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ORIGINAL ARTICLE

Disease prevalence in a rural Andean population of central Peru: a focus on autoimmune and allergic diseases

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Abstract

Introduction The hygiene hypothesis, formulated to explain the increased incidence of allergic and autoimmune diseases observed in industrialized countries, remains controversial. We reflected upon this hypothesis during a medical mission to rural and impoverished villages of central Peru.

Materials and methods The mission was carried out in July 2015 to aid three Andean villages located near Cusco, and comprised 10 American physicians, 4 nurses, and 24 students. After recording the vital signs, patients were triaged by nurses based on the major complaint, visited by physicians, and prescribed medications. Physicians wrote their notes on a one-page form and established diagnoses purely on clinical grounds, without laboratory or imaging testing. Physician notes were then analyzed retrospectively in a de-identified and double-blinded fashion.

Results A total of 1075 patients (357 men and 718 women) were visited during 5 consecutive clinic days, 840 being adults and 235 <18 years of age. The most common complaints were back pain, stomach pain, headache, and vision loss. Osteoarthritis, gastritis, visual disturbances, and parasitic infections dominated the diagnostic categories. Thirty-seven patients (3 %) were diagnosed with an allergic or autoimmune disease, mainly represented by asthma, rheumatoid arthritis, and Hashimoto's thyroiditis, a prevalence that was not significantly lower than that reported in industrialized countries.

Conclusions Although a study of this nature cannot definitively support or refute the hygiene hypothesis, it does provide a novel snapshot of disease prevalence in rural Andean villages of central Peru. The study could serve as a basis to implement basic public health interventions and prepare for future missions to the same or comparable regions.

Keywords Hygiene hypothesis · Autoimmunity · Epidemiology

Introduction

The "hygiene hypothesis" was proposed by Strachan [1] to explain the increased prevalence of allergic diseases in countries that enjoy "improved household amenities and higher standards of personal cleanliness". A few years later, the same hypothesis was used to explain the increased prevalence of autoimmune diseases reported in Western countries [2]. In essence, this hypothesis envisions a direct relationship between the cleanliness of the environment in which humans live and the incidence of allergic and autoimmune conditions: the cleaner and more devoid of infectious agents the environment is, the greater the incidence of allergy and autoimmunity. Recently, Clarke et al. [3] reported that living in rural, thus less "clean",

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areas during early childhood significantly reduced the risk of developing papillary thyroid cancer in adulthood. Over the past two decades, several studies have evaluated the association between environmental infections (mainly parasitic) and autoimmune diseases such as multiple sclerosis and [4, 5] inflammatory bowel disease [6], suggesting that exposure to microbes imprints and calibrates the immune system so as to not overreact against the host. In keeping with these findings, Shoenfeld et al. have demonstrated that the experimental administration of helminth products, such as phosphorylcholine combined with tuftsin, ameliorated morbidity and mortality in a murine model of systemic lupus erythematosus [7], highlighting new interventional approaches based on infectious agents for the treatment of autoimmune and allergic diseases [8]. While the mechanism underlying the hygiene hypothesis remains to be defined, recent evidence suggests that parasite-driven protection is associated with induction of regulatory T cells [9] as well as regulatory B cells [10].

Peruvian Quechua can overall be considered a population not enjoying household amenities and not having higher standards of personal cleanliness. They are indigenous Amerindians, descendant of the Incas, who currently make up to 45 % of the Peruvian population. They are typically rural and impoverished [11], and often rely on folk medicine for the treatment of various diseases [12]. Centuries of exposure to high altitude (i.e., higher than 2500 m above sea level) have induced genetic polymorphisms and physiological responses that allow Quechua to survive chronic hypoxia and cold temperatures. Several studies have revealed these genetics and environmental adaptions (summarized in Supplemental Table 1) by comparing Quechua born and raised at high altitude to those born and raised at sea level. On the contrary, only limited information is available regarding autoimmune diseases in Andean populations. Toloza et al. [13] analyzed the prevalence of psoriasis and psoriatic arthritis in 8191 consecutive patients seen at the arthritis clinic in the Juliaca Hospital of Puno over a period of 3 years (2008–2011). The authors identified 16 cases, yielding a period prevalence (0.2 %) that is not significantly different from the lifetime prevalence of psoriasis observed in Denmark in 2001 [14].

Recently, we participated in a medical mission to Andean villages of central Peru organized by the non-profit charity *Hands Across the Americas*. We took this opportunity to analyze the overall disease prevalence in patients attending the mission clinics, reflect upon the hygiene hypothesis, and provide a benchmark for guiding future missions in similar areas.

Materials and methods

Settings

The medical mission was carried out in the three rural villages of Huarocondo (day 1), Ancahuasi (days 2–3), and Anta (days 4–5) over the course of 5 days in July 2015. These villages, located at approximately 50 km from Cusco, are situated at about 3300 m above the sea level and comprise a population of approximately 30,000 Amerindian people. Patients came spontaneously to the clinic and were seen on a first-come, first-served basis until the day was over. The mission was conducted by 10 American physicians and 4 nurses, with the assistance of 24 students. After registration, patients were seen by a nurse to record vital signs [blood pressure, heart rate, respiration rate, temperature (mainly in children), and body weight], and then triaged to the various physicians (5 internists, 2 gynecologists, 1 pediatrician, 1 otorhinolaryngologist, and 1 psychiatrist) according to the major complaint. Physicians hand-wrote notes and prescriptions on a printed one-page form and established diagnoses purely on clinical grounds, without the aid of laboratory or imaging studies. These diagnoses reflected the clinical expertise of the participating physicians, none of whom had received specialized training in autoimmune and allergic diseases. Following the visit, patients were escorted to a tent pharmacy where they received instructions and medications. Medications, donated by various institutions or purchased through private donations, had been shipped from the United States prior to the mission.

Study design

This cross-sectional study analyzed after completion of the mission the clinical notes physicians had taken. Physicians were unaware of the study and thus provided an unbiased assessment of the disease prevalence in this region. De-identified patient notes were manually entered into a FileMaker database (FileMaker Inc., Santa Clara, CA), and then analyzed with Stata (software release 14, from Stata Corporation, College Station, TX). The study was considered exempt from institutional review board evaluation on the basis of federal regulation 45 CFR 46.101(b) (research involving the study of existing data recorded in such a manner that subjects cannot be identified). Differences in means between two groups were assessed by Student's *t* test, and differences in proportions by Fisher's exact test. Simple linear regression was used to analyze the association of blood pressure with age, and heart rate with age.

Results

Demographics

A total of 1075 patients were examined by ten physicians in 5 days. Of the patients, 235 were children (<18 year old, 123 boys and 112 girls) and 840 adults (234 men and 606 women). The majority of patients (961 of 1075, 89 %) were seen by only one physician; the remaining minority (114, 11 %) had more than one visit, for a total of 1196 visits (Supplemental Table 2). Age ranged from 6 months to 107 years (Fig. 1a). In children, age had a median of 4, a mean of 6, and a standard deviation of 5 years, and did not differ between males and females (Fig. 1b). In adults, age had a median 56 years, a mean of 55, a standard deviation of 19, and was significantly greater in males (61 ± 18) than females (53 ± 20, $p < 0.0001$, Fig. 1b).

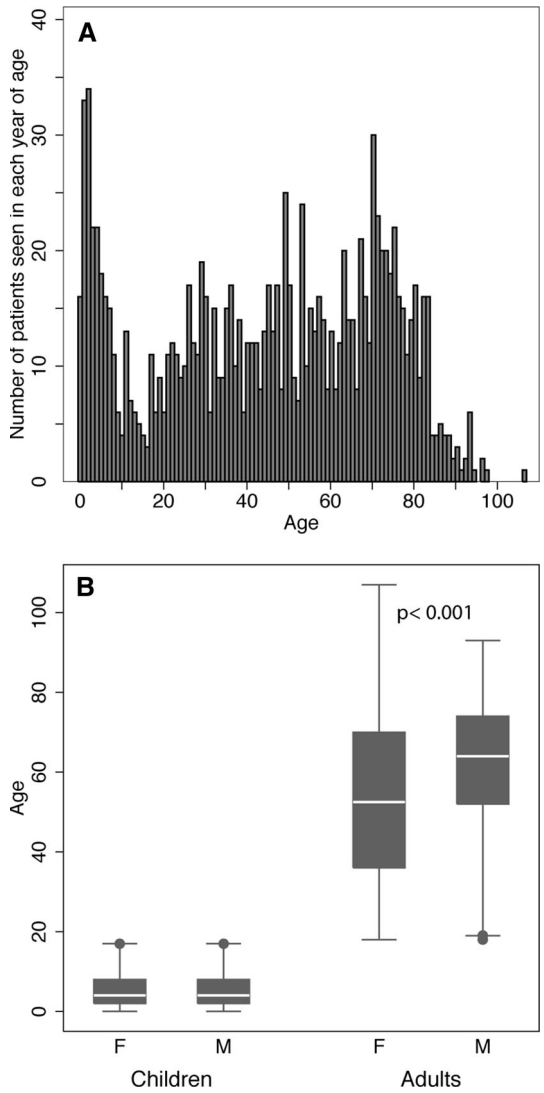

Fig. 1 **a** Age distribution of the 1075 patients seen according to their age. **b** Distribution of the patient ages according to gender (male or female) and group (children or adults)

Vital signs

Blood pressure was measured in most adults (808 of 840, 96 %, 582 women and 226 males), and in a few children (17 of 235, 7 %). The overall prevalence of hypertension (defined as a systolic pressure >140 mmHg and/or a diastolic pressure >90 mmHg) in men was 27 % (60 of 226), a value similar to the one (30 %) reported in the 2011–2012 National Health and Nutrition Examination Survey [15]. In women, the prevalence of hypertension was significantly lower than in men (76 of 582, 13 %, $p < 0.001$), and lower than that (28 %) reported in the United States [15]. The mean arterial blood pressure was significantly associated with age, increasing about 2.5 mmHg (95 % confidence interval from 2 to 2.9, $p < 0.001$) for every decade increase in age (Fig. 2a).

Resting heart rate was measured in most adults (738 of 840, 88 %) and a few children (20 of 235, 9 %). It was normal (i.e., comprised between 60 and 100 beats per minute) in the majority of patients. One patient, seemingly asymptomatic, was found to have a heart rate of 162 and shortness of breath; treatment with metoprolol was started and arrangements were made to transfer him to an emergency department. Five additional patients had heart rates between 105 and 115, but were asymptomatic and left untreated. A significant proportion of patients (78 of 1075, 7 %) had a heart rate below 60. They were also asymptomatic and left untreated. Heart rate did not significantly change with age (Fig. 2b).

Reasons for the visit

A total of 2299 complaints were reported by the patients who elected to come to the clinic. The most common complaint was back pain (223 of 2299, 10 %), followed by stomach pain (208, 9 %), headache (206, 9 %), large joint pain (184, 8 %), and vision loss (169, 7 %, Table 1).

Diagnoses

A total of 1661 diagnoses were established by the visiting physicians. The most common diagnosis was osteoarthritis (343 of 1661, 21 %), followed by gastritis (149, 9 %), visual disturbances (124, 7 %), and parasitic infections (119, 7 %, Table 2). The latter ones were more commonly found in children (104 of 235, 44 %) than in adults (15 of 840, 2 %, $p < 0.001$). Thirty-seven of the total 1075 patients (3 %) were diagnosed with diseases considered allergic or autoimmune, the most common of which were asthma, rheumatoid arthritis, and Hashimoto's thyroiditis (Table 3).

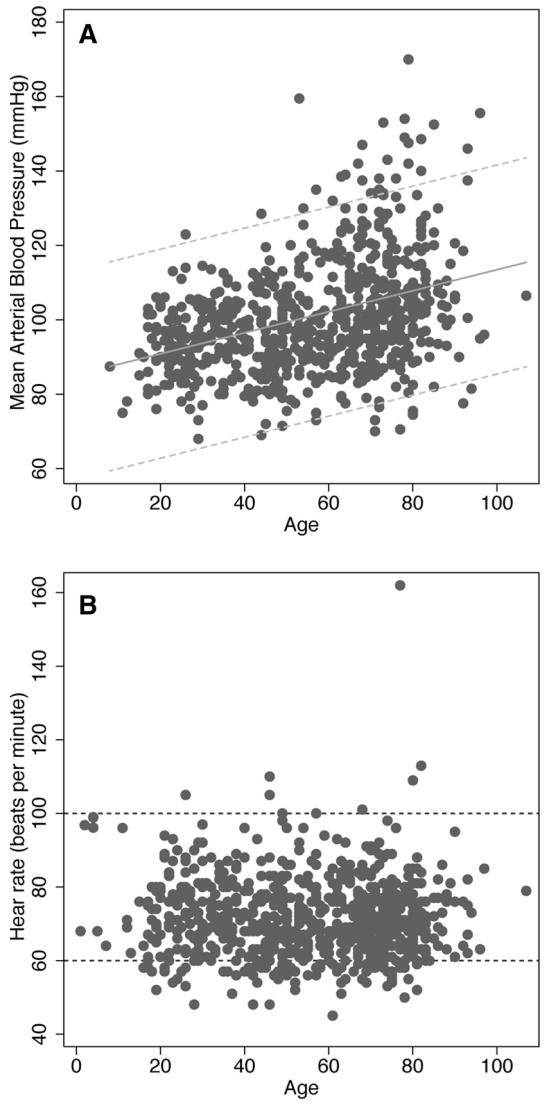

Fig. 2 Blood pressure and heart rate. **a** Significant association of mean arterial blood pressure with age. *Dotted lines* represent the 95 % confidence interval around the linear fit. **b** Lack of association between heart rate and age. *Dotted lines* represent the upper (100) and lower (60) normal beats per minute

Medications prescribed

A total of 1648 medications were prescribed by the visiting physicians, mainly represented by acetaminophen (361 of 1648, 22 %), ibuprofen (261, 16 %), albendazole (118, 7 %), ranitidine (116, 7 %), and metronidazole (79, 5 %, Table 4).

Discussion

This study analyzed the overall prevalence of diseases affecting Amerindian people living in a rural and mountainous region of central Peru. Given its cross-sectional and

Table 1 Reasons for the total 2299 visits, classified according to their origin

	Number	Percentage
Head	655	28
Headache	206	
Vision loss	169	
Hearing loss	93	
Tooth pain	27	
Sore throat	26	
Lacrimation	20	
Others	114	
Joints and muscles	632	27
Back pain	223	
Large joints pain	184	
Others	225	
Gastrointestinal	336	15
Stomach pain	208	
Diarrhea	23	
Abdominal pain	22	
Constipation	21	
Acid reflux	21	
Others	41	
Genitourinary	218	10
Vaginal discharge	91	
Pelvic pain	44	
Dysuria	28	
Vaginal pruritus	12	
Vaginal bleeding	6	
Others	37	
Heart and lungs	157	7
Cough	61	
Chest pain	30	
Runny nose	28	
Difficult breathing	15	
Others	23	
Constitutional	137	6
Appetite loss	69	
Fever	28	
Weight loss	23	
Cold intolerance	5	
Others	12	
Neuropsychiatric	82	3
Domestic problems	17	
Sadness	12	
Difficulty sleeping	8	
Anxiety	6	
Loneliness	4	
Others	35	
Skin	43	2
Rash	19	

Table 1 continued

	Number	Percentage
Itchiness	8	
Photosensitivity	3	
Dryness	2	
Hair loss	2	
Others	9	
Trauma	39	2

unbiased nature, the study offers a novel snapshot of this population health, as assessed on purely clinical grounds (i.e., without the aid of imaging or laboratory tests).

The most prevalent diseases were those caused by the environment in which patients lived and worked. Osteoarthritis, the inevitable consequence of years of physical labor in the agricultural fields, involved mainly the back, hands, knees, and shoulders, and often caused significant impairment. Gastritis was likely attributable to the beverages Quechua people drink. Households, often lacking running water, make large use of *chicha de jora*, a corn-derived beer that dates back to Incan times. It is cheap and considered by the locals more a way of life than a drink, endowed with health benefits for all ages. Although *chicha*'s composition is not fully characterized, its alcoholic content is not negligible (around 2 %) and can contribute to gastric irritation upon prolonged usage. In addition, the yeasts responsible for *chicha*'s fermentation have a phenotype that markedly differs from that of traditional *Saccharomyces cerevisiae* strains [16]. Vision impairment was common in both children and adults, an expected consequence of living at high altitude where exposure to ultraviolet radiation is higher [17]. For example, in children living in mountainous regions of Nepal the most common ocular morbidity (38 of 140 subjects, 27 %) was myopia [18]. In adults, high altitude has been associated with increased prevalence of dry eye syndrome, cataract, corneal thickness, photokeratitis, and retinopathy [19, 20].

Parasitic infections were commonly diagnosed in children. The type of parasite was not characterized in this study, but it was most likely *Taenia solium* tapeworm since it is endemic in much of Peru, with the greatest prevalence in rural communities [21]. In adults, bacterial and viral infections of the upper respiratory tract and bacterial and fungal infections of the female genitourinary tract were the most common. Since the early days of autoimmunity (mid 1950s), infections have been considered a cause, or trigger, of autoimmunity [22, 23]. Indeed there are animal models where autoimmunity is induced by infection, for example the Theieler's virus model of multiple sclerosis in mice

Table 2 Diagnoses (No. = 1661) established by the physicians, classified according to the organ system

	Number (%)
Joints and muscles	400 (24 %)
Osteoarthritis	343
Sciatica	7
Degenerative disc disease	6
Others	44
Gastrointestinal	333 (20 %)
Gastritis	149
Parasitic infestation	118
Gastroesophageal reflux	32
Biliary stone disease	11
Gastro-enteritis	8
Others	15
Eyes and ENT	326 (20 %)
Keratitis (dry eye syndrome)	69
Cataract	55
Tooth cavities and abscesses	52
Earwax blockage	12
Pharyngitis	12
Others	126
Genitourinary	172 (10 %)
Vaginitis	43
Urinary tract infection	42
Vaginosis	39
Pelvic inflammatory disease	17
Benign prostatic hyperplasia	10
Others	21
Heart and lungs	147 (9 %)
Hypertension	59
Upper respiratory infection	23
Rhinitis	21
Bronchitis	19
Asthma	7
Allergic rhinitis	4
Others	18
Skin	107 (6 %)
Eczematous dermatitis	48
Pterygium	12
Dermatitis	9
Varicose veins	5
Onychomycosis	4
Vitiligo	4
Others	25
Neuropsychiatric	83 (5 %)
Depression	24
Migraine	17
Anxiety	8
Guillain–Barré disease	4

Table 2 continued

	Number (%)
Others	30
Endocrine	60 (4 %)
Diabetes type 2	16
Malnutrition	14
Obesity	14
Hashimoto thyroiditis	4
Thyroid nodules	4
Others	8
Recent trauma or wound	33 (2 %)

Table 3 Frequency of allergic and autoimmune diseases diagnosed solely on clinical grounds in 1075 Amerindian Peruvian patients

	No.	% of 1075
Asthma	7	0.7
Rheumatoid arthritis	5	0.5
Hashimoto thyroiditis	4	0.4
Allergic rhinitis	4	0.4
Guillain–Barré syndrome	4	0.4
Vitiligo	4	0.4
Food allergy	2	0.2
Addison's disease	1	0.1
Celiac disease	1	0.1
Fibromyalgia	1	0.1
Giant cell arteritis	1	0.1
Postpartum thyroiditis	1	0.1
Psoriasis	1	0.1
Temporal arteritis	1	0.1
Total	37	

Table 4 Distribution of 1648 medications prescribed by ten physicians, according to the pharmaceutical class

Pharmaceutical Class	Number prescribed (%)
Analgesics	635 (38 %)
Acetaminophen	361
Ibuprofen	261
Others	13
Antimicrobials	431 (26 %)
Albendazole	118
Metronidazole	79
Clindamycin	47
Amoxicillin	45
Fluconazole	45
Others	97
Gastrointestinal drugs	220 (13 %)
Ranitidine	116
Tums	49
Omeprazole	28
Others	27
Heart and lungs drugs	145 (9 %)
Benadryl	30
Hydrochlorothiazide	22
Enalapril	16
Lisinopril	15
Sudafed	14
Albuterol	13
Others	35
Eyes and ENT drugs	115 (7 %)
Dry eye drops	76
Nasal spray	12
Earwax removal drops	11
Erythromycin eye drops	9
Others	7
Skin topicals	74 (4 %)
Hydrocortisone cream	45
Antibiotic ointment	7
Desitin	4
Others	18
Neuropsychiatric drugs	18 (1 %)
Fluoxetine	8
Cyclobenzaprine	5
Others	5
Prednisone	10 (0.6 %)

[24]. In humans, however, proving that infections cause autoimmunity has been challenging. In more recent years (late 1980s), actually, the opposite hypothesis has been formulated. According to the "hygiene hypothesis", infections protect from autoimmunity, so that populations living in less "clean" environments should have a lower prevalence of autoimmunity [1, 2]. In keeping with the hygiene hypothesis, parasitic infections have been shown to promote beneficial (T-helper 2) immune responses and suppress pro-inflammatory (T-helper 17) ones [25]. The literature, however, remains unclear regarding the complex relationship between infections and autoimmunity. In this study, autoimmune and allergic conditions were diagnosed at a prevalence of 3 %, which appears lower than what has been reported in developed countries. For example, recent analyses quote a prevalence of autoimmune diseases around 5 % [14, 26, 27] and allergic diseases as high as 44 % [28]. Nevertheless, it is important to emphasize that our findings of 3 % prevalence are likely an underestimate of the true prevalence, as diagnoses relied purely on the

clinical skills of participating physicians, none of whom received specialized training in clinical immunology. This limitation makes it difficult to establish whether rural populations living in central Peru are protected from autoimmunity and allergy through the hygiene hypothesis mechanism.

Andean people seen in the clinics appeared to have poor dental care, low standards of personal hygiene, and marginal understanding of the importance of disease prevention. At the same time, they showed a stronger sense of community and willingness to help each other than what is found in most modern societies. They also benefited from a low prevalence of conditions that are prominent in the American society. For example, obesity was estimated to be around 5 % of the patients attending the clinic, a value markedly lower than that reported in the United States: 17 % in children and 35 % in adults [29]. Similarly, cardiovascular diseases were seldom diagnosed. In addition, we noted that hair loss, in either men or women, was a rarity, as was the graying of the hair, even in advanced age.

It is difficult to quantify the benefits a medical mission like this one can have on the indigenous population. The lack of follow-up data and interaction with local physicians prevents us from drawing meaningful conclusions. In the short term, the mission certainly provided relief by delivering medications (such as antibiotics and anti-inflammatory) that are not easily available to this population. Long-lasting benefits can perhaps arise if studies like this foster a stronger collaboration with the local health system, promote the implementation of electronic medical records and thus patient follow-up, refine the medication inventory based on the observed disease prevalence, and identify practical objectives for future missions. For example, programs could be implemented to promote better dental hygiene, regular eye exams, and safer sexual practices to reduce the incidence of genitourinary infections. Naturally, century–ingrained dietary and work practices cannot be easily changed. Nevertheless knowing what these practices are should better equip future missions for providing more targeted relief and novel health care solutions.

In summary, the study reports the prevalence of diseases found in rural and mountainous Andean villages of central Peru, providing a foundation for designing basic public health interventions in the same or comparable regions.

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Compliance with ethical standards

Conflict of interest None.

Human and animal rights Not applicable to this retrospective study.

Informed consent No informed consent was necessary as the study in fact was considered exempt from institutional review board evaluation on the basis of federal regulation 45 CFR 46.101(b) (research involving the study of existing data recorded in such a manner that subjects cannot be identified).

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