*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*
*e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 12 Ver. X (December. 2016), PP 94-97*
*www.iosrjournals.org*

# Cardiovascular Risk Factors in Acromegaly

Aem Haddam, Ns Fedala*, L Ahmed Ali*
*Department Of Diabetology , Bab El Oued Hospital*
**Department Of Endocrinology Bab El Oued Hospital ,Algiers, Algeria*

## I. Introduction

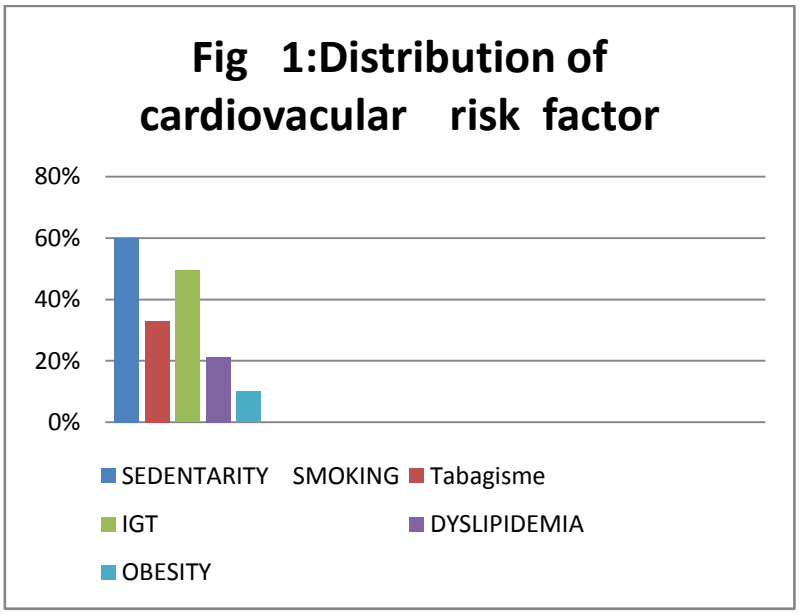
Individualized by Pierre Marie in 1886 Acromegaly is a disease characterized by a dysmorphic syndrome acquired, to which it owes its name and by many consequences (rheumatologic, cardiovascular, respiratory, metabolic effects ) that determine prognosis (1).
They are in fact all the more severe as the excess of GH has been prolonged and important. Among these complications, cardiovascular disorders are important to treat precociously because they cause increased morbidity and mortality. Analysis of the determinants of this mortality indicates that approximately 60% of patients die from cardiovascular pathologies, 25% from respiratory complications and 15% from cancer.
The survival of untreated acromegaly patients would be reduced by about 10 years. An untreated acromegaly is still evolving and its natural evolution is fatal. Only early treatment lets hope for a cure of the disease , limit deformation and prevent complications (1)(2)
The objective of this study is to report the cardiovascular complications observed in acromegaly

**Population, Methodology**

This is a 15-year retrospective study (2000 to 2015) involving 75 cases of patients in our department of endocrinology . In all cases hypersomatropism was related to a pituitary adenoma. The following cardiovascular risk factors were studied: family history of cardiovascular disease (AF), smoking, sedentary lifestyle, body mass index, prevalence of hypertension, diabetes mellitus, tolerance disorders Carbohydrate as well as dyslipidemia.

## II. Results

The average age of patients is 39.01 years [9-73 years] with a sex ratio of 0.57. The duration of the disease is 6.36 ± 4.4. The mean GH level was 53.02 ng / ml [1.74-78] One third of the patients are tobacco and two thirds of the patients are sedentary . HTA is found in 20% of cases (n: 15 cases) , family history of hypertension in 40% (n: 30 cases) and Obesity in 13.3% (n: 10 cases). Abnormalities in carbohydrate metabolism were found in 49.3% of cases with glucose intolerance (10%), diabetes mellitus (37.3%), and moderate hyperglycaemia (1.33%). A family history of diabetes mellitus was observed in 34.66% Dyslipidemia was found in nearly a quarter of cases (n: 16, 21.33%) with mixed dyslipidemia (13.33%), hypertriglyceridemia (5.33%) and hypercholesterolemia (2.66%). Nearly one third of patients have at least three cardiovascular risk factors, half have at least two risk factors and 10% of patients have all risk factors (Fig1)



## III. Discussion

Several pathological conditions are associated with abnormal GH secretion. In general, the causes for hypersecretion or hyposecretion of GH involve tumors in the hypothalamus or the pituitary (1). Chronic hypersecretion of GH leads to giantism or acromegaly, depending on whether the hypersecretion occurs before or after complete ossification of the epiphyseal plates in the skeletal system. Chronic hypersecretion of GH before the epiphyseal plates have ossified causes exaggerated and prolonged growth in long bones, resulting in giantism. Some individuals have grown to 8 feet tall or more (4) .

In adults chronically elevated GH levels result in acromegaly. No increase in height occurs because of the ossified epiphyseal plates. The condition does result in an increased diameter of fingers, toes, hands, and feet; the deposition of heavy bony ridges above the eyes; and a prominent jaw (5). The influence of GH on soft tissues results in a bulbous and broad nose, and enlarged tongue, thickened skin, and sparse subcutaneous adipose tissue. Nerves frequently are compressed as a result of the proliferation of connective tissue (5)(6). Because GH spares glucose usage, chronic hyperglycemia results, frequently leading to diabetes mellitus and the development of severe atherosclerosis (7).

The prevalence of acromegaly, per million individuals, is 40, 69 and 63 with a respective annual incidence of 3 to 4. The age of onset of the disease is difficult to specify since the onset is insidious and progressive. It is 32.7 years (8 to 62 years) for men, and 34.9 years (9 to 64 years) for women. It strikes with equal frequency men and women (8) (9).

Cardiovascular events are the cause of increased morbidity and mortality. Indeed, arterial hypertension is 2 to 3 times more frequent than in the general population. It appears to be largely due to the hypervolemia characteristic of acromegaly, the result of the increase in the sodium pool due to the stimulating action that GH exerts on the cell-dependent sodium-potassium-ATP pump Tubular kidneys (10).

Hypervolemia increases renal blood flow and glomerular filtration, which inhibits the renin-angiotensin system . Therefore , hypertension of acromegaly is blood pressionn dependent to low renin. When acromegaly is cured, blood pressure improves in about 40% of cases, but only normalizes in about 15% of cases (11).

This improvement in blood pressure goes in the same direction as the elimination of the hydrosodic overload observed immediately after intervention on the pituitary, with reduction of the volume. The fact that hypertension is inconsistently cured with acromegaly suggests that other mechanisms are involved and / or that it is secondarily autonomous (12).

Hypersomatotropism is responsible for a visceromegaly that can affect several organs. The frequency of cardiomegaly is not negligible. It is observed in 60 to 70% of cases. It is better evaluated by ultrasound as confirmed by necroscopic and radiological studies. There are two evolutive stages (13).

Hyperkinetic hypertrophic Cardiomyopathy is the first observed; The left ventricular hypertrophy which characterizes it Is either concentric or predominant on the septum (which is peculiar to acromegaly) or isolated septal. It can be observed even in the absence of arterial hypertension, coronary artery disease, valvulopathy and diabetes mellitus. This myocardial hypertrophy is also peculiar since it is usually accompanied by no alteration of the ventricular function (13).

The hemodynamic studies show that the cardiac output is increased: the heart rate is moderately accelerated but especially the volume of systolic ejection is greatly increased. The increase in cardiac output is accompanied by a decrease in systemic arterial resistance which, if sufficient, maintains normal blood pressure . At this stage, filling pressures, which can also be measured during right catheterization (pulmonary capillary pressures for the left ventricle, right atrial for the right ventricle), are normal (14) .

Hypertrophic and hyperkinetic acromegalic cardiomyopathy could result from a direct effect of GH on the myocardium, which would determine an increase in ventricular mass, or even contractility, similar to that seen with GH treatment of The normal or hypopituitary man or in the rat whose myocardium, subjected to a chronic hypersecretion of GH, improves both contractility and energy efficiency. However, in some cases, myocardial contractility appears to be altered (13)(14).

Cardiomyopathy may also represent cardiac adaptation to chronic hypervolaemia and / or hypermetabolism characteristic of acromegaly. In the absence of effective treatment, the clinical picture may worsen and progress to congestive cardiomyopathy. This leads to left or overall cardiac insufficiency, with increased filling pressures, ventricular dilatation, and decreased cardiac output to low or normal values. Disorders of the ventricular rhythm or conduction may be added. Coronary artery disease, hypertension and / or diabetes, favored by hypersomatotropism, could precipitate the evolution of cardiomyopathy towards the congestive stage (12).

Such developments can be observed independently and seem especially favored by the prolonged course of acromegaly. It should be noted, however, that even at this stage, reduction in GH levels can lead to an improvement in heart failure in the short to medium term. The reasons leading to the transition to heart failure

remain hypothetical: depletion of the overloaded ventricle due to organomegaly and hypermetabolism, decreased ventricular compliance when the extent of fibrosis becomes critical ... .. In fact, it is the intricacy of these phenomena that is at issue (10)

The histological study shows that hypertrophy of the myocardial fibers is almost constant and that interstitial fibrosis is very often associated with it. Lymphocytic infiltration, which may extend to myocarditis, is frequent. These changes, almost constant in cases of hypertension, are also frequent in its absence (15)

Coronary artery disease and atheromatosis may possibly be associated but appear to be mostly due to the elderly (16).

Described in 3 to 15% of cases, it can aggravate acromegalic cardiomyopathy. GH stimulates lipolysis and antagonizes the antilipolytic action of insulin, hence the increase of non-esterified fatty acids in acromegaly. Endogenous hypertriglyceridemia, type 4, Increase in VLDL (very low density lipoprotein), mild and moderate, is common in acromegaly. It is probably the result of an increase in hepatic synthesis of VLDL (possibly due to hyperinsulinism) and decreased catabolism (decreased lipoprotein lipase). The reduction in the level of GH, whether by surgery or octreotide, results in the reduction of triglycerides in 10 to 20% of the acromegals ( 17) (18).

Anomalies of glucose tolerance are also observed . There is a patent diabetes mellitus that requires the use of insulin in one third of the cases (1) (2). This diabetes plays an aggravating role in the evolution of the cardiovascular pathology of acromegals (19). The healing of acromegaly leads to its improvement, even its disappearance. Sleep apnea (SA) can also be observed.They affect 60-80% of acromegals (more often men). These SA contribute to cardiovascular pathology. In the vast majority of cases, apneas are obstructive (but a third of the patients also have central apneas) (20). They are related to the anatomical changes caused by mandibular and maxillary growth, soft tissue thickening, particularly in the palate and uvula, and changes in the angulation of the different bone segments, explaining hypercollapsibility of the lateral and posterior walls of the hypopharynx. The hypertrophy of the tongue also plays a role as well as that of submaxillary submax glands (20)(21).

After treatment of acromegaly, the apnea-hypopnea index improved, as well as the index of obstructive and the oximetry. However, if some patients, cured of their acromegaly, their SA disappear, others keep it, Justifying a nocturnal positive pressure ventilation (21).

In our series, the incidence of cardiovascular risk factors conforms to those of the literature concerning the frequency of various atherogenic risk factors in acromegaly patients (20 to 56% for diabetes, 16 to 46% for intolerance to Glucose and 20-50% for HTA) (4). . Because of the high prevalence of complications associated with acromegaly and some of which constitute true cardiovascular risk factors, screening and early management are necessary in all patients in order to improve the prognosis and reduce Morbidity and mortality. The incidence of risk factors in a population of acromegals is higher than the general population. This is explained by the lipolytic effect and insulin resistance of growth hormone. Thus to reduce the morbidity and mortality of these patients at very high cardiovascular risk, It is necessary to act early and efficiently on its factors.

## IV. Conclusion

Acromegaly is a serious disease by its metabolic, cardiovascular and neoplastic repercussions. Cardiovascular complications are the leading cause of acromegalic mortality. Because of their high prevalence, rigorous follow-up is required in all patients

## References


[1]. Colao A, Ferone D, Marzullo P, Lombardi G. Systemic complications of acromegaly: epidemiology, pathogenesis, and management. Endocr Rev 2004;25:102-52.
[2]. Wright AD, Hill DM, Lowy C, Fraser TR 1970 Mortality in acromegaly. Q J Med 34:1–16.
[3]. Holdaway IM, Rajasoorya C. Epidemiology of acromegaly. Pituitary 1999;2:29-41.
[4]. Giustina A, Casanueva FF, Cavagnini F, Chanson P, Clemmons D, Frohman LA, et al. Diagnosis and treatment of acromegaly complications. J Endocrinol Invest 2003;26:1242-7.
[5]. Molitch ME. Clinical manifestations of acromegaly. Endocrinol Metab Clin North Am 1992;21:597-614.
[6]. Lieberman SA, Bjorkengren AG, Hoffman AR. Rheumatologic and skeletal changes in acromegaly. Endocrinol Metab Clin North Am 1992;21:615-31.
[7]. Biermasz NR, van Thiel SW, Pereira AM, Hoftijzer HC, van Hemert AM, Smit JW, et al. Decreased quality of life in patients with
[8]. acromegaly despite long-term cure of growth hormone excess. J Clin Endocrinol Metab 2004;89:5369-76.
[9]. Holdaway IM, Rajasoorya C. Epidemiology of acromegaly. Pituitary 1999;2:29-41.
[10]. Etxabe J, Gaztambide S, Latorre P, Vasquez JA 1993 Acromegaly: An epidemiological study. J Endocrinol Invest 16:181–187.
[11]. Hejtmancik MR, Bradfield JY, Herrmann GR 1951 Acromegaly and the heart: A clinical and pathologic study. Ann Intern Med 34:1445–1456.
[12]. Maison P, Demolis P, Young J, Schaison G, Giudicelli JF, Chanson P. Vascular reactivity in acromegalic patients: preliminary evidence for regional endothelial dysfunction and increased sympathetic vasoconstriction. Clin Endocrinol (Oxf) 2000;53:445-51.
[13]. Sacca L, Cittadini A, Fazio S. Growth hormone and the heart. Endocr Rev 1994;15:555-73.
[14]. Clayton RN. Cardiovascular function in acromegaly. Endocr Rev 2003; 24:272-7.
[15]. Bihan H, Espinosa C, Valdes-Socin H, Salenave S, Young J,Levasseur S, et al. Long-term outcome of patients with acromegaly and
[16]. congestive heart failure. J Clin Endocrinol Metab 2004;89:5308-13.

[17]. Lie JT, Grossman SJ 1980 Pathology of the heart in acromegaly: anatomic findings in 27 autopsied patients. Am Heart J 100:41–52.
[18]. Giustina A, Casanueva FF, Cavagnini F, Chanson P, Clemmons D, Frohman LA, Gaillard R, Ho K, Jaquet P, Kleinberg DL, Lamberts SW, Lombardi G, Sheppard M, Strasburger CJ, Vance ML, Wass JA, Melmed S Diagnosis and treatment of acromegaly complications. J Endocrinol Invest 2003 ; 26:1242–1247
[19]. Dekkers OM, Biermasz NR, Pereira AM, Romijn JA, Vandenbroucke JP 2008 Mortality in acromegaly: a metaanalysis. J Clin Endocrinol Metab 93:61–67
[20]. Holdaway IM, Bolland MJ, Gamble GD 2008 A meta-analysis of the effect of lowering serum levels of GH and IGF-I on mortality in acromegaly. Eur J Endocrinol 159:89–95
[21]. Melmed S 2006 Medical progress: acromegaly. N Engl J Med 355:2558–2573
[22]. Herrmann BL,Wessendorf TE, AjajW, Kahlke S, Teschler H, Mann K. Effects of octreotide on sleep apnoea and tongue volume (magnetic resonance imaging) in patients with acromegaly. Eur J Endocrinol 2004;151:309-15.
[23]. Ip MS, Tan KC, Peh WC, Lam KS. Effect of Sandostatin® LAR® on sleep apneoa in acromegaly: correlation with computerized
[24]. tomographic cephalometry and hormonal activity. Clin Endocrinol (Oxf) 2001;55:477-83.