Extensive evidence indicates that genetic predisposition is a central element in susceptibility to AD even if environmental (i.e. infections, drugs assumption, UV exposure, etc.) or stochastic factors are involved in the induction and maintenance of autoimmunity process.

Several authors reported an increased prevalence of systemic AD in non-Caucasian populations, and different genetic and/or environmental factors have been hypothesized to justify this difference.

Anti-nuclear antibodies (ANA) are autoantibodies directed against various nuclear antigens (DNA, RNA, histones, acidic nuclear proteins, or complexes of these molecular elements), and may represent diagnostic markers for different systemic AD, including systemic lupus erythematosus, Sjögren’s syndrome, scleroderma, polymyositis, and mixed connective tissue disease. ANA positivity can be detected at low titre in healthy subjects, probably as expression of immune system activation. A high titre ($\geq 1:80$) of ANA positivity in Caucasians has been reported in 5-15% of blood donors, with an increased prevalence in women and elderly.

Filipinos is a mixed genetic and ethno-linguistic population, anthropologically classified as Polynesians, representing the second largest Asiatic immigrant population in Italy, and in absolute the first immigrant population in the city of Rome (about 25,000 presence).

The aim of this study was to evaluate the prevalence of ANA in subjects of two different racial groups (Filipinos and Italians) living in the same area and therefore potentially exposed to the same environmental features.

**Patients and Methods**

Eighty Filipinos (M/F = 22/58; age 43 ± 8 – range 25-65 years) migrated to Italy and sixty...
ians (M/F = 14/46; age 41 ± 10 years – range 25-69 years), were consecutively enrolled in this study. We recruited Filipinos (FIL) during Filipino social functions and festivals held in Rome, and Italians (ITAL) during pre-intervention evaluation for aesthetic surgery in our Hospital. Subjects with a history of AD, cancer and/or drug abuse were excluded. A written informed consent was provided by all subjects before the beginning of the visit.

Demographic characteristics, lifestyle behaviour (including cigarette smoking and dietary habits), physician-diagnosed diseases, medication history and family history for AD were determined using structured questionnaires. All subjects underwent blood sample collection, and serum was stored at -20°C, until assay.

**Laboratory Assessment**

ANA were detected through indirect immunofluorescence (IIF) on commercial Hep-2 cell substrate (ImmunoConcepts, Sacramento, CA, USA), at a 1:80 serum dilution in phosphate buffered saline (PBS). Two observers, using positive and negative reference samples in each run, evaluated the results. Fluorescence intensity was scored semiquantitatively in four categories ranging from 0 to 4+, relative to the intensity of the negative and positive controls, as indicated by international guidelines. A sample was considered positive for ANA if a score of at least 2+ was obtained and the positivity was confirmed after a ≥ 1:160 dilution.

**Statistical Analysis**

Data were analysed using the Prism statistical package (Graphpad Instat, version 3). Categorical variables were compared using Fisher exact’s test. Continuous variables were analyzed by the Student t-test and Mann Whitney U-test for parametric and nonparametric data, respectively. Odds Ratio (OR) and 95% Confidence Interval (CI) were calculated using standardized methods. P-value < 0.05 was considered significant.

**Ethical Consideration**

The study, performed according to the principles of the Declaration of Helsinki, was approved by the Ethical Committee of the University “Campus Bio-Medico” of Rome, Italy.

**Results**

In Table I are reported data about demographic, habits and clinical aspects of our studied groups.

Mean time of Italy residence among FIL was 15 ± 7 years (range 1-32 years); they moderately changed their alimentary habits towards Mediterranean diet. A relevant percentage of FIL was house servant, factory worker or labourer with low school attendance. Two-third of ITAL were freelancer or employed as secretary or clerk, with higher education level. Sixteen FIL (20%) and

<table>
<thead>
<tr>
<th>Table I. Epidemiological and clinical features of studied groups.</th>
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<tbody>
<tr>
<td><strong>Filipinos no. 80</strong></td>
</tr>
<tr>
<td>M/F</td>
</tr>
<tr>
<td>Age, years – mean ± SD (range)</td>
</tr>
<tr>
<td>Smoking (≥ 5 cig./day), no. (%)</td>
</tr>
<tr>
<td>Mean time in Italy, years – mean ± SD (range)</td>
</tr>
<tr>
<td>Familial history of autoimmune disease, no. (%)</td>
</tr>
<tr>
<td>Arthralgia, no. (%)</td>
</tr>
<tr>
<td>Raynaud’s phenomenon, no. (%)</td>
</tr>
<tr>
<td>Past thrombotic episode, no. (%)</td>
</tr>
<tr>
<td>History of abortion, no. (% on female)</td>
</tr>
<tr>
<td>Disease(s), no. (%)</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
</tr>
<tr>
<td>Allergopathies</td>
</tr>
<tr>
<td>Non autoimmune thyropathies</td>
</tr>
<tr>
<td>Others *</td>
</tr>
<tr>
<td>Drug(s)# assumption, no. (%)</td>
</tr>
<tr>
<td>Oral estrogesterin drug(s) assumption, no. (% on female)</td>
</tr>
</tbody>
</table>

*Headache; irritable bowel syndrome; gastroesophageal reflux. #Antihypertensive drugs; oral hypoglycemic agents; non steroidal anti-inflammatory drugs (NSAIDs); anti-allergic drugs; anti-anxiety agents.

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seventeen ITAL (28%) smoked at least 5 cig./day. Hypertension, diabetes and allergies were the most prevalent diseases in our study groups, and anti-hypertensive tablets and hypoglycaemic agents were the main drugs taken, with no differences between the two groups. Oral estroprogestin treatment was reported in about 15% and 24% of FIL and ITAL women, respectively. Family history for AD was present in 15 (18.7%) FIL and in 14 (23.3%) ITAL, respectively.

ANA positivity was found in 19/80 (23.7% - M/F = 6/13) FIL and in 5/60 (8.3% - M/F = 1/4) ITAL (P = 0.02 – OR 3.43; 95% CI 1.2-9.8) (Figure 1). Of note, about 90% of FIL-ANA positive were resident in Italy from more than 10 years. Of those, 17% were < 40 years of age, 28% were 40-50 years old and 42% were more than 50 years old.

The evaluation of possible AD related clinical manifestations disclosed that persistent arthralgia was present in 16 (20%) FIL and in 14 (23.3%) ITAL; photosensitivity was reported in 15 (18.7%) FIL and in 13 (21.7%) ITAL and Raynaud’s phenomenon was present in only 1 (1.2%) FIL woman and in 4 (6.7% - 3 women and 1 man) ITAL. No skin or mucosal lesions were present in the clinical history or at the moment of the visit in any subject. Previous venous thrombotic events were reported in 3 (3.7%) FIL and in 2 (3.3%) ITAL, whereas history of spontaneous abortion was present in 10 (12.5%) Asiatic women and 6 (10%) ITAL. However no one subject fulfilled classification criteria for any AD.

Discussion

Although ANA presence is relevant for systemic AD diagnosis13, this study confirmed that ANA positivity in healthy subjects is not a rare condition. In fact, autoantibodies detection with no clinic manifestations of AD is quite common, probably as expression of immune system activation due to subclinical infection, drug assumption or as a false positive of laboratory testing, resulting in low specificity14.

Even if a high prevalence of ANA was documented in healthy Asiatic children15, no data are available about Filipinos, both in their own countries and in migrants.

In our study we observed a Filipino population with a long term residence in Italy (on average 15 years) and with a relevant modification of their life-style through occidental habits. In this population we found a high prevalence of ANA, above all in females and elderly, compared to Italians.

Specific HLA class I alleles in combination with high risk DR-DQ haplotypes may explain the differences in autoantibodies positivity in our studied groups. Thus, a previous study of HLA class II loci in the Filipino population revealed an unusual distribution of DRB1 alleles and haplotypes, which was strikingly different to other Polynesians and white populations16. Moreover, Filipinos contain a DR-DQ haplotype unique of this population17. Otherwise, the prolonged exposition to western environmental factors (i.e. infective agents, polluting, smoke, and drugs) different from their own countries, on a genetic background “prone” to autoimmunity, could explain our results. Indeed, we observed that over 90% of autoantibodies positive subjects migrated to Italy from more than ten years.

It is likely that the different socio-economic conditions between ITAL and FIL subjects, could have influenced our results. Frequently, migrant populations live in lower socio-economic conditions compared to native, and this could be associated with poorer health condition. The resulting different exposure to environmental agents18-19 could offer an explanation for the higher prevalence of autoantibodies detection in FIL migrated subjects compared to the ITAL population.

Furthermore, the oral estroprogestin (EP) and/or other drugs assumption, although not statistically significant between our study groups, could be an other possible explanation for the high ANA prevalence in Filipinos. Estrogens have pleiotropic effects on the immune system and modulate the development of autoimmunity, not always resulting in exacerbation20. Asiatic women have different habit in estrogen assumption21 and the adaptation to European habits could have influenced their immune system response.

![Figure 1. Antinuclear antibodies (ANA) prevalence in Filipinos and Italians.](image-url)
Of course, data about prevalence of antinuclear autoantibodies in Filipinos, living in their native country could be helpful in understanding the real predisposition to AD of this population. Future studies should be interesting in this respect.

Although, autoantibody detection could represent a transient condition due to an unspecified immune system stimulation (i.e. acute infectious episode), a high-titre positivity is more suggestive of a real autoimmunity process and should have some clinical significance\(^\text{14}\). The medical follow-up of these positive subjects should allow us to reveal disease state because autoantibodies can be detected many years before that the diagnosis of AD can be made\(^\text{22}\).

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