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Abstract

Acromegaly is a rare and insidious disease characterized by chronic excess growth hormone, leading to various morphological changes and systemic complications. Despite its low prevalence, acromegaly poses a significant socioeconomic burden on patients and healthcare systems. This review synthesizes the current state of knowledge on the psychosocial burden, disability, impact on daily life, and cost of acromegaly disease, focusing on the quality of life, partnership, medical care and treatment afflictions, participation in daily activities, professional and leisure impairment, and cost of treatment for acromegaly and its comorbidities. It also examines management strategies, coping mechanisms, and interventions aimed at alleviating this burden. A comprehensive understanding of the extent of the socioeconomic burden in acromegaly is crucial to develop effective strategies to improve treatment and care. Further research is warranted to explore the myriad factors contributing to this burden, as well as the efficacy of interventions to alleviate it, ultimately enhancing the quality of life for patients with acromegaly.

Keywords: acromegaly, pituitary, socioeconomic burden, quality of life, disability, absenteeism, cost of illness

Significance

Acromegaly defines a rare endocrine disorder resulting from excess growth hormone due to pituitary tumors. Even when biochemical remission is achieved and maintained, significant impairments persist in the daily life of patients. Our review highlights the substantial psychosocial, emotional, and financial impacts beyond physical difficulties experienced by patients with acromegaly and emphasizes how these are often exacerbated by diagnostic delays and treatment side effects. Moreover, it elucidates the complexities of managing acromegaly, underscoring the need for comprehensive strategies to improve diagnostic accuracy, mitigate treatment repercussions, and address patients' emotional needs. Providing a comprehensive perspective, the review lays the groundwork for informing health policy and tailoring patient care to a more personalized approach for improved patient outcomes.

Introduction

Acromegaly is an insidious disease resulting from a chronic excess growth hormone that slowly leads to a wide variety of morphological changes (such as coarsening of facial features or enlargement of the hands, feet and soft tissue) and systemic complications,[1] among others hypertension, diabetes, arthropathy, and cardiovascular disease (to name a few). It is a rare disease with an estimated prevalence of around 50-70 patients per million people,[2] but there is evidence of increasing prevalence in the last decades.[3] Furthermore, regional variations in epidemiology have been described.[4–6] Unsurprisingly, many healthcare professionals hardly ever get to see a patient with acromegaly and may therefore not be prepared to identify the disease. Additionally, differences in medical practice, documentation, and likely cultural differences can influence the reporting of symptoms and screening patterns in geographically different populations.[7] The slow progression of symptoms makes it often difficult even for their treating physicians to link the signs of affected patients with the underlying disease. For these reasons, acromegaly remains largely unrecognized for a period of several years,[8] during which the devastating effects of the condition continue. The longer the delay until diagnosis is, the higher morbidity and mortality are.[9] Even worse, while adequate therapy may restitute some function, only a few comorbidities are truly reversible.[10] As such, this would be a new impetus to rather consider acromegaly as a condition leading to physical, emotional, and psychological sequelae, instead of referring to "persistent symptoms of acromegaly" which insinuates that they are still (and falsely) reversible.

Rare diseases inherently bear the potential for increased psychosocial burden due to a lack of understanding by peers, often difficult diagnostic processes, and a paucity of efficient treatment strategies. This also imposes an economic burden on patients and the health system to an extent that is more often than not poorly understood.[11] In acromegaly, morphological changes with facial disfigurement have an important impact on patients, especially in women. The disability faced by organ complications such as heart failure and severe arthropathy also has far-reaching implications not only in the medical work-up but also in the social and work life of those who suffer from this disease. There is an intricate interplay of

several factors that lead to an increased socioeconomic burden of acromegaly, many of which may not be perceivable at first sight, such as racial disparities.[12] Several questionnaires have been constructed and validated to examine disease perception, quality of life, and other patient-reported outcomes,[13] some specific to acromegaly such as AcroQoL and Acro-TSQ.[14–16] Patient-reported outcomes are considered crucial in the evaluation of disease activity. Recently, harmonization and the development of core outcome sets for clinical practice and research have been advocated.[17] Over the past decades and especially in recent years, numerous studies have focused on the socioeconomic burden that acromegaly imposes. In this review, we aim to summarize the current state of knowledge on the psychosocial burden, disability, impact on daily life, and the cost of acromegaly illness.

Methods

Our search strategy to assemble the literature for this narrative review consisted of querying PubMed for the following terms: "acromegal*" combined with "soci*", "economic", "cost", "burden", "quality of life", "qol", "disability", "impairment", "partner*", "psych*", "work", "absenteeism", and "coping". We screened all articles published between 2001 and 2023 for relevance. A manual review of the reference list of all retrieved articles was performed to identify additional references not indexed by PubMed or not identified by the above-mentioned search terms. The final reference list was defined based on the relevance of each paper to the scope of this review.

Socioeconomic burden

The burden imposed by acromegaly on patients and their surroundings is multilayered and complex. Firstly, there is the burden imposed by the complex diagnostic path: patients have many different physician encounters and quite some time passes until the correct diagnosis is made.[18] Only then does adequate treatment start, effectively meaning an invasive procedure and a 50-50 chance of subsequent (and most likely lifelong) medical treatment. Besides the emotional burden that accompanies interventions, there are potential side effects and costs of the treatment as well. Of course, several comorbidities may already have developed or still progress that lead to loss of functioning, maybe even in the context of liabilities that cannot be fulfilled anymore. This imposes additional costs on the patient and society. Naturally, as is the nature of chronic diseases, this impairs quality of life in several dimensions. And it affects the support community of the patient, namely family and friends.

Psychosocial burden

In an article published in 2006, in *Neuroendocrinology* covering the costs involved in medical care for acromegaly patients, the principal author Robert Knutzen—a patient with acromegaly himself and CEO, Chairman of the Board and Co-founder of the Pituitary Network Association—makes an intimate confession of being able to "relate to the prolonged course of treatment for kidney stones, migraine headaches, weight gain, sexual and emotional disorders, sleep apnea, plus innumerable developing skin tags and cysts for many years before recognition of acromegalic status."[19] That same article also presents accounts of other patients, picturing the suffering of a syndromic disease (as well as its economic burden). Similarly, in another article Jill Sisco—president of the online support group Acromegaly Community—points out what she and other patients experienced: "For a patient living with acromegaly, the cost and burden of delay of diagnosis can be substantial and, in many cases, irreversible. Not just the monetary factors should be considered, but also the mental, physical, and hormonal tolls that are taken from delays."[20] Patients in a recent study accompanying a virtual education program expressed "quality of life/mental health" to be the most important personal care goal. About a third of the patients classified "quality of life/mental health" as an unmet need.[21]

Quality of life

The impairment of quality of life in acromegaly has been described in numerous cross-sectional as well as interventional studies with conflicting results. Several studies reported beneficial effects on quality of life in biochemically controlled patients due to medical treatment. In one such study, 27 patients completed three validated questionnaires at six predetermined time points before, during, and after treatment. Several domains of the questionnaires improved during treatment, mainly in the first year of treatment.[22] The last evaluation took place 2.5 years after diagnosis and quality of life was still reduced in acromegaly patients compared to the general population despite successful treatment. In another study during a 4-year follow-up in patients with long-term biochemical control of acromegaly, the scores in the AcroQoL questionnaire were progressively impaired,[23] especially in patients that underwent radiotherapy. Another longitudinal study that followed 58 patients over 5.7 years also came to the conclusion that impaired quality of life persisted despite long-term biochemical remission,[24] particularly in the subscales "Appearance" and "Physical Function" of the AcroQoL. Compared to healthy controls, quality of life remains low even if there are improvements from successful therapy.[25] The importance of long-standing and/or poorly controlled morphometric changes in psychosocial well-being is accentuated by the fact that in most studies female patients with acromegaly scored worse in terms of quality of life than their male counterparts.[22,26,27] Remarkably, radiotherapy also plays an important role in worsening the quality of life,[23,26–28] but this has not uniformly been reported.[29] The presence and frequency of comorbidities,[30] diagnostic delays, lack of diagnostic acumen in medical care provision,[31] as well as depression and anxiety are predictive of worse quality of life in acromegaly.[32] Patients often have difficulty accepting the disease and its consequences.[33] On the contrary, patients who learn to accept their illness have a better quality of life.[34] Overall, treatment leads to improvements even though not full restitution of quality of life: a recently published meta-analysis by Broersen et al.[35] identified 46 studies that count a total of 3301 patients with acromegaly that describe an improvement in symptoms and quality of life during treatment in both treatment-naive patients and previously treated patients with acromegaly.

Impact on partnership

Partner support is an important part of a patient's support environment. But caregiving has both negative and positive consequences that can even lead to a poorer quality of life than the

patient being cared for with certain chronic diseases.[36] Little is known about the partners of patients with acromegaly and how the disease affects them. In a study by Andela et al.,[37] focus group interviews of partners of people with pituitary disease were conducted, highlighting concerns related to pituitary disease and negative beliefs about medication, coping challenges, relationship issues, social issues, and unmet needs in care. The focus group discussions also revealed difficulties in the relationship during active disease and treatment periods with some accounts of a lasting negative impact. However, some partners reported a strengthening of their relationship through the common fight against chronic disease and the hardships it comes with. Another study compared the perception of acromegaly in remission in the patient–relative dyad by interviewing 27 patients in remission and their relatives. Both patients and their relatives completed a set of questionnaires. Relatives accurately assessed the body image of the patient, but the answers in other domains diverged. The quality of life of relatives was not altered.[38]

An essential aspect to consider when evaluating the socioeconomic burden of patients with acromegaly in this context is the impact on their sexual functioning. Aspects of sexuality have been investigated especially in male patients.[39–41] On the one hand, tumor mass as well as treatment-related damage from surgery or radiation may alter pulsatility of gonadotropin secretion and therefore lead to hypogonadotropic hypogonadism. However, acromegaly comorbidities, such as cardiovascular disease, hypertension, sleep apnea, and diabetes, are associated with decreased sexual functioning, mainly promoting a decline in erectile function, desire, and arousal. Whether or not growth hormone (GH) and/or insulin-like growth factor I (IGF-I) exert direct effects on sexual function is not fully elucidated.[39]

A noteworthy cross-sectional study conducted in Italy aimed to investigate this area, among other factors, in a sample of 223 acromegaly patients from five referral centers.[42] The results revealed that sexual dysfunction was a prevalent problem in most of these patients, with women experiencing more severe impairments: 60% of men experiencing erectile dysfunction, of which 25% had severe impairment, as well as sexual dysfunction identified in 77% of women, especially in presence of concomitant cardiovascular disease. In addition, distortion of body image and mood disorders appeared to be important modulators of sexual functioning in female patients with acromegaly. Interestingly, the Italian study showed higher scores of sexual desire in female patients with full disease control, unlike a prior single-center study from Turkey.[43]

Afflictions from medical care and treatment

One of the most fundamental principles of the medical profession is expressed in the Latin phrase "primum non nocere" which loosely translates as "firstly, do no harm". Yet, virtually all treatments come with side effects that may harm our patients. In the context of acromegaly, this is true for surgical intervention, medical treatment, and radiotherapy alike. These have been reviewed elsewhere thoroughly, for example,[44] even subtle technical differences may have an impact on patient care: misclassification of remission status can occur due to improper laboratory readings, as reference ranges from IGF-I measurements differ between assays[45] and even across continents.[46]

The inherent differences between the various approved substances in the medical treatment of acromegaly have led to assumptions on their effect on treatment burden and quality of life. There are some data to support some of these hypotheses, for example, the beneficial effects of long-acting somatostatin analogs approved for self- or partner-injection.[47] Equally, studies investigating the impact of pegvisomant—which needs to be injected more frequently but achieves biochemical remission in a higher proportion of cases—came to the conclusion of superior improvement of quality of life.[48,49] However, it seems that an effective treatment leads to comparable measures of quality of life, regardless of the drug used to achieve that goal.[50] Furthermore, negative beliefs associated with medical treatment lead to more negative perceptions of the disease and worse disease-specific quality of life.[51]

In a large study assessing patient-reported outcomes ($n = 195$), 52% of patients treated with somatostatin analogs reported worsening symptoms toward the end of the dosing interval, frequent injection-related symptoms, a feeling of loss of independence, and repeated work loss days.[52] Even though patients admitted an overall satisfaction with their treatment, they wished for alternatives preferably without injections. Oral formulations of medical treatment could therefore be an anticipated improvement.[53]

Patients report symptoms more frequently and with greater severity than their medical providers.[54] This mismatch underscores an unmet need for patients to recognize their symptoms and suffering more accurately. It also illustrates how medical providers guide treatment decisions primarily on biochemical parameters, not considering other clinical findings more closely. This can lead to poorer patient care and outcomes.

Impairment of participation in daily activity

Disability

Chronic exposure to growth hormone and consequently IGF-I leads to various changes that cause disability in affected patients. For a more detailed and comprehensive look at acromegaly complications, we refer to two exhaustive and excellent reviews.[1,55]

A major concern for many patients is the occurrence of arthropathy in up to 80% of patients,[56,57] which persists despite long-term biochemical control.[58–60] Thus, leading to a chronic condition characterized by pain, joint stiffness, and ultimately loss of function. Although classically this affects the spine and knees primarily, it can also affect the hips, hands, and shoulders.

A key contributor to disability in patients with acromegaly is the deficiency of other pituitary axes: It has been observed that more than 40% of acromegaly patients are affected by hypopituitarism.[61] Among the various manifestations of hypopituitarism, corticotropic deficiency has been particularly associated with severely impaired quality of life and disability.[62] This highlights the importance of recognizing and addressing hypopituitarism in the context of acromegaly to mitigate its impact on the socioeconomic burden of patients.

Acromegaly patients suffer from excess mortality, mostly reversible with adequate treatment.[63,64] Mortality has decreased over the past decades probably due to improvements in the medical care of patients with acromegaly.[65,66] The main reasons for increased mortality are cardiovascular and malignant diseases. Cardiomyopathy in acromegaly is characterized by biventricular concentric hypertrophy and diastolic

dysfunction leading to cardiac dysfunction. At this stage, the patient's exercise capacity decreases. It can progress further to a loss of systolic function that culminates in explicit clinical congestive heart failure,[67] severely limiting the prognosis and quality of life.[68]

Acromegaly also leads to deficits in cognitive function and memory.[69–75] In a questionnaire-based study, patients with active acromegaly reported dysfunction with respect to concentration/distractibility and ability to learn.[69] In another study from Spain, a longer duration of untreated acromegaly was associated with more severe neurocognitive complications, while both patients with active disease and biochemical remission performed poorly in memory tests, especially those assessing visual and verbal recall.[74] This was also reported by a study from the Netherlands.[72] A German study found deficits in attention, memory, and/or executive function in 37 of 55 patients with acromegaly investigated.[73] Even though changes in macroscopic brain architecture were previously described by the group, no simple relationship between an individual estimate of a patient's brain volumetric changes and cognitive dysfunction could be found.[73,76] A large multicentric study from Italy comprising 223 patients found a prevalence of approximately 10% of cognitive dysfunction, notably visuospatial and verbal working memory problems in female patients.[42] A comprehensive review of all studies that investigated cognitive dysfunction in acromegaly has recently been published.[75]

But not only cognition and memory are altered: In a systematic review of the literature, psychiatric disorders were observed in up to 63% of patients with acromegaly, mainly depression or affective disorders.[77] Acromegaly patients often experience a diverse array of emotional and psychological changes.[78] These may include personality alterations resulting from diminished self-esteem, distorted body image, disruptions in interpersonal relationships, social withdrawal, and decreased impulsivity, initiative, and spontaneity. Additionally, these patients may exhibit significant mood lability, particularly in relation to anxiety and depression. In a focus group study, specific fears and other psychological problems were identified (fear of collapsing, fear of recurrence, panic, persisting thoughts, problems with an altered personality, anger, jealousy, sadness, and frustration).[33] In another study, patients reported more anticipatory worries and pessimism, higher fear of uncertainty, higher fatigue, and asthenia.[79] While schizophrenia and manic-depressive psychoses have been reported in some cases, they remain relatively rare occurrences. In addition to the psychosocial burden experienced by patients themselves, their partners or spouses have also reported a negative impact on their own psychosocial well-being due to the consequences of the disease.[37]

In summary, the multitude of physical and psychological challenges faced by patients with acromegaly account for their impaired participation in daily activities, whether it involves household duties or leisure pursuits.

Impairment of professional activity

Understandably, the factors leading to disability described in the previous section also lead to impairment of professional activity. In an Italian study, the disease-related unemployment rate was 8%.[80] A study investigating work disability in 241 patients with pituitary disease (amongst them 41 patients with acromegaly) showed that these patients were more often without a paid job.[81] Among those with paid jobs, 41% reported health-related absenteeism in the previous year. The three most frequently reported work-incapacitating issues among patients were predominantly found within the mental and social domains. These findings align with the outcomes of the aforementioned focus group study, in which patients treated for pituitary tumors reported work-related challenges stemming from reduced functional capacity, difficulties in concentrating, and obstacles in collaborating with others.[33] In a French online survey respondents also mentioned the impact of the disease on their professional life.[82] A common problem in the work environment of patients with acromegaly is disease-related absenteeism.[83–85] Essentially, this also means a loss of income, which can become quite substantial. In a questionnaire-based study of 106 acromegaly patients recruited from a patients' advocacy group, the average number of days unable to work due to the disease was 34 days, resulting in a $6702 loss of income per person.[86] However, financial loss can be further aggravated by impaired productivity. The same study pointed out that patients with an increased burden of the disease need more help with daily activities such as household chores and depend on household services, which introduces additional costs. This leads to an altered socioeconomic status which was also shown in a large population study from Denmark.[87]

In addition to the limitations imposed by the disease itself, treatment can introduce additional restrictions. In patient-reported outcome studies, patients frequently mentioned that injections interfered with their daily life, leisure, and work activities.[88] Notably, in another study 16% of patients reported experiencing repeated lost working days as a consequence of the injections.[52] Acro-TSQ correlates well with the Work Productivity and Activity Impairment Specific Health Problem Questionnaire (WPAI:SHP) that assesses the impact of an intervention on work productivity.[89] Thus, it could serve in the future in the scope of clinical studies to track the impact of effective treatments on the burden of the disease.

Cost of treatment of acromegaly and its comorbidities

As already laid out in previous sections, acromegaly comes with a cost related to loss of income and impaired productivity.[90] In addition to that, treatment of acromegaly is costly and includes one-time expenses such as the cost of surgery, as well as recurring expenditures related to drugs and comorbidity. Although acromegaly is classified as a rare disease, its treatment has led to the growth of a profitable market.[44] Studies evaluating the cost-effectiveness of various acromegaly treatments have been conducted in multiple contexts, examining different stages of the treatment process.[91] Despite providing valuable insights, these studies have faced certain limitations, leading to a general classification of moderate quality. To enhance the reliability of these analyses, future economic models should be designed in accordance with recommended health economics guidelines while prioritizing transparency in the research process. However, valuable insights on the economic burden of healthcare systems can be gained from these analyses.

Many studies have analyzed medical claims from databases in the United States.[84,92–95] All these studies conclude that acromegaly increases costs manyfold. An important driver of costs was inpatient hospitalizations.[93,94] Comorbidities

increased the odds of hospitalization.[93] Cardiovascular complications nearly tripled the odds of hospitalization and increased the annual mean cost by $13 331. Comorbidity-related cost is an important factor in the economic burden of acromegaly.[96]

Numerous studies have estimated treatment-associated expenses and made comparisons between various treatment methods, including surgery, radiotherapy, and medical therapy. Considering the recurring costs of medications that typically require lifelong administration at regular intervals, it is not unexpected that these studies often conclude that one-time interventions are more cost-effective.[95] There is a point to be made about expert neurosurgeons who play a crucial role in these savings.[97] However, even surgical costs vary substantially depending on postoperative complications (regardless of the outcome in terms of acromegaly cure).[98]

Real-world treatment sequences may vary substantially from economic models, rendering such calculations imprecise. An example is the outcome of surgery that can lead to remission and therefore low follow-up cost, but in about half of the cases, further treatment is required. Furthermore, longer injection intervals in lanreotide can induce savings[99–101] which most models do not consider. Additionally, pasireotide as a treatment option is taken into account only in a minority of these studies.[102–105] Two recent analyses from Europe (namely Spain and France) have therefore constructed complex decision tree models aiming at a holistic approach taking into account success and failure rates from the literature and incorporating comorbidities and complications.[104,105] Both studies found pasireotide to be associated with a very high cost per gained quality-adjusted life years compared to treatment with pegvisomant (or even pegvisomant in combination with first-generation somatostatin analogs). However, in a Brazilian study, the most cost-effective option was lanreotide, while pegvisomant scored poorer than pasireotide.[106] Interestingly, a study from Italy showed that the annual cost per patient did not differ significantly between controlled and uncontrolled patients.[107]

Some studies looked at the possibilities of reducing overall costs by optimizing the resources used. Two studies found reduced costs in long-term medical therapy when it was initiated pre-operatively.[108,109] Combining somatostatin analogs with pegvisomant might be an economically reasonable procedure, as it could lower the necessary doses and, therefore, the treatment-related cost.[110]

Studies assessing the cost-effectiveness of various acromegaly treatments have been conducted in multiple contexts, examining distinct stages of the treatment process. Despite providing valuable insights, these studies have faced certain limitations, leading to a general classification of moderate quality. To enhance the reliability of these analyses, future economic models should be designed in accordance with recommended health economics guidelines while prioritizing transparency in the research process.

Management strategies

Coping

Acromegaly patients reported using less effective coping strategies in a study in the Netherlands.[111] Upon investigating patients' perception of their disease, it has been demonstrated that individuals with acromegaly exhibit altered perceptions of the disease.[70,112] Patients receiving medical treatment for acromegaly tend to perceive a more chronic timeline of their disease compared to those in remission without medical treatment.[51] Furthermore, for patients who used medications to treat acromegaly, negative beliefs about their medication were associated with greater perceptions of the illness and greater impairments in the specific quality of life of the acromegaly. Many patients do not seem to accept their disease at all, and there are sometimes feelings of frustration, sometimes leading to alcohol intake.[33] It was suggested that a targeted intervention might help stimulate patients to use a more active coping strategy and seek social support instead of avoiding a coping strategy.[111]

Interventions and other measures to alleviate the socioeconomic burden

Not many studies have investigated how to improve the socioeconomic burden of acromegaly, but there are several key concepts that have been proposed. In their reasoning, both Knutzen[19] and Sisco[20] argue that timely diagnosis would be crucial to reduce the number of comorbidities, which has been shown numerous times to be the most important predictor of impaired quality of life (as outlined above). This has been propagated by other authors as well.[18,113] A method that could ease early diagnosis is the use of computer-aided face recognition paired with artificial intelligence,[114–116] but so far there is no real-world implementation of these systems. Various screening procedures have been investigated to aid in identifying patients with acromegaly in large-scale populations, but overall none of the proposed strategies proved worthwhile and thus specific screening mechanisms could not be established.[117–121] Another approach identified dyads of common clinical conditions in acromegaly to establish the relative risk of their occurrence in patients with acromegaly compared to controls,[122] for example, the combination of arthropathy and sleep apnea was 10 times more likely in patients with acromegaly than without. However, due to the high prevalence of these conditions in the general population, this approach would produce a high number of patients requiring further tests. There are no calculations on whether this would be cost-efficient. Another aspect that deserves attention is considering the impact of the gender of acromegaly patients on the burden it imposes on daily personal and professional life. Few data currently exist on this dichotomy; however, in the study published by Dal et al.,[87] female gender was associated with a significantly worse socioeconomic status as compared to male, stressing that a personalized approach according to gender could also be a lever on which to act.

Improving medical care for patients with acromegaly is an urgent need. This requires experienced physicians and trained staff (such as nurses and psychologists) who are knowledgeable about this particular disease, its treatment, and potential pitfalls. This is also true of all other diseases affecting the pituitary. Consequently, the term "Pituitary Centers of Excellence" was coined a few years ago and describes interprofessional centers of expertise in the domain of pituitary disease.[123] As an advocate and spokesperson for the acromegaly patient population, Robert Knutzen responded to this paper to stand up for this concept.[124] Recently, the Pituitary Society published distinct criteria for the definition of Pituitary Tumor Centers of Excellence.[125]

Several interventions have been published aiming to improve the outcomes of the psychosocial burden of patients with acromegaly. As pointed out by Jawiarczyk-Przybyłowska et al.,[34]

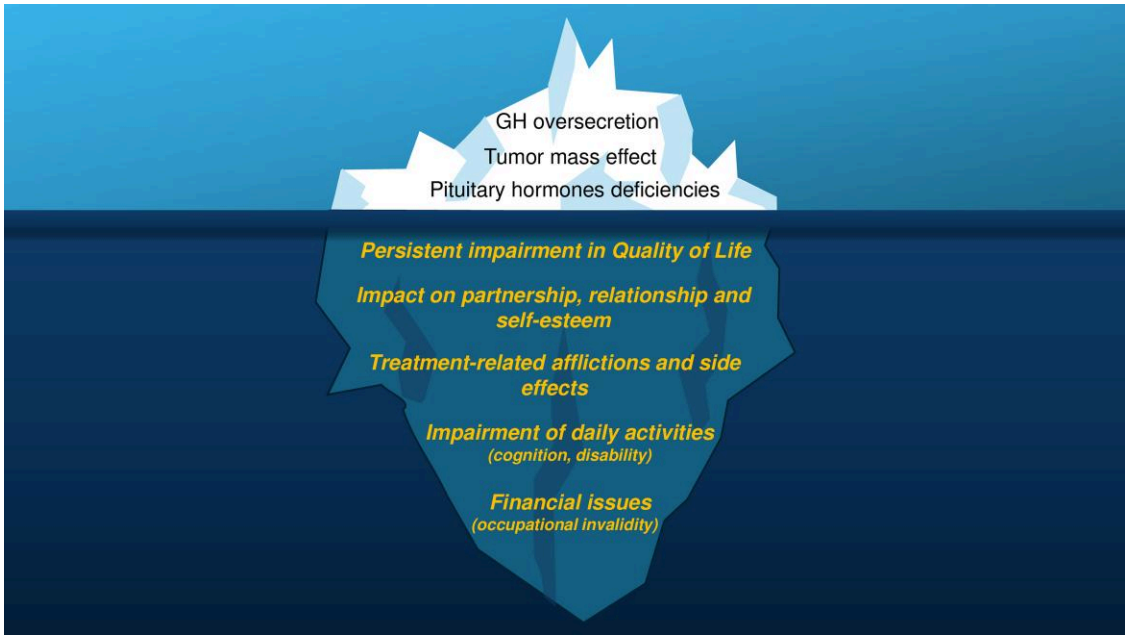

Figure 1. Graphic representation of acromegaly as a disease. The upper part symbolizes the essential concerns of the medical community. Conversely, the larger submerged part symbolizes the invisible, less well-managed handicaps at the root of the persistent socioeconomic burden of acromegaly, even in controlled patients.

the level of illness acceptance is a strong predictor of quality of life. They argued that "inclusion of patient's acceptance of the illness into a clinical routine would promote holistic, patient-centered care and empower doctor–patient partnership where patients' expectations and perceptions are constantly tracked". A small study with 23 patients with acromegaly exposed 10 of these patients to a technique called "Think healthy and feel the difference" conveyed in nine weekly group sessions.[126] The remaining 13 patients did not receive this intervention and served as controls. Participants completed the Short Form 36 Question Health Survey (SF-36) and the Beck Depression Inventory at baseline, after the intervention, and 9 months later. The results showed an improvement in the mental health of the intervention group compared to the control group, which was noticeable immediately after the intervention and maintained at the 9-month follow-up. An education program for pituitary tumor patients established in southern France led to significant quality of life improvements in terms of physical and psychic limitation scores, as determined by the assessments accompanying this program. These changes persisted at follow-up evaluation where patients reported improved self-management of pituitary disease and improved self-efficacy.[127] A recent and timely publication investigated the effectiveness of a virtual education program, covering an international audience amongst which 78 of the participating patients suffered from acromegaly. The programs consisted of patient-centered livestream education by a multidisciplinary team of pituitary experts and patient presenters. The attitudes before and after the event were recorded, and patients were asked to complete short answer surveys to collect care goals and unmet needs related to treatment. The intervention significantly reduced the number of patients who felt hopeless, considered being at the mercy of the disease, or simply feeling lonely.[21] Recently, a study carried out in Spain and Italy evaluated changes in quality of life, mood, pain, sleep, self-compassion, life satisfaction, blood pressure, and heart rate after a structured mindfulness program following a strict protocol.[128] The intervention led to better sleep hygiene, reductions in pain scores and an improvement in self-compassion.

A rather timely approach used a virtual education program that counted 653 participants from 37 different countries.[21] In this study, patient-centered livestream education was provided by a multidisciplinary team of pituitary experts and patient presenters. Attitudes were evaluated before and after the event showing a decrease in pessimistic valuation, but an unchanged anxiety about the diagnosis of acromegaly. Interestingly, patients judged "Quality of Life/Mental Health" to be the most common personal care goal.

Summary

Acromegaly is a rare disease characterized by a chronic excess of growth hormone, leading to morphological changes and systemic complications. The slow progression of symptoms often results in delayed diagnosis, causing devastating effects on patients and imposing significant socioeconomic burdens on them and the health system. Patients with acromegaly experience a poor quality of life, an impact on partnership and sexual functioning, and potential harm from medical care and side effects of treatment.

The disease leads to disability and impaired professional activity due to complications such as arthropathy, hypopituitarism, increased mortality rates, cognitive deficits, psychiatric disorders, and emotional and psychological changes. This results in disease-related unemployment, reduced functional capacity, absenteeism, loss of income, and impaired productivity, further exacerbating the socioeconomic burden, usually experienced by the patients as the "hidden face" of acromegaly (Figure 1).

Managing acromegaly patients involve addressing coping strategies and implementing interventions to alleviate the

burden. This requires a multi-modal approach. Research suggests that targeted interventions promoting active coping and social support may be beneficial. This requires interdisciplinary teams consisting of expert endocrinologists, neurosurgeons, psychologists, and nurses alike, ideally within the frame of Pituitary Centers of Excellence. Furthermore, a timely diagnosis is crucial to reduce comorbidities and improve quality of life, but current screening procedures are ineffective. Computer-aided face recognition with artificial intelligence offers potential but lacks real-world implementation. Improving medical care through the establishment of Pituitary Centers of Excellence and implementing psychosocial interventions, such as group sessions, education programs, and mindfulness programs, can significantly improve patients' quality of life and reduce the socioeconomic burden of acromegaly.

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