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ARTICLE

Post-surgery Quality of Life in Patients with Acromegaly Using SF36 Quality of Life Questionnaire-prospective Study

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ABSTRACT

Introduction: Acromegaly is chronic progressive disease with multisystem involvement characterised by an excess secretion of growth hormone and increased circulating insulin like growth factor 1 concentration.
Aims and Objectives: To assess surgical outcome of acromegaly patients at tertiary care institute using SF 36 quality of life questionnaire. SF-36 scores comprise 3 components: the physical component summary (PCS), the mental component summary (MCS) and role-social component summary (RCS).
30 acromegaly patients admitted in Guwahati medical college were enrolled in study and followed up post operatively for surgical remission. All participants completed the SF-36 preoperatively, 1 year and 2 years postoperatively.
Material and Method: Out of 30 patients 6 patients had surgical remission post operatively on the basis of postoperative glucose suppressed GH Level done after 12 weeks. Preoperatively subscale scores (physical functioning, role physical, general health) which were below the set standards for the normal population show significant postoperative improvements along with mental health (MH) scores. Similarly, PCS, MCS and RCS scores changed significantly after surgery. We also compared the QOL of 6 patients whose peak GH level was < 0.4 μg/L during postoperative oral glucose tolerance testing with those patients whose nadir GH level was ≥ 0.4 μg/L. There was significant difference between partial and complete remission group in subscale score role physical, social function and mental health. Similarly, PCS and RCS score significantly different in partial and complete remission group than MCS score.
Conclusions: QOL is considerably reduced in patients with acromegaly compared to general population which improves significantly after surgical treatment. Patients achieving the new remission criteria had significant improvement in physical and social components than those who did not.

1. Introduction

Acromegaly is a chronic illness characterised by changes in appearance, skeletal deformities and various metabolic disorders. In 95% of cases, acromegaly is caused by excessive secretion of the growth hormone (GH) by a hormonally active adenoma of the anterior lobe of the pituitary gland (GHoma) which in turn leads to excessive secretion of insulin-like growth factor-1 (IGF-1). Excessive secretion of IGF-1 results in bone and soft tissue proliferation in the distal extremities, the jaw, tongue, lips, nose and the frontal eminence. Disease control by vari-

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ous means can improve metabolic function, improve life expectancy and reduce morbidity [1-3]. Metabolic abnormalities associated with acromegaly lead to cardiac hypertrophy, heart failure and increased incidence of ischemic heart disease which is the leading cause of death in patients with acromegaly [4-5]. The introduction advanced surgical techniques have significantly improved the cure rate of acromegaly patients [6-8]. Remission of acromegaly is usually defined on the basis of 3 month post-operative suppressed GH< 1 ug/l, however according to a new consensus guideline based on GH suppression to < 0.4 µg/L and age and sex adjusted IGF 1 level is recommended [9]. We do not know the effect of surgical remission on the post-operative QOL in patients with acromegaly and also of new consensus criteria. So, we conducted this study to assess the effect of surgical treatment on quality of life using SF36 questionnaire in a prospective cohort of acromegaly patients. We also evaluated the quality of life in patients who have achieved remission according to new consensus criteria.

2. Material Methods

30 newly diagnosed acromegaly patients (14 men and 16 women) based on clinical, biochemical and radiological features with an average age of 44.5 years (range 21-67) were included in study. The diagnosis of acromegaly was confirmed with post oral glucose tolerance test (OGTT) GH >1.0 µg/L, and IGF-I level was above the upper normal range for age and sex. Patients were treated using transsphenoidal surgery performed by a senior neurosurgeon during period of 2015-2019. IGF-1 normalization was achieved in 6 out of 30 patients (20%) according to new consensus criteria (peak GH level during the OGTT of < 0.4 µg/L). All participants underwent an OGTT 3 months post-surgery and based on that peak GH level were divided into old consensus criteria (nadir GH level during the OGTT of < 1 µg/L or >1ug/L): the complete remission group or the not in remission group. Complete remission group was further divided according to a new consensus guideline into: the complete remission group and the partial remission group (postoperative nadir GH level during the OGTT of < 0.4 µg/L or ≥ 0.4 µg/L). We compared the clinical and biochemical characteristics, and postoperative SF-36 scores between the two groups. We also did pre- and post-surgical hormonal profile and follow-up patients 3 monthly.

3. Survey Methods

We conducted thorough Clinical and biochemical examinations pre- and 3-month post- surgery. The validity and reliability of SF-36 have been already established in Indian population and has been used to assess health outcomes in several diseased population [10,11]. All 30 patients completed SF 36 quality of life questionnaire at the assessment. The quality-of-life questionnaire evaluates 12 items regarding a patient's general well-being, each item has multiple questions under it and all questions have 5 possible answers. All questions are scored on a scale of 1–5. The items are scored in various scales: physical functioning, daily activities, symptoms, social, psychological, general health perception, sleep, sexual health, pain, energy, body image and cognition. Higher the scores poor is the quality of life. We compared the pre- and post- operative quality of life questionnaire scores. All patients completed preoperative questionnaire. In this questionnaire, responses to questions around physical symptoms — My body has enlarged/ grown enormously — could be given as "not important", "slightly important", "important"," fairly important" or "very important". We also assessed the severity of obstructive sleep apnoea with the help of polysomnography which is shown by the apnoea hypopnea index (AHI).

4. Statistical Analysis

Subjects were divided based on remission criteria. Spearman correlation coefficients were calculated between the change in IGF-I levels and SF 36 scores. Non-parametric tests (Mann-Whitney U and Kruskal-Wallis one-way ANOVA) were performed to test the statistical significance of differences between different groups. All statistical analyses were performed with SPSS software and a $p<0.05$ was considered statistically significant. Informed consent was obtained from all the individual participating in study.

5. Results

Table 1 shows the baseline characteristics of individuals. A total of 14 males and 16 female individuals Patient with mean age of 44.5 years (21-67) and mean duration of symptoms7.6 years (4 years-15 years) were included. Dyslipidaemia was the most common co-morbidity (80%), followed by hypertension (73%) and diabetes (60%). Coronary artery disease was present in 8 (26%) patients at baseline with none of them having history of cerebrovascular accident or malignancy. Acral enlargement was the most common symptom (73%) followed by arthralgia and fatigue (66%) (Table 2). Hyperprolactinemia (53%) was the most common hormonal abnormality followed by low cortisol (40%), hypothyroidism(30%), hypogonadism (23%) and diabetes insipidus (10%) (Table 3).

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Pituitary macroadenoma was found in (83%), followed by microadenoma(10%) and empty Sella (6.6%). On immunohistochemistry 24 patients had somatotroph adenoma, 4 patients had mamo-somatotroph adenoma and 2 patients had pleurihormonal adenoma. All patients were treated with surgery for IGF-1 normalization. Preoperative mean stimulated GH level was 66.4±55.4 ng/ml (1.5-185) and postoperative stimulated GH was 6±4.9 ng/ml (0.1-16) which was significant (p-0.003). The preoperative IGF-1 levels ranged from 344.0 µg/L to 1400.0 µg/L (mean: 797.3 ± 275.1 µg/L). There was a significant reduction in postoperative serum IGF-1 levels (388 ± 200 µg/L, p -0.003). No significant change in proportion of patients with hypertension, diabetes mellitus, or hyperlipidaemia, AHI. Fewer patients required hormonal replacement post operatively at 12month (Hyperprolactinemia-8, Hypothyroidism-4, low cortisol-6, hypogonadism-5, diabetes insipidus-1). Figure 1 shows Preoperative and postoperative (12 month and 24 month) subscale scores. Preoperative physical functioning (PF), role physical (RP), general health (GH) was below the national standard value as indicated by the boxed value. Significant postoperative improvements were observed for the physical functioning (PF) (53±10.4 vs 60±8.7 vs 63.3±6.7, p<0.0001), role physical (RP) (50.1±8.7 vs 60±9.9 vs 60.8±13.3, p<0.0001), general health (GH) (47.5±8.3 vs 63.6±8.1 vs 62.1±8.8, p,0.001) and mental health (MH) (58±7.8 vs 64.8±6.8 vs 70±6, p<0.0001) scores but not in bodily pain (BP) (62.8±9.1 vs 63.5±9.2 vs 63.6±9.1, p-0.934), vitality (VT)(65.1±7.2 vs 65.3±7.1 vs 65.6±7.6, p-0.965), social functioning (SF) (64.6±7.7 vs 64.8±7.7 vs 65.8±7, p-0.969), role emotional (RE) (63.1±8 vs 63.3±7.6 vs 63.5±7.6, p-0.986). Figure 2 shows the preoperative and postoperative results of PCS, MCS, and RCS score. The baseline score was close to the national standard. The PCS, MCS and RCS scores did change significantly after surgery. Figure 3 shows pre-operative and post-operative subscale score in patient group. There was significant difference in subscale score between partial and complete remission group in role physical (RP) (57.6±12.7 vs 71.4±9.8, p-0.014), social function (SF) (63.4±7.8 vs 70.7±6, p-0.05) and mental health (MH) (68.4±5.7 vs 75±4, p-0.009). Similarly, PCS (64.2±4.4 vs 67.5±4.6, p<0.012) and RCS (60.9±5.4 vs 69.2±5.4, p<0.0001) score significantly different in partial and complete remission group than MCS score (62.7±5.3 vs 67.1±5, p-0.064).

Table 1. Table showing baseline characteristics with radiological and immunohistochemistry character of individuals

Baseline Characters	N-30
Male: Female	14:16
Age(years)	44.5 (21-67)
Duration of symptoms(years)	7.6 (4-15)
Adenoma characteristics	
Macroadenoma	25(83%)
Microadenoma	3(10%)
Empty sella	2(6.6%)
Immunohistochemistry hormonal secretion	
GH Secreting	24(80%)
GH+Prolactin	4(13.3%)
Pleurihormonal	2(6.6%)

Table 2. Showing predominant symptoms in individual patients

Symptoms(N-30)	Number of patients
Acral enlargement	22(73%)
Coarse facial features	18(60%)
Hoarse voice	16(53%)
Excessive sweating	16(53%)
Arthralgias	20(66%)
Sleep apnoea	14(46%)
Headache	12(40%)
Hypogonadal symptoms	8(26%)
Visual deficit	10(33%)
Fatigue	20(66%)

Table 3. Showing predominant hormonal abnormality in individual patients

Hormonal abnormality(n-30)	Number preoperative	Number postoperative
Hypothyroidism	9(30%)	4(13%)
Hypocortisolism	12(40%)	6(20%)
Hypogonadism	7(23%)	5(16%)
Hyperprolactinemia	16(53%)	8(26%)
Diabetes Insipidus	3 (10%)	1(3%)

Table 4. Showing preoperative and postoperative characteristics of patients

Characteristics	Preoperative	Postoperative (12 month)	p value
Diabetes Mellitus	18(60%)	14(46%)	-
Hypertension	22(73%)	20(66%)	-
Dyslipidaemia	24(80%)	20(66%)	-
OSA	16(53%)	11(36%)	
Mild (AHI:5-20)	8(50%)	5(45%)	-
Moderate (AHI:20-40)	4(25%)	4(36%)	
Severe (AHI>40)	4(25%)	2(18%)	
CAD	8(26%)	8(26%)	-
CVA	0	-	-
Cancer	0	-	-
GH (Glucose stimulated)	66.4±55.4 ng/ml	6±4.9 ng/ml	0.003
IGF 1	797.3 ± 275.1 µg/l	388 ± 200 µg/l	0.003

OSA(Obstructive sleep apnea), CAD(Coronary Artery Disease), CVA(Cerebrovascular accident)

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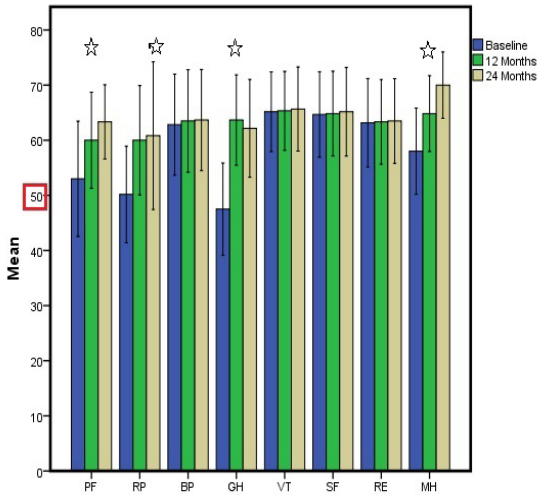

Figure 1. Showing preoperative and postoperative subscale score

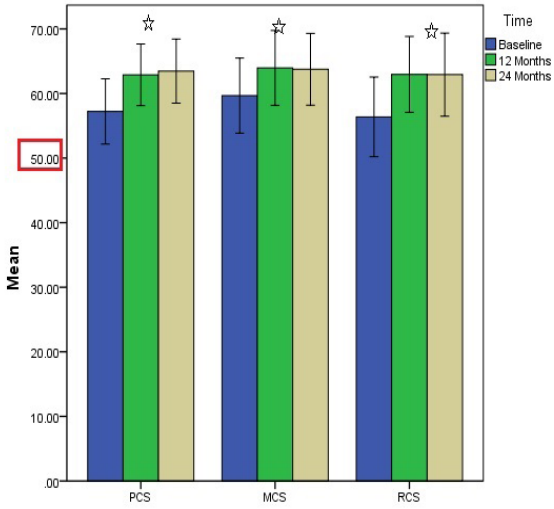

Figure 2. Showing preoperative and postoperative component score

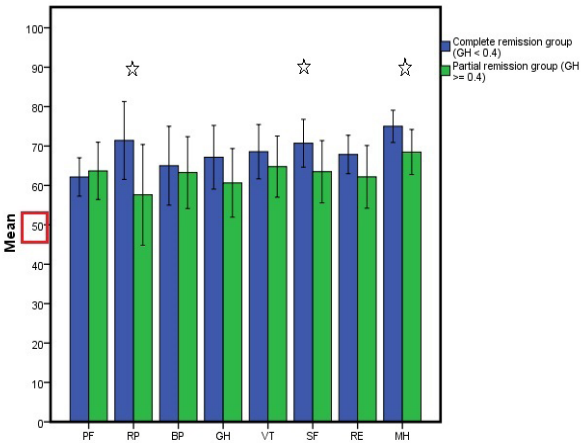

Figure 3. Showing subscale score in complete and partial remission group

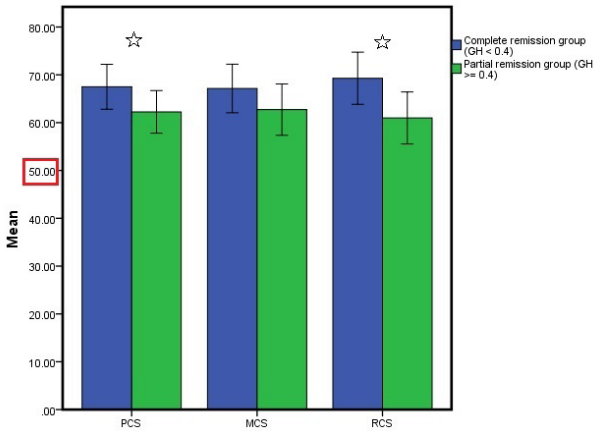

Figure 4. Showing component score in partial and complete remission group

6. Discussion

Acromegaly is associated with various disabilities with poor quality of life. There are very few prospective studies reporting postoperative changes in QOL among patients treated by surgery alone.

Our study showed preoperative SF-36 scores were lower in acromegaly patients than that of the general population in subscales, including physical functioning, role physical, general health which indicate that acromegaly significantly affects patient's physical condition, self-perception as well as participation. We found that postoperative there was significant improvement in physical component, mental component and role social component of SF36 QOL questionnaire. Sardella et al. [12] on the other hand found that surgical cure resulted in improvements in the mental components as compared to physical or role-social components of SF 36 QOL questionnaire. Yoshida et al. [13] in acromegaly patients reported higher psychological scores in patients with surgically achieved disease control. Biermasz et al. [14] found better physical function in surgically cured acromegaly patients.

Shingo Fujio [15] using SF-36 questionnaire found MCS score improved significantly postoperatively while there was no significant difference in PCS, RCS and MCS scores between complete and partial remission groups. We, on the contrary found that there was significant postoperative improvement in PCS, RCS and MCS scores but MCS score did not change significantly between complete and partial remission group.

All of our patients achieved IGF-1 normalization by surgery alone, and fewer number of patients required postoperative hormone replacement therapy. Several comorbidities, such as joint pain due to severe arthritis, myopathy and hypertension, impairs postoperative improvement

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in physical and emotional subscale score in some patients with acromegaly even after achievement of postoperative cure.

Gilbert et al. [16] in his study showed improvements in health perception and fatigue during medical treatment among newly-diagnosed with acromegaly. In addition, Sardella et al. [12] in Acromegaly patients observed improvements in psychological and appearance domains after a 6-month course of a somatostatin analog. Matta et al. [17] reported higher AcroQoL psychological subscale scores in controlled acromegaly patients compared to patients with uncontrolled disease.

There was significant difference in subscale score between partial and complete remission group in role physical (RP), social function (SF) and mental health (MH). In a similar study Renata Aparecida Elias Dantas [18] in acromegalic patients found the scores obtained on SF-36 domains were higher in patients with controlled disease and statistical differences were found in the domains Role Physical, Pain, Vitality, Role Emotional.

Kauppinen Mäkelin et al. [19] in his study reported that a post OGTT nadir GH level in the 0.3– 1.0 µg/L range could achieve the best QOL but not < 0.3 µg/L. Post OGTT nadir GH level <0.3 µg/L might have GH deficiency and adversely affect QOL. None of our patients developed post OGTT low GH suggestive of GH deficiency although we could not perform GH secretory function in our patient group.

Significant number of patients present with diabetes mellitus, hypertension and hyperlipidaemia pre-operatively which decreased post-surgery. However, the dose of antidiabetic and antihypertensive medication decreased in some cases but antihypertensives could not be withdrawn which could be due to irreversible remodelling of vascular system.

Small sample size has limited the generalization of our study. We need large studies to evaluate the effects of the surgical remission on the QOL of patients with acromegaly.

Some of the limitations of our study are, we have used SF-36 questionnaire which may be less sensitive when compared with disease-specific questionnaires, such as the AcroQoL questionnaire. OGTT will change depending upon the time of its performance [20]. We have performed OGTT at 3 months interval which could be different at 1 year when we administered SF36 questionnaire. We have evaluated SF 36 scores at baseline, 1 year and 2 years post-surgery but patient's score can change at any time. Therefore, long term studies with extended follow-up is needed to confirm the long-term effects of surgery. Finally, further studies are needed to gather information regarding the impact of GH deficiency on postoperative QOL.

7. Conclusions

Acromegaly is debilitating illness with multisystem involvement and poor QOL. Our study showed that acromegaly leads to low preoperative SF-36 QOL scores compared to the general population. Surgical remission leads to an improvement in the mental, physical and social domain of SF 36 QOL scores. There were significant differences in physical and social scores of QOL between complete and partial remission group. Although, small sample size has limited the generalisation of the finding of our study, there are few prospective studies reporting postoperative changes in QOL among patients cured solely by surgery. We need further large-scale long-term studies with extended follow-up to evaluate the effects of surgery as well as newer stricter remission criteria on QOL.

Contributor Ship Statement

Dr Dipti Sarma developed the research concept presented here along with Dr Manoj Gedam. Dr Manoj contributed to the study design and managed the database, participated in the data analysis. All authors have read and approved the final draft of the manuscript.

Conflict of Interest

No conflict of interest.

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Patient Consent

Informed verbal consent was obtained from the patient or primary caregiver.

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