The disease results from the interaction between the person’s genetic makeup and his outer environment. The proportionate role of both the factors varies from disease to disease. There are some diseases with unclear etiology; Vitiligo is one of them.

The purpose of this paper is to show the application of Epidemiology and the statistical methods to understand the disease causation.

The epidemiological study of skin conditions among school children in Urban and Rural areas of Surat district carried out by the author brought out the following observations.

(A) Epidemiological observations:

1. Vitiligo affects both sexes
2. Multiple cases of Vitiligo seen in some families (sharing common gene pool and common home environment)
3. Prevalence of Vitiligo varied insignificantly in various home environments (It may be presumed that role of environment is proportionately very low in causation of Vitiligo)
4. Significantly higher proportion of affected students had outwardly normal (apparently unaffected) parents (suggesting effect of environment)
5. Cases of Vitiligo were seen more commonly in certain communities (castes) (as most of the marriages are within the caste, this indicates that there could be genetic base)

The above observations suggest the genetic base in Vitiligo. How to test it?

(B) A case-control study can help to understand this. It is an inquiry in which groups of individuals are selected in terms of whether they do (the cases) and do not (the controls) have the disease of which the etiology is to be studied, and the groups are then compared with respect to existing or past characteristics judged to be of possible relevance to the etiology of the disease.

The cases may be selected from the hospital or detected through survey and their controls are selected from the same administrative area, hospital patients, relatives or associates (classmate, work-mate) of the cases depending upon the feasibility.

Various studies attempted to explore the etiology of Vitiligo and ultimately concluded that the disease results from the interactions of genes and environment. However, the relative importance of genes and environment could not be judged.
School children from the urban (15350) and the rural (4425) areas of Surat district were screened for the detection of Vitiligo cases.

The Dermatologist of Civil Hospital Surat confirmed cases of Vitiligo.

The control for each Vitiligo case was selected preferably from the same class in the school. The criteria used for matching were age, sex, religion and caste, Socio-economic status, home sanitary condition, residence and the duration of stay in the area. The control student should match Vitiligo cases in at least 4 / 6 criteria in addition to home sanitary condition. More than one control students were selected for each Vitiligo case to compensate the drop out.

Home visits were paid to each Vitiligo case and its control spending equal time to elicit the required information. During home visits attempt were made to examine all available family members. Enquiry was also made to know the occurrence of Vitiligo in non-available family members and in the previous generations. Thus, a comprehensive family history of three or four generations was obtained. Based on this Pedigree of each case and its control was prepared, analysed and findings are presented here.

In this study, 56 families of each of the Index Vitiligo case and control were studied.

**OBSERVATIONS:**

**Familial aggregation:**

Total 9.7% of the relatives of Index Vitiligo cases had Vitiligo as compared to 5.0% relatives of the controls students. The difference observed was significant at 0.001 level (d=4.87). As the home sanitary condition was matched in cases and controls, this observation strongly suggests the genetic basis of Vitiligo.

This is further supported by the findings that significantly higher percentage of FIRST Degree relatives of Index cases were affected (11.9%) as compared to SECOND Degree relatives (5.72%) (d=3.2, p <0.002) while no such difference was observed between FIRST and SECOND Degree relatives of the control students. (d=1.74, p > 0.05).

Table: 1

<table>
<thead>
<tr>
<th>Percentage of affected individuals</th>
<th>Index case</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>All relatives</td>
<td>9.77 (47 / 1504)</td>
<td>5.0 (63 / 1260)</td>
</tr>
<tr>
<td>FIRST Degree relatives (parents, brothers, sisters, sibs)</td>
<td>11.9 (40 / 336)</td>
<td>2.3 (7 / 304)</td>
</tr>
<tr>
<td>SECOND Degree relatives (First cousins, uncles, grand parents)</td>
<td>5.72 (52 / 909)</td>
<td>1.23 (34 / 804)</td>
</tr>
</tbody>
</table>

1) Number of Families studied = 112
   a) With affected student index case = 56
   b) With unaffected student as control = 56

2) Number of affected index students with Outwardly normal parents = 40 (71.4%)
Pedigree analysis to determine the nature of Inheritance:

i) Sex linked inheritance can be ruled out because (a) Vitiligo affects both sexes and females are predominantly affected (b) Father-son transmission, which is absent in sex-linked inheritance, is observed in Vitiligo.

ii) In autosomal dominant conditions, the disease tend to manifest early in life and tend to be more severe.\(^8\) Vitiligo is not a serious condition and manifest between the age 6-15 years in a majority of the cases.\(^5\) The possibility of autosomal dominant inheritance can, therefore be ruled out.

iii) In the present study, out of 56 Index Vitiligo cases, 40 cases (71.4 \%) had apparently normal (outwardly normal) parents. This observation suggests the autosomal recessive nature of inheritance.

(b) Statistical Test to support Autosomal Recessive Inheritance:

In autosomal recessive conditions the heterozygous parents (outwardly normal) will have one fourth (1 / 4 = 25 \%) of their offspring homozygous and affected. However, in human genetics, such families are ascertained only through the occurrence in them of at least one affected member (in the present study the affected student i.e. index case). Since we do not have any means to recognize the outwardly normal heterozygous parents whose children are fortunate to escape this condition, a collection of sibship containing at least one affected child is a biased sample. In these ascertained families, we found more affected children than expected one fourth (25 \%) (in the present study it was 28.72 \%) Table: I.

So it is necessary to prove whether the deviation of the observed value (28.72 \%) from the expected value (25 \%) is significant or not. For this, a Statistical test “ Bias of Ascertainment” \(^8\) is applied. This test is shown step by step in Table: II Expected number of affected children and variance for each size of sibship are calculated by multiplying the figures in the columns (a x d) and (b x c) respectively. The square root of such variance (22.838) will give the Standard Deviation (SD) (4.78)

Since the observed value (i.e. observed number of affected children-56) falls within the range of 2 SD from the expected number of affected children (65.3166), the deviation is not significant. Similarly X\(^2\) square statistics applied to the observed number and expected number of affected children in each size of sibship was found insignificant (X\(^2\) = 4.518, d.f. = 6, p > 0.05). Therefore our hypothesis of Autosomal Recessive nature of Inheritance in Vitiligo is supported. So the observed proportion of affected children (28.72 \%) in the ascertained sibship in the present study does not deviate significantly from the expected proportion of 25 \%.

In light of the present observations, it is concluded that Genes primarily decide Vitiligo. However, delayed phenotypic manifestation of Vitiligo in susceptible individuals may be related to some environmental factors, probably microenvironment, which may be identified by a prospective study.
<table>
<thead>
<tr>
<th>Sibship size</th>
<th>Proportion of affected children in ascertained sibship (a)</th>
<th>Variance of affected children (b)</th>
<th>Number of sibship included in present study (c)</th>
<th>Number of sibs in the present study (d)</th>
<th>Affected children Observed</th>
<th>Affected children Expected (a x d)</th>
<th>Variance of affected children in the present study (b x c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0000</td>
<td>0.000</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
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<td></td>
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<td>3</td>
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<td>0.263</td>
<td>8</td>
<td>24</td>
<td>9</td>
<td>10.3376</td>
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<td>0.3657</td>
<td>0.420</td>
<td>12</td>
<td>48</td>
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<td>5</td>
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<td>0.502</td>
<td>8</td>
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<td>10</td>
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<td>4.016</td>
</tr>
<tr>
<td>6</td>
<td>0.3041</td>
<td>0.776</td>
<td>4</td>
<td>24</td>
<td>6</td>
<td>7.2984</td>
<td>3.104</td>
</tr>
<tr>
<td>7</td>
<td>0.2885</td>
<td>0.970</td>
<td>5</td>
<td>35</td>
<td>11</td>
<td>10.0975</td>
<td>4.850</td>
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<tr>
<td>8</td>
<td>0.2778</td>
<td>1.172</td>
<td>2</td>
<td>16</td>
<td>6</td>
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<td>9</td>
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<td>1.380</td>
<td>1</td>
<td>9</td>
<td>1</td>
<td>2.4327</td>
<td>1.380</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>40</td>
<td>196</td>
<td>56</td>
<td>65.3166</td>
<td>22.838</td>
</tr>
</tbody>
</table>

The predicted and the observed values of affected children according to their sibship size- Statistical testing of Recessive Hypothesis. SD = \sqrt{22.838} = 4.78

Reference:

Note: Values stated in Column number (a) and (b) are taken directly from the Book “Human Genetics” by Mc Kusick, page No: 138