

## Association between Diabetes Mellitus and Heart Failure

Domma A. M.<sup>(1)</sup> And Gamal M.A.B.<sup>(2)</sup>

<sup>1</sup>, Faculty of Pharmacy, Al Margeb Univ. Libya, <sup>(2)</sup> Faculty of Pharmacy, Alazhar Univ., Egypt.

---

**Abstract:** Heart failure is a major and growing public health issue.

**Objective:** The aim of this study was to describe the association between diabetes mellitus and heart failure.

**Methods:** In this study 150 (78 males and 72 females) participants of Libyan attended Emergency department and Intensive Care in Tajoura National Heart Center and Tripoli Medical Center, were selected during the period from 4/2013 to 11/2013, with diagnosis of heart attack and their age range from 30-80 years old.

**Results:** In the present study the prevalence of heart failure increased by increasing age and is more common in patients with age range 61-70 years old in both males and female patients. Also the percentage of diabetic patients with heart attack, whatever males or females is significantly higher than non diabetic patients. This indicates very strong relation of diabetes with heart attack. The relation between heart attack development and hypertension in diabetic female patients was clear. On contrast to the results obtained with female patients; the number of male patients with heart attack and suffering from hypertension is slightly less than male patients with normal blood pressure. Concerning the lipid profile of patients under investigation, the result showed that high percentages of diabetic patients with heart attack, having normal lipid profile were encountered in this study. This means that serum cholesterol and triglycerides levels do not discriminate well between individuals with and without heart attack in case of diabetic patients.

**Conclusion:** Heart failure in diabetic patients is an important health problem and the results of this study firmly established the epidemiologic link between diabetes and heart failure. The risk of heart failure was increased approximately 6-fold in men and fourfold in women. There is well association between diabetes and heart failure that is linked at least in part to hypertension as in some cases of female patients. We can conclude that diabetes predicted heart failure independent of coexisting hypertension or coronary disease. Also we have to concentrate on the third possible mechanism that link diabetes mellitus to heart failure development in which diabetes may cause a cardiomyopathy.

---

### I. Introduction

Diabetes mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects of insulin secretion, insulin action, or a combination of both. In type 1 diabetes, it is due to a virtually complete lack of endogenous pancreatic insulin production, whereas in type 2 diabetes, the rising blood glucose results from a combination of genetic predisposition, unhealthy diet, physical inactivity, and increasing weight with a central distribution resulting in complex pathophysiological processes<sup>(1)</sup>. Recent estimates suggest that 195 million people throughout the world have diabetes and that this number will increase to 330, maybe even to 500 million, by 2030<sup>(2)</sup>. In developed countries, the prevalence of diabetes mellitus is higher in the elderly (over 65 years) population<sup>(3)</sup>.

Diabetes and cardiovascular diseases often appear as the two sides of a coin: on one side, diabetes mellitus has been rated as an equivalent of coronary heart disease, and conversely, many patients with established coronary heart disease suffer from diabetes or its pre-states<sup>(4)</sup>. Diabetes increases the risk of heart failure, independent of coronary heart disease and hypertension and may cause a cardiomyopathy. The term diabetic cardiomyopathy was initially introduced based upon postmortem findings in four diabetic adults who had risk of heart failure in the absence of coronary heart disease<sup>(5)</sup>.

There is a well established association between diabetes and heart failure that is linked at least in part to coronary heart disease and hypertension. Associations have also been reported between absolute blood glucose levels, glycemic control, and heart failure. The Framingham Study firmly established the epidemiologic link between diabetes and heart failure during 18 years of follow-up, compared with patients free from diabetes and in a general population of elderly. The risk of heart failure was increased 2.4-fold in men and fivefold in women<sup>(6)</sup>.

**Subjects and methods:** This study included one hundred and fifty patients who will present to Emergency department and intensive care unit in Tajoura National Heart Center and Tripoli Medical Center with diagnosis of heart failure during the period from 4/2013 to 11/2013. Samples of 10 ml. of blood were obtained from

each patient involved in the study, in non-heparinized tubes for the biochemical analysis for determination of serum glucose, triglycerides and cholesterol. The level of serum glucose were determined according to the method described by Tinder (Enzymatic colorimetric assay)<sup>(7)</sup> while the level of serum triglycerides were determined by GPO-PAP method as described by Young and Panstner<sup>(8)</sup> and Fossatic and Principe<sup>(9)</sup>. Serum cholesterol were determined by CHOD-PAP (Enzymatic colorimetric method) as described by Richmond<sup>(9)</sup>. Statistical analysis of the results; the difference between means +SD was tested at  $P < 0.05$  using Duncan's multiple range tests<sup>(10)</sup>.

## **II. Results**

Distribution of patients involved in according to their age and sex were illustrated in figure (1), 3.9% of males and 5.6% of female patients were less than 40 years old; 15.4% males and 5.6% females having ages ranged from 40-50 years old. Age range 51-60 years old included 25.6% of males and 22.2 % of females. However age range 61-70 included 33.3% of males and 43% of females. Finally 21.8 % of males and 23.6% of females were more than 71 years old. This findings indicated that heart failure is more common in patients with age range 61-70 years old in both males and female patients, where females are more liable to heart attack (43%) than male patients in the same age range (33.3%). This is followed by age range of 51-60; and age group older than 71 years, where the rate of heart attack is more or less equal in both males and females. Heart attack slightly more in male patients (25.6%) than female patients (22.2%) in patients with age range of 51-60 years, while in patients with age older than 70 years, the rate of heart attack is slightly more in female patients (23.6%) than male patients (21.8%). Moreover, the rate of heart attack in patients with younger age (less than 50 years), is much more common in males compared with females.

The incidence of heart attack in hypertensive and non hypertensive patients were illustrated in figure (2&3). The results indicated that in case of female patients with heart attack and suffering from hypertension the percentage (**65.3**) is significantly higher than females with normal blood pressure (**34.7**). This is not the case concerning male patients, where the percentage of male patients with heart attack and suffering from hypertension is (**44.9**) and those with normal blood pressure (**55.1**). On contrast to the results obtained with female patients; the number of male patients with heart attack and suffering from hypertension is slightly less than male patients with normal blood pressure. This means that there is a difference between males and females concerning the relation between blood pressure and occurrence of heart attack.

The incidence of heart attack in diabetic and non diabetic patients was illustrated in figure (4&5). The results indicated that the percentage of diabetic patients with heart attack, whatever males or females is significantly higher than non diabetic patients. The percentage of diabetic male patients with heart attack is (**85.9**) and that of non diabetic patients is (**14.1**). Also the percentage of diabetic female patients with heart attack is (**80.6**) and that of non diabetic patients is (**19.4**). This indicates the most important relation of diabetes with heart attack. Incidence of heart attack in patients according to hypertension and diabetic states was illustrated in figure (6 & 7).

The distribution of diabetic patients with heart attack in the study according to their age and their lipid profiles were illustrated in figures (8 & 9). The results indicated that in case of diabetic male patients the percentages of those having hypercholesterolemia and hypertriglyceridemia were 7.4 % and 22.4% respectively. However in case of diabetic female patients the percentages of those having hypercholesterolemia and hypertriglyceridemia were 3.4% and 20.7% respectively. This means that there is no clear evidence that increased total blood cholesterol and triglycerides concentration play an important role in development of heart attack in the diabetic patients involved in this study, if compared with the high percentage of diabetic patients with heart attack and having normal lipid profile.

## **III. Discussion**

Heart failure is a major and growing public health issue. In spite of significant advances in management and treatment, the mortality of patients with heart failure remains high. Heart failure is also a major cause of morbidity; chronic heart failure results in almost 1 million hospitalizations each year in the U.S. This has a major impact on health care expenditure. A better understanding of the mechanisms leading to heart failure may also help to design preventive strategies<sup>(10)</sup>.

In the present study the prevalence of heart failure increased by increasing age. These results indicated that heart failure is more common in patients with age range 61-70 years old in both males and female patients, where females are more liable to heart attack (43%) than male patients in the same age range (33.3%). The results of the current study agree with other studies which indicated that as the population ages increases the number of patients with heart failure increases and the economic burden of heart failure will inevitably increase. In 1991, the total inpatient and outpatient costs for heart failure were estimated to be \$38 billion (5.4% of the health care budget that year)<sup>(11)</sup>.

Considerably less is known about the prevalence of the combination of diabetes and heart failure and less information is available on the incidence of the combination of diabetes and heart failure. However the available information indicated that diabetes mellitus is a well known and important risk factor for cardiac disease. While the most common cardiac manifestation in diabetic patients is coronary artery disease, diabetes mellitus also appears to be strongly linked to heart failure<sup>(12)</sup>.

The first demonstration of an increased risk of heart failure in patients with diabetes mellitus was reported by Kannel and McGee based on data obtained from 20 years follow-up of the Framingham cohort. The incidence of heart failure according to sex and diabetic status showed an increased risk of heart failure was observed in patients with diabetes mellitus. In a study by Tenenbaum et al in patients with ischemic heart disease, the incidence of heart failure at 6 to 9-year follow-up was 35.7% in non diabetic patients, 39% in patients with impaired fasting glucose and 45.7% in diabetic patients<sup>(13)</sup>.

Prevalence of heart failure and glucose abnormalities varies somewhat in different studies. The prevalence of heart failure has been estimated to be 0.6–6.2% in Swedish men and these increases with age. This is similar to the overall prevalence of heart failure among both genders in the Rotterdam population and the Reykjavík Study. The most recent and extensive data on the prevalence of diabetes and heart failure are from the Reykjavík Study, showing that the prevalence of the combination heart failure and diabetes is 0.5% in men and 0.4% in women, increasing with increasing age. Heart failure was found in 12% of those with diabetes compared with only 3% in individuals without diabetes. Thus, there was a strong association between diabetes and heart failure<sup>(14)</sup>. Incidence of heart failure and glucose abnormalities among British outpatients, has been reported to be around 4/1000 person-years, rising with age<sup>(15)</sup>.

The results of the present study agree with that of previous study in that the percentage of diabetic patients with heart attack, whatever males or females is significantly higher than non diabetic patients. The percentage of diabetic male patients with heart attack is (85.9%) and that of non diabetic patients is (14.1%). Also the percentage of diabetic female patients with heart attack is (80.6%) and that of non diabetic patients is (19.4%). This indicates very strong relation of diabetes with heart attack. The results of the current study is different from the results of the above studies in that the percentage of diabetic patients suffering from heart attack is greater than that reported by other authors.

Various mechanisms may link diabetes mellitus to heart failure development by at least 3 mechanisms: **firstly**, associated comorbidities or risk factors such as hypertension may play a role; **secondly**, diabetes accelerates the development of coronary atherosclerosis; **thirdly**, experimental and clinical studies support the existence of a specific diabetic cardiomyopathy related to microangiopathy, metabolic factors or myocardial fibrosis.

Associated comorbidities or risk factors may partly account for the increased risk of heart failure in diabetic patients. These cardiovascular risk factors such as dyslipidaemia, hypertension, hypercoagulability, obesity and inflammation are part of the insulin resistance syndrome<sup>(16)</sup>.

The increased risk of atherosclerosis in diabetic patients may also contribute significantly to the increased risk of heart failure. Coronary artery disease is the underlying cause of heart failure in approximately two thirds of patients with left ventricular systolic dysfunction. Diabetes mellitus is associated with a markedly increased risk of coronary artery disease. In the Framingham study, the incidence of coronary artery disease was increased in diabetic subjects. In the study by Haffner et al, the seven-year incidence rate of myocardial infarction in diabetic subjects without prior myocardial infarction at baseline was 20.2% versus only 3.5% in non-diabetic subjects without prior myocardial infarction at baseline. This increased risk of atherosclerosis in diabetic subjects has been attributed to diverse mechanisms such as endothelial dysfunction or altered haemostatic factors (higher levels of fibrinogen, plasminogen activator-inhibitor-1 or VonWillebrand factor, or altered platelet function<sup>(17 & 18)</sup>).

There are also data to suggest that diabetes mellitus may predispose to heart failure development through the existence of a specific diabetic cardiomyopathy. The exact mechanism(s) by which diabetes mellitus may induce heart failure independent of epicardial coronary artery disease is (are) unknown but several hypotheses have been advanced; these include microangiopathy, metabolic factors, and fibrosis. Intramyocardial microangiopathy has also been observed in diabetic hearts; combined with functional abnormalities related to endothelial dysfunction, diabetic microangiopathy may explain the reduced coronary blood flow reserve observed in diabetic patients. Metabolic factors may also play a role in the development of myocardial dysfunction; hyperglycemia, impaired myocardial glucose uptake, and increased turnover of free fatty acids may all contribute to diabetes mellitus-related myocardial dysfunction<sup>(19 & 20)</sup>.

Finally, experimental and clinical data also point to a potential role for myocardial fibrosis in diabetic cardiomyopathy; intramyocardial accumulation of collagen is a well-demonstrated consequence of diabetes mellitus; moreover, the deposition of advanced glycation end products may result in increased left ventricular stiffness and consequently to diastolic dysfunction<sup>(21)</sup>.

In summary, various mechanisms may induce a specific diabetic cardiomyopathy. Whether this diabetic cardiomyopathy alone may cause heart failure is however unknown; another possibility is that these myocardial alterations related to diabetes mellitus may predispose to the development of heart failure in response to other insults such as coronary artery disease or hypertension. After an acute myocardial infarction, decreased compensatory responses of non-infarcted area have been described in diabetic patients. Similarly, a synergistic effect may exist between diabetes mellitus and hypertension for the development of myocardial fibrosis<sup>(22)</sup>.

The results of the present study indicated that in case of female patients with heart attack and suffering from hypertension the percentage (**65.3**) is significantly higher than females with normal blood pressure (**34.7**). This conclusion agrees with that observed in the Framingham cohort, diabetic women had higher blood pressures and were more obese than non-diabetics; diabetic women had<sup>(23)</sup>.

The same observation has been reported in heart failure populations in other studies, for example, diabetic patients were older and were more likely to have a history of hypertension than non-diabetic patients, 54% of diabetics had hypertension versus 38% of non-diabetics<sup>(24)</sup>.

Another evidence that relates development of heart attack to hypertension in diabetic female patients included in the current study, on comparing the percentage of the diabetic and hypertensive (**58.4%**) with the diabetic and nonhypertensive (**22.2%**) female patients, where there is a significant difference observed between the two groups.

An opposite observation was found concerning male patients in the current study, where the percentage of male patients with heart attack and suffering from hypertension is (**44.9**) and those with normal blood pressure (**55.1**). On contrast to the results obtained with female patients; the number of male patients with heart attack and suffering from hypertension is slightly less than male patients with normal blood pressure. This means that there is a difference between males and females concerning the relation between blood pressure and occurrence of heart attack. These results can be explained by the fact although hypertension may in part explain the higher incidence of heart failure in diabetic patients; other mechanisms must also play a role. Indeed, in most of the studies discussed previously, diabetes or poor glycemic control remained significantly associated with heart failure after adjustment for important baseline clinical variables including age, sex, and hypertension<sup>(25 & 26)</sup>.

Also this was clear from the results of this study on comparing the percentage of the diabetic and hypertensive (**44.9%**) with the diabetic and nonhypertensive (**41.0%**) male patients, where there is no significant difference observed between the two groups. This means that we cannot associate heart attack in diabetic male patients to hypertension and other mechanisms that may link diabetes mellitus to heart failure development must be considered.

The result of this study showed that diabetic male patients having hypercholesterolemia and hypertriglyceridemia were 7.4 % and 22.4% respectively and diabetic female patients having hypercholesterolemia and hypertriglyceridemia were 3.4% and 20.7% respectively. Also nearly there is no difference in lipid profile in diabetic females and diabetic males. However high percentage of diabetic patients with heart attack and having normal lipid profile were encountered in this study. This means that serum cholesterol and triglycerides levels do not discriminate well between individuals with and without heart attack in case of diabetic patients. The reason of this may be attributed to changing the dietary habits of patients for better direction with regard to the quantity and quality of dietary fat intake. On the other hand, increased cholesterol level in some of patients in the study may be attributed partly to alterations in the genetic characters. Also, high intakes of total fat have increased serum cholesterol<sup>(27)</sup>.

Our finding was in agreement with the result concluded that heart attack has been reported to present in normocholesterolemic subjects or hypercholesterolemic ones<sup>(27)</sup>.

From the above results and discussion we can conclude that diabetes predicted heart failure independent of coexisting hypertension or coronary disease. Also we have to concentrate on the third possible mechanism that links diabetes mellitus to heart failure development in which diabetes may cause a cardiomyopathy. The term diabetic cardiomyopathy was initially introduced based upon postmortem findings in four diabetic adults who had heart failure in the absence of coronary heart disease. Diabetic cardiomyopathy has been defined as ventricular dysfunction that occurs in diabetic patients independent of a recognized cause (eg, coronary heart disease, hypertension). However, the frequency with which this occurs is not well defined and there is some evidence that diabetic cardiomyopathy is uncommon in patients with type 1 diabetes in the era of intensive insulin therapy<sup>(28 & 29)</sup>. Also diabetes alone or in combination with a variety of risk factors (hypertension, hypercholesterolemia) can impair endothelial function. Increased oxidative stress brought about by hyperglycemia may be an important link between diabetes and vascular events<sup>(30)</sup>.

References

- [1]. DeFronzo R. A. 2004: International Textbook of Diabetes Mellitus. 3<sup>rd</sup> ed. Chichester , West Sussex, Hoboken, NJ: John Wiley.
- [2]. Wild S., Roglic G., Green A., Sicree R., King H. 2004: Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*; 27:1047–1053.
- [3]. Tuomilehto J., Borch-Johnsen K., Molarius A., Forsen T., Rastenyte D., Sarti C. and Reunanen A. 1998: Incidence of cardiovascular disease in Type 1 (insulin-dependent) diabetic subjects with and without diabetic nephropathy in Finland. *Diabetologia*, 41:784-790.
- [4]. Zarich S., Nesto R. 1989: Diabetic cardiomyopathy. *Am Heart J*; 118:1000.
- [5]. Konduracka E., Gackowski A. and Rostoff P. 2007: Diabetes-specific cardiomyopathy in type 1 diabetes mellitus: no evidence for its occurrence in the era of intensive insulin therapy. *Eur Heart J*; 28:2465.
- [6]. Kannel W. B., Hjortland M., Castelli W. P. 1974: Role of diabetes in congestive heart failure: the Framingham study. *Am J Cardiol*; 34:29–34.
- [7]. Tindler, P. 1969: Enzymatic colorimetric method for glucose determination. *Ann. Clin. Biochem.*, 6:24-27.
- [8]. Young D. and Pastaner L. 1975: Triglycerides determination. *Clin. Chem.*, 21:373D.
- [9]. Fossatic P. and Principe L. 1982: Triglycerides determination. *Clin. Chem.*, 28:2077-2080.
- [10]. Levit K. R., Lazenby H. C., Cowan C. A. and Letsch S. W. 1990: National health expenditures. *Health Care Financ Rev* 1991, 13:29-54
- [11]. O'Connell J. B. 2000: The economic burden of heart failure. *Clin Cardiol*, 23:III6-10
- [12]. Tuomilehto J., Borch-Johnsen K., Molarius A., Forsen T., Rastenyte D., Sarti C. and Reunanen A. 1998: Incidence of cardiovascular disease in Type 1 (insulin-dependent) diabetic subjects with and without diabetic nephropathy in Finland. *Diabetologia*, 41:784-790
- [13]. Tenenbaum A., Motro M., Fisman E. Z., Leor J., Boyko V., Mandelzweig L. and Behar S. 2002: Status of glucose metabolism in patients with heart failure secondary to coronary artery disease. *Am J Cardiol* , 90:529-532
- [14]. Thrainsdottir I. S., Aspelund T., Thorgeirsson G., Gudnason V., Hardarson T., Malmberg K. 2005: The association between glucose abnormalities and heart failure in the population based Reykjavik Study. *Diabetes Care*; 28:612–616.
- [15]. Johansson S., Wallander M.A., Ruigo'mez A., Garcia Rodr'iguez L. A. 2001: Incidence of newly diagnosed heart failure in UK general practice. *Eur J Heart Fail* .;3:225–231.
- [16]. Martens F. M., Visseren F. L., Lemay J., de Koning E. J. and Rabelink T. J. 2002: Metabolic and additional vascular effects of thiazolidinediones. *Drugs*, 62:1463-1480.
- [17]. Knobler H., Savion N., Shenkman B., Kotev-Emeth S. and Varon D. 1998: Shear-induced platelet adhesion and aggregation on sub endothelium are increased in diabetic patients. *Thromb Res*, 90:181-190
- [18]. Shechter M., Merz C. N., Paul-Labrador M. J. and Kaul S. 2000: Blood glucose and platelet-dependent thrombosis in patients with coronary artery disease. *J Am Coll Cardiol*, 35:300-307.
- [19]. Nitenberg A., Paycha F., Ledoux S., Sachs R., Attali J. R. and Valensi P. 1998: Coronary artery responses to physiological stimuli are improved by deferoxamine but not by L-arginine in non-insulin-dependent diabetic patients with angiographically normal coronary arteries and no other risk factors. *Circulation*, 97:736-743.
- [20]. Nahser P.J. Jr, Brown R. E., Oskarsson H., Winniford M. D. and Rossen J. D. 1995: Maximal coronary flow reserve and metabolic coronary vasodilation in patients with diabetes mellitus. *Circulation*, 91:635-640.
- [21]. Asif M., Egan J., Vasam S., Jyothirmayi G. N., Masurekar M. R., Lopez S., Williams C., Torres R. L., Wagle D. and Ulrich P. 2000: An advanced glycation end product cross-link breaker can reverse age-related increases in myocardial stiffness. *Proc Natl Acad Sci U S A*, 97:2809-2813.
- [22]. van Hoven K. H. and Factor S. M. 1990: A comparison of the pathological spectrum of hypertensive, diabetic, and hypertensive-diabetic heart disease. *Circulation*, 82:848-855.
- [23]. Kannel W. B. and McGee D. L. 1979: Diabetes and glucose tolerance as risk factors for cardiovascular disease: the Framingham study. *Diabetes Care*, 2:120-126.
- [24]. Dries D. L., Sweitzer N. K., Drazner M. H., Stevenson L.W. and Gersh B. J. 2001: Prognostic impact of diabetes mellitus in patients with heart failure according to the etiology of left ventricular systolic dysfunction. *J Am Coll Cardiol*, 38:421-428
- [25]. Iribarren C., Karter A. J., Go A.S., Ferrara A., Liu J. Y., Sidney S. and Selby J. V. 2001: Glycemic control and heart failure among adult patients with diabetes. *Circulation*, 103:2668-2673.
- [26]. Stratton I. M., Adler A. I., Neil H. A., Matthews D. R., Manley S. E., Cull C. A., Hadden D., Turner R. C. and Holman R. R. 2000: Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Bmj*, 321:405-412.
- [27]. Di-Mascio R., Marchioli R. and Vitullo F. 1995: Serum cholesterol and risk of ischemic stroke. *Prev Med*, 24:128.
- [28]. Boudina S. and Abel E. D. 2007: Diabetic cardiomyopathy revisited. *Circulation*; 115:3213.
- [29]. Konduracka, E., Gackowski A., Rostoff P., 2007: Diabetes-specific cardiomyopathy in type 1 diabetes mellitus: no evidence for its occurrence in the era of intensive insulin therapy. *Eur Heart J*; 28:2465.
- [30]. Giugliano D., Ceriello A. and Paolisso G. 1995: Diabetes mellitus, hypertension, and cardiovascular disease: the role of oxidative stress? *Metabolism*. 44:363–368.

Figure (1): Distribution of patients included in the study according to their age and sex.

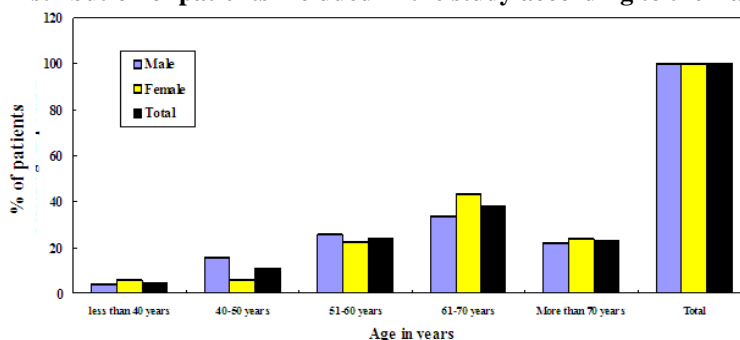


Figure (2): Percentage of heart attack in hypertensive and non hypertensive male patients.

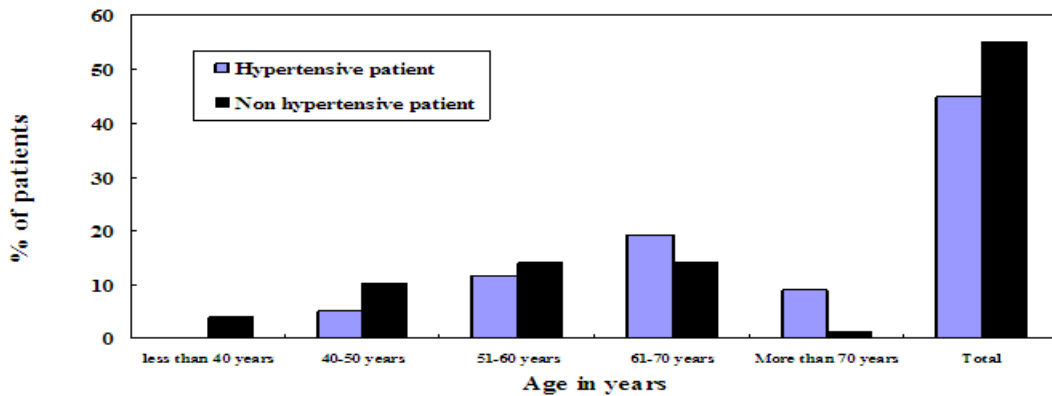


Figure (3): Percentage of heart attack in hypertensive and non hypertensive female patients.

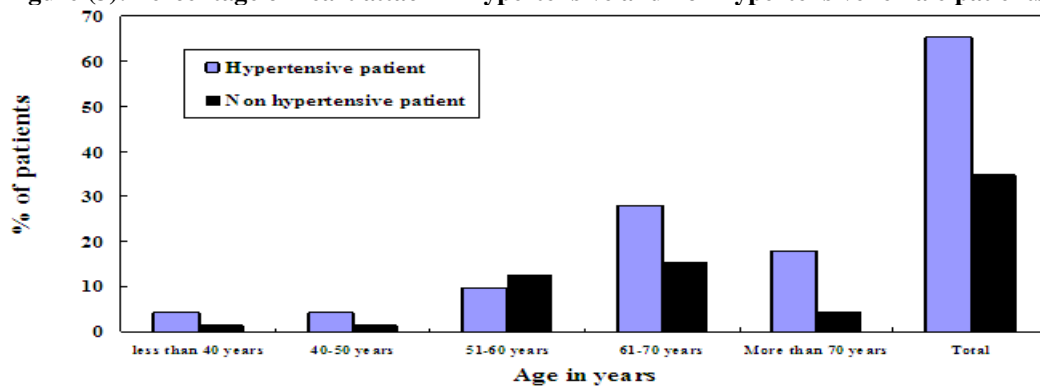


Figure (4): Percentage of heart attack in diabetic and non diabetic male patients.

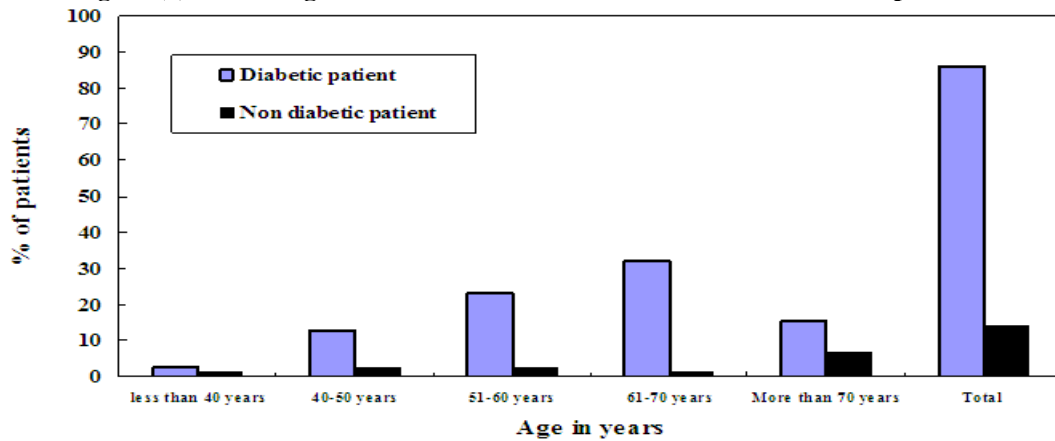


Figure (5): Percentage of heart attack in diabetic and non diabetic female patients.

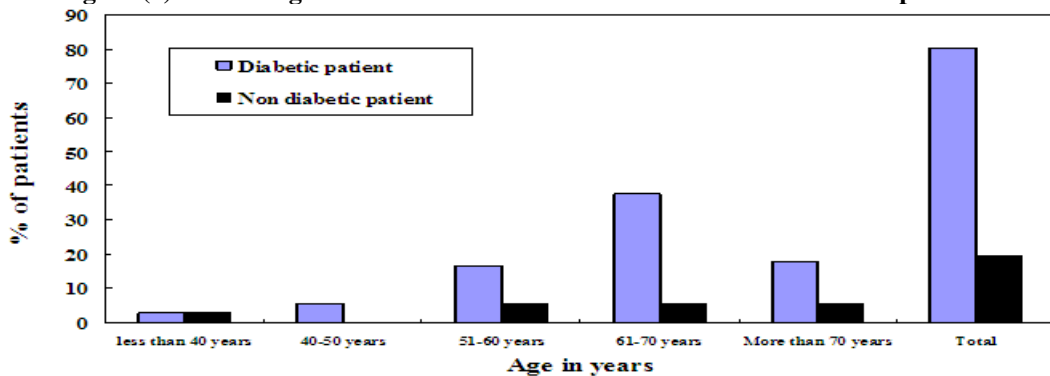


Figure (6): Incidence of heart attack in male patients according to hypertension and diabetic states.

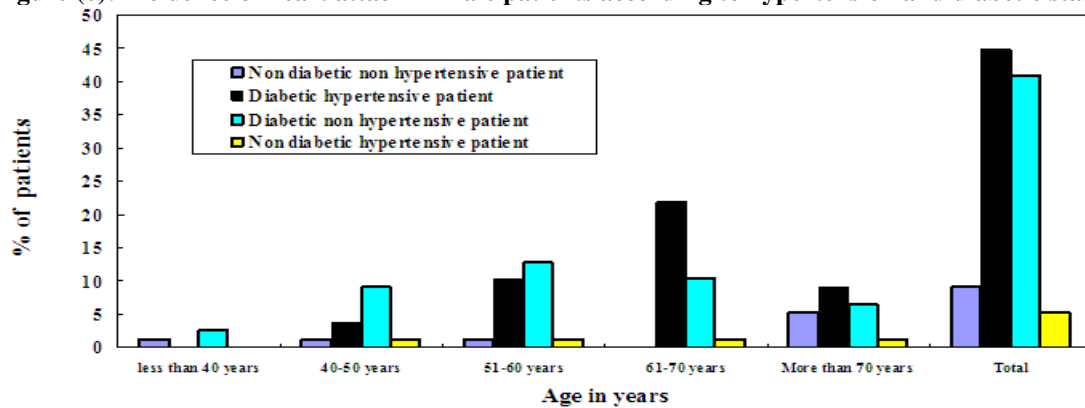


Figure (7): Incidence of heart attack in female patients according to hypertension and diabetic states.

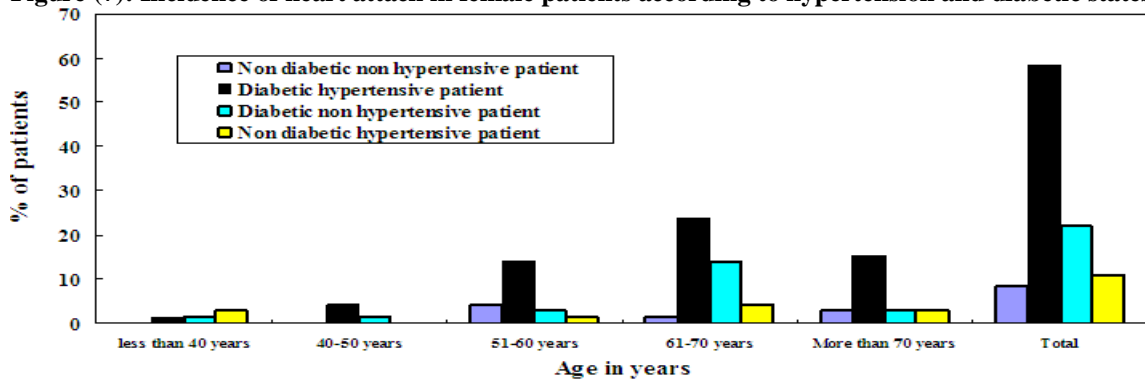


Figure (8): Incidence of heart attack in male patients according to their lipid profile.

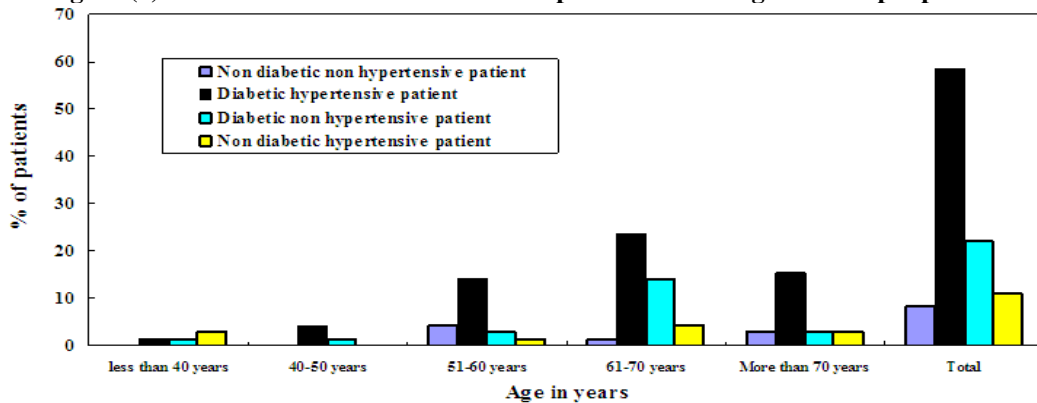


Figure (9): Incidence of heart attack in female patients according to their lipid profile.

