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ASSESSMENT OF CLINICAL SPECTRUM OF PATIENTS PRESENTING WITH ACROMEGALY IN A TERTIARY CARE HOSPITAL

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Abstract

OBJECTIVE

To determine the frequency of different clinical presentations in acromegaly including facial features, headache, visual problems, acral enlargement, oral changes, infertility and polydipsia.

MATERIAL & METHODS

This cross-sectional study was carried out in the Endocrinology Department of Jinnah Postgraduate Medical Centre Karachi. The total sample of 83 Participants of any gender, aged 18-60 years with acromegaly diagnosed with either an elevated level of insulin-like growth factor -1 above that for their reference population or a plasma growth hormone level of ≥1 µg/L following an oral glucose tolerance test with 75g glucose and having at least one of the clinical profiles of acromegaly were included in the study through non-probability purposive sampling. All the patients underwent clinical assessment to determine acromegaly features which include facial changes, severe headache (VAS ≥ 4), prolonged visual symptoms, acral enlargement, oral changes, infertility (≥12 months), and polydipsia (>3L/day).

RESULTS

The mean age of the participant was noted as 32.25 ± 11.43 years. Among them 48.2% were male while 51.8% were female. The clinical features of acromegaly were noted as headache 65.1%, decrease vision 32.5%, amenorrhea 18.1%, galactorrhea 4.8%, infertility 14.5%, increase and decreased liver growth (16.9% and 9.6%), skin changes 44.6%, increase body hair 21.7% while decrease libido was noted in 25.3% patients.

CONCLUSION

The present study identified headache, acral enlargement, visual abnormalities, and skin changes as the most frequent features of acromegaly in patients with acromegaly. Thorough clinical evaluations are critical for early detection and treatment. More detailed understanding and better results could be reached through larger sample sizes, longitudinal designs, and biochemical or genetic analyses, which highlights the importance of future research.

INTRODUCTION

Acromegaly is an endocrine disorder characterized by increased levels of Growth hormone (GH) and insulin-like growth factor-1 (IGF-1) [1]. The annual global incidence of acromegaly is reported to be 13 cases per 100,000 population with more than 95% patients eventually being diagnosed with Growth Hormone-secreting pituitary neuroendocrine tumor [2]. Acromegaly may also result from ectopic production of GH-releasing hormone which is commonly seen in neuroendocrine tumors of lungs and pancreas, and pheochromocytoma [3]. Other causes of acromegaly include familial isolated pituitary adenoma, MEN 1 and 4, neurofibromatosis 1, Carney Syndrome and exogenous growth hormone [4].

Growth hormone excess may present in the form of gigantism and acromegaly depending upon epiphyseal fusion before disease onset [5]. Gigantism results from disease onset before epiphyseal fusion and leads to increase in linear growth while acromegaly develops due to growth hormone excess after epiphyseal and has various clinical manifestations including acral enlargement, facial features (frontal bossing, jaw protrusion, nose enlargement and coarse facial features) and organomegaly [6]. Besides classical clinical manifestations, chronic growth hormone excess is also known to be associated with various cardiovascular, respiratory, musculoskeletal and neurological comorbidities [7].

Diagnosis of acromegaly is based on raised serum growth hormone and IGF-1 levels, though increased IGF-1 levels are also observed in conditions including chronic liver disease, chronic kidney disease, malnutrition and poorly controlled diabetes [8]. Goals of treatment in acromegaly include normalization of growth hormone and IGF-1 levels which are achieved with trans-sphenoidal surgical excision of adenoma, radiotherapy or medical treatment options in patients who are unfit for surgery [9]. Various studies have attempted to determine the frequencies of different clinical manifestations in acromegaly.

Al-Dahmani et al, reported that headache (82.4%), facial features (82.4%) and acral enlargement (79.7%) were the most common presentations of acromegaly [10]. While Slagboom et al, reported that among patients diagnosed with acromegaly, most common clinical presentations included acral enlargement (90%), facial features (65%), oral changes (62%) and headache (49%) [11]. Varlamov et al, reported that the most common signs observed in acromegaly patients included acral enlargement (68.5%), facial features (38.4%), macroglossia (31.9%), truncal obesity (25.5%) and goiter (17.1%) [12].

Acromegaly is a rare disease characterized by endocrine disturbances which can vary in clinical presentation widely including facial changes, headache, visual disturbance, acral enlargement, oral change, gonadal insufficiency and polydipsia [13,14]. This insidious course gives rise to high delays in diagnosis and high morbidity.This study aims to determine the frequency of these clinical features in a local population to enhance early recognition and improve diagnostic accuracy, ultimately supporting better patient outcomes.

MATERIAL & METHODS

This cross-sectional study was carried out in the Endocrinology Department of Jinnah Postgraduate Medical Centre Karachi. Participants of any gender, aged 18-60 years with acromegaly diagnosed with either an elevated level of insulin-like growth factor -1 above that for their reference population or a plasma growth hormone level of ≥1 µg/L following an oral glucose tolerance test with 75g glucose and having at least one of the clinical profiles of acromegaly were included in the study through non-probability purposive sampling. Patients with BMI < 18.5, severe DCLD (Child Pugh Class C) or renal failure (eGFR <

15 ml/m or maintenance hemodialysis requirement), active untreated systemic infection, poorly controlled diabetes (HbA_1C > 8.5%), pregnant and lactating women were excluded from the study.

A predesigned form was used to collect baseline demographic and clinical data such as age, gender, residential status, and duration of symptoms. A comprehensive clinical assessment (history and physical examination) of each patient was performed to assess the clinical manifestations of acromegaly (facial features (frontal bossing jaw protrusion, nose enlargement, or coarse features), symptomatic moderate to severe ongoing headache (Visual Analog Scale [VAS] score ≥ 4), visual symptoms > 1 month duration, acral enlargement (progressive increase in shoe size or glove tightness), oral changes (increased spacing of teeth macroglossia), infertility (failure to conceive after at least 12 months of regular unprotected intercourse), and polydipsia (>3 liters daily water intake). Data were analysed using version 26.0 of SPSS. Abstract Background Descriptive statistics such as mean with standard deviation and frequency with percentage were reported. The statistical test of significance was applied using P-value ≤ 0.05 as criteria of significance.

RESULTS

Table I summarize the demographic and baseline characteristics of the 83 study participants. The mean age of the participants was 32.25 ± 11.43 years, with 54.2% older than 30 years and 45.8% aged between 18 and 30 years. The mean body mass index (BMI) was 26.76 ± 6.07 kg/m², with nearly equal proportions having a BMI ≤27 kg/m² was noted in (50.6%) and >27 kg/m² in (49.4%).The average pulse rate was 85.05 ± 13.56 bpm of which 26.5% were above normal rates (>90 bpm) and 73.5% had normal rates (60–90 bpm). Mean systolic blood pressure (SBP) was noted as 122.29 ± 17.43 mmHg), and 100–120 mmHg was noted in 59.0% of participants while 41.0% of participants recorded higher SBP values > 80mmHg. Mean diastolic blood pressure (DBP) was noted as 79.94 ± 13.12 mmHg, among those, 55.4% had DBP in the range of 60–80 mmHg, 44.6% were higher than this range. There were 48.2% males and 51.8% females in the study. In terms of marital status, 53.0% were married, 41.0% were single, and 6.0% were divorced.

Table I: Characteristics of Study Participants (n=83)

Variable	**n (%)**
Age (Mean ± SD) = 32.25 ± 11.43	
18 - 30 years	38 (45.8)
>30 years	45 (54.2)
Body Mass Index (Mean ± SD) = 26.76 ± 6.07	
19 - 27 kg/m²	42 (50.6)
>27 kg/m²	41 (49.4)
Pulse (Mean ± SD) = 85.05 ± 13.56	
60 - 90 bpm	61 (73.5)
>90 bpm	22 (26.5)
SBP (Mean ± SD) = 122.29 ± 17.43	
100 - 120 mmHg	49 (59.0)
>120 mmHg	34 (41.0)
DBP (Mean ± SD) = 79.94 ± 13.12	
60 - 80 mmHg	46 (55.4)
>80 mmHg	37 (44.6)
Gender	
Male	40 (48.2)
Female	43 (51.8)
Marital Status	
Single	34 (41.0)
Married	44 (53.0)
Divorced	5 (6.0)

Table II summarizes the clinical features of individuals with acromegaly. The most common clinical features were noted as headache (65.1%). In distribution of visual abnormalities decrease vision was noted in (32.5%), temporal field defect (8.4%), blurring (7.2%), LEB+RVFD (3.6%), and blindness (1.2%). Enlargement of the acral was reported in 39.8% of patients, and skin changes were noted in 44.6%, which are common characteristics of acromegaly. Among the female participants, menstrual irregularities such as amenorrhea (18.1%) and oligomenorrhea (9.6%) were documented. Infertility affected 14.5% of participants and 25.3% were afflicted with decreased libido. Acne occurred in 18.1% of patients, while 16.9% had increased linear growth and 9.6% had decreased linear growth. Importantly, even within abnormal range, we found a fraction of patients with normal parameters in certain domains, including vision (47.0%) and acral features (55.4%), highlighting the variable clinical presentation of acromegaly.

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Table II: Distribution of Clinical Manifestations in Acromegaly Patients (n=83)			
Headache, *n (%)*	Yes	54	65.1%
	No	29	34.9%
Vision, *n (%)*	Blind	1	1.2%
	Blurring	6	7.2%
	Decrease	27	32.5%
	LEB+RVFD	3	3.6%
	Normal	39	47.0%
	Temporal Field Defect	7	8.4%
Menstruation, *n (%)*	Amenorrhea	15	18.1%
	Menopause	6	7.2%
	Normal	11	13.3%
	Not Applicable	40	48.2%
	Oligomenorrhea	8	9.6%
	Polymenorrhea	1	1.2%
	Primary Amenorrhea	2	2.4%
Galactorrhea, *n (%)*	Yes	4	4.8%
	No	39	47.0%
	Not Applicable	40	48.2%
Infertility, *n (%)*	Yes	12	14.5%
	No	37	44.6%
	Unmarried	34	41.0%
Linear Growth, *n (%)*	Increase	14	16.9%
	Decrease	8	9.6%
	Normal	61	73.5%
Acral Growth, *n (%)*	Increase	33	39.8%
	Decrease	4	4.8%
	Normal	46	55.4%
Skin Changes, *n (%)*	Yes	37	44.6%
	No	46	55.4%
Body Hair, *n (%)*	Increase	18	21.7%
	Decrease	10	12.0%
	Normal	55	66.3%
Libido, *n (%)*	Decrease	21	25.3%
	Normal	62	74.7%
Genital Size, *n (%)*	Decrease	13	15.7%
	Normal	27	32.5%
	Not Applicable	43	51.8%
Erection, *n (%)*	Normal	29	34.9%
	Abnormal	11	13.3%
	Not Applicable	43	51.8%
	Yes	7	8.4%

Vaginal Dryness, *n (%)*	No	36	43.4%
	Not Applicable	40	48.2%
Acne, *n (%)*	Yes	15	18.1%
	No	68	81.9%

***LEB+RVFD**: Left Eye Blind + Right Visual Field Defect*

DISCUSSION

Acromegaly is a rare but serious hormonal disorder because of excessive growth hormone (GH) production, usually due to a pituitary adenoma. The clinical spectrum varies widely, with patients presenting gradual changes that are often subtle, leading to delayed diagnosis [15]. Common features were enlarged hands and feet, facial changes (e.g. protruding jaw, enlarged nose, and thickened skin), and joint pain [16]. Additionally, patients may experience hypertension, diabetes, and sleep apnea, which are linked to the metabolic efforts of excess GH. Cardiovascular complications such as cardiomegaly, and heart failure are important risks, due to prolonged exposure to high GH levels [17]. Other manifestations were the increased risk of malignancies, especially colorectal cancer [18]. Early diagnosis and treatment typically involving surgery, radiotherapy, and medication to control GH levels are crucial to prevent morbidity and mortality. Timely management can lead to a favorable prognosis by alleviating symptoms and reducing the risk of long-term complications.

Giustina et al. emphasized the criteria in diagnosing and determining remission in acromegaly emphasizing the value of accurate diagnostic tests like IGF-1 levels and the oral glucose tolerance test (OGTT) [19]. They outlined remission as normalized IGF-1 levels and suppressed GH post-OGTT, stressing the requirement for long-term follow-up because of potential tumor recurrence. The study by Ambrosio et al reports acromegaly in older patients, adding that due to subtle symptom presentation and the overlap with age-related changes, diagnosis is often delayed [20]. The study emphasizes the need for careful management, considering comorbidities, and the associated risks with treatment options i.e. surgery and radiotherapy. AlDallal reports the diagnostic challenges in acromegaly noting that the condition is frequently misdiagnosed, due to its gradual onset, and the broad range of symptoms that can mimic other health problems [21]. At last, Zahr and Fleseriu gave an update on treatment strategies, reviewing the role of medical therapies such as somatostatin analogs, GH receptor antagonists, and dopamine agonists for patients with persistent disease or those who are not surgical candidates [22]. They also stress the value of handling comorbidities, such as diabetes and cardiovascular disease, which are associated commonly with acromegaly. Together, these sources emphasize the importance of early diagnosis, careful management, and ongoing monitoring to reduce complications and improve patient outcomes.

In our study, the clinical features of acromegaly were noted as headache 65.1%, decrease vision 32.5%, amenorrhea 18.1%, galactorrhea 4.8%, infertility 14.5%, increase and decreased liver growth (16.9% and 9.6%), skin changes 44.6%, increase body hair 21.7% while decrease libido was noted in 25.3% patients.

The study of Espinosa de los Monteros AL, et al reported clinical features headache (72.1%), and acral growth (96.9%) [4]. Another study reported the frequency of headache (82.4%), facial features (82.4%) and acral enlargement (79.7%) [10]. Slagboom, et al, stated the most common clinical presentations were acral enlargement (90%), facial features (65%), oral changes (62%), and headache (49%) [11] while the research conducted by Varlamov, et al observed acral enlargement (68.5%), facial features (38.4%), macroglossia (31.9%), truncal obesity (25.5%) and goiter (17.1%) [12].

The differences between our findings and those published in the literature as revealed by the systematic review may be related to the size of the sample size in each study, the symptoms may be statistically underpowered, and the population characteristics of the various study samples such differences in genetic, environmental, and health care access factors that can influence clinical features and disease course in acromegaly. In addition, several

studies may differ on diagnostic thresholds and criteria for defining and measuring acral enlargement, facial changes, or other subtle features of the disease which may be clinically overt only in a proportion of patients.

The strength of the study to have a thorough assessment of the local manifestations of acromegaly and this could address a gap between clinical diagnosis and awareness of symptoms of the disease. Finally, standardized clinical parameters like VAS scores and IGF-1/GH levels help ensure reliable assessment of symptoms. The cross-sectional design represents a limitation as we cannot infer progression of symptom course, and the use of non-probability purposive sampling also limits the generalizability of our results. The absence of biochemical correlations and treatment outcomes data in the study is another limitation due to the key role of linking symptom severity to treatment effect. The sample size of 83 are still small to represent target population, so robust statistical analysis for rarer symptoms (e.g. blindness, LEB+RVFD) are limited.

To overcome these limitations, longitudinal study designs are suggested for future studies to follow the natural course of symptoms and treatment response more closely. More generalizable findings would be obtained with a local sample batch for diverse populations. Furthermore, the inclusion of biochemical markers and genetic profiling might reflect the pathophysiology of acromegaly and the heterogeneity better. Multicentre studies or collaborative networks would also help ensure a larger database and increase generalizability. Even with its limitations, this study represents a substantial first step towards an enhanced understanding of the pattern of clinical features of acromegaly in this local context and it highlights the imperative for early and accurate diagnosis in order to maximize patient benefit.

CONCLUSION

The present study identified headache, acral enlargement, visual abnormalities, and skin changes as the most frequent features of acromegaly in patients with acromegaly. Thorough clinical evaluations are critical for early detection and treatment. More detailed understanding and better results could be reached through larger sample sizes, longitudinal designs, and biochemical or genetic analyses, which highlights the importance of future research.

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