

12-Year Dynamics for Acromegaly Morbidity in the Regions of the Republic of Uzbekistan According to the Register

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Abstract Numerous investigations from various global regions and in nations with different healthcare systems revealed that the prevalence of acromegaly ranged from 0.2 to 13.7 instances per 100,000 people. Disease diagnosis is still frequently seen as having been delayed. Men are verified to have the condition in their fifth decade of life, while women are diagnosed between the ages of 38 and 56. Of the 526 patients that had been registered by January 1, 2019, 195 (37.07%) were men and 331 (62.93%) were women. Comparative investigation has revealed that between 2007 and 2019, the prevalence of acromegaly rose nationally. While acromegaly diagnosis declined over time in Djizzak and Samarkand, it improved in Tashkent city, Navoiy, and the Tashkent area. Over a 12-year period, the prevalence of acromegaly increased steadily nationwide. This statewide study can be used to inform local planning for initiatives aimed at raising the standard of care for acromegalic patients and lowering mortality and disease-related comorbidities.

Keywords Acromegaly, Prevalence of acromegaly, Acromegaly morbidity

1. Introduction

Several studies, from different geographical areas worldwide, in countries with unlike healthcare systems, showed acromegaly prevalence from 2.8 to 13.7 cases per 100,000 population [14,17]. Agustsson TT et al [3] and Aagaard C et al [13] reported of 13.3–13.7 cases of acromegaly per 100,000. Regions with high prevalence of acromegaly include Iceland and Malta showing >13 cases per 100,000 individuals [7,10]. Studies in South Korea and Sweden discovered prevalence rate between 2.8 and 3.3 cases per 100,000 [16,24].

Diagnosis of disease, to the date, considered significantly delayed in many cases. The presence of the disease is confirmed on the 5th decade of life in men (36.5–48.5 years-old), while women diagnosed between 38 and 56 years-old [7,13,16,21,24]. A period from disease manifestation to diagnosis varies across the studies from 3 to 25 years (average 4.5–5 years) [7,22,24]. These contribute to high macroadenomas frequency at diagnosis, which may result in less radical outcome of surgical treatment [3,4,6,7,13,21,24].

Current estimates of uncontrolled disease suggest decreasing life expectancy [5,19]. Number of studies showed increased mortality rate in patients with acromegaly by 2–3 times comparing with control group of the same age and sex [19]. Mostly, death caused by cardio-vascular and respiratory complications, and malignant disease [5,19]. Two meta-analyses showed inverse dependence between disease control and mortality rate – the better control, the lower mortality rate [8,11]. Additionally, remission of the disease, decrease of growth hormone levels, normalization of IGF-1 concentrations and somatostatin analogues administration contribute to lower mortality rates [11]. Decreased mortality rate with control improvement to population levels in acromegaly, except after radiation therapy, demonstrated across studies [8]. Sherlock M et al found that after radiation therapy the mortality rate of patients with acromegaly doubled compared to general population [23].

In recent years, a number of studies have shown significance of nationwide or regional registries for acromegaly reflecting their effectiveness in better diagnosis, follow-up and treatment [19]. Uzbek nationwide registry for acromegaly was developed in 2007 and included patients from 1971 to 2007. Registry was designed for single examination with no option to follow patients. Thus, we developed new database with updated profiles to cover and survey acromegaly and its complications.

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The aims of this study were to assess comparative analysis of morbidity with acromegaly for 12-year period.

2. Materials and Research Methods

Five hundred twenty six patients with GH-producing adenoma contributed to Uzbek acromegaly registry. All patients have been examined and registered from 1971 to 2019 i.e. forty eight-year period.

All patients underwent examinations including radioimmune tests for LH, FSH, Prolactin, TSH, GH, IGF-1, IGFBP-3, Cortisole, Testosterone, Estradiol, free T4, computed or/and magnetic tomography of sellar region, ultrasound of thyroid and internal organs, ophthalmologic exam. To classify complications, we divided patients into three groups: with cardiovascular events, metabolic deviations, respiratory, bone-skeletal problems and neoplasms.

3. Results

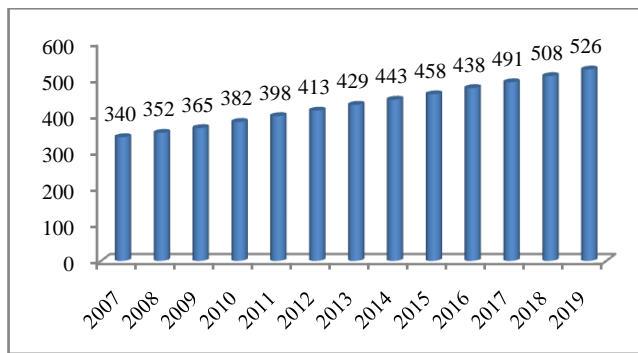


Figure 1. 12-year growth of acromegaly cases nationwide in the Republic of Uzbekistan

Of 526 patients included in registry by 01/01/2019, 195 were males (37.07%) and 331 females (62.93%). Figure 1

demonstrates a growth of cases with acromegaly across Uzbekistan.

As presented in Figure 1, new acromegaly cases grew for twelve-year period. Thus, in 2007, there were 340 patients in the registry and from the period of 2007 to 2018, 186 new patients were diagnosed and included in registry [2,15]. Table 1 shows the 12-year demographic features of acromegaly across Uzbekistan.

Table 1. Morbidity, mortality and prevalence rates of acromegaly for 12-year period

Year	Prevalence	Morbidity	Mortality
2007	1,3	0,03	0,01
2008	1,3	0,04	0,01
2009	1,3	0,05	0,007
2010	1,4	0,06	0,01
2011	1,4	0,06	0,01
2012	1,5	0,05	0,01
2013	1,5	0,06	0,02
2014	1,4	0,04	0,01
2015	1,5	0,05	0,009
2016	1,5	0,05	0,009
2017	1,5	0,05	0,006
2018	1,5	0,05	0,01
2019	1,6	0,05	0,02

As seen from table 1, acromegaly prevalence had a trend to grow, while comparing with other studies with prevalence of 2.8 to 13.7 cases per 100,000, Uzbekistan showed relatively low prevalence with 1.6 patients per 100,000 [14,17]. At the same time, morbidity numbers remained at 0.05–0.06 levels as well as morbidity data have not changed significantly varying from 0.007 to 0.02 cases per 100,000. On the other hand, prevalence rates varied across the regions of the country (Table 2).

Table 2. Acromegaly prevalence rates in Uzbekistan across regions by 01/01/2019

Regions	Population by 01.01.2019 (mln.)	Acromegaly cases	Prevalence per 100,000	Prognosis
Republic of Karakalpakstan	1,87	26	1,4	74
Andijan	3,06	26	0,8	121
Bukhara	1,89	33	1,7	76
Djizzak	1,35	9	0,7	54
Kashkadarya	3,2	23	0,7	128
Navoiy	9,74	24	2,4	39
Namangan	2,75	55	2	110
Samarkand	3,79	33	0,9	152
Surxandarya	2,56	21	0,8	103
Syrdarya	8,29	14	1,7	33
Tashkent	2,89	80	2,8	116
Fergana	3,68	48	1,3	147
Khorezm	1,83	47	2,6	73
Tashkent city	2,51	87	3,5	100
Republic of Uzbekistan (total)	33,25	526	1,6	1330

Table 2 demonstrates significant variations through the parts of Uzbekistan with lowest 9 cases of in Djizzak and the highest 87 persons in Tashkent city. Furthermore, regions with larger contribution were Tashkent city (16.54%), Tashkent (15.21%) and Namangan (10.46%) regions. In addition, significantly lower data revealed in Djizzak (1.07%) and Syrdarya (2.66%) regions. It is worth to note, that population in Djizzak and Syrdarya regions live in long-distance rural areas with difficulties to reach closest medical facilities, which complicates relevant medical care for such patients.

Unlike evaluations discovered in regions for prevalence rates. Thus, variations observed in Djizzak and Kashkadarya regions (0.7 per 100,000) with the largest number of 3.7 patients per 100,000 in Tashkent city. Prognostic data suggest that 1330 people have acromegaly, i.e. 60% of patients remain undiagnosed. Little growth trend and prevalence rate demonstrate poor diagnosis of condition and patients' compliance. Further, we compared prevalence estimates in acromegaly between 2007 and 2019 (Fig. 2)

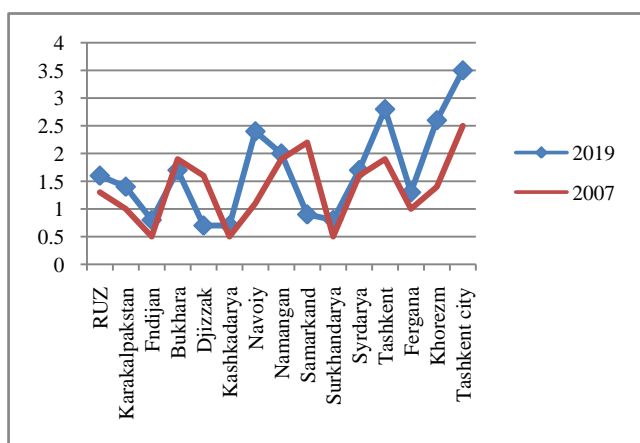


Figure 2. Comparative evaluation of acromegaly prevalence across the regions

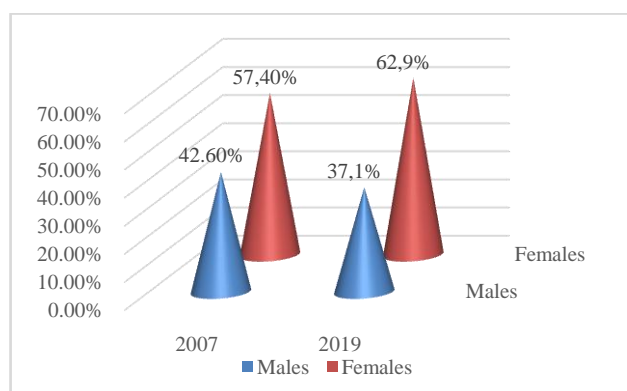


Figure 3. Sex-associated relationship of acromegaly prevalence

Comparative analysis have shown that prevalence of acromegaly increased nationwide between 2007 and 2019. Diagnosis of acromegaly improved in Tashkent city, Navoiy and Tashkent regions, whereas in Djizzak and Samarkand it decline over the time. To decrease the number of undiagnosed patients we need to improve population awareness, particularly, in other medical disciplines, as well as to perform

screening studies. Recent clinical practice guidelines of Endocrine Society suggest the measurement of IGF-1 without the typical manifestations of acromegaly, but who have sleep apnea syndrome, type 2 diabetes mellitus, debilitating arthritis, carpal tunnel syndrome, hyperhidrosis, and hypertension [14]. Additionally, we learned relationship of acromegaly prevalence with the sex of patients for 12-year period (Fig. 3).

In 2007, there were 340 patients diagnosed with acromegaly in Uzbekistan, of which 145 were males (42.6%) and 195 females (57.4%). By 2019 the group of patients verified with acromegaly consisted of 331 females (67.9%) and 195 males (37.1%) (Table 3).

Table 3. Acromegaly cases in males and females in Uzbekistan across the country

Regions	Females		Males		Total	
Andijan	13	50,00%	13	50,00%	26	4,94%
Bukhara	21	63,64%	12	36,36%	33	6,27%
Tashkent city	64	73,56%	23	26,44%	87	16,54%
Djizzak	6	66,67%	3	33,33%	9	1,71%
Kashkadarya	12	52,17%	11	47,83%	23	4,37%
Navoiy	11	45,83%	13	54,17%	24	4,56%
Namangan	35	63,64%	20	36,36%	55	10,46%
Karakalpakstan	17	65,38%	9	34,62%	26	4,94%
Samarkand	18	54,55%	15	45,45%	33	6,27%
Surkhondarya	14	66,67%	7	33,33%	21	3,99%
Syrdarya	11	78,57%	3	21,43%	14	2,66%
Tashkent	48	60,00%	32	40,00%	80	15,21%
Fergana	35	72,92%	13	27,08%	48	9,13%
Khorezm	26	55,32%	21	44,68%	47	8,94%
Total	331	62,93%	195	37,07%	526	100,00%

Majority of regions represented by female patients, except for Navoiy region, where number of male patients contributed to 54% of cases.

Age-related relationships, learned from registry, shown in figure 4.

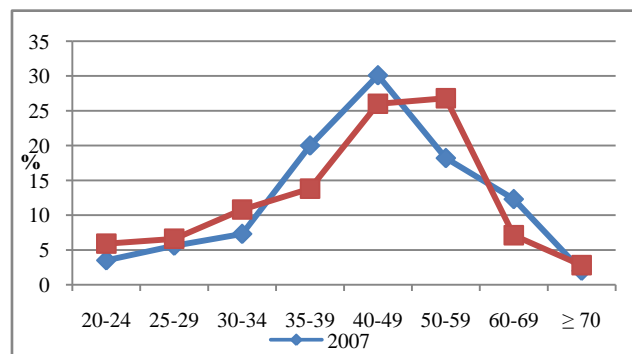


Figure 4. Age-related cases of acromegaly for 12-year period

The most frequent prevalence rate between the ages of 40 and 59 years and constitutes 52.8% of all patients. Morbidity rates increase by 40 to 49 years (26%) and remain at higher levels by 50 to 59 years.

4. Discussion

Acromegaly is debilitating neuroendocrine condition causing multiorgan affection that leads to high disability and mortality rates. There are variety of literature data regarding the prevalence of acromegaly [3,7,9,17,24]. Our results suggest that prevalence of acromegaly by 2019 constituted 1.6 per 100,000 with significant fluctuations across the country (between 0.7 in Djizzak and Kashkadarya to 3.7 per 100,000 in Tashkent city). Equivalent prevalence rate estimates with other countries observed in Tashkent city (3.7) and Tashkent (2.8), Khorezm (2.6), Navoiy (2.4) regions. Lack of early diagnosis is the one of the essential reasons for low prevalence in Djizzak (0.7), Kashkadarya (0.7), Andijan (0.8) and Surkhandarya (0.8) regions. Compared to recent epidemiologic studies, our data correlates with international estimates (between 2.8 to 13.7 cases per 100,000) [3,7,13,22,24]. Tjornstrand *et al* showed 3.3 per 100,000 in Sweden [24], as well as Mestron *et al* demonstrated 3.4 per 100,000 prevalence of acromegaly in Spain.

Epidemiological studies for acromegaly in relation with sex of the patients vary in data numbers [9,17,18,20]. According to Fernandez *et al* [115], Daly *et al* [96] and Agustsson *et al* [28] morbidity with acromegaly more often seen in males, while Gruppette *et al* [9] and Kwon *et al* [16] reported higher numbers in female patients. Moreover, there are studies, which found no sex-specific differences in prevalence and morbidity of acromegaly [4,24]. In our study, we found that acromegaly morbidity is more common in female patients and for twelve-year period female/male ratio showed growth from 1:1.3 to 1:1.7.

It is acknowledged that morbidity rate among patients with acromegaly is higher than in general population [8,11]. In 2018 6 patients died, of which cardio-vascular events contributed to 59.5%, and morbidity rate constituted 0.02 ppm. Morbidity rate in our work remains on low level comparing to the world statistics, where this feature as twice as high the general population, which confirms that patients with acromegaly need better surveillance to follow main causes of mortality.

5. Conclusions

Acromegaly prevalence growth showed progressive growth across the country through 12-year period. This nationwide research can be applied to the local planning of actions with the objective of improving the quality of care for acromegalic patients and reducing the mortality rates and complications associated with disease.

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