown increased blood pressure or hypertension. It is reported that metabolic syndrome expand hypertension related cardiac and renal damage. The treatment of subjects with the metabolic syndrome is important to decrease the risk of cardiovascular and renal diseases, diabetes and hypertension and organ damage in the future. In present study, it was reviewed with a number of related articles on the role of hypertension (as one of the metabolic syndrome components) in metabolic syndrome.

Key words: Hypertension, metabile syndrome, disease

INTRODUCTION

There are many definitions for metabolic syndrome. The metabolic syndrome is described by obesity, high blood glucose, low level of high-density lipoprotein (HDL), high triglyceride, and high blood pressure. These are risk factors for cardiovascular disease (CVD) (Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, 2001). Several definitions of Metabolic Syndrome described in the World. World Health Organization's (WHO) decided to make to standardize the criteria. The National Cholesterol Education Program (NCEP) suggested the concept of Metabolic Syndrome (Shepherd *et al.*, 1995).

The Third Report of the National Cholesterol Education Program Adult Treatment Panel (ATP III) introduced a definition in 2001. ATP III is the most used definition in many studies. Subjects have taken in account having metabolic syndrome if they had any three or more of the following, according to the ATP III Criteria: (Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, 2001):

- Abdominal obesity: Waist Circumference highers than 102 and 88 cm in males and females, respectively
- Hypertriglyceridemia: Serum triglycerides level more than 150 mg dL⁻¹
- Low HDL-cholesterol: Serum HDL-cholesterol lowers than 40 and 50 mg dL⁻¹ in males and females, respectively

- High blood pressure: SBP highers than 130 mmHg and DBP highers than 85 mmHg or on treatment for hypertension
- High fasting glucose: Serum glucose level highers than 110 mg dL⁻¹ or on treatment for diabetes

Many studies have been approved the importance of the metabolic syndrome in different populations as a predictor of vascular disease (Shepherd et al., 1995; Downs et al., 1998; Ballantyne et al., 2001). Several studies have been shown that the metabolic syndrome is one of the significant public health problems in the World. The prevalence of metabolic syndrome alternates in different ethnic groups (Meigs et al., 2003; Cameron et al., 2004; King and Zimmet, 1998). There are many factors that can affect the metabolic syndrome prevalence and its components such as ethical differences, regimen, physical activity, age and sex (Cameron et al., 2004). One of the main causes of death among women in the world is cardiovascular disease (Lloyd-Jones et al., 2009). Studies among Italian, Korean, Chinese and Iranian populations have been shown that prevalence of metabolic syndrome were 3-3.5% (Trevisan et al., 1998), 13.8% (Kim et al., 2007), 17.8% (Gu et al., 2005) and 18.35% (Eshtiaghi et al., 2010) for females, respectively. The frequency of metabolic syndrome among Fars and Sistanee females were 20.62% and 23.75%, respectively (Marjani et al., 2012; Marjami et al., 2012). Studies in Greece and USA

have shown that prevalence of metabolic syndrome was similar in both gender (males and females) (Athyros et al., 2005; Cameron et al., 2004). Some studies indicated that females to be much more frequently (Cameron et al., 2004; Ramachandran et al., 2003), while in some other studies the metabolic syndrome was found to be more common among males (Ramachandran et al., 2003). The prevalence of metabolic syndrome depended on age progresses. In a study in Turkey, it has been shown that the prevalence of metabolic syndrome changes in different age groups. It was shown that the prevalence of the metabolic syndrome was 15.3, 23.1, 28.0, 26.0 and 20.5% among people aged from 30 to 39, 40 to 49, 50 to 59, 60 to 69, 70 to 79 and ≥80 years old, respectively (Sanisoglu et al., 2006). In other study in US, it has been reported that the prevalence of the metabolic syndrome was 16.5, 40.3 and 46.4% for males and 19.1, 33.8 and 56.0%, respectively, for females aged from 20 to 39, 40 to 59 and ≥60 years old, respectively. It was found that there is an association between older age groups and a higher prevalence of metabolic syndrome (Ford et al., 2006). One of the most effective determining factors of cardiovascular risk and disease is blood pressure. Hypertension is in many cases underrated and undiagnosed. It is suggested that there are different mechanisms to play a role in the blood pressure elevation in different subjects. Many studies have been shown that the metabolic syndrome confers an elevated risk of cardiovascular disease and mortality (Lakka et al., 2002; Ridker et al., 2003; Sattar et al., 2003; Isomaa et al., 2001). It has been revealed that the metabolic syndrome may be increased in hypertensive patients (Schillaci et al., 2004). It seems that the association between increased cardiovascular risk and metabolic syndrome may be depended on an elevated incidence of preclinical cardiovascular and renal alterations in hypertension and metabolic syndrome patients (Isomaa et al., 2001; European Society of Hypertension, ESH-ESCGC, 2003; Vakili et al., 2001; Cerasola et al., 1996; Karalliedde and Viberti, 2004). Study of Reaven et al. (1996) have been shown that metabolic alterations may play in the blood pressure regulation. Many studies have indicated that there is an association between insulin resistance and blood pressure (Every et al., 1993; Manolio et al., 1990; Chen et al., 1995) and some other studies were not in agreement with these findings (Dowse et al., 1993; Collins et al., 1990; Muller et al., 1993). Some findings have been shown that there is an association between the metabolic syndrome and hypertension in 50% of patients (Reaven et al., 1996). Ethnic variations in the association between the metabolic syndrome and hypertension have been shown in many studies (Ferrinin et al., 1987; Shen et al., 1988;

Howard et al., 1996; Pollare et al., 1990; Edwards et al., 1998). Some studies have indicated that there are different relationships between the metabolic syndrome and hypertension in people who live in different areas, but their ethnicity is the same (Manolio et al., 1990; Chen et al., 1995; Zimmet et al., 1994). In present study, it was reviewed with a number of related articles on the role of hypertension (as one of the metabolic syndrome components) in metabolic syndrome.

DIFFERENT OBSERVATIONS

The metabolic syndrome is highly frequent worldwide. It can be seen in nearly one-third of patients with hypertension. The metabolic syndrome significantly elevates the risk of cardiovascular disease and renal damage. Because of the relationships among different components of metabolic syndrome, it is difficult to understand the cause of these diseases. It has been identified that obesity and insulin resistance may play a significant role in the elevation of blood pressure and the progression of hypertension. In spite of the fact that its exact mechanisms are not completely clear. More than 80% of individuals with the metabolic syndrome have shown a blood pressure in the high normal or hypertension. Studies have shown that patients with metabolic syndrome have a 5.5-fold risk of diabetes and 2-fold risk of hypertension when compared with subjects without metabolic syndrome (Franklin, 2005). Some studies have shown the relationship of the high prevalence of blood pressure abnormalities in the metabolic syndrome and incidence of organ damage (Mancia et al., 2007). These studies have shown that all components of the metabolic syndrome donate to elevated blood pressure. This can promote cardiac, renal and brain tissue damages (Khan et al., 2007; Reaven, 2001). The importance of hypertension depends on as risk factors in the progression of cardiovascular disease and the main cause of morbidity and mortality. Hypertension often stays undiagnosed. It may cause kidney damage and heart failure (Kearney et al., 2005). The association of elevated blood pressure and metabolic abnormalities has been identified long time before the metabolic syndrome be approved (Kannel, 1996). Before 1997, hypertension was explained if blood pressure value was above 160/90 mmHg. The definition of hypertension alterates if an elevation in systolic or diastolic blood pressure of 5 mmHg occurre, which is associated with an elevation in cardiovascular disease (Kannel, 1995). In 1997, the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure suggested a value of 140/90 mmHg for the

general population and 130/85 mmHg for diabetic subjects JNC, 1997). In 2003, this committee suggested a value of 130/80 mmHg for diabetic (Chobanian et al., 2003). In 2003, the European Society of Hypertension and Cardiology also mentioned a new definition of blood pressure as a value under 120/80 mmHg (GC, European society of hypertension, ESH-ESCGC (2003). Choi et al. (2003) have been shown that blood pressure was not related to other cardiovascular disease risk factors. Study of Saad et al. (1991) indicated that there is an association between blood pressure and insulin resistance among different ethnic groups. In the study of Chen et al. (1995) on Chinese people have shown that hypertention was linked to the metabolic syndrome in females. Vazquez et al. (2003) reported that 62% hypertensive patients were seemed to have metabolic syndrome. Schillaci et al. (2004) have found that metabolic syndrome is a useful index for detection of future cardiovascular disease in hypertensive patients. Their results have been shown that metabolic syndrome increases cardiovascular disease risk in hypertensive patients. In a study has been shown that the prevalence of metabolic abnormalities collaborated with hypertension in two control and hypertensive groups (0.8 to 35.3%, respectively). Most of the hypertensive patients (Approximately 91.3%) have shown one associated cardiovascular risk factor (Rantala et al., 1999). There is an association between the metabolic syndrome and the risk of diabetes mellitus and cardiovascular disease. The prevalence of metabolic syndrome in Japanese type 2 diabetic patients was 26.37%. It has been shown that the prevalence was higher in males than females (45.9, 28.0%, respectively) (Shimajiri et al., 2008). A study indicated that the overall prevalence was 32.6% in Korean people. The prevalence was reported to be 46.9% in males and 65.1% in females (Kim et al., 2008). The Saudis with type 2 diabetes has been shown that the overall prevalence was 22.64% (19.49 male, 25.17% female) (Ahmed, 2008). Reported that the prevalence of metabolic syndrome in type 2 diabetic patients was 53.27% in females and 48.71% in males. They have found that the prevalence of metabolic syndrome in Gorgan was significantly high when compared with findings (Marjani and Moujerloo, 2011). Diabetes mellitus and hypertension are interdepended diseases. Diabetes mellitus make people susceptible to cardiovascular disease (Epstein and Sowers, 1992; The National High Blood Pressure Education Program Working Group, 1994). A study has shown that patients with diabetes have a 2-fold risk of hypertension when compared with subjects without diabetes (The National High Blood Pressure Education Program Working Group, 1994). Genetic differences and lifestyle may be important factors in promoting to hypertension and diabetes mellitus in

different subjects. The prevalence of hypertension and diabetes seems to be elevating in developed countries. Studies have shown that the prevalence of hypertension and diabetes elevates with age (Mogensen, 1990; Mykkanen et al., 1994). Hypertension causes diabetic retinopathy and blindness (The National High Blood Pressure Education Program Working Group, 1994). It is suggested to identify both hypertension and diabetes and treatment of subjects must begin quickly. Hypertension frequently causes the progress of nephropathy in many diabetic subjects (Mogensen, 1990; Mykkanen et al., 1994).

CONCLUSION

One of the important components of metabolic syndrome is hypertension. Many studies suggested that metabolic syndrome expand hypertension related cardiac and renal damage. Hypertension is closely collaborated with the metabolic syndrome. The influence of blood pressure regulation on mortality and cardiovascular disease is important. It looks like to confer a higher cardiovascular risk on the top of the risk caused by blood pressure enhancement. Alterations in lifestyle in developed and developing countries cause the epidemic growth of overweight and obesity, metabolic abnormalities, diabetes mellitus, cardiovascular disease and death. The first therapeutic step suggestion is alterations in lifestyle. It is important to change dietary habit and elevates daily activation. Initiation of antihypertensive treatment is needed to reduce blood pressure levels. The aim of treatment of individuals with the metabolic syndrome is to decrease the high risk of cardiovascular and renal diseases, diabetes and hypertension and organ damage.

REFERENCES

Ahmed, A.A., 2008. The prevalence of metabolic syndrome among type 2 Saudi diabetic patients: A particular view in Gurayat Province. Middle East J. Family Med., 6: 3-7.

Athyros V.G., E.S. Ganotakis, M. Bathianaki, I. Monedas and I.A. Goudevenos *et al.*, 2005. MetS-Greece Collaborative Group. Awareness, treatment and control of the metabolic syndrome and its components: A multicentre Greek study. Hellenic J. Cardiol., 46: 380-386.

Ballantyne C.M., A.G. Olsson, T.J. Cook, M.F. Mercuri, T.R. Pedersen and J. Kjekshus, 2001. Influence of low high-density lipoprotein cholesterol and elevated triglyceride on coronary heart disease events and response to simvastatin therapy in 4S. Circulation, 104: 3046-3051.

- Cameron, A.J., J.E. Shaw and P.Z. Zimmet, 2004. The metabolic syndrome: Prevalence in worldwide populations. Endocrinol. Metab. Clin. N. Am., 33: 351-375.
- Cerasola, G., S. Cottone, G. Mule, E. Nardi and M.T. Mangano *et al.*, 1996. Microalbuminuria, renal dysfunction and cardiovascular complication in essential hypertension. J. Hypertens, 14: 915-920.
- Chen, C.H., S.T. Tsai, J.H. Chuang, M.S. Chang, S.P. Wang and P. Chou, 1995. Population-based study of insulin, C-peptide and blood pressure in Chinese with normal glucose tolerance. Am. J. Cardiol., 76: 585-588.
- Chobamian, A.V., G.L. Bakris, H.R. Black, W.C. Cushman and L.A. Green et al., 2003. The seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure: The JNC 7 report. J. Am. Med. Assoc., 289: 2560-2571.
- Choi, K.M., J. Lee, K.B. Kim, D.R. Kim and S.K. Kim et al., 2013. Factor analysis of the metabolic syndrome among elderly Koreans: The South-West Seoul study. Diabetic Med., 20: 99-104.
- Collins, V.R., G.K. Dowse, C.F. Finch and P.Z. Zimmet, 1990. An inconsistent relationship between insulin and blood pressure in three Pacific island populations. J. Clin. Epidemiol., 43: 1369-1378.
- Downs, J.R., M. Clearfield, S. Weis, E. Whitney and D.R. Shapiro et al., 1998. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: Results of AFCAPS/TexCAPS. Air force/Texas coronary atherosclerosis prevention study. J. Am. Med. Assoc., 279: 1615-1622.
- Dowse, G.K., V.R. Collins, K.G.M.M. Alberti, P.Z. Zimmet, J. Tuomilehto, P. Chitson and H. Gareeboo, 1993. Insulin and blood pressure levels are not independently related in Mauritians of Asian Indian, Creole or Chinese origin. J. Hypertension, 11: 297-307.
- ESH-ESCGC, 2003. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J. Hypertens, 21: 1011-1053.
- Edwards, K.L., C.M. Burchfiel, D.S. Sharp, J.D. Curb and B.L. Rodriguez et al., 1998. Favors of the insulin resistance syndrome in nondiabetic and diabetic elderly Japanese-American men. Am. J. Epidemiol., 147: 441-447.
- Epstein, M. and J.R. Sowers, 1992. Diabetes mellitus and Hypertension. Hypertension, 19: 403-418.
- Eshtiaghi, R., A. Esteghamati and M. Nakhjavani, 2010. Menopause is an independent predictor of metabolic syndrome in Iraman women. Matutritas, 65: 262-266.

- Every, N.R., E.J. Boyko, E.M. Keane, J.A. Marshall, M. Rewers and R.F. Hamman, 1993. Blood pressure, insulin and C-peptide levels in San Luis Valley, Colorado. Diabetes Care, 16: 1543-1550.
- Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, 2001. Executive summary of the 3rd report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III). J. Am. Med. Assoc., 285: 2486-2497.
- Ferrinin, E., G. Buzzigoli and R. Bonadonna, 1987. Insulin resistance in essential hypertension. N. Engl. J. Med., 317: 350-357.
- Ford, E.S., C. Li, G. Imperatore and S. Cook, 2006. Age, sex and ethnic variations in serum insulin concentrations among U.S. youth: Findings from the National Health and Nutrition Examination Survey 1999-2002. Diabetes Care, 29: 2605-2611.
- Franklin, S.S., 2005. Hypertension in the Metabolic Syndrome. In: Metabolic Syndrome and Related Disorders (Ishwarlal and Jialal (Eds.). Vol. 4, Mary Ann Liebert, Inc., Irvine, pp. 287-298.
- Gu D, K. Reynolds X. Wu J. Chen and X. Duan *et al.*, 2005. Prevalence of the metabolic syndrome and overweight among adults in China. Lancet, 365: 1398-1405.
- Howard, B.V., E.T. Lee, J.L. Yeh, O. Go, R.R. Fabsitz, R.B. Devereux and T.K. Welty, 1996. Hypertension in adult American Indians: The strong heart study. Hypertension, 28: 256-264.
- Isomaa, B., P. Almgren, T. Tuomi, B. Forsen and K. Lahti *et al.*, 2001. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care, 24: 683-689.
- JNC, 1997. The sixth report of the joint national committee on prevention detection evaluation and treatment of high blood pressure. Arch. Intern. Med., 157: 2413-2446.
- Kannel, W.B., 1995. Framingham study insights into hypertensive risk of cardiovascular disease. Hypertens Res., 18: 181-196.
- Kannel, W.B., 1996. Blood pressure as a cardio vascular risk factor: Prevention and treatment. JAMA, 275: 1571-1576.
- Karalliedde, J. and G. Viberti, 2004. Microalbuminuria and cardiovascular risk. Am. J. Hypertens, 17: 986-993.
- Kearney, P.M., M. Whelton, K. Reynolds, P. Munter, P.K. Whelton and J. He, 2005. Global burden of hypertension: Analysis of worldwide data. Lancet, 365: 217-223.

- Khan, S.H., F.A. Khan, A. Ijaz, A. Sattar, M. Dilwar and R. Hashim, 2007. Hypertension and metabolic syndrome: Impact of clustering of hypertension in subjects with metabolic syndrome. Pak. Med. Sci., 23: 903-908.
- Kim, H.M., J. Park, S.Y. Ryue and J. Kim, 2007. The effect of menopause on the metabolic syndrome among Korean women the Korean national health and nutrition examination survey, 2001. Diabetes Care, 30: 701-706.
- Kim, W.Y., J.E. Kim, Y.J. Choi and K.B. Huh, 2008. Nutritional risk and metabolic syndrome in Korean type 2 diabetes mellitus. Asia Pac. J. Clin. Nutr., 17: 47-51.
- King, H. and P. Zimmet, 1998. Trends in the prevalence and incidence of diabetes: Noninsulin dependent diabetes mellitus. World Health Stat, 41: 190-196.
- Lakka, H.M., D.E. Laaksonen, T.A. Lakka, L.K. Niskanen, E. Kumpusalo, J. Tuomilehto and J.T. Salonen, 2002. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. J. Am. Med. Assoc., 288: 2709-2716.
- Lloyd-Jones, D., R. Adams, M. Carnethon, G. De Simone and T.B. Ferguson et al., 2009. Heart disease and stroke statistics - 2009 update: A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation, 119: e21-e181.
- Mancia, G., M. Bombelli, G. Corrao, R. Facchetti and F. Madotto *et al.*, 2007. Metabolic syndrome in the Pressioni arteriose monitorate E Loro Associazioni (PAMELA) study: Daily life blood pressure, cardiac damage and prognosis. Hypertension, 49: 40-47.
- Manolio, T.A., P.J. Savage, G.L. Burke, K. Liu and L.E. Wagenknecht *et al.*, 1990. Association of fasting insulin with blood pressure and lipids in young adults. The CARDIA study. Arteriosclerosis, 10: 430-436.
- Marjani, A. and M. Moujerloo, 2011. The metabolic syndrome in type 2 diabetic subjects in Gorgan, Iran. J. Pak. Med. Assoc., 61: 458-461.
- Marjani, A., N. Shahini, O.A. Atabay and R.G. Tabari, 2012a. Prevalence of metabolic syndrome among sistanee ethnic women. Adv. Stud. Biol., 4: 363-372.
- Marjani, A., S. Hezarkhani and N. Shahini, 2012b. Prevalence of metabolic syndrome among fars ethnic women in north east of Iran. World J. Med. Sci., 7: 17-22.
- Meigs, J.B., P.W.F. Wilson, D.M. Nathan, R.B. D'Agostino, K. Williams and S.M. Haffner, 2003. Prevalence and characteristics of the metabolic syndrome in the San Antonio heart and framingham offspring studies. Diabetes, 52: 2160-2167.

- Mogensen, C.E., 1990. Prevention and treatment of renal disease in insulin-dependent diabetes mellitus. Semin Nephrol., 10: 260-273.
- Muller, D.C., D. Elahi, R.E. Pratley, J.D. Tobin and R. Andres, 1993. An epidemiological test of the hyperinsulinemia-hypertension hypothesis. J. Clin. Endocrinol. Metab., 76: 544-548.
- Mykkanen, L., S.M. Haffner, J. Kuusisto, K. Pyorala and M. Laakso, 1994. Microalbuminuria precedes the development of NIDDM. Diabetes, 43: 552-557.
- Pollare, T., H. Lithell and C. Berne, 1990. Insulin resistance is a characteristic feature of primary hypertension independent of obesity. Metabolism, 39: 167-174.
- Ramachandran, A., C. Snehalatha, K. Satyavani, S. Sivasankari and V. Vijay, 2003. Metabolic syndrome in urban Asian Indian adults-a population study using modified ATP III criteria. Diabetes Res. Clin. Pract., 60: 199-204.
- Rantala, A.O., H. Kauma, M. Lilja, M.J. Savolainen, A. Reunanen and Y.A. Kesamemi, 1999. Prevalence of the metabolic syndrome in drug-treated hypertensive patients and control subjects. J. Int. Med., 245: 163-174.
- Reaven, G.M., 2001. Insulin Resistance, Compensatory Hyperinsulinemia and Coronary Heart Disease: Syndrome X Revisited. In: Handbook of Physiology Section 7: The Endocrine System Vol. 2: The Endocrine Pancreas and Regulation of Metabolism, Jefferson, L.S. and A.D. Cherrington (Eds.). Oxford University Press, New York, pp: 1169-1197.
- Reaven, G.M., H. Lithell and L. Landsberg, 1996. Hypertension and associated metabolic abnormalities. The role of insulin resistance and the sympathoadrenal system. N. Engl. J. Med., 334: 374-382.
- Ridker, P.M., J.E. Buring, N.R. Cook and N. Rifai, 2003. C-reactive protein, the metabolic syndrome and risk of incident cardiovascular events: An 8-year followup of 14,719 initially healthy American women. Circulation, 107: 391-397.
- Saad, M.F., S. Lillioja, B.L. Nyomba, C. Castillo and R. Ferraro et al., 1991. Racial differences in the relation between blood pressure and insulin resistance. N. Engl. J. Med., 14: 733-739.
- Samisoglu, S.Y., C. Oktenli, A. Hasimi, M. Yokusoglu and M. Ugurlu, 2006. Prevalence of metabolic syndrome-related disorders in a large adult population in Turkey. BMC Public Health, Vol. 6.
- Sattar, N., A. Gaw, O. Scherbakova, I. Ford and D.S. O'Reilly et al., 2003. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland coronary prevention study. Circulation, 108: 414-419.

- Schillaci, G., M. Pirro, G. Vaudo, F. Gemelli, S. Marchesi, C. Porcellati and E. Mannarino, 2004. Prognostic value of the metabolic syndrome in essential hypertension. J. Am. Coll. Cardiol., 43: 1817-1822.
- Shen, D.C., S.M. S hieh, M.M.T. Fuh, D.A. Wu, Y.D.I. Chen and G.M. Reaven, 1988. Resistance to insulin-stimulated-glucose uptake in patients with hypertension. J. Clin. Endocrinol. Metab., 66: 580-583.
- Shepherd, J., S.M. Cobbe, I. Ford, C.G. Isles and A.R. Lorimer *et al.*, 1995. Prevention of coronary heart disease with pravastatin in men with hyper cholesterolemia. N. Engl. J. Med., 333: 1301-1308.
- Shimajiri, Y., K. Tsunoda, M. Furuta, Y. Kadoya, S. Yamada, K. Nanjo and T. Sanke, 2008. Prevalence of metabolic syndrome in Japanese type 2 diabetic patients and its significance for chronic vascular complications. Diabetes Res. Clin. Pract., 79: 310-317.
- The National High Blood Pressure Education Program Working Group, 1994. National high blood pressure education program working group report on hypertension in diabetes. Hypertension, 23: 145-158.

- Trevisan, M., J. Liu, F.B. Bahsas, A. Menotti and the Risk Factor and Life Expectancy Research Group, 1998. Syndrome X and mortality: A Population-based study. Am. J. Epidemiol., 148: 958-966.
- Vakili, B.A., P.M. Okin and R.B. Devereux, 2001. Prognostic implications of left ventricular hypertrophy. Am. Heart J., 141: 334-341.
- Vazquez, V.A., C.A. Vazquez, R.O. Calderin, E.F. Buchaca, N.M.C. Alvarez, R.J. Paneque and J. Luno, 2003. [Metabolic syndrome in patients with essential hypertension]. Nefrologia, (Article in Spanish) 23: 423-431.
- Zimmet, P.Z., V.R. Collins, G.K. Dowse, K.G.M.M. Alberti and J. Tuomilehto et al., 1994. Is hyperinsulinaemia a central characteristic of a chronic cardiovascular risk factor clustering syndrome? Diabetic Med., 11: 388-396.