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Helicobacter pylori Infection and Atrophic Corpus Gastritis on Patients with Intellectual Disability: Challenges in the Clinical Translation of Personalized Medicine

Pekka Kaipainen and Markus Kaski

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Abstract

The purpose of this chapter is to clarify the prevalence of *Helicobacter pylori* infection (HPI) and atrophic corpus gastritis (ACG) in patients with intellectual disability (ID) and review the literature surrounding them. We measured the levels of pepsinogen I, pepsinogen II, gastrin-17b (basal), and *Helicobacter pylori* antibodies from 243 patients with intellectual disability living in Rinnekoti Research Centre at Lakisto area during 2009–2011. We determined the levels of hemoglobin, mean cell volume (MCV), hematocrit, and the mean amount (MCH) and concentration (MCHC) of red cell hemoglobin, the counts of erythrocytes, leucocytes, and thrombocytes. About 43% had high level of *Helicobacter pylori* antibodies and 6% ACG. Our results show that Helicobacter pylori infection occurs approximately twice the rate it appears in the normal population. Also, the incidence of ACG was higher among patients with ID than normal population. ID may be a risk of getting the *Helicobacter pylori* infection (HPI) and ACG. In addition, it was found that the level of thrombocytes was increased in HPI group compared to normal group and decreased in ACG group compared to normal group. This study shows that there is clearly a need to investigate (test) more stomach condition in patients with ID.

Keywords: helicobacter, *Helicobacter pylori*, pepsinogen, gastritis, atrophic corpus gastritis, intellectual disability, personalized medicine

1. Literature review

1.1. *Helicobacter pylori* infection

Helicobacter pylori is a common Gram-negative bacterium, which may colonize the human stomach, wherein it can induce various gastroduodenal disorders (chronic gastritis, ulceration, atrophic corpus gastritis, and gastric cancer). However, only a small part of the people, who are colonized, develops associated diseases. It is estimated that *H. pylori* infection (HPI) affects more than half of the adult population worldwide [1] and is responsible for 75% of all gastric cancer cases [2]. In Finland and many other countries, the prevalence of *H. pylori* is decreased in last decades, in Finland to the level of approximately 15% of population [3]. Intellectually disabled children are a vulnerable subgroup and may experience higher rates of infections and morbidities [4]. *H. pylori* infection and gastric cancer occur at higher rates in subjects with ID than in the general population [5]. In institutionalized patients with intellectual disability (ID), *Helicobacter pylori* infection (HPI) occurs twice the rate it appears in the normal population [6–8]. It is suggested that the transmission of HPI occur via an oral-oral or fecal-oral pathway. Ohwada et al. [9] concluded that a high frequency of mild norm chromic anemia in institutionalized people with ID was observed. According to them, medications and chronic inflammation may increase the risk of anemia. Telaranta-Keerie et al. [10] noted the prevalence of 3.5 % of population for atrophic corpus gastritis (ACG) and also found that ACG may cause impairment in secretion of intrinsic factor, resulting in vitamin B12 deficiency. Because of these observations, we decided to evaluate the hematological values of our patients with ID. ACG can be autoimmune in origin or it can appear as multifocal atrophic gastritis (MAG) [11, 12]. According to Telaranta-Keerie et al. [10], MAG is always HPI-initiated. Achlorhydric or hypochlorhydric stomach with ACG may result in malabsorption of vitamin B12, micronutrients, and medicines [13]. It is well known that the stomach must be acid in order to absorb B12. Many people already suffer from borderline B12 deficiency—this is a difficult vitamin for the body to assimilate, but essential for normal biochemistry. Therefore, achlorhydria may be associated with vitamin B12 deficiency in the setting of pernicious anemia. Parenteral vitamin B12 may be important in selected patients. Achlorhydria is associated with thiamine deficiency in the setting of bacterial overgrowth [14–16]. In addition, increasing evidence accumulates that *H. pylori* infection may interfere with many biological processes and have a role in birth of several other extra-gastroduodenal manifestations including among others iron deficiency anemia, immune thrombocytopenic purpura, metabolic syndrome and diabetes mellitus, nonalcoholic fatty liver disease, coronary artery disease and cerebrovascular disorders [17]. Because of these facts, ACG is important disease to be diagnosed and recognized [18, 19]. It has been observed that *Helicobacter pylori* infection can cause rumination and numerous other behavioral disorders [20]. *Helicobacter pylori* are associated with gastric atrophy and gastric carcinoma [21].

1.2. The role of epidemiology in understanding the health effects of *Helicobacter pylori* in intellectual disability

H. pylori infection appears to be almost universal among certain groups of people with intellectual disability and appears to be a relatively silent condition in this population, even in

those with more virulent strains [22]. The ID is potentially at risk of significant but preventable morbidity and mortality from the disease consequences of this infection [23]. The efficacy of standard treatment protocols appear lower than that in the general population, and in some, the side effects are more prominent [24]. The diagnosis of *H. pylori* infection can be made with reasonable clinical certainty using the fecal antigen test (and serology under some conditions) or, in those with greater abilities, using the urea breath test [25]. Although eradication of infection does not change the level of maladaptive behavior or intellectual disability, it may reduce the risk of the disease consequences of *H. pylori*. Given the clinical silence of the infection, the virulence of the strains, the acceptability of the diagnostic tests, and knowledge of the risk factors for infection, despite a possible lower eradication rate and higher rate of side effects, a strong argument can be made to proactively screen for and treat *H. pylori* infection among groups of people with intellectual disability who have a history of institutionalization, greater levels of intellectual disability or maladaptive behavior, or live with flatmates with hypersalivation or fecal incontinence [5].

Intellectually disabled children are a vulnerable subgroup and may experience higher rates of infections and morbidities [4]. *H. pylori* infection and gastric cancer occur at higher rates in subjects with ID than in the general population [5, 7]. Many children with ID and neurological impairments are not able to co-operate with performance of noninvasive test such as UBT [7]. In addition, because of limitations in their intellectual and adaptive functioning, such children are unable to report their symptoms. Behavior of people with ID is often difficult to explain and reactions may be similar on physical and emotional stress that is why they may be misunderstood and over medicated. One of the main reasons to begin this research study in our research center—Rinnekoti Research Centre—was the fact that patients with ID very often have difficulties to recognize, localize and indicate their symptoms. Although life-long *H. pylori* associated morbidities are well known, relatively few studies have addressed the status of *H. pylori* infection in people with ID [5].

1.3. Helicobacter infection and gastric neoplasia

As discussed above, *Helicobacter pylori* are one of the world's most common pathogens with a colonization of about 60% of the general population [26, 27]. It is estimated that *H. pylori* infection affects more than half of the adult population worldwide [1] and is responsible for 75% of all gastric cancer cases [2]. No mode of transmission is fully known, however, many factors may contribute such as socio-economic and poor living standards, poor nutrition and physical activity, and possibly poor access to health services. However, most individuals never develop clinical disease [28].

Gastrointestinal problems in handicapped children with neurodevelopmental disabilities are chronic and present long-term management problems. These conditions include dysphagia (60%), chronic pulmonary aspiration (41%), gastroesophageal reflux (32%), abdominal pain and gastritis (32%), constipation (74%), and malnutrition (33%) [29]. Growth failure and malnutrition are common in children with cerebral palsy, particularly in those with spastic quadriplegia, of which 85% report feeding problems [30, 31]. In addition, 20–30% of hemiplegic and diplegic cerebral palsy children are underweight for age [26, 32]. There are multifactorial causes:

insufficient food intake, feeding problems, increased nutrient losses from vomiting or diarrhea, and alterations in energy requirements in epileptic or metabolic syndromes where increased muscle tone or involuntary movements are seen. What is now clear is that undernutrition in cerebral palsy is often correctable and that providing a balanced diet and better nutrition can result in improvement in long-term spasticity, appearance, and effect of these children [33].

Good number of studies have been published in persons with intellectual disability, however, large-scale scientific studies have not been published with a population case-control study [22, 32, 34]. Harris et al. [35] (10) reported that hospital residents under 40 years of age had a 87% prevalence of HP compared with 24% for controls, whereas the overall prevalence for all ages was 87% for residents, and 43% for controls in hospital residents with severe learning disabilities. A larger study including 338 intellectually disabled and 254 controls from Holland (12) found a prevalence of 5% in children and 50% in the elderly in the general population, whereas 83% of the disabled and 27% of the healthy employees were infected. The presence of HP was significantly associated with male gender, longer duration of institutionalization, an IQ below 50, rumination, and a history of upper abdominal symptoms. Another study was conducted to determine the occurrence of HP infection in persons, who presented with severe dyspeptic symptoms and to monitor clinically the effect of treatment [36]. Over a 1-year period, a total of 43 persons (total population in care was 224) had severe dyspeptic symptoms and 42 persons (98%, 26 males, 16 females, mean age 45 years, mean institutionalization 20 years) had HP.

1.4. Treatment regimens used for *H. pylori* eradication

H. pylori infection is most likely acquired by ingesting contaminated food and water, and through person to person contact. *H. pylori* infections are usually treated with antibiotics to help prevent the bacteria from developing a resistance to any particular antibiotic. *Helicobacter pylori* infection causes progressive damage to gastric mucosa and results in serious disease such as peptic ulcer disease, MALT lymphoma, or gastric adenocarcinoma in 20–30% of patients [37]. Most persons who are infected with *H. pylori* never suffer any symptoms related to the infection; however, *H. pylori* causes chronic active, chronic persistent, and atrophic gastritis in adults and children. Infection with *H. pylori* also causes duodenal and gastric ulcers. Infected persons have a two- to six-fold increased risk of developing gastric cancer and mucosal-associated-lymphoid-type (MALT) lymphoma compared with their uninfected counterparts. The role of *H. pylori* in nonulcer dyspepsia remains unclear [38]. Therapy for *H. pylori* infection consists of 10 days to 2 weeks of one or two effective antibiotics, such as amoxicillin, tetracycline (not to be used for children <12 years), metronidazole, or clarithromycin, plus either ranitidine bismuth citrate, bismuth subsalicylate, or a proton pump inhibitor [39, 40]. H pylori eradication rates were higher for a 7-day antibiotic regimen containing lansoprazole, amoxicillin, and clarithromycin (LAC), when used as first-line therapy compared with levofloxacin, amoxicillin, and lansoprazole (LAL) [39]. Yoon et al. [40] investigated the efficacy of a moxifloxacin-containing triple therapy as second-line therapy for *H. pylori* infection as well as the effect of treatment duration and antibiotic resistance on the eradication rate [40].

Combination drug therapy regimens commonly used to treat *H. pylori* infection includes a proton pump inhibitor (PPI) plus clarithromycin plus amoxicillin or metronidazole and a proton pump inhibitor plus a bismuth compound plus metronidazole plus tetracycline. However, all medicines have side effects. But many people don't feel the side effects or they are able to deal with them [38, 41, 42].

1.5. *Helicobacter pylori* infection and oxidative stress

Oxidative stress results from the damaging action of reactive oxygen species. These molecules react with proteins, lipids, or DNA, altering their structure and causing oxidative damage to the cells. Reactive oxygen species (ROS) are produced during normal and physiological process, which inevitably leads to the generation of oxidative molecules: superoxide ($O_2\bullet^-$), hydrogen peroxide (H_2O_2), or hydroxyl radical ($\bullet OH$). Oxidative stress is implicated in a large number of diseases: cancer (oxidative damage to DNA causes mutations that can lead to carcinogenesis), atherosclerosis (atherosclerotic plaques are made from oxidized fat), and neurodegenerative diseases (oxidative damage is a central component of nerve cell destruction). Indicators of oxidative stress have been detected in muscles and blood of ID patients. Oxidative damage can alter the blood-brain barrier, which could explain some of the cognitive problems experienced by patients.

There is an increasing evidence that microbial pathogens induce oxidative stress in infected host cells [43–45] and this may represent an important mechanism leading to epithelial injury in *H. pylori* infection [46].

Oxidative stress could well play a role in the altered epithelial proliferation, increased apoptosis, and increased oxidative DNA damage [47–49] associated with *H. pylori* infection.

Evidence for this includes increased levels of reactive oxygen species (ROS) measured in the mucosae of infected patients [48, 50, 51]. While activated, ROS-releasing phagocytic leukocytes recruited to the gastric mucosa during infection represent one obvious source of oxidative stress [43, 50].

The mechanism of tissue damage and cell proliferation in H. Pylori infection remains unknown, although cytokines, chemokines, growth factors, including nitric oxide synthase and potent neutrophil. Derive reactive oxygen metabolism have all been proposed to contribute to such damage [52–54]. HP infection is associated with the increased production of free radicals in the gastric mucosa [50]. Accumulated free radicals in the tissue initiate lipid peroxidation of cell membranes and threaten cell integrity. Antioxidant may be useful in HP-related mucosal disease [47]. Evidence suggests that microbial pathogens induce oxidative stress in infected host cells [43–45], which represents an important mechanism causing damage to the epithelial in *H. pylori* infection [55]. *Helicobacter pylori* is the major cause of acute and chronic gastritis, gastric, and duodenal ulcer and increased incidence of gastric adenocarcinoma and elevated gastric mucosa lymph proliferation. Reactive oxygen species have been suggested as one of the main causes of cell injury in *H. pylori* associated gastritis. *H. pylori* mutants that are defective in RuvC have increased sensitivity to DNA-damaging agents and to oxidative stress, exhibit reduced survival within macrophages, and are unable to establish successful infection in a mouse model [56].

2. Research study

2.1. Material and methods

GastroPanel test (Biohit Oyj, Helsinki) was used. The test consisted of measurement of plasma pepsinogen I, pepsinogen II (PG I, PG II and PG I/PG II ratio), *H. pylori* IgG antibodies (HpAb) and gastrin-17-basal by the ELISA method. Test results, together with a short interpretation of the results are created by the GastroSoft software. The GastroSoft software uses an algorithm that is based on the levels of PG I, PG II, HpAb, and gastrin-17-basal in plasma as measured by GastroPanel. When the results showed a low PG I level (<30 μg/l) and/or a low PG I/PG II ratio (<3), the GastroSoft interpretation was "moderate or severe atrophic corpus gastritis". Cases fulfilling these criteria were considered to have advanced ACG. If PG I level and PG I/PG II ratio were normal but the patient had an elevated HpAb result (≥30 EIU), this was interpreted as "nonatrophic *H. pylori* gastritis". When the levels of all the biomarkers were within their reference ranges (PG I ≥ 30 μg/l and PG I/PG II ratio ≥ 3, HpAb below 30 EIU), the GastroSoft interpretation was "healthy, normal stomach mucosa".

2.2. Laboratory determinations and reagents

Vacuette serum tubes were used to obtain serum samples and vacuette K2EDTA tubes were used to obtain hematological samples. Hemoglobin, mean cell volume (MCV), hematocrit, erythrocytes, thrombocytes, and leukocytes were assayed with Sysmex KX-21 N analyzer. All used reagents were reagent grade. All laboratory determinations were controlled with the control samples from Labquality Ltd., Helsinki, Finland. All enzyme immunoassays were done with BP 800 reader.

2.3. Study population

The study material consisted of blood samples from patients with intellectual disability (243 individuals). Patients with ID lived in groups containing 6–8 persons during 2009–2011. Age was from 10 to 80. The whole group consisted 157 male and 86 female patients with ID. Sanitary facilities were common for each group as normal family living. The personnel taking care of these patients was living with them for 24 hours per day with 8–10 hours shifts.

3. Results

We measured the levels of pepsinogen I, pepsinogen II, gastrin 17-beta, and *Helicobacter pylori* antibodies from 243 patients with intellectual disability (157 male patients and 86 female patients). Results are shown in **Tables 1** and **2** and **Figures 1**–**4**. The prevalence of subjects with ACG, HPI, and normal stomach mucosa is shown in **Table 1**. Among male patients, 7% had ACG, while among female patients, 4.7% had ACG. 6.2% of all patients had ACG. Among male patients, 45.2% had HPI, while among female patients, 39.5% had HPI. About 43.2% of all

Populations	Number of patients	Advanced corpus gastritis	Elevated helicobacter pylori antibodies	Healthy stomach mucosa
	No.	No. (%)	No. (%)	No. (%)
Patients (male)	157	11 (7,0%)	71 (45,2%)	75 (47,8%)
Patients (female)	86	4 (4,7%)	34 (39,5%)	48 (55,8%)
Total	243	15 (6,2%)	105 (43,2%)	123 (50,6%)

Table 1. Prevalence of subjects with advanced atrophic corpus gastritis (ACG), elevated *Helicobacter pylori* antibodies, and normal stomach mucosa in male and female patients with ID.

patients had HPI. Among male patients, 47.8% had normal stomach mucosa, while among female patients, 55.8% had normal stomach mucosa. About 50.6% of all patients had normal stomach mucosa (**Table 1**). Differences in the levels of pepsinogen II, PG I/PG II, and *Helicobacter pylori* antibodies between HPI group and normal group were statistically extremely significant. Differences in the levels of pepsinogen I, PG I/PG II, and *Helicobacter pylori* antibodies between ACG group and normal group were also statistically extremely significant. Differences in the levels of hemoglobin, hematocrit, erythrocytes, and leucocytes between HPI group and normal group were not statistically significant. The level of thrombocytes was increased in HPI group compared to normal group and decreased in ACG group compared to normal group. These differences were statistically significant. Differences in the MCHC, MCH, and MCV were not statistically significant between these groups. Same results were between ACG group and normal group (**Table 2**).

Determinations	ACG	HPI	Normal	Reference values	Unit	p-value	p-value
	(N=13)	(N=87)	(N=100)			ACG vs Normal	HPI vs Normal
	(M ±SD)	(M ±SD)	(M ±SD)				
Age	50 ±11	43 ±16	35 ±21			0,0003	0,0056
Pepsinogen I	25 ±12	127 ±68	103 ±60	30-165	µg/l	6,99 E-21	0,01
Pepsinogen II	15,2 ±8,5	21,0 ±14,9	9,6 ±6,9	3-15	µg/l	0,02	1,27 E-09
PEP I/PEP II	2,4 ±2,2	7,7 ±4,5	12,3 ±6,6	3-20		9,22 E-17	8,24 E-08
Gastrin 17-beta	44 ±81	14 ±20	9 ±14	5-30	pmol/l	0,12	0,06
H.pylori antibodies	77 ±45	85 ±26	12 ±10	<30	EIU	5,99 E-05	3,35 E-45
B-Hb	138 ±16	136 ±16	134 ±14	male 134-167 female 117-155	g/l	0,39	0,47
B-Hkr	0,41 ±0,04	0,39 ±0,04	0,39 ±0,04	male 0,39-0,5 female 0,35-0,46		0,24	0,96
B-Eryt	4,5 ±0,5	4,5 ±0,5	4,4 ±0,4	male 4,3-5,7 female 3,9-5,3	E12/L	0,77	0,52
E-MCV	92 ±5	88 ±4	89 ±5	82-98	fl	0,11	0,28
E-MCH	31 ±2	30 ±2	31 ±2	27-33	pg	0,53	0,78
E-MCHC	339 ±11	346 ±13	341 ±12	320-360	g/l	0,42	0,03
B-Tromb	167 ±52	225 ±88	201 ±70	150-360	E9/L	0,04	0,04
B-Leuk	5,7 ±2,3	6,1 ±2,1	6,0 ±2,4	3,4-8,2	E9/L	0,62	0,77

Table 2. Five gastro and eight hematological parameters in groups with advanced corpus gastritis (ACG), *Helicobacter pylori* antibodies (HPI), and healthy stomach mucosa (normal).
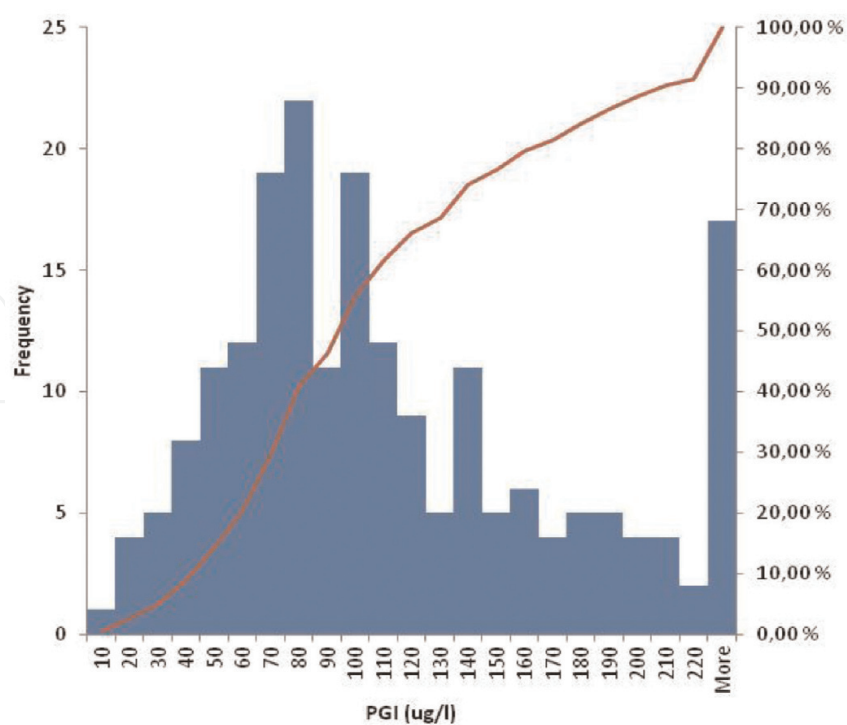
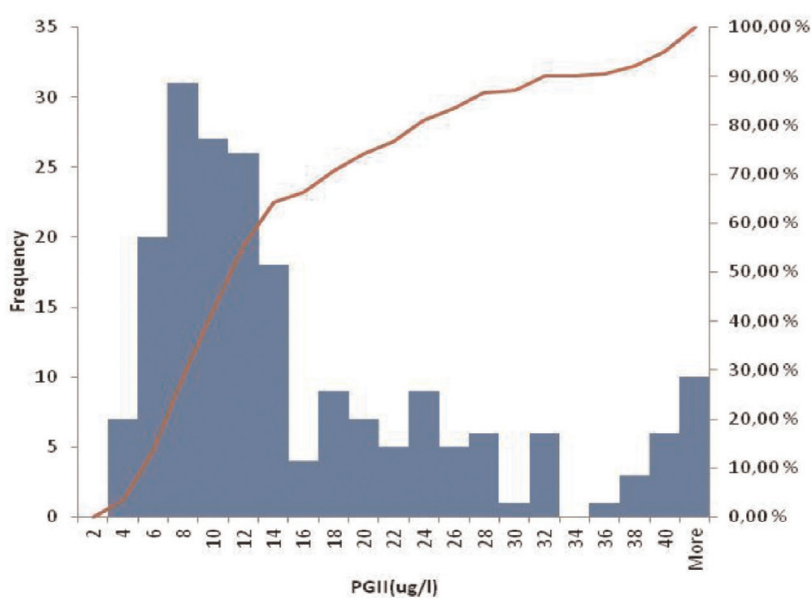**Figure 1.** The levels of pepsinogen I on 243 patients with ID.

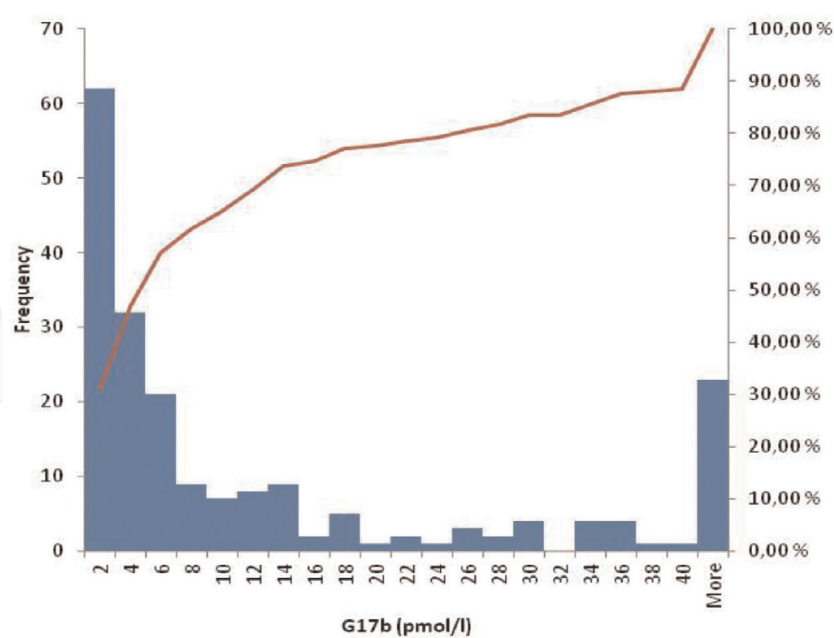**Figure 2.** The levels of pepsinogen II on 243 patients with ID.

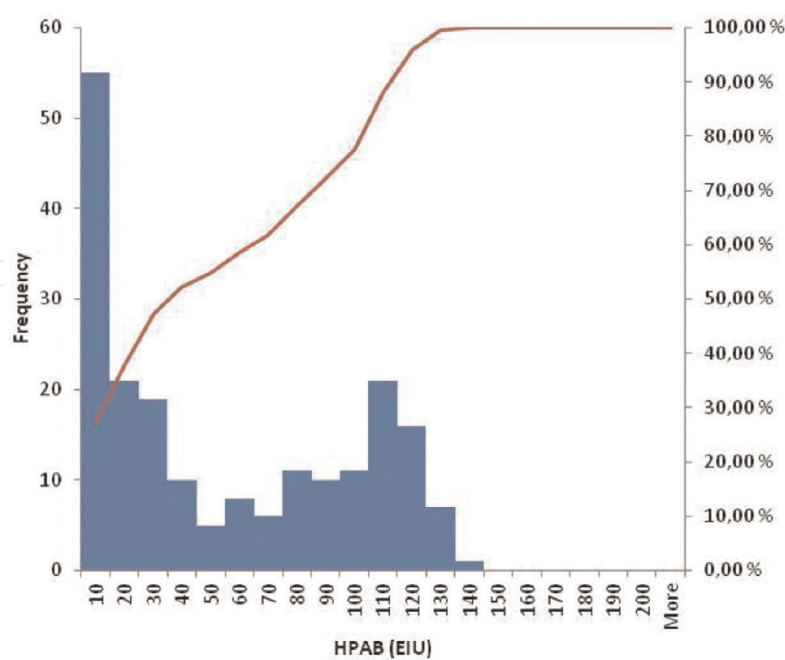**Figure 3.** The levels of Gastrin 17-b on 243 patients with ID.

Figure 4. The levels of H. pylori antibodies on 243 patients with ID.

4. Discussion

This study provides an overview of the best available evidence on the prevalence of *H. pylori* infection obtained from patients with intellectual disability.

The level of ID and environmental factors may be related to the risk of infection with *H. pylori* [7]. According to Merrick, 43 persons (total population in care was 224) had severe dyspeptic symptoms. Wallace et al. [7] showed that adults with ID may be at risk of infection with HPI. According to their results, a long period of institutionalization living with other patients predisposes to HPI. *Helicobacter pylori* among patients with ID living in hospitals are common [7]. In institutionalized patients with intellectual disability (ID), *Helicobacter pylori* infection (HPI) occur twice the rate it appears in the normal population [6–8]. However, this trend has not been before observed in Finland. The patients with ID lived in groups containing 6–8 persons. Sanitary facilities were common for each group as normal family living. It is suggested that the transmission of HPI occur via an oral-oral or fecal-oral pathway. The mechanism of transmission of this pathogen is not known exactly. But it is known that the rate of this disease is increased with age and other living conditions. According to our findings, patients with ID and age of 50 and living for a long time in group residences are high at risk to get *Helicobacter pylori* infection and also so atrophic corpus gastritis. Because well-being of patients with ID is important, we decided to determine also the hematological values of these people. We did not find any big differences between the patients with healthy and sick stomach mucosa. The count of thrombocytes was increased in HPI group and decreased in ACG group. Thrombocytes have an important role in inflammation [57]. They participate in inflammatory response to *H. pylori* infection by activation and aggregation as well as acting as a source of inflammatory mediators and modulating the activity of other inflammatory cells in stomach mucosa [58]. The volume of thrombocytes may be increased during infection. Their persistent activation and enhanced destruction production process during infection may lead to decreased amounts of them [59]. However, it seems that there lacks association between *H. pylori* infection and various markers of systemic inflammation including thrombocyte/lymphocyte ratio in adults with chronic asymptomatic *H. pylori* infection [60]. *Helicobacter pylori* infection and its consequences may be severe to people with ID. Wallace et al. [7] concluded that if this infection leads to increased levels of maladaptive behavior, this could result in loss of social opportunities, sedative drug use and so decrease of well-being. The mental pressure among workers in institutions for people with ID will increase. Böhmer et al. [61] and Schryver et al. [62] found that *Helicobacter pylori* infection is an occupational risk in healthcare workers working in institutions for people with ID. This observation gives the reason to also investigate all workers taking care of patients with ID.

Proujansky et al. [20] stated that rumination may be a possible symptom of *Helicobacter pylori* infection. Rumination occurs more frequently in patients with ID. Dentists play the important role in finding patients with rumination. From these patients, it is important to investigate *Helicobacter pylori* infection and treat it. Ohwada et al. [9] found that the prevalence of anemia was increased on patients with ID. According to their results, most patients showed a normocytic norm chromic anemia pattern. They say that medications and inflammation may increase the risk of anemia. We did not find differences on hemoglobin levels between the patients with normal and sick mucosa of stomach. We need more research on this field.

Wallace et al. [63, 64] reported that 7% of institutionalized adults with ID treated for *Helicobacter pylori* infection and test negative at the end of treatment are at risk of reinfection. They suggest that patients with ID should retest at an interval of approximately 3–5 years after apparent eradication. More research is needed to evaluate the effects of *Helicobacter pylori* infection on pain and use of drugs on patients with ID. Taking care of this infection, we can probably increase the level of well-being of these patients and so to decrease the physical and physiological pressure of workers in institutions for people with ID. Many studies have explored the association of *H. pylori* with hypermethylation of specific genes [65, 66] as well as hypomethylation of genes [67, 68]. Further research is required to elucidate the exact mechanisms of inflammation and tumor suppression, which might provide new opportunities for personalized treatment options.

The poor prognosis of patients with a negative *H. pylori* status might be the result of a more aggressive form of gastric cancer [69, 70]. The present study demonstrates that *H. pylori* positivity is a beneficial prognostic indicator in patients with intellectual disability, independent of other clinic pathologic variables. In clinical practice, patients with curatively resected gastric cancer who are negative for *H. pylori* may need more careful follow-up and more aggressive antitumor treatment to prolong life expectancy. Further research is required to elucidate the exact mechanisms of inflammation and tumor suppression, which might provide new opportunities for personalized treatment options. We believe that the current prospective study is the first to confirm *H. pylori* status as a favorable prognostic factor in a large number of intellectual disability patients with *Helicobacter pylori* infection and atrophic corpus gastritis in Finland, thus validating the effect of *H. pylori* infection status on survival in intellectual disability patients.

Antibiotic susceptibility should be checked in all patients, ideally, before the start of eradication treatment. The knowledge of local antibiotic resistance and consumption pattern is important in selecting a reliable regimen [71–73]. Future development for *H. pylori* therapy should be directed to overcome individualized antibiotic resistance. Warneke et al. [74] investigated various phenotypic and genotypic biomarkers of gastric cancer (GC) and concluded whether these biomarkers are suitable for the identification of GC subtypes, are they of prognostic significance, and should any of these biomarkers be considered to tailor patient treatment in the future. There remains a need to better understand the prognostic factors affecting the cure rate of *Helicobacter pylori* infection might lead to the development of novel prevention strategies and therapeutic targets. Therefore, personalized medical approach will likely increase the cure rate of *H. pylori* infection [75].

A complete history could also do away with the need for additional testing and increased medical expenses for the patient and the healthcare system as a whole.

Acknowledgements

Author details

Pekka Kaipainen[1]* and Markus Kaski[2]

*Address all correspondence to: pekka.kaipainen@nordlab.fi

1 Nordlab Kokkola, Kokkola, Finland

2 Rinnekoti Research Centre, Espoo, Finland

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