Association of Hygiene Hypothesis with High prevalence of Allergy and Autoimmune Diseases: FMT industry

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Abstract—Prevalence of Allergy and Autoimmune Diseases are high in developed countries, but not in developing countries. Helminth infection were associated with lower level of allergy but the mechanism is not yet clear. In hygiene countries like UK, Japan and Korea, Fecal Microbiota Transplantation (FMT) has gained interest as novel therapy and prevention and reach to medicine industrial manufactures. This study will support it by associate Hygiene Hypothesis (HyHy) and the high prevalence of Allergy and Autoimmune Disease. Systematic review and Bayesian network analysis in EBSCO host search engine were used. Result from dynaMed Evidence Based, Point-of-care Reference e Journals: Dentistry, Medical and Nursing has describe 9 literatures support the association of Hy-hy/parasite infection with Allergy and/or Autoimmune Diseases: 2 publications of meta-analysis are chosen and supported by 5 cross sectional, longitudinal, causal-effect design, and 2 clinical and animal trial. Conclusions: Low-middle-high income countries has a life style of HyHy pattern support FMT industrial medicine and travelling to developing countries with broad diversity bacteria and worm in therapeutic and prevention potential, supported by sub-saharan and tropical forest developing countries.

Keywords— Hygiene hypothesis, allergy, autoimmune diseases, FMT industrial medicine, traveling to developing countries.

I. INTRODUCTION

A firmed increase of global prevalence in allergic diseases mainly among children in the last few decades. Over the years, where several epidemiological studies have reported an inverse association between parasitic worm infections and allergies. The relationship between helminthes infection and allergies is urgent as research aims move to approach the potential of therapy and prevention in using helminths and their products for allergic disorders. Using infectious disease high prevalence countries as a source of prevention and treatment of allergy and autoimmune diseases (AD). Knowledge of much references in the association of HyHy-Allergy. Molecular aspect of epitope mapping of bacteria and worm vs. lifestyle in low-middle-high income population are associated with Most of Autoimmune Diseases are costly but Fecal Microbiota Transplantation (FMT) is an effective potential therapy and vaccine. Traveling to developing countries with high biodiversity microbiota are also promising.

II. MATERIAL AND METHOD

Systematic Review and Bayesian analysis using EBSCO host DynaMed: Evidence –Based, point-of Care Reference, e-Journal: Dentistry, Medical and Nursing search engine. First, searching with CINAHL plus with developing the knowledge for the aims of study. Using the following search terms: Autoimmune Diseases, Hygiene Hypothesis, Epidemiology and AD, Atopic Sensitization, Asthma, T1D, IBS, MS, Rheumatoid Arthritis, Ulcerative Colitis, Allergic Diseases. Epidemiology AND Autoimmune Disease and UK (263), AND Japan (259). FMT are growing (4550), FMT and Meta-analysis (12), FMT and UK (34), FMT AND Japan (66). FMT industry (3), Hygiene Hypothesis AND Autoimmune Disease (117), Helminth AND Autoimmune diseases (148), Worm and Autoimmune (36), Worm and Hygiene Hypothesis (17), Epidemiology AND Meta-analysis and Rheumatoid Arthritis (27). Second step, all are screening abstract or title: excluded the not relevant and the duplicates by Bayesian analysis. Since we were interested in explanatory factors of bacteria and worm epitope sequencing are filtered. In the third step, screening full text publications, excluded since not relevant, duplicated and extracted for Table. Association of Hygiene Hypothesis or parasite infection AND Allergy/ Autoimmune Diseases. The selection was mainly performed by one reviewer and confirmed by the co-authors.
III. DISCUSSIONS

3.1 Dry and Wet climate

From clinical to molecular aspect of inflammation markers in savanna (warm and dry climate) with dormant bacteria and worm in dry season, and also in tundra (cold and dry) where no worm no bacteria in all season are searched by us. Meanwhile AD have been found in low prevalence in wet and warm (tropical rainforest) or hot and humid (sub-Saharan) countries, whereas allergy and AD are epidemic in clean countries. Dormant bacteria in dry season are specific physics-chemistry antigens and broad spectrum of variable microbiota implies rich of epitope of protein from known FMT. Figure 1 of Flowchart and Table 1 showed the association of Hygiene Hypothesis with allergy and AD.1,2,4,11

| TABLE 1 | DESCRIPTION OF IDENTIFIED 9 LITERATURES ON HYGIENE HYPOTHESIS(WORM-BACTERIA)-ALLERGY/AUTOIMMUNE DISEASES |
|---|---|
| **Study** | **Design** | **Population** | **Hygiene Hypothesis autoimmune measure** | **Epitope / synthetic vaccine measure** |
| Figueiredo 2013 | Comparison of high vs. low infection | Environmental condition in Latin American | Aeroallergen | Immunologic phenotypes, atopy, asthma |
| Obeng 2014 | Cross-sectional | 1385 Ghanaian Schoolchildren | Schistosome infection | Mite Atopy but not wheeze & asthma |
| Hamid 2011 | A longitudinal study | Semi urban and rural areas of Flores, Indonesia | Intestinal helminth infections | Allergy |
| Xu 2015 | Randomized Controlled Trial (RCT) | Metabolic syndrome subjects | Fecal Microbiota Transplantation | Beyond intestinal disorders |
| Lopez-Isac 2016 | Meta-analysis | Meta-genome-wide association (meta-GWAS) | Systemic Sclerosis (SSc) and Rheumatoid Arthritis (RA) | Top single-nucleotide polymorphism |
| Colman 2014 | Systematic review and Meta-analysis | 18 studies of FMT primary therapeutic agent for 122 pts with 79 ulcerative colitis, 39 Crohn’s disease, 4 IBD | Clinical remission and/or mucosal healing | IBS as autoimmune disease |
| Puentes F 2016 | Animal model of autoimmune disease | Tolerogenic potential of fusion protein in 10 transgenic mouse model | Parasite proteins containing repeats are essential invasion ligands | Ability to evade the host immune system |
| Ajendra 2016 | Experimental | NOD mice after insulitis started in T1D process | Inflammation of the pancreatic islets | Helminth antigens as a new potential therapeutic approach against AD |
| Lagier 2014 | Review | Longitudinal CT of Recurrent CDI patients | FMT frozen, antigens | Extensive use and wide industrialization of FMT against AD |
Figure 1. Flowchart of the 9 identified literature: 2 meta-analysis, 2 review, 3 cross sectional, longitudinal, cause-effect design, 2 experimental (animal/ human) which associated hygiene hypothesis/parasite infection with allergy and autoimmune diseases

Improved hygiene and little infections in childhood influence the development of allergic and autoimmune diseases. It has been reported in Latin America (Urban Brazil), a tropical rainforest area. Lifestyle factors with microbial exposure are associated with allergy prevalence also reported in developed countries.

Not only microbial exposure, helminth infections are also associated with low prevalence of allergy, till FMT are used as therapy in Autoimmune Diseases. Including metabolic diseases. Systematic sclerosis and rheumatoid arthritis has been identified have a common susceptibility locus of gene.

3.2 Proinflammatory cytokine as hygiene hypothesis marker

Parasite proteins contains repeats which induce immunosuppression and induce down-regulation of TNF-α (cytokine proinflammation) and TGF-β (cytokine profibrosis) make potential application for the treatment and prevention of autoimmune diseases.

Entering of helminth antigens increase the protective effect stipulated by antigen-peculiar therapies and symbolizes a new approach for potential therapy against AD including T1DM. The use of microbiota which has been frozen facilitates transplantation, and per oral are at least as effective as other invasive methods and to keep from occurring the risk of anesthesia. The use of pills form, already test as clinical trials, will certainly be the beginning landmark for the width use and broad industrialization of fecal microbiota transplantation.

Treatment with helminthes and worms ova mitigated the clinical symptoms of numbers autoimmune diseases in animal model and in patients. Tuftsin-PC (TPC), a novel helminth-based compound, reduced proinflammatory cytokines and induced the expression of anti-inflammatory cytokine, as well as expansion of Treg and Breg cells, also histological analysis guide to a new approach for a natural therapy for beginning rheumatoid arthritis onset, one of autoimmune diseases.

The role of transfer of immune cells adoption in worm-influenced regulation of allergy and autoimmune diseases, was supported by animal experiments. The chronic diseases for families economic burden, health systems, governments and the association between national policy maker and international economic pressure and politics have a large impact on chronic diseases risk and countries ability in responding them, the potential of wet and warm climate area double burden of infectious and chronic diseases.
3.3 Economic income and Hygiene Hypothesis

How the present of chronic conditions in certain multimorbidity patterns, which could have great burden on public health at several levels in low-, middle-, and high-income countries has been identify and describe in several countries to the advancement of preventive actions to decrease their prevalence and also give increase to new, understandable approaches for the management of these co-existing conditions. The association of individuals raised in hygiene environment have a higher of developing Allergy and Autoimmune Diseases was supported by random or fixed-effect meta-analyses.

IV. LIMITATION

These Systematic review has several limitation 1) Non published literature on all autoimmune diseases may limit the validity of our findings, but these inflammatory bowel diseases and rheumatoid arthritis study are a real phenomenon which is already attracted peoples from developed and clean countries with AD burden. However, we used meta-analysis with partly overlapping data bases for our literature search on bacteria and worm cell wall antigens. And we found a large number of papers fulfilling the criteria of our search in these HyHy-AD prevention and therapeutic. 2) Another potential problem in this systematic review is that studies mainly used in the searching steps are depended on the vocabulary synonyms (not find in general, but many in specific such as autoimmune diseases could be Rheumatoid arthritis, recurrent CDI, IBS, T1D, atopic sensitization, asthma etc.) but not in Lupus Erythematosus. Different chances changes choices used give different results may be misleading. We intended to manage this problem in an additional work, by dividing the using chosen specific to generic into 2 broad categories: prevention and therapeutic findings.

V. SUMMARY

Epitope of FMT, bacteria, wall of worm are all rich of ranges epitopes and could be present in therapeutical and prevention potential. These epidemiological studies from developing/ tropical rainforest area countries, present to hygiene developed countries is similarly paralleled with low-middle- high- income population, vaccination and therapeutic fighting against autoimmune diseases. Hygiene hypothesis / FMT has association with novel treatment for Allergy and Autoimmune Diseases. Further knowledge and education to policy maker and global politic doer from local to global will support the industries in FMT.

VI. CONCLUSION

Low-middle-high income countries has a life style of Hygiene hypothesis. The low- and middle economic income in development countries have similar pattern with population in developing countries, which support FMT industrial medicine and travelling to developing countries. Broad diversity bacteria and worm in therapeutic and prevention potential, supported by sub-saharan and tropical rainforest developing countries.

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