Humanistic and Economic Burden of Retinitis Pigmentosa in Japan: Findings from a Literature Review

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Background

- Inherited retinal dystrophies (IRDs) are a group of eye diseases caused by gene mutations which result in the gradual degeneration of the light sensitive cells (rods and cones) on the back of the eye (the retina)[1].
- Among IRDs, Retinitis pigmentosa (RP) and Leber's congenital amaurosis (LCA) are rare genetic diseases, clinically diagnosed with progressive loss of peripheral vision that eventually leads to near-total blindness, as well as photophobia[2-4].
- RP often becomes symptomatic during childhood or early adulthood with visual field (VF) constrictions and poor night vision as rods in the (mid) periphery degenerate. In contrast, LCA affects both rods and cones right from birth[5-9].

Objectives

- To assess the humanistic and economic burden of RP in Japan.

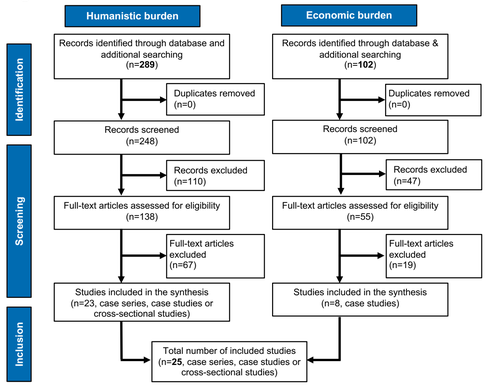
Methods

- A systematic literature review was previously published on the burden of RP Worldwide[10-11]. This was conducted through PubMed and Medline databases for publications in English language only.
- Due to the lack of findings in the English language literature related to Japan, an additional literature review was conducted in the country's ICHUSHI database for publications in Japanese on humanistic and economic burden of RP.
- The search was restricted to Japanese population for articles published from 2005 to 2020.
- Observational studies and case reports were included with relevant humanistic data on patient reported outcome, disease burden and/or economic data on direct/ indirect costs, work life related burden, education, presenteeism/absenteeism, or resource utilization.

Results

- Based on the inclusion criteria, a total of 25 publications was included (**Figure 1**):
  - 23 papers were identified from a humanistic burden perspective
  - 8 papers were identified from an economic burden standpoint

Figure 1: PRISMA Flowchart

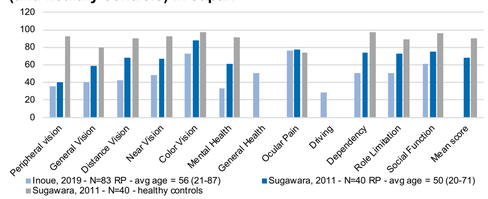


Humanistic Burden

Clinical Burden

- RP is found to be a leading cause of vision impairment between 18 to 49 years old[12].
- All findings mention RP patients experiencing symptoms such as photophobia, night blindness, progressive loss of visual acuity, and visual field defects leading to blindness
  - RP is associated with a deteriorating visual field expressed by a worsening mean deviation in Humphrey field analyser (HFA), a worsening foveal threshold (FT), a worsening sensitivity of central 4 test points in HFA 10-2 perimetry (CENT4), and a worsening sensitivity of central 12 test points in HFA 10-2 perimetry (CENT12) with time[13].
  - Similarly, visual acuity also deteriorate with the progression of the disease displayed by increasing values in logarithm of the minimum angle resolution (LogMAR) with time[13-14].
  - Takeuchi et al. 2018[15] reported that the median visual field area for better eye was significantly narrower in RP patients having car accident compared to those who do not, although no significant difference were observed in visual acuity.
  - Functional Vision Score (FVS) estimating the general visual ability[14] has been recorded for 150 patients during 14 years in Suyama et al. 2018[17]. In the 38 patients remaining after attrition, the functional vision is shown to significantly decrease with disease progression[17].
  - Night blindness is described as a major clinical feature independent of the disease onset[18].

Figure 2: VFQ-25 Scores for Retinitis Pigmentosa patients (and healthy controls) in Japan



*Avg, average

Mental Health

- The following findings shed light on the impact of the RP disease on the patient psychological well-being:
  - Depression has been experienced by 26% of RP patients[21].
  - Anxiety is reported in 37% of RP patients[21].
  - Mental health has been described as one of the category with the lowest score within the VFQ-25. Compared to healthy controls, mental health is significantly more present and impairing in the RP case[14,19] (**Figure 2**).
  - Social workers report RP patients suffering from anxiety (i.e. regarding their vision changes) and aim in their daily practice to encourage positive thinking[22].
  - The fear of injury and anxiety walking alone for RP patient is a target for improvement by low-vision clinics[23].
- Published case-report record patients being worried about various aspects such as their daily activities, social interactions, professional life, personal life, progression of their disease and fear of blindness. They also mention having heavy concerns related to the disease evolution or their future within the society[24-27] (**Figure 3**).

Quality of Life

- Studies report that Japanese RP patients endure substantial humanistic burden including low vision-related quality of life (QoL), and substantial risk of car accidents:
  - In the two studies describing the Visual Function Questionnaire (VFQ-25) scores for RP, mental health, peripheral vision and driving are reported to be particularly impacted by the disease[14,19] (**Figure 2**).
  - In the double arms study from Sugawara et al. 2011[20], RP patients are shown to have significant lower VFQ-25 scores in peripheral vision, general vision, distance vision, near vision as well as, dependency, social function and mental health compared to controls (**Figure 2**).

Figure 3: Concerns and worries from Retinitis Pigmentosa patients

Aoshima et al., 2018[24]; Kanagawa et al., 2013[25]; Yamanouchi et al., 2010[26]; and Tsuruoka et al. 2012[27]

Daily Living Activities Burden

- Cases of autonomy limitations was recurrently found when searching for RP:
  - Mobility and functional vision appear highly impacted following the wide range of devices and visual aids used by patients (**Figure 4**).
  - Patients beneficiating from low vision care and trainings for PC use, white cane use, gaiting or eating[27-30].
  - In their work life, patients do also rely on devices[24].
  - Patients tend to self-limit themselves from driving[15] (**Figure 5**) and refrain to be going out at night alone[31].
  - Rehabilitation for low vision is also an option to cope with the disability[29,32].

Figure 4: Percentage of visual aids or assistive devices used by Retinitis Pigmentosa patients for daily activities in Japan

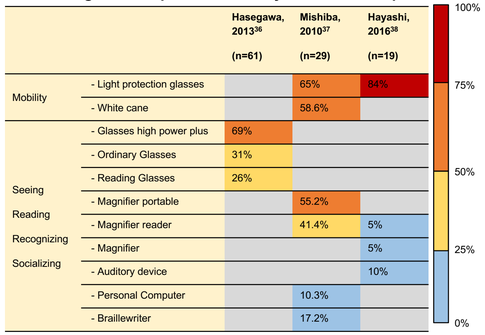
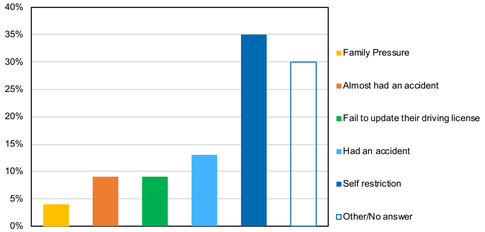


Figure 5: Reasons for quitting driving for Retinitis Pigmentosa Patients

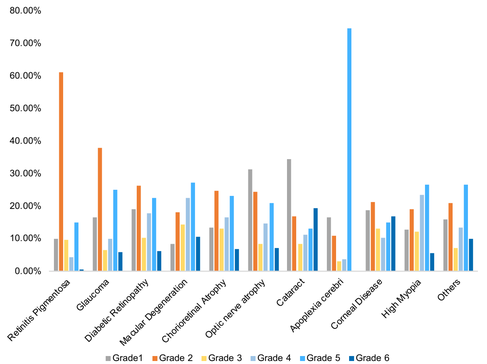


Disability Certification

- Disability Certification in Japan provide financial support:
  - In 2020, majority of RP disability certification holders were of Grade 2[33] (**Figure 6**).*

*Out of 7 grades level, Grade 1 is the most severe status on the Japanese disability certification scale.

Figure 6: Proportion of Grade per Diseases



Morizane et al, 2020[33]

Economic Burden

- Employed patients had to endure several limitations at work including limited mobility, challenges in productivity or social interactions. A total of 10 patients (8 published case studies) experienced difficulties at work.
  - 4 patients found challenging to commute or to navigate within their office[24-25,34-35].
  - 3 patients took leave of absence from work or/and eventually quit their job[27,29,32].
  - 2 patients reported difficulties in professional relationships/work social interactions[25,32].
  - 2 patients reported the negative impact of work environment on her/his mental health[24-25].
  - 3 patients received support from an occupational physician[24-25,34].
  - 3 patients benefitted from work environment adaptation/relocation (i.e. office adaptation, work from home)[30,34-35].
- No relevant information was available on education or supported direct/indirect cost.

CONCLUSIONS

- This literature review provides a glance on the humanistic and economic burden for RP patients in Japan from last fifteen years.
- RP was reported to be a major cause of visual impairment at working-age.
- The insights from this review showed that RP patients had endured heavy burden in their daily lives with respect to autonomy, mobility and professional life.
- Additionally, it has also suggested potential mental health burden among the RP patients.
- Due to limited findings, no clear economic burden can be drawn
- Despite the frequent utilisation of various assistive tools, support provided to compensate for their visual field loss does not seem to be common.

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