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Posted Date: 3 December 2024

doi: 10.20944/preprints202401.0861.v2

Keywords: alopecia areata, cost of illness, economic burden

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The Economic Burden of Alopecia Areata in Romania

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Abstract: Background: Alopecia areata is a skin disease that affects patients' quality of life and social participation and it exerts an economic burden of patients and implicitly their family. To date, this is the first study to quantify the economic burden of alopecia areata for both pediatric and adult patients. Objective: This cost of illness study seeks to quantify the economic burden of alopecia areata for patients aged <20 years and 20+ years for both mild and severe forms of alopecia areata using retrospective and prospective data sources, both incidence and prevalence-based approaches. This cost of illness study is mixed as it employs both top-down and bottom-up approaches. Results: The results of this cost of illness study show that for adults, for both prevalence and incidence-based approach, the highest costs are the direct costs attributable to medical services and associated costs, and the indirect costs due to work absenteeism. Regarding the pediatric population segment, the highest costs were due to treatment, associated expenses and productivity costs inquired by caregivers. Conclusion: This is the first study to quantify the burden of alopecia areata in Romania, for both pediatric and adult patients. Our study highlights that out-of-pocket costs pose an immense burden on patients and their caregivers. Our estimations emphasize that patients with AA should be considered when planning health services delivery and health services and medicine reimbursement.

Keywords: alopecia areata; cost of illness; economic burden

Introduction

Alopecia areata (AA) affects patients of all ages, sexes, and ethnicities, with variations among categories being observed(1). For example, in terms of sex differences, some studies point out that men are diagnosed earlier by 4.7 years than women, while other studies have shown contrary results (2,3).

The burden of alopecia areata in 2019 remained approximately constant at the global level, although, when comparing 1990 with 2019, slight decreases in global age-standardized incidence rates (ASIRs) for both men (287.26 vs. 279.16) and women (549.03 vs. 531.68)(4) were noticed. When comparing adult with minor patients there was a difference of 0.08% among age-standardized prevalence rates (0.18% in adults and 0.10% in pediatric patients). Regarding age predominance, one study reported that patients aged 21–40 were the most affected, while patients aged 40–49 were the second most affected(5). Based on ethnicity, the highest, respectively, the lowest prevalence were among Asian patients (414/100.000) and White patients (168/100.000)(6). In terms of the geographical distribution of disease burden, countries with a high (ASIR – 518.91) and high-middle (ASIR – 408.62) socio-demographic index (SDI) were the most affected. In Eastern Europe, ASIRs were similar in 1990 (389.49) and 2019 (387.84)(4).

AA affects patients and their caregivers on multiple domains. Shi and colleagues showed in a secondary analysis of registry data that poor quality of life (reported by over 54.7% of the included

 doi:10.20944/preprints202401.0861.v2

patients) was associated with age (20-50 years), modification in physical appearance (skin- and hair-related), and sex (female), as well as to several social factors (such as job or family related stress)(7). A hospital-based multicenter study conducted in Korea reported that quality of life worsened in both family members and pediatric patients as the severity of the disease increased. This study also reported that as the disease progressed, the annual cost of treatment in the majority of patients was over $1,000(8). Patients affected by AA, both adults and children, were more often (compared to controls defined as healthy adults) diagnosed with anxiety and/or depression(9).

AA also poses an economic burden. A study assessing the healthcare utilization patterns in the US, in a sample of adolescent patients with AA listed a total cost per patient of $9,397 (the highest - $7,480 was due to payer medical costs, while the lowest was due to payer cost for dermatology appointments - $922)(10). Another US-based study reported for AA adult patients (characterized by an average age of 40.3 years and predominantly female - 61%), healthcare costs of $11,241.21 (for all-causes), while $419.12 due to alopecia (11). Other studies in Europe have confirmed the economic burden of alopecia areata. A real-world analysis conducted in Italy emphasized that the economic burden attributable to health services was of €1,715 per AA patient(12). A comparison analysis conducted in Spain showed that the cost difference between AA patients without (€821,2) and with systemic treatment (€886,6) is of €65.4(13).

Our study is the first study in Romania to quantify the economic burden in patients diagnosed with alopecia areata of different ages. By focusing on this gap, we aim to offer a policy tool for patients and stakeholders alike as cost of illness studies are of utterly importance for policymaking and advocacy, among others.

Methodology

This cost of illness study was conducted from a societal perspective and quantified the direct medical and non-medical costs and indirect costs for patients with alopecia areata. The reference year was 2022. We computed the economic burden by including several data sources, such as: the 2021 GBD study and National Institute of statistics(14), IQVIA, National Institute for Health Services and Management, a financial controlling firm as well as prospective online survey, thus incorporating retrospective and prospective data sources.

From the Global Burden of Disease 2021 Study, we retrieved epidemiological data for AA, for Romania, for 2021, for both sexes and description of health state based on which severity level could be assessed (health state name: “Disfigurement, level 1” and corresponding lay description:” has a slight, visible physical deformity that others notice, which causes some worry and discomfort.”) and L2 (health state name: “Disfigurement, level 2” and corresponding lay description: “has a visible physical deformity that causes others to stare and comment. As a result, the person is worried and has trouble sleeping and concentrating.”)(15). Severity levels included in the survey (prospective source) ranged between S0 (0% hair fall) to S5 (100% hair fall). Per expert opinion and considering the description of the GBD health states for AA, severity levels S0, S1 (1-24% hair fall), S2 (25-49% hair fall) were incorporated in L1, while S3 (50-74% hair fall), S4 (75-99% hair fall), and S5 in L2.

We retrieved crude numbers for prevalence (<20 years: 3,792.18, 20+ years: 37,548.63) and for incidence (<20 years: 6,964.62, 20+ years: 65,413.8) for two age bands: <20 and 20+. Considering that the age band from the survey that was used as input for this model, we included one patient (that responded to the survey), aged between 18 to 25 years, in the 20+ years group considering that there are more years covered by 20+ as opposed to <20. From IQVIA, we used an average cost per prescription – 52 RON (€10.54). This estimate excluded “white prescriptions” (for over-the-counter medicine) and the average cost amounted to 52 RON (with partially or total reimbursed prescriptions were included) based on data collected from 3,700 pharmacies for alopecia areata.

From Hospital Consulting data (financial controlling firm), we used the average cost for inpatient hospitalizations for both adult and pediatric patients with alopecia areata in 2022 and the average length of hospital stays for both adult and pediatric patients for 2022. These estimates are based on yearly updated data, from different hospitals in based of coverage and profile. The average cost for hospitalization for adult AA patients was 1,295 RON (€262.61) and for pediatric AA patients

 doi:10.20944/preprints202401.0861.v2

was 1,321 RON (€267.88). The average length of hospital stay for adult AA patients was 6.03 days and for pediatric AA patients was 3.85 days.

From the National Institute of statistics (INSSE)(16) we used the mean gross salary for 2022 - 6,126 RON (€1,242) which, together with the number of working days for 2022 (251 working days)(17) and the number of missing days reported by adult AA patients or caregivers of pediatric AA patients from the prospective survey, were used to compute the indirect costs attributable to absenteeism from work.

Additional variables used from the prospective survey were cost for treatments, medical services, associated costs (transport, hotel, associated costs) and missing days from work for patients and caregivers that were working full-time or part-time. We excluded missing days reported for patients that were aged over 65 years (thus being considered retired) and from patients and caregivers that were under 65, but have checked (retired due to illness) when completing the survey. We also excluded missing days that exceeded the number of working days within a year.

The average cost for treatment, for adult AA patients was 1701 RON (€344.9) – L1, and 1387 RON (€281.3) – L2 while for pediatric AA patients is 510 RON (€103.4) – L1 and 1595 RON (€323.4) – L2. The average cost for medical services for adult AA patients is 1928 RON (€391) – L1, and 1732 RON (€351.2) – L2. This cost was omitted for the survey on pediatric AA patients. Lastly, the average associated costs for adult AA patients is 3450 RON (€700) – L1 and 3868 RON (€784.4) – L2; while for pediatric AA patients is 1867 RON (€378.6) – L1 and 2500 RON (€507) – L2. The item for medical services was not included in the survey for pediatric AA patients and therefore, this cost category is reported only for adult AA patients. Missing data (for adult patients – for all cost variables; for pediatric patients – only for associated costs) was imputed using the "mice" R package(18).

Lastly, from the National Institute for Health Services and Management (SNSPMN)(19), we used alopecia areata hospital related-discharges that had as the main discharge diagnosis "L63.9 – alopecia areata, unspecified". There were 72 hospitalizations, this representing the total number of hospitalizations that had an AA diagnosis as a main diagnosis, including both adult and pediatric AA patients.

Based on the patients retrieved from the survey (n=41 – adult AA, n=4 – pediatric AA), we calculated the proportions corresponding to each severity level. In the next steps, we took these proportions and calculated the corresponding number of prevalent and incident cases (for both mild and severe cases), for both population segments (<20 years and 20+ years) based on the GBD 2021 data. Next, we took the prevalence and the total number of patients working full-time and of caregivers of pediatric patients that were working full-time to extrapolate these results at the national level. We repeated this steps for incidence. For hospitalizations, considering that we have received the total number of patients and not the total for adults and pediatric AA patients, we took the prevalence for both ages to calculate the proportions of cases corresponding to each age group. Next, we took the total number of prevalent cases and the estimates corresponding to each severity and the obtained numbers for each age groups. We repeated these steps for the incidence data. The obtained estimates were used as cost multipliers.

We report total and average cost per patient per severity levels (L1 and L2) and per age group (<20 and 20+ years). Taking into account the multiple sources presented, we calculated the costs using bottom-up and top-down approaches. Bottom-up was used to compute three costs (for treatment, medical services, and associated costs), top-down for one cost (hospitalizations), and lastly, a hybrid (combining these two approaches) for costs due to absenteeism from work.

All costs were converted in EUR (1 EUR = 4.9313), the value being based on an average of exchanged rates for 2022(20). A research protocol was submitted and approved by the Institutional Review Board - Public Health (IRB-PH), Babes-Bolyai University (no. 151122-003).

Results

AA Incidence and Prevalence

 doi:10.20944/preprints202401.0861.v2

Based on the GBD prevalence-derived results, there were 18,317 L1 and 19,232 L2 AA patients aged 20+ years. For the second age group, <20 years, there were 2,845 L1 and 948 L2 AA patients. As for the incidence-derived results, there were 31,909 L1 AA and 33,505 L2 AA patients aged 20+ years, while for those aged <20 years, there were 5,224 L1 and 1,741 L2 AA patients.

Full-time workers

There were 12,211 L1 and 6,411 L2 patients that were full-time workers (based on GBD prevalence) and 21,273 L1 and 11,168 L2 (based on the GBD incidence). Regarding caregivers of AA patients, there were, based on the prevalence data, 1897 for both L1 and L2 AA patients. As for the second approach, which was incidence-based, the number of caregivers was of 3823 for both L1 and L2 patients.

Hospitalizations

For patients <20 years, there were 7 hospitalizations (5 for L1 and 2 for L2) and 65 for those aged 20+ (32 for L1 and 33 for L2) when using the GBD prevalence. Moreover, when using the GBD incidence, the derived number remained unchanged for both <20 and 20+ years.

Costs Adult AA Patients

The total cost of alopecia areata for adult patients in Romania in 2022 was of €97,950,652.6 for mild (L1) and severe (L2) cases based on the prevalence-based approach. The costs for mild cases were the following: €50,672.9 for hospitalizations, €6,318,256.2 for treatment, €7,161,433.3 for medical services, €12,814,805 for associated expenses, and €33,153,262 for productivity losses. The average cost € 2,608.6 (Table 1). The costS for severe cases were €52,256.4 for hospitalizations, €5,409,280.3 for treatment, €6,754,775.4 for medical services, €15,085,145 for associated expenses and €11,150,766 for productivity losses. The scenario for which the treatment cost (collected via the survey) was replaced with the average cost per prescription, decreased the total cost for treatment to €193,150.7 for L1 and to €202,799.3 for L2 AA patients.

The total cost of alopecia areata for adult patients in Romania in 2022 was of €170,562,808.4 for mild and severe cases based on the incidence-based approach. The costs for mild cases were €50,672.9 for hospitalizations, €11,006,673.5 for treatment, €12,475,524.1 for medical services, €22,323,941 for associated expenses, and €57,756,886.2 for productivity loss. The costs for severe cases were €52,256.4 for hospitalizations, €9,423,770 for treatment, €11,767,822 for medical services, €26,280,563 for associated expenses, and €19,424,700 for productivity loss. Average costs are available in Table 1. Percentages corresponding to each cost and for each approach are reported in Table 2.

Table 1. Average costs by severity (20+ years).

	Prevalence	**Incidence**	**Prevalence (2nd treatment cost scenario)**	**Incidence (2nd treatment cost scenario)**
Average/all	€2,608.6	€2,607.4	€2,306.8	2,305.7
Average/L1	€3,248.3	€3,247.2	€2,913.9	€2,912.8
Average/L2	€1,999.4	€1,998.2	€1,728.7	€1,727.5

Table 2. Cost percentages by scenario and costing approach for adult AA patients.

	Prevalence	**Prevalence (2nd treatment cost scenario)**	**Incidence**	**Incidence (2nd treatment cost scenario)**

 doi:10.20944/preprints202401.0861.v2

Direct medical				
Treatment	11.97%	0.46%	11.98%	0.46%
Medical services	14.21%	16.07%	14.21%	16.07%
Hospitalizations	0.01%	0.12%	0.06%	0.07%
Direct non-medical				
Associated costs	28.48%	32.21%	28.50%	32.23%
Indirect costs				
Productivity-related costs (due to absenteeism)	45.23%	51.15%	45.25%	51.17%

Costs Pediatric AA Patients

The total cost of alopecia areata for pediatric patients in Romania in 2022 was of €3,348,773 for mild – L1 and severe – L2 AA patients, based on a prevalence-based approach. The costs attributable to mild cases were €294,232.8 for treatment, €920,198.5 for associated expenses, €5,156.7 for hospitalizations, and €241,425.8 for caregiver productivity costs. The costs attributable to severe – L2 cases were €358,914.7 for treatment, €480,603.5 for associated expenses, €2,062.7 for hospitalizations, and €1,046,178 for productivity costs. The scenario for which the cost associated to the treatment (collected via the survey) was replaced with the average provided by IQVIA, decreased the total of treatment was to €30,000.2 for L1 and to 9,996.5 for L2 AA patients.

The total cost of alopecia areata for pediatric patients in Romania in 2022 was of €6,373,828 for mild – L1 and severe – L2 AA patients, based on an incidence-based approach. The costs attributable to mild cases were €540,271.3 for treatment, €1,689,672 for associated expenses, €5,156.7 for hospitalizations, and €486,542.3 for caregiver productivity costs. The costs attributable to severe – L2 cases were €659,146.1 for treatment, €882,627.3 for associated expenses, €2,062.7 for hospitalizations, and €2,108,350 for productivity costs. The scenario for which the cost associated to the treatment (collected via the survey) was replaced with the average annual cost for treatment, decreased the total cost of treatment was to €55,086.5 for L1 and to 18,358.7 for L2 AA pediatric patients. Average costs are available in Table 3. Percentages corresponding to each cost and for each approach are reported in Table 4.

Table 3. Average costs by severity (<20 years).

	Prevalence	**Incidence**	**Prevalence – (2nd treatment cost scenario)**	**Incidence - (2nd treatment cost scenario)**
Average/all	€882.9	€915.12	€721.2	€1,383.9
Average/L1	€513.54	€521	€420.7	€428.1
Average/L2	€1,991.3	€2,097.8	€1,623.3	€1,729.7

Table 4. Cost percentages by scenario and costing approach for pediatric AA patients.

	Prevalence	**Prevalence (2nd treatment cost scenario)**	**Incidence**	**Incidence (2nd treatment cost scenario)**
Direct medical				

 doi:10.20944/preprints202401.0861.v2

Treatment	19.50%	1.46%	18.82%	1.4%
Medical services	0%	0%	0%	0%
Hospitalizations	0.22%	0.26%	0.11%	0.14%
Direct non-medical				
Associated costs	41.83%	51.21%	40.36%	49.02%
Indirect costs				
Productivity-related costs (due to absenteeism)	38.45%	47.07%	40.71%	49.45%

Discussion

To our knowledge, this is the first study to assess the costs for patients (children and adults alike) diagnosed with alopecia areata. For pediatric patients, costs due to treatment, associated expenses and productivity were attributable the highest share of the total costs, while costs due to hospitalizations, the lowest attributable economic burden. For adult patients, costs due to associated expenses and productivity were attributable the highest share of the total costs, while costs due to hospitalizations, the lowest attributable economic burden.

Our results highlight how burdening can be an unequal distribution of health services as well as (lack of) treatment reimbursement for treatment options.

Out-of-pockets costs have been representing an important component of the economic burden of AA in German speaking countries as well (such as Germany, Switzerland or Austria). In the sample consisting patients that were mostly employed and female, over three quarters of them reported monthly (non-reimbursed) AA-related OOP costs. The average ranged between €38.4 ± 59.8 (for hair-related items – i.e., wigs – and cosmetic products) and €15.3± 32.9 (for medicines)(21). Another study, conducted by the National Alopecia Areata Foundation, in 2019 emphasizes the financial burden among patients with AA, indicating that for AA-related expenses, patients needed to cut costs for other expenses (such those on food, clothes, or leisure activities), with a range of annual costs between $537 and $3300. The expenses posing the highest economic burden were "headwear or cosmetic options in the past year", "copays/out-of-pocket deductibles for doctor visits in the past year", and "medications (over the counter and prescription) for hair loss in the past year"(22). Among adolescents, the cost per patient, per year in the US was of $7,480 for medical costs, $1,918 for pharmacy costs, $922 for dermatologist, and $1,597 of OOPs costs(10).

Patients with severe AA – L2 – represented a lower number as compared to those with mild AA – L1 – for both adult and pediatric AA cases. However, patients with severe types of hair loss (as well as those having a lower level of hair loss) report health-related quality of life impairments which interferes with their daily activities, social and work life, in addition to causing emotional stress(23). The study by Catwright and colleagues, has shown that greater impact of the disease is reported in female patients in aspects related to emotional and personal life, while men reported a greater impact of the disease in work-related activities(24). Among children and adolescents, decreased quality of life is negatively influenced by the degree of AA severity, as well as mental health-related impairments, such as anxiety and depression(25). Boys (among children and adolescents) reported a poorer QoL as they were bullied more frequently (more frequent in severe AA cases) and implicitly affecting school participation(26,27). Moreover, worse quality of life among minor patients corresponds with worse quality of life among caregivers(28). Thus, psychological support should be provided to both patients and family members. Worse quality of life and severe AA has been documented to influence unemployment rates and work-related repercussions(29–31).

In terms of productivity-related costs, our study only focuses on the cost of productivity due to missing days from work. Thus, future studies on AA patients in Romania (conducted either

 doi:10.20944/preprints202401.0861.v2

nationally, regionally, or locally) should add instruments on absenteeism and also presenteeism. In order to capture how AA negatively influences work-related activities, future studies should incorporate WPAI – Work Productivity and Activity Impairment, a previously validated tool(32). Gandhi and colleagues emphasize in their study how the burden of AA highly affects productivity and cognitive activity when in working environments(33). Other studies also point out that patients with AA, in addition to having a higher level of work absenteeism, they also have a higher risk of losing their job/having difficulties in finding one (which are further explained by the mental health-related complications posed by this pathology)(29,34,35). In terms of financial burden attributable to work absenteeism, the annual median lost wage reported by AA patients was of $500(36). In our study, the average cost due to absenteeism ranged between €127.3 (L1) and €551.5 (L2) for caregivers of pediatric AA patients, and between €340.4 (L1) and €434.8 (L2) for adult AA patients.

A systematic review and meta-analysis (based on fourteen studies) highlight that patients with AA are suffering from anxiety (between 8% and 19.1%) as opposed to non-AA controls or healthy controls. As for pediatric patients with AA, up to 8% suffer from separation anxiety, and up to 16% of generalized anxiety disorder(9). The results of the meta-regression pointed out that, based on the data that anxiety had a moderate effect on the quality of life in patients with AA (when measured with DLQI)(9). Another review highlights that having a diagnose of AA represents a risk factor for developing depression(37).

Strengths

Our CoI employs a nationally representative source – data from the GBD study – as well as hospital discharges with AA as a main diagnosis, in order report a comprehensive economic burden of AA in Romania. In addition, our CoI study quantifies the burden among adults and children alike. The results of our CoI incorporate associated costs, which, are usually overlooked as the main focus can be on either direct medical or indirect costs. Another strength of our study lays in the fact that it presents estimated costs using both incidence and prevalence-based approaches.

Limitations

A limitation of our CoI is represented by the fact that although the cost categories retrieved from the prospective survey on the burden of alopecia areata for minors as well (under 18) from their formal/informal caregivers covered major cost categories, we do not have data on the cost of specific treatments or other items – i.e., wigs – used by AA patients.

Although we report data on the cost of treatment, medical services, and associated costs (transportation, hotel, or other non-medical expenses), our CoI did not distinguish between formal and informal caregivers and does not account for the economic burden generated due to paid care of patients with alopecia areata with formal caregivers.

With this study, we provide the burden of alopecia areata in terms of economic costs and its impact on the health-related quality of life in 2022, in Romania and provide evidence that this disease yields considerable costs that is burdening an already resource scarce health system.

Author Contributions: Conceptualization SS, RZ, DAG, ACN, CV, and RO; data curation SS, DAG, RZ; formal analysis SS, DAG; funding acquisition SS, RZ; investigation and methodology SS, RZ, DAG, ACN, CV, and RO; project administration SS, ACN, RO, RZ; supervision SS, ACN, CV, RO; writing - original draft SS, DAG; writing - review and editing SS, RZ, DAG, ACN, CV, and RO. All authors read and approved the final manuscript.

Funding: An academic grant by Pfizer Global Grants, tracking number 75036377, supported this study. The study was conducted independently, without contributions or communication with the company.

Data Sharing: The data that support the findings of this study are available from the corresponding author, DAG, upon reasonable request.

Conflicts of Interests: Stefan Strilciuc has received an academic grant by Pfizer Global Grants. Rozalina Lapadatu has received an academic grant by Pfizer Global Grants. Rodica Olteanu has received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events, support for

 doi:10.20944/preprints202401.0861.v2

attending meetings and/or travel and participation on a Data Safety Monitoring Board or Advisory Board from Pfizer, Lilly, and AbbVie. In addition, Rodica Olteanu also reports an unpaid leadership or fiduciary role in other board, society, committee or advocacy group. The other authors declare no conflicts of interest.

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