# ADDIS ABABA UNIVERSITY
# SCHOOL OF GRADUATE STUDIES

## A Comparative Genetic-Epidemiological Study of Some Human Disease Traits and ABO Blood Groups among Different Population Categories in Harari Region of Ethiopia

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*ABSTRACT*

*A comparative Genetic-Epidemiological analysis was carried out in Harari Region of Ethiopia (Region-13) on the spectrum, frequency, and distribution of some selected human traits which have been described by several previous scientific investigations as being genetically determined: (1) Genetic diseases which are found under various disease classification categories of the Ethiopian Ministry of Health's "List of Causes for Tabulation of Morbidity and Mortality" and (2) the ABO blood groups. From all available medical data of 10-years (1984-1994 E.C.), a total sample of more than 12,000 cases of the various selected disease conditions were collected from hospital inpatient belonging to different Population Categories (PCs) characterized by different 'Local Ethno-Geographic' backgrounds; and 279 blood samples were taken from informed volunteers of the normal population with different ethnic origins-Oromo, Amhara, and Harari. The genetic disease samples collected from hospital records of inpatient populations were grouped into four basic PCs that closely follow or approximate their historical settlement patterns as well as current administrative boundaries of Harari Region, which are both presumed to be based upon and reflect the ethnic identities or composition of their respective inhabitants; the blood samples were grouped into three groups based on the ethnic origin of the volunteers. (I) The statistical analysis results with regard to the RFD of disease traits were found to be age and sex specific among the compared PC pairs. PC-1 was found to be the most distinctive population category of all in its RFD of those disease traits classified under Dxgroup-2 (Neoplasms), Dxgroup-3 (Deficiency Diseases- Diabetes Mellitus and Diabetes Insipidus), and Dxgroup-6 (Diseases of the Nervous System and Sense Organs- Epilepsy, Cataract, and Glaucoma). PC-1 showed no significant variation from any of the other PCs in its RFD of: Dxgroup-1 (Malaria), Dxgroup-9 (Diseases of the Digestive System), Dxgroup-10 (Diseases of the Genito-Urinary System), and Dxgroup-11 (Diseases Associated with Pregnancy, Child Birth, and the Puerperium). (II) The statistical tests concerning the ABO blood group samples obtained from the three major ethnic groups in Harari Region showed that (1) Phenotypic heterogeneity test: the total chi-square values for homogeneity were non-significant both among the (i) Oromo, Amhara, and Harari entries, and (ii) Oromo and Amhara entries with Chi-square=5.932, df=6, $p>0.05$ and Chi-square=4.332, df= 3, $p>0.05$, respectively, indicating phenotypic homogeneity. (Similar tests on the other possible data combinations could not be performed due to insufficient*

*data.) (2) Genetic-equilibrium test: (i) the Chi-square values for genetic equilibrium were non-significant for both the Oromo and Amhara entries indicating random intra-ethnic mating to the extent of reaching genetic equilibrium. (Similar tests on the Harari entry could not be performed due to insufficient data.) (ii) the total Chi-square values for genetic equilibrium were non-significant for the combined entries of the Oromo, Amhara, and Harari as well as the combined entries of the Oromo and Amhara indicating either that (a) there is random inter-ethnic mating between the populations from which the samples were taken, or (b) the samples were taken from different ethnic populations each of which are randomly mating within themselves and are all at genetic equilibrium as well as possessing similar proportions of the alleles at the ABO locus. (iii) the total Chi-square values for genetic equilibrium were significant for the combined entries of the Oromo and Harari as well as the combined entries of the Amhara and Harari indicating that the Harari do not engage in random inter-ethnic reproductive mixing with neither the Amhara nor the Oromo, although they are genetically closer to the later than the former ethnic group.*

## *I. INTRODUCTION*

### *1. BACKGROUND: THE STUDY OF HUMAN BIOLOGICAL TRAIT VARIATIONS*

### *1.1. HUMAN BIOLOGICAL TRAIT VARIATION*

Variation is a common observation in human populations. The chance that two individuals selected at random from a population will have the same genetic and phenotypic patterns or variants is infinitesimally small, except perhaps for identical twins. While some of these variants may represent mutational 'noise' and may be entirely neutral in survival value, it is likely that many polymorphisms had some selective advantage in the past (Motulsky, 1980). For example, genetic variations might determine or act as the substrate for the differential predisposition/susceptibility or resistance to various diseases. In other words, it is possible that the genetic identity of an individual, and genetic variation among the population at large, underlies differences in the phenotypes (e.g. health/disease profiles) of different populations.

### *1.2. "HEALTH" AND "DISEASE" STATES AS EXPRESSIONS OF HUMAN BIOLOGICAL TRAIT VARIATION*

"Disease' and 'Health' states are variants of the natural human attributes, i.e., the two human conditions are the extremes of the distributions of essentially any phenotype with specific causation which often involves a combination of different factors: A Spectrum of Causality (Weiss, 1993).

In broad terms, the causal spectrum of any health/disease related variations includes factors, which, relative to an individual, are (Weiss, 1993):

- Intrinsic- inherent biological factors (Nature)
- Extrinsic- external environmental factors (Nurture), and
- Both intrinsic and extrinsic- (Nature and Nurture)

One of the major intrinsic factors is the genetic identity or constitution of the individual and the genetic pool of populations in general; traits that are wholly or in part genetically determined are known as Genetic Traits and, if disease related, Genetic Diseases (GDs) (Weiss, 1993). Particularly, one would expect that genes involved in the biochemical, metabolic, or

immunologic processes related to the mechanism of a given disease state would be more likely to be implicated in its causation or etiology and prognosis.

### *1.3. GENETIC VARIATION AS HELTH RISK FACTOR*

Geneticists are interested in establishing whether there is a "cause-and-effect" relationship between genotypes and phenotypes, disease related or not. Human geneticists made their greatest contribution in medicine by the elucidation of how genetic factors affect the health states of individuals from the moment of conception to death (Goodman, 1970).

However, people have known for long that some traits including disease traits tend to "run in families" or are "heritable", thus acknowledging the role of genetics in the generation and transmission of human variations; and it can be assumed that the evolution of man's concepts and practices regarding procreation, mating, marriage, kinship, ethnicity, etc., emanate directly from such knowledge about heredity.

Human genetic variation was first scientifically associated with disease related traits by the English physician and biochemist, Archibald Garrod (1902) who was studying the epidemiology of a recessive trait, known as Alkaptonuria, characterized by significant familial aggregations (Goodman, 1970).

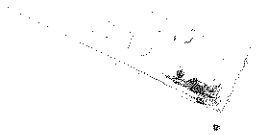
The identification of the genetic determination of Alkaptonuria made it one of the first applications of Mendel's laws to human disease traits and pointed out that genes can directly cause disease traits or determine the liability of individuals to be exposed to risk factors (predisposition), and when exposed, to actually manifest the traits; it also launched formal Genetic-Epidemiology (Weiss, 1993).

### *1.4. BURDEN OF GENETIC DISORDERS*

It is now universally acknowledged that there are several genetic disorders or that the susceptibility/resistance to various diseases is genetically determined (WHO, 1999):

- Single-gene/Monogenic disorders.
- Polygenic disorders.

- Congenital malformations (CMs).
- Genetic predispositions.



Besides the enormous emotional, practical, and financial burdens on families genetic disorders can result in (WHO, 1999):

- Premature death.
- Long years of ill health and disability.

The burden of genetic disorders also falls on the health care resources of every country especially as the relatively high morbidity and mortality rates due to infections and malnutrition come under control. Worldwide it is estimated that (WHO, 1999):

- Genetic diseases account for a third of all pediatric admissions and are a significant cause of childhood deaths worldwide.
- About 5% of children are born with a congenital or hereditary disorder and almost 40% of adults are genetically predisposed to common diseases during their lifetime.
- About 3 million infants are born annually with major CMs and most of them die in the first three years of life.
- In developed countries, even under the best of conditions, congenital and genetic disorders account for a quarter of deaths under the age of one and 23% between one and four.
- Diabetes mellitus alone affects at least 140 million people, with many of these cases being genetically predisposed. It alone accounts, on average, for 8% of the total health budgets in industrialized countries.
- About 250 million people, or 4.5 % of the world population, carry a potentially pathological haemoglobinopathy gene.
- Every year, 300 000 infants are born with major haemoglobin disorders, prevalence varying from under 0.1 births per 1,000 in some parts of the world to more than 20 per 1,000 in parts of Africa.

Compounding the problem is the fact that only very few GDs can be treated effectively by medical intervention (Simpson and Globus, 1992). Generally, now it is possible to reduce the effect on mortality, disability and reproductive fitness in (Table-1):

- Just under a third of single gene disorders.
- About 50% of congenital abnormalities.
- 2% of chromosomal disorders.

However, little can be done for the majority of genetic disorders, inherited or sporadic and, therefore, pending the development of treatments, the main goal remains to be prevention approaches (Simpson and Globus, 1992):

- Carrier-detection screening programs for some common and easily identifiable genetic disorders.
- Prenatal diagnosis to identify some inborn errors of metabolism, hematological disorders and chromosomal abnormalities, by cytological analysis of amniotic fluid cells and fetal blood sampling.
- Moreover, several problems are associated with some of these (treatment and prevention) approaches:
    - When therapy is available, it is often required for life and is unpleasant or expensive.
    - Prenatal diagnostic technologies are complicated, expensive, and not without some risks to the fetus.

***Table-1. Some Genetic Diseases that are Treatable*** *(Source: Simpson and Globus, 1992)*

| DISEASE | METHOD OF TREATMENT |
|---|---|
| | DIETARY RESTRICTION OF SUBSTRATE |
| *Phenylketonuria* | *Phenylalanine* |
| *Galactosemia* | *Galactose* |
| *Maple syrup urine disease* | *Leucine, isoleucine, valine* |
| *Lactase deficiency* | *Lactose* |
| *Fructose intolerance* | *Fructose* |
| *Lipoprotein lipase deficiency* | *Neutral fats* |
| *Refsum syndrome* | *Phytanic acid* |
| *Favism (G6PD deficiency)* | *Fava beans* |
| | ADDITION OF A DEFICIENT END PRODUCT |
| *Orotic aciduria* | *Uridine* |
| *Hypophosphatemic rickets* | *Vitamin D & phosphate* |
| *Congenital adrenal hyperplasia* | *Cortisol* |

| | |
|---|---|
| *Menkes syndrome* | *Copper* |
| *Familial goiters* | *Thyroxine* |
| DEPLETION OF EXCESSIVE SUBSTANCE | |
| *Wilson disease* | *Copper (by penicilleamine)* |
| *Familial hypercholesterolemia* | *Sterol (by bile binding resins)* |
| *Gout* | *Uric acid (by several drugs)* |
| SURGICAL REPAIR & REMOVAL | |
| *Cleft lip & cleft palate* | *Surgical repair* |
| *Hereditary sphercytosis* | *Splenectomy* |
| *Familial polyposis of colon* | *Colectomy* |
| *Medullary thyroid carcinoma syndrome* | *Thyroidectomy* |
| REPLACEMENT OF A MISSING GENE PRODUCT | |
| *Juvenile onset diabetes* | *Insulin* |
| *Pituitary dwarfism* | *Growth hormone* |
| *Hemophilia* | *Factor VIII* |
| *Lysosomal storage disease* | *Various enzymes* |
| *Agammaglobulinemia* | *Gamma globulin* |
| ORGAN & TISSUE TRANSPLANTATION | |
| *Fabry disease* | *Kidney* |
| *Severe combined immunodeficiency* | *Bone marrow* |
| *Thalassemia* | *Bone marrow* |
| *Lysosomal storage disease* | *Bone marrow* |
| GENE THERAPY | |
| *(Experimental)* | *Addition of normal allele; replacement or correction of abnormal allele* |

Many of the disease conditions that afflict humanity originated deep in the past, when *Homo sapiens* was still confined to Africa (De Stefano *et al.*, 1998). Therefore, analyzing Africa's diversified human genetic resources, and particularly that of Ethiopia, which is a good candidate for the region where modern humans evolved, is important in understanding not only the genetic control of diseases but also for finding effective treatment methods for non-genetic contagious diseases.

In the Ethiopian context, it can be said that there are very few studies performed and published to be reviewed concerning genetically determined human disease/health conditions, which could be an indication of the lack of awareness or resources to do so. In addition, those available 'studies' are mostly case reports of disease conditions known to be genetically determined in individual patients presenting themselves to hospitals or health care centers (Table-2).

This trend is similar to the whole of Africa (except South Africa and Egypt), which has been greatly underrepresented in studies of genetic variation, disease related or not, compared with

other continents. This is despite Africa's extremely high human genetic diversity found even between closely related or located groups (De Stefano *et al.*, 1998).

***Table-2. Some Published Studies about Genetically Determined Health Conditions in Ethiopia.***

| Study Titles | Author |
|---|---|
| -A Preliminary Survey for G-6-PD Deficiency & Hemoglobin-s in Ethiopia. | Perine, P. L (1974). |
| - Congenital Malformations of Anus & Rectum in Ethiopian Childeren. | Jhonson, O., Yohannes G. & Demissie H. (1981). |
| - Haemophilia in an Ethiopian Family. | Mulugeta, M. & Edemariam T. (1983). |
| - A *Forme Fruste of* Marfan Syndrome Presenting with Ectopia Lentis & Late Systolic Click. | Biru, M. (1983). |
| - ABO & Rhesus Blood-Type Frequencies in data from Hospitals & the Red Cross in Ethiopia. | Seifu, S. & Kifle, D. (1985). |
| - True Hermaphroditism: A Case Report. | Sebhat, A. (1988). |
| - Achondrogenesis: A Case Report. | Amha, M. (1988). |
| -Leukemia in Children's Hospitals, A.A. | Tilahun, T. and Abubeker, B. (1988). |
| - Testicular Feminization Syndrome: Four Case Reports. | Sebhat, A. (1989). |
| - Melkersson-Rosenthal Syndrome. | Mekonnen, A. (1989). |
| - Leukaemia in Childeren/Adult Ethiopians. | Tilahun, T. & Abubeker, B. (1988)/Milkias, S. (1990). |
| -A Case Report of Xeroderma Pigmentosum. | Nega, W. H. (1991). |
| -The Prune Belly Syndrome: Triad Syndrome. | Tilahun, T. (1993). |
| -Familial Polyposis in Two Ethiopians. | Biru, M., Jhonson O. & Yehyes N. (1994). |

The logical starting point in the investigation of the genetic basis or control of disease/health conditions is to systematically look for and identify or ascertain the existence of epidemiological variations in populations from phenotypic or other available data (Miller and Farmer, 1982).

This thesis deals with the epidemiological variations of some traits the expressions of which have been shown to be genetically influenced or determined to varying degrees. More specifically, it is concerned about the frequency and distribution of those human conditions commonly referred to as "Non-Communicable/Contagious Genetic Diseases" (NCGD) and the ABO blood types among people with different Ethno-Geographic backgrounds in the Eastern part (Harari Region) of Ethiopia.

Before delving into the details of the present study, however, it is customary to present its backgrounds in the form of reviews of the available literature. The emphasis of the reviews will be on the scientific methodologies employed to investigate disease-related variations since the present study mostly deals with the epidemiologic variations of pathologic traits.

## *1.5. SCIENTIFIC METHODS OF INVESTIGATING HUMAN BIOLOGICAL TRAIT VARIATIONS*

Several biological studies are concerned with the investigation of human biological trait variations:

- Causes (e.g. genetic and/or environmental)
- Extent (e.g. frequency and distribution)
- Consequences (e.g. health or disease)

There are two broad and complementary approaches towards the investigation of human variation (disease related or not): Epidemiology and Genetic-Epidemiology.

### *1.5.1. EPIDEMIOLOGY: APPROACH TOWARDS THE INVESTIGATION OF THE CAUSES, FREQUENCY, AND DISTRIBUTION (NATURAL HISTORY) OF HUMAN TRAITS.*

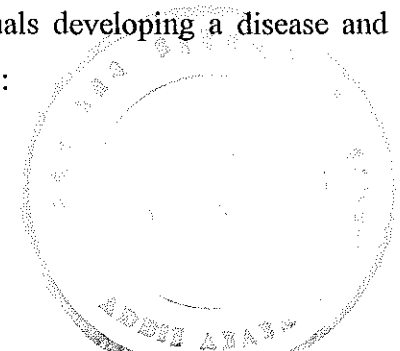
The word 'epidemiology' is derived from Greek: "studies upon people" (Miller and Farmer, 1982). First developed as a scientific field in the course of investigating outbreaks of infectious diseases in the 19$^{th}$ century, modern methods of epidemiological enquiry are now used in the investigation of practically types of human conditions.

The first step in epidemiology is appropriate surveillance to gain basic knowledge (Minimum Basic Data Sets- MBDS) about the condition(s) being investigated that can be used to infer their natural history (Barker and Rose, 1990). It is usually a complex exercise that involves the investigations of:

- The characteristics of affected and susceptible individuals or populations.
- The characteristics of individuals or populations who appear exceptionally resistant.
- The types of exposure to external factors necessary for the disease to occur.

Few diseases have a single cause; rather most have a spectrum of causation. Epidemiological methodologies are designed to identify and distinguish between factors that play a role in the causal spectrum of diseases: epidemiological variables. Three main categories of epidemiological variables affect the chance of individuals developing a disease and thus the frequency and distribution of disease (Farmer *et al*, 1996):





- Time (when?)
- Place (where?)
- Personal characteristics (who?)

#### *1.5.1.1. Variation of Disease Epidemiology with Time*

Such variations include (Farmer *et al*, 1996):

- *Long Term Trends:* temporal variations that do not conform to readily identifiable natural cyclic patterns.
- *Periodic Changes (Including Seasonality):* more or less regular or cyclic variations in disease incidence associated with the natural history of the disease.
- *Epidemics:* temporary increases in the incidence of disease in populations above the level expected from experience.

#### *1.5.1.2. Variation of Disease Epidemiology with Place*

Such Variations include (Farmer *et al*, 1996):

- *Broad Geographical Differences:* geographical variations following broadly homogenous natural ecological patterns, national administrative boundaries or territories, countries or regions, which encompass common social, cultural, and racial (ethnic) groups.
- *Local Differences:* variations limited by localization within the distribution area of possible cause.

#### *1.5.1.3. Variation of Disease Epidemiology with Personal Characteristics*

A) Variation related to age (Farmer *et al*, 1996):

- In infancy: due to immaturity and genetic defects.
- In later life: due to physiological changes, degenerative processes, genetic defects, and cumulative effects of exposure.
- 'Cohort-effect': due to exposures to the same noxious agent of individuals born at a particular point in time and, therefore, carry enhanced risk.

B) Variation related to sex/gender (Farmer *et al*, 1996):

- Due to intrinsic biological differences.
- Due to socio-economic tasks.

C) Variation related to ethnicity (Farmer *et al*, 1996):

- Genetic factors: due to the distinctive genetic-pool of members of the group.
- Non-genetic factors: dietary habits, cultural and religious practice, etc.

***Table-3. Prevalence of Genetic Disorders in Some Population Groups*** **(Source: Goodman, 1970)**

| Ethnic Group | Genetic Disorder | Mode of Inheritance |
|---|---|---|
| *Africans* | Hemoglobinopathies, namely Hbs, | |
| | Hbc, and persistent HbF | Autosomal Dominant |
| | α- and β- Thalassemia | Autosomal Recessive |
| Armenians | Familial Mediterranean Fever | Autosomal Recessive |
| Chinese | (- Thalassemia | Autosomal Recessive |
| | G-6-PD Deficiency, Chinese Type | X-linked Recessive |
| Japanese, Koreans | Acatalasia | Autosomal Recessive |
| | Dyschromatosis Universalis Hereditaria | Autosomal Recessive |
| | Oguchi's Disease | Autosomal Dominant |
| Jews (Ashkenazic) | A-(- Lipoproteinemia | Autosomal Recessive |
| | Bloom's Disease | Autosomal Recessive |
| | Dystonia Musculorum Deformans | Autosomal Recessive |
| | Factor XI (PTA) Deficiency | Autosomal Recessive |
| | Familial Dysautonomia | Autosomal Recessive |
| | Gaucher's Disease | Autosomal Recessive |
| | Niemann-Pick Disease | Autosomal Recessive |
| | Pentosuria | Autosomal Recessive |
| | Spongy Degeneration of Brain | Autosomal Recessive |
| | Stub Thumbs | Autosomal Dominant |
| | Tay-Sachs Disease | Autosomal Recessive |
| Jews (Sephardic) | Familial Mediterranean Fever | Autosomal Recessive |
| | G-6-PD Deficiency, Mediterranean Type | X-linked Recessive |
| Mediterranean People | Familial Mediterranean Fever | Autosomal Recessive |
| Greeks | G-6-PD Deficiency | X-linked Recessive |
| Italians | Thalassemia (Mainly () | Autosomal Recessive |

C) Variation related to family (Farmer et al, 1996):

- Genetic factors: common genetic inheritance.
- Non-genetic factors: common environment and culture.

D) Variation related to occupation and socio-economic status (SES) (Farmer et al, 1996):

- Exposure to special risks in working environment.
- Life-styles, dietary habits, etc. related to the level of income.

#### *1.5.1.4. Interactions of Epidemiological Variables*

Separate epidemiological variables can interact with each other in such a way that their combined effect is more or less than otherwise. Individual variables can be separately analyzed if circumstances arise in which one of the variables can be kept constant while the others change. For example, the relative effects of heredity and the environment on disease susceptibility can be investigated by (Eylenbosch and Noah, 1988):

- Comparison of the health profiles of twins raised in different conditions.
- Comparison of the health profiles of different ethnic groups living side by side in similar circumstances.
- Comparison of the health profiles (for example, disease frequency) of migrant populations with those living in their place of origin.

#### *1.5.1.5. Epidemiological Associations*

The observation that a disease is statistically associated with a suspected agent may not be necessarily a proof of causality (Farmer et al., 1996). Types of evidence to distinguish a causal from a fortuitous association include:

- *Strength of Association:* The stronger the association the more likely it is to be causal.
- *Consistency:* Conformation of the same association in analogous studies of different populations.
- *Gradient:* Correlation with the distribution, amount, and duration of exposure (population-dose response).
- *Time Sequence:* Exposure precedes expression or onset.
- *Specificity:* Specificity of distribution (incidence/prevalence) to exposure.
- *Biological Plausibility:* Compatibility with known biological activity.
- *Experimental Models:* Reproducibility in closely related animal experimental models.
- *Preventive Trials:* Reduction of incidence subsequent to control or removal of suspected cause.

### *1.5.2. GENETIC-EPIDEMIOLOGY (GE): AN INTERDISCIPLINARY APPROACH TOWARDS THE FREQUENCY, DISTRIBUTION, AND GENETIC DETERMINATION OF HUMAN TRAITS.*

Genetic-epidemiological studies about the genetic determination of various human conditions, particularly diseases, employ interdisciplinary methodologies compatible with genetic principles (Weiss, 1993). It is a population concept of causality for genetic inference with the main objective of understanding whether and how genotypes are causally related to disease phenotypes based on differential disease susceptibilities, frequencies, and distribution among specific families, racial or ethnic groups, populations, geographical locations, etc.

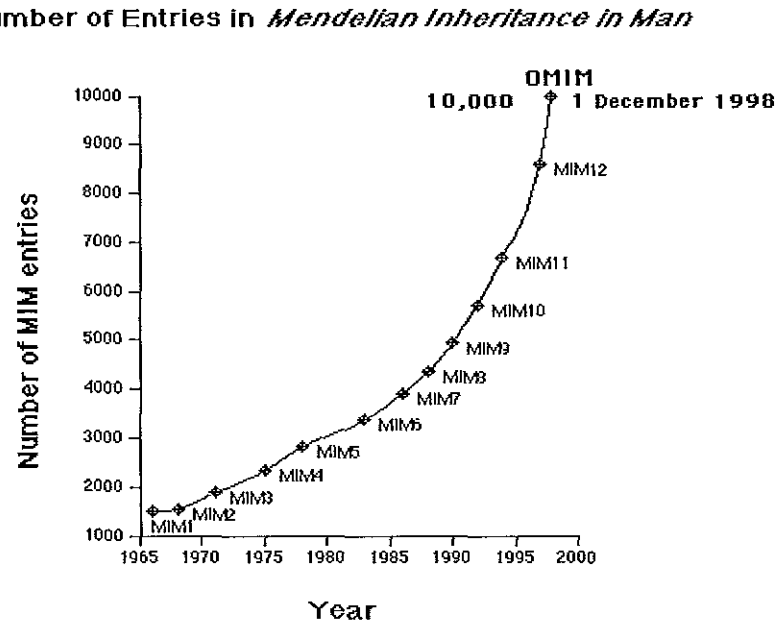



***Fig. 1- Number of Entries in Mendelian Inheritance in Man*** *(Source: Brandon Brylawski Online Mendelian Inheritance in Man, OMIM (TM). McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD), 2000. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/)*

In earlier investigations of the role of genetics in human trait variations geneticists concentrated on the better-delineated rare variants while the medical profession acknowledged general 'genetic predispositions' but disregarded incorporating genetic approaches into the studies of disease-related variations: pathogenesis and treatment response (Motulsky, 1980). Recent approaches include interdisciplinary professional collaboration between epidemiologists,

geneticists, doctors, clinicians, pathologists, immunologists, technicians, etc. Such collaboration has led to the birth of Genetic-Epidemiology and a rapid increase and refinement of knowledge regarding the genetic bases of several human traits, including diseases (Fig.1).

### *1.5.2.1. Genetic-Epidemiological Tools*

The study of the genetic aspects of human traits, and especially disease-related traits, is bedeviled by a host of problems unique to the field in addition to those others common to general epidemiology. These include (Motulsky, 1980):

- Ambiguous disease definitions
- Ascertainment difficulties
- Heterogeneity of disease traits
- Lack of sufficient and easily accessible data that can be statistically analyzed
- Ethical issues, i.e., the necessity to rely on observational data (Natural Experiment).

Genetic-epidemiologists, therefore, employ various scientific approaches in the observation and analysis of variation and integrate them with standard epidemiological measures of causation and association to infer the relationships between genetic and phenotypic variation. Some of these methods are (Simpson and Globus, 1992):

- Pedigree/Segregation Analysis.
- Twin Studies.
- Association and Linkage Analysis.
    - Gene-Marker Association Studies.
    - Linkage Analysis and Mapping.
- Cytogenetics.
- Molecular Genetics.
- Population Genetics.
- Evolutionary Genetics.
- Teratology.
- Medical/Clinical Genetics.

The unifying influence of genetic principles in these scientific approaches to the epidemiological investigation of diseases is demonstrable.

### *1.5.2.2. Genetic-Epidemiological Models for the Causal Spectrum of Traits/Phenotypes*

At the population level, the objective in GE is to understand how genotypes are causally related to phenotypes (Hassted, 1980). There are at least two relevant meanings of the concept of causation in biology:

- *Physiological or Mechanistic*: the direct mechanism of action of the locus of interest.
- *Epidemiological*: a strictly probabilistic association between the occurrence of alleles and phenotypes of interest in a population or sample as specified by penetrance functions.

There are different GE models designed to explain or infer the cause-and-effect relationships between genes and phenotypes. They represent various hypotheses about, or specifications of, relevant components of statistical associations that would be predicted by phenomena specific to the behavior of genes (Hassted, 1980).

Three main factors determine the 'genetic-causal-spectrum' or 'genetic architecture', of a phenotype (Weiss, 1993):

- The distribution of allelic effects on a trait, at loci that affect it.
- The frequency distribution of alleles and genotypes involved.
- The relationships among different loci, and between them and the environment, in their causal effects.

Although a model for the genetic-causal-spectrum begins to bridge the gap between the probabilistic and physiological causations, it is developed for application to epidemiological, not physiological data, and is often designed for a specific kind of population or sample. The current repertoire of genetic models usually provide for (Hassted, 1980):

- Only or at most a few loci with very large effects on penetrance compared to those of any other loci.
- A large number of loci with individually very small effects typically treated in aggregate.

- Environmental effects.

The objectives of the models are to (Hassted, 1980):

- Infer that genetic factors are involved.
- Describe their frequency, variation, and mode of action.
- Locate and identify the genes so that the phenotype becomes as predictable as possible and physiological mechanisms can be determined.

There are also model free studies in GE that use the same general databases as do other epidemiological studies- frequency distribution measures (prevalence and incidence) - with one important conceptual difference: in GE, genes/genotypes are considered the main risk factors (Weiss, 1993).

While GE methodologies take advantage of evolution-based constraints on the distribution of human genetic variation, the application of GE is itself constrained by the ethical necessity to rely mostly on observational rather than experimental data (Weiss, 1993). This places a premium on the ability to find and analyze samples that are most revealing of underlying human genetic mechanisms. The most important samples are population sub-divisions with definable levels of genetic relationship or variation:

- Families, including twins.
- Ethnic groups, including isolates.

#### *1.5.2.3. Population Sub-divisions, the Unique History of Mutations, and Clonal Diseases*

A classic problem in human genetics has been the estimation of how often new mutations leading to a given disease occur that explains their persistence or epidemiology in a given population. Based on phenotypic data, it was assumed that only a few alleles could exist at a locus, of which new copies arose via recurrent mutation at a rate generally estimated to be about $10^{-5}$ per locus per generation, providing a slow but continuous supply of a given mutant allele (Wallace, 1981).

However, at the nucleotide sequence level, the probability that the same mutation will recur is very small. For example, in a cistron (coding DNA stretch) the mutation rate per nucleotide is no more than $10^{-8}$ per meiosis. Moreover, mutational events can occur essentially at every step in gene expression (Weiss, 1993):

- Promoter-site mutations leading to incomplete or depleted mRNA transcription
- Deleted intron-exon splice sites.
- Added splice sites.
- Activated cryptic splice sites.
- Altered mRNA polyadenylation sites.
- Altered translation initiation or termination sites.
- Deletion-fusion mutations bringing together parts of separate genes.

At the core of modern evolutionary genetics is the realization that evolutionary forces generate genetic and phenotypic variants unique to the populations in which they arise. This concept is referred to as "the infinite alleles" or "unique mutation" model (Weiss, 1993):

- Different mutations uniquely arise in different populations and the longer populations have been isolated the more genetically different they become. Eventually, different clones of mutant alleles will become fixed in each population and locality (Weiss, 1993).
- Clonal diseases are caused by the effects of alleles descended from some common original pathogenic mutation.
- GDs may often be clonal in ethnic groups and isolates or individual families, but even in the larger general population, only a small number of clones of mutations may cause them. Since these will usually be specific to each population, their identification is important to reconstruct the unique history of populations from the distribution of such mutations.

The identification of the clonal nature of GDs is important to (Weiss, 1993):

- Understand the genetic basis of a disease or any other trait.
- Reconstruct the unique history of populations from the epidemiological pattern of such mutations and their phenotypic consequences.

The genetic-epidemiological study of small reproductively isolated, endogamous human population sub-divisions (e.g., cultural and/or religious sects, geographically isolated groups, etc.) often reveals that they have elevated frequencies of rare recessive GDs through homozygosis (Weiss, 1993):

- Founder individuals of isolates may non-randomly sample the alleles of their source population producing a 'founder effect'.
- The smaller population size of isolate leads to more rapid drift effects, which can raise a random selection of alleles to much higher frequency than previously.
- Isolates experience high frequencies of consanguineous marriages in their pedigree, either by social rules or simply because a high fraction of the available mates are also relatives (e.g., cousins of various types).

Generally, founder effect, small population size, rapid drift, and inbreeding make random sets of otherwise rare alleles (e.g., recessive disease-related alleles) much more common in isolates. On the other hand, inbreeding has less sever effects in populations that historically practice consanguineous marriage or endogamy, which is consistent with the theory that continued inbreeding gradually eliminates detrimental recessive genes acting on the reduced fitness (inbreeding depression) of recessive homozygotes (Arthur and Elain, 1990).

## *2. BACKGROUND: THE PEOPLES OF HARARI REGION OF ETHIOPIA*

Ethiopia has been described as an "Ethnic Museum" and each of its diverse people deserves to be studied intensively on its own terms, as bearer of a bounded system and a unique culture (Donald, 1974). The chief assumptions associated with this view are:

- Ethiopia is the origin of the human race.
- Ethiopia is a country of extraordinary ethnic diversity.

The delineation of groups of people on the basis of their ethnic identity is of particular concern in Genetic-Epidemiology since ethnicity is taken as a major genetic-epidemiological factor (Farmer *et al.*, 1996)

The term 'ethnic' is derived from the Greek word "ethnos", meaning 'tribe' or 'race' (Gould and Kolb, 1964). The term is also associated with "ethos" or "custom" implying that an ethnic group is ordained by the laws of social learning besides biological or genetic determinants and is applied to any group of people that differs in one or more aspects of its biologically and socially transmitted ways of life from other groups. Therefore, the ethnic group has a separate social status by virtue of the unique personal and social traits it exhibits, such as genealogy, physical appearance, religion, language, national or geographical origins, etc.

For any population or group, beyond any genealogical claims, ethnic identity is a matter of the ways in which the members identify and construct themselves as a bounded group, the ways in which they convey, perpetuate, and adopt perceptions of their history as a community, or how the life of an individual conforms to their collective precepts of tradition (Gibb, 1997).

In general, the label "ethnic group" tends to be used very loosely to describe a number of personal and collective characteristics including those that are genetically determined, for example, skin pigment and some that have nothing to do with genetics, for example, birth place and religion (Gould and Kolb, 1964).

Issues of ethnic identity in general and the delineation of groups of people on the basis of ethnicity have become paramount within the contemporary political climate of Ethiopia which calls for a reconstruction of administrative boundaries along ethno-geographic lines; and in a way, the current "Ethnic Federalism" of Ethiopia provides an analytic opportunity in the search for realistic evidence for the bases and the ways in which ethnic groups are constructed as separate, definable entities, the motivations for ethno-geographic categorization, as well as the possible implications of such categorizations (Gibb, 1997).

Identification as a member of any given ethnic group in Ethiopia is concomitant to (Gibb, 1997):

- Common genealogy.
- Common language.
- Common environment.
- Cultural and historical identification with geographical location.
- Participation in the way of life of the group'.

- Acceptance within the traditional forms of social organization.
- And, more recently, political allegiance.

It is often difficult in epidemiological studies to disentangle these ethnic characteristics and their effects from one another. The effect of ethnicity on the distribution of any human trait and particularly on the incidence/prevalence of disease is best studied in communities where members of different ethnic groups live side-by-side in more or less similar circumstances (Farmer *et al.*, 1996).

The Harari People National Regional State or Region-13, which is the smallest regional state in Ethiopia with its inhabitants composed of various ethnic groups, closely approximates this epidemiological concept or requirement and was, therefore, selected as the study site for this research.

### *2.1. ETHNIC COMPOSITION AND POPULATION ESTIMATES OF HARARI REGION*

The pivotal location of Harari Region at the crossroads for the meeting of people and produce has made the ethnic composition of its inhabitants one of the most diverse in Ethiopia. In recognition of the historic and current ethnic diversity that it harbors, UNESCO has named Harar, the capital city of Harari Region covering a small area of about 350km$^2$, "The Living Museum". The original inhabitants and founders of Harar are a small population known as the 'Adare' in Amharic, the 'Harari' in English, and who refer to themselves as the *'Ge usu'* (Gibb, 1997).

Population estimations based on ethnic designations is a complicated process due to the fluidity inherent in the use of "ethnicity" as a construct and the various ways by which groups are referred possibly reflecting the agendas of those who so delineate and the historical context in which they are being so delineated (Gibb, 1997) (Table-4).

***Table-4. Population Estimates and the Distribution of Ethnic Groups in Harari Region*** *(Source: Ethiopian Central Statistics Bureau, 1994).*

| Ethnic Group | Census (1994) | | | | Extrapolation | | | |
|---|---|---|---|---|---|---|---|---|
| | PC-123 (All) Count | PC-123 (All) % | PC-12 (Urban) % | PC-3 (Rural) % | PC-1 % | PC-23 % | PC-2 % | PC-13 % |
| *Argoba* | 992 | 0.76 | 0.02 | 1.78 | 0.01 | 0.94 | 0.02 | 1.21 |
| *Somalie* | 2199 | 1.68 | 1.61 | 1.77 | 1.19 | 1.80 | 1.83 | 1.59 |
| *Tigre* | 2244 | 1.71 | 2.93 | 0.01 | 2.18 | 1.59 | 3.33 | 0.71 |
| *Gurage* | 4140 | 3.16 | 5.42 | 0.00 | 4.03 | 2.94 | 6.15 | 1.31 |
| *Harari* | 9374 | 7.15 | 11.91 | 0.50 | 34.56 | 0.26 | 0.00 | 11.56 |
| *Amhara* | 42781 | 32.62 | 55.12 | 1.25 | 40.94 | 30.53 | 62.57 | 14.14 |
| *Oromo* | 68564 | 52.28 | 21.98 | 94.55 | 16.33 | 61.31 | 24.95 | 69.16 |
| *Others* | 845 | 0.64 | 1.02 | 0.13 | 0.75 | 0.62 | 1.15 | 0.33 |
| *Total* | 131139 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

*PC: Population Categories as defined in this thesis.*
*Assumptions in the extrapolation:*
*(1) All Hararis living in PC-12 (9098) live in PC-1, leaving 76378-9098=67280 to be occupied by the rest of the population, i.e., 17226 in PC-1 and 50054 for PC-2.*
*(2) The other ethnic groups are proportionally distributed in PC-1 and PC-2. E.g. Argoba in PC-1=(15*17226)/67280 and in PC-2=(15*50054)/67280.*

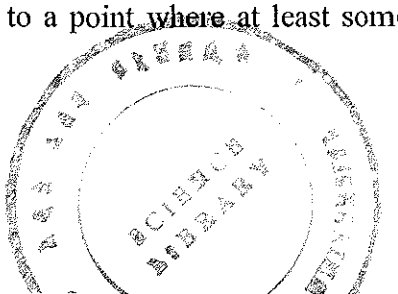
Although, the census figure provides no indication of ethnic group distributions beyond the "Urban and Rural" dichotomy, significant changes in the ethnic composition of Harar have taken place during the 19th century, especially since the expulsion of the Italians in 1941, creating a general picture of decreasing proportions of indigenous to non-indigenous inhabitants (Table-5). The most notable result is that while the Ge usu' were once numerically dominant in Harar, it is now clear that the Ge usu' are a minority group and virtually all of them live within the old city walls, Djugal (Gibb, 1997).

*Table-5.* ***Population Size Changes of Harari Region by Ethnic Group: 1877-1994*** *(Source: Harari People National Regional State, Conservation Strategy, 1998)*

| Ethnic group | Population size of 1877 | | Population size of 1994 | | Change in % |
|---|---|---|---|---|---|
| | № | % | № | % | |
| Harari | 24,500 | 59 | 9,374 | 7 | -88 |
| Oromo | 6,000 | 14 | 68,564 | 52 | 271 |
| Somalie | 5,000 | 12 | 2,199 | 2 | -83 |
| Amhara | 3,000 | 7 | 42,781 | 33 | 371 |
| Others | - | - | 8221 | 6 | - |

The huge influx of migrants, which brought about such extreme changes in the ethnic composition of Harar, probably marks the most important factor that altered the closed or insular traditional way of life of the Hararis by bringing them to a point where at least some Hararis





begun to consider themselves "Harari-Ethiopians" and not just as "Ge usu'- people of the city" (Waldron, 1973).

On the other hand, for the Ge usu' themselves, awareness of their increasing numerical inferiority and exclusive urban orientation are all the more reasons to 'safeguard' their ethnic identity in multi-ethnic Harar/Ethiopia which, indirectly, can further contribute to their relative reproductive isolation (Gibb, 1997).

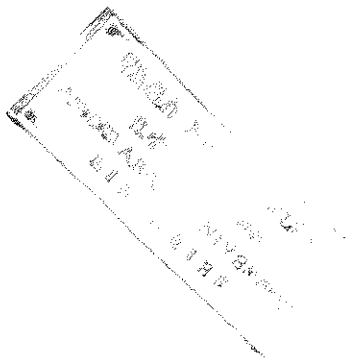
### *2.2. THE HARARI (GE USU'): IDENTITY AND PERSISTENCE IN MULTI-ETHNIC HARAR*

The *Ge usu'* have been described as a 'one-city-culture', a cultural group created and defined within a single geographic center. As the Harari term of self-reference, '*Ge usu'*- "People of the city", suggests, their orientation and perception of themselves is critically understood in terms of the urban environment, which their history has developed (Gibb, 1997). Before the huge influx of other populations started, the Harari and their old walled city of Harar represented the 'perfect' Population Category.

The walled city of Harar is the traditional homeland of the *Ge usu'* and is a relatively small, defined space of 60 hectares contained within a wall punctuated by six gates. In distinguishing the newer areas of the city of Harar which have developed in this century, the *Ge usu'* refer to the wall and the original city contained within it as 'Djugal', which literally means 'the wall'. Due to lack of space and the historical tendency of the *Ge usu'* to exclude visitors, especially those not of the Muslim faith, the majority of the new comers in Harar established themselves in what is now the 'New City' surrounding Djugal (Gibb, 1997).

With great consistency, many of the essential aspects of *Ge usu'* culture are referred to as '*Ge*', "of the city", which is an indication that the old city is vitally important in the expression of Harari ethnic identity (Waldron, 1966). For example:

- *Ge sinan*- language of the city
- *Ge gar* and *Ge garach*- house/houses of the city
- *Ge ada*- culture of the city
- *Ge kahatach*- daughters of the city



- *Ge usu'*- people of the city

Despite incorporation in to the greater Empire of Ethiopia, the Harari people have developed in comparative isolation and their cultural institutions and day-to-day interactions have remained relatively self-contained. The wall has served as both a physical and symbolic boundary separating the *Ge usu'* and their traditional homeland from others to the extent that the rest of the population of Harar, and the government itself, affected the Harari way of life only in matters which connect them to the world outside the old city walls (Waldron, 1966).

Western travelers and scholars have made much of this relative isolation and the resultant endogamy of the Harari. The famous European explorer, Sir Richard Burton (1854) was one of the first to describe the Harari as a unique entity:

- "A peculiar population, descendants of a once mighty race, a distinct self-governed cultural isolates whose inhabitants communicated through the medium of Harari, a peculiar dialect confined within the city walls, unintelligible to any save the citizens".

A recent scholar, Sidney Waldron (1966), states:

- "The *Ge usu'* present a tight knit, a relatively endogamous group with their own internal system of administration, protected by the physical structure of the city with its circumscribing wall, and linguistically, culturally, and religiously different from the dominant Amhara".
- "Contact with the world beyond the wall by the *Ge usu'* is limited as they live as "an island, remaining aloof from the outside world seemingly by choice".
- "While maintaining boundaries between themselves and other groups, the *Ge usu'* are, however, enmeshed in a complex of overlapping indigenous social institutions which are responsible for their overwhelming degree of internal social cohesion and solidarity".

Another very recent scholar, Camilla Gibb (1997), comments:

- "The Harari have historically occupied the apex of a pyramid of ethnic stratification over the neighboring ethnic groups a situation which helped them to maintain their cultural

boundary and ethnic identity while engaging in daily transactions with the other ethnic groups living in Harar".

Other culturally defining unique characteristics such as birth and marriage, wedding ceremonies, architecture, house furnishing styles, traditional dresses, basketry, etc have also been used by several scholars to distinguish the *Ge usu'* from the rest of Harar's populations.

For the *Ge usu'* themselves, however, identification as a *Ge usu'* citizen is primarily dependent upon membership and participation in at least three fundamental *Ge usu'* institutions or social organizations which structure Harari society (Gibb, 1997):

- The kinship or genealogy group- *Ahli,*
- The friendship group- *Gailach/Marinach*, and
- The community organization- *Afocha.*

The kinship system is described as conforming to a "bifurcate collateral" model although not integrated into any corporate kin groups such as, clans or lineages, and provides a network of relations throughout the city, which ultimately interrelates all Hararis (Gibb, 1997).

The network of relations are based on a concept of a limited number of original households, of which there are in the order of 300 named households, each of which refers to the founders of a family line or genealogy by name. All *Ge usu'* have household names which indicate that every individual is ultimately related through the founders of the original households. The founders are historically assumed to be Sheikh Abadir and his 43 companions, who came from the Arabian Peninsula in the early 1200s, with whom the intimate core of the Hararian national identity is deeply associated (Gibb, 1997).

For example, an Ethiopian scholar, Mohammed Abdulrahiman Quorum (1984), has prepared the "*Chokti Kitab*", a list of household names (*Ishara Sum*) each paternal line ending somewhere in the original households, which strengthens the claims that all Geusu are related. In addition, most Hararis, particularly the elders, are aware of their household names and could name several of their forefathers which is one form of the recognition of the Ahli (a system of kin reckoning) as the first of the fundamental forms of *Ge usu'* social organization (Gibb, 1997).

## *2.3. BIRTH AND MARRIAGE AMONG THE HARARI: THE DEMAND FOR A BRIDE FROM HARAR (GE KAHATACH)*

Birth and marriage are two events which provide considerable insight about the Harari concept and practice of procreation and the importance that the *Ge usu'* attach to the issues of endogamy, fertility, and the perpetuation of the group; and, although marriage is an honorable exercise for any of our (Ethiopia's) ethnic groups, the highest esteem with which the Harari regard marriage is considered exceptional by Tsedale, 1983.

The *Ge usu'* kinships are attainable primarily through genealogy, strengthened by a firmly established structure of social organization, conformity, and homogeneity. In the social organization of personal life among the '*Ge usu'*, the individual develops along a culturally preconceived route of maturation, i.e., internalizes the rules of the *Ge ada-* culture of the city. Among these, marriage and birth are perhaps the greatest events: in marriage, single individuals become part of a marital union and honor the order of the *Qurr'an* and can then take on full adult responsibilities, producing children, and join in the community organization or *Afocha* (Gibb, 1997).

The average age of marriage amongst the *Ge usu'* is estimated by *Qadis* (Muslim judges) to be between 25 and 35 years for a woman, and 25 to 40 years for a man, figures which may partly reflect the rigorous *Ge usu'* prerequisites for marriage. The *Ge usu'* take their time in choosing mates so that they could thoroughly check out both partners (*Aruz and Aruzit*) and their extended families with regard to ethnicity, upbringing, and wealth (Alemayehu, 1981).

The *Shawwal Eid* celebration, held in February of every year, is another clear manifestation of the desire of the Ge usu' to monitor the 'purity' of the group in marriage. *Shawwl Eid* is the traditional occasion for premarital courtship and choosing a marriage partner. As an exclusively *Ge usu'* tradition, during which non-*Ge usu'* are involved in neither the celebrations nor the prospective liaisons that might arise from it, this occasion underlies the community's preference for endogamous marriages (Gibb, 1997).

This is especially true in these days with a huge proportion of the *Ge usu'* community scattered throughout the world and increasing numbers of young men living abroad seeking brides from

Harar. It is common to find female relatives enlisted by a young male relative of theirs living abroad who defers to their suggestions knowing that they have had opportunities to monitor the bride to be and investigate the ethnic composition, moral reputation, financial well-being and, these days equally as important, the political affiliations of her extended family. These arrangements also meet the other reasons for the demand for a bride from Harar since, if a girl has been raised as an ideal *Ge kahatach* (Daughter of the city):

- Her first language will be *Ge sinan*,
- She will be educated in *Qurr'an*,
- She will have internalized the principles of *Hawa mahal* (manners and civility),
- She will be skilled in the traditional tasks or arts of basketry and the preparation of Ge usu' cuisine.

Such engagement procedures according to a traditional formula despite the bridegroom's absence can be taken as an indication of the strong sense of the need and desire to marry within the group building up in order to survive as a distinct group (Gibb, 1997).

However, there are some scholars who challenge the portrayal of the *Ge usu'* as a totally 'socially and ethnically exclusive' group in present day Ethiopia. For example, Gibb (1997) who stayed and worked among the Harari in Harar, makes the following observations:

- "Although it may have been the case that there did exist an active campaign among the *Ge usu'* to ensure membership (to friendship and other community organizations) was only open to individuals accepted to be full-blooded *Ge usu'* in genealogical terms, in present day Harar it is difficult to maintain a pretence of ethnic exclusivity or purity of the *Ge usu'*.
- "While the degree of *Ge usu'* purity is still an issue at the theoretical level within the traditional institutions, and while individuals often refer to others on the basis of the degree to which they are *Ge usu'*, it is a question of degree alone and definable by context."
- "In many cases ethnicity can be and is overlooked where an individual has been a fully participating and identified member of the *Ge usu'* society."

The last reference is to the Harari concept of '*Ge limad'*- "learning the way of life of the city", i.e., the process of becoming a member of the people of the city through 'enculturalization' or assimilation through time. It is argued that, in as far as ethnic differences exist in and around Harar, and in as much as it is the *Ge usu'* who sit at the pinnacle of such an ethnically-structured class hierarchy, the aspirations of non-*Ge usu'* individuals into this 'prestige' category can also be realized through the pursuit of *Ge limad* which involves (Gibb, 1997):

- Acquisition and practice of Islam which has developed in-situ,
- Practice of the culture of the city, *Ge ada*, and finally,
- Acceptance into the primary social institutions of Ge *usu'* life.

In general, *Ge limad* is thought to cast doubt on the usual picture of ethnic exclusion within the principal *Ge usu'* social structures because it overrides the potential to promote the *Geusu'* as a closed ethnic category, making it possible for any one to adopt or internalize *Ge ada* and become a full member of the *Ge usu'*.

However, these are not common occurrences and, in any case, an entire family of non-*Ge usu'* is not permitted to live in the city and hence, an ethnic boundary is preserved, managed by the *Ge usu'* people (Waldron, 1966).

It is also pointed out that from the historical perspective, *Aw* (father) Abadir, the founding Muslim Sheik who came from Saudi Arabia, is renowned for having consolidated many of the indigenous tribes in and around Harar while introducing them to Islam (Gibb, 1997). The implication is that, since his followers were established from this consolidation process, the origins of the group to which he became 'father' were heterogeneous and what came into existence as a definable group known as the *Ge usu'* has been produced within the context of inter-ethnic relationships.

Moreover, in the current century the relative numerical and socio-economic preeminence of the *Ge usu'* has diminished, and therefore, although their primary social institutions still exist as the fundamental means through which individual *Ge usu'* are organized, the 'self-contained' entity able to 'self-govern', and remain 'aloof' from the rest of Harar's inhabitants, may no longer be possible (Gibb, 1997).

However, even Gibb, who strongly advocates a "Demand for New Perspective" on the notion of the "exclusivity" of the *Ge usu'* and sites several evidences for their "inter-ethnic solidarity", admits that:

- "For the *Ge usu'*, while endogamy is considered ideal, consanguinity at the level of patrilateral cross-cousin marriages (like the Arab preference) is perhaps too insular for a group which appears to me to increasingly fear its extinction".

It is possible, therefore, to safely assume that the Ge usu's idea of "inter-ethnic solidarity" does not include "inter-ethnic marriage". On the contrary, they have for long erected both subtle and not so subtle mechanisms for preventing what they consider 'unacceptable' mating. Examples of these mechanisms include (Gibb, 1997):

- Female infibulations to prevent pre-marital sex or ensure virginity before marriage.
- Conduct arranged marriages.
- Overall alienation or ostracization of those members of the group who engage in inter-ethnic marriages.
- Maintenance of unfavorable or negative stereotypes of other ethnic groups as manifested by the stigmatization of *Toyach* (neighborhoods) on the basis of their non-*Ge usu'* ethnic composition, while on the other hand, demonstrating a considerable amount of pride by the residents of those *Toyach* which have managed to remain exclusively *Ge usu'*.

Such mechanisms, besides the rigorous birth and marital traditions mentioned before, offer the strongest evidence of the ways by which the persistence of the identity of the *Ge usu'* has been ensured through the ages despite enormous challenges in multi-ethnic Harar-Ethiopia.

In conclusion, it can be inferred that the *Ge usu'*, existing as they do as a tiny minority engulfed by other much larger ethnic groups, have for long erected social structures and principles which permit necessary transactions between themselves and the other inhabitants of Harar while safeguarding their overall ethno-geographic identity. These are achieved primarily through (Waldron, 1966):

- Control of information, personnel, and goods and services,

- Control of sexuality, prohibiting both premarital sex and inter-ethnic marriage,
- Practice of endogamy,
- Exclusion of non-Ge usu' and maintenance of unfavorable or negative stereotypes of other ethnic groups.

In any case, however, beyond any possible genealogical claims which emphasize the genetic implications of inter-ethnic relationships in Harar, most of the socio-economic and cultural issues raised in connection with the 'non-ethnic exclusivity' of the *Ge usu'* are no more than "confounding epidemiological variables" to the essential question of this thesis which can be stated as:

- "Whether or not there is random inter-ethnic marriage or reproductive mating between the various ethnic groups living in Harar, especially, between the *Ge usu'* and the other inhabitants?"
- "Whether or not the people of Harar, indigenous or not, have a homogenous/heterogeneous genetic-pool, at least at the "ethnic group" level of organization of human populations".

In other words, the changing fortunes of the various ethnic groups in Harar relate to the present genetic-epidemiological study only in as far as they have phenotypically demonstrable impact through inter-ethnic marriage and birth, the two social factors that can modify the genetic-pool of populations.

To put the real issues of this thesis in the form of a single question: "Is marriage or reproductive mating random among the inhabitants of Harari Region?"

These questions are important in this thesis because one of its major premises (hypothesis) relates to the distinctive assumption of the general heterogeneity of the genetic-pool or identity of the different ethnic groups (and other population groups as defined in this thesis) inhabiting Harari Region, especially relative to the *Ge usu'* people as an ethnic group prone to endogamy or consanguinity (consanguineous marriages).

## *II. OBJECTIVES*

The objectives of this study, as well as its underlying procedural and analytic logic, can be outlined within the following contexts.

Human populations have come through time to be subdivided and hierarchically structured in such a way that there are founders of a community as in reproductive mates or parents, siblings, families, and immediate or distant relatives which may give rise to specific Population Categories (PCs) each with their own geographically, socially, and biologically determined characteristics (ethno-geographic characteristics). Thus, each resultant Population Category possesses several distinguishing characteristics, and associated levels of variation that are determined by virtue of the extent of the members' shared environmental factors and ways of life operating in concert with their common ancestry or genealogy, if any.

The health and/or disease profiles of populations are among such basic distinguishing characteristics; and the objective of this research is to statistically analyze the relative frequency distribution (incidence/prevalence) of some of these characteristics among various Population Categories in Eastern Ethiopia, Region-13. It is particularly concerned with the epidemiology of those human conditions that are known to be affected or determined by genetic factors.

The epidemiology of genetic traits depends on several characteristics of the population wherein the basic genetic factors responsible for the traits in question occur. For example, genetic defects responsible for disease phenotypes are caused by pathogenic spontaneous or induced mutations, which, according to modern evolutionary principles, are usually unique and localized to the population wherein they arise, can only be passed on to subsequent generations or across population subdivisions, such as ethnic and geographic barriers, only through reproductive mating (for example, inter-ethnic mating). That is why cases of a given genetic disease that arise in members of a given population tend to be clonal, i.e., due to alleles that constitute a clone of descendants of the original specific pathogenic mutation(s). The localization of specific mutations is also maintained by small population sizes, as in the case of earlier human populations and some contemporary ethnic groups, e.g. the *Ge usu'* in Harar..

Therefore, different mutations may uniquely arise in different population groups causing correspondingly variable incidence/prevalence (Relative Frequency Distribution, RFD) of the phenotypes that they affect; and the longer populations have been reproductively isolated, the more divergent their genetic pool becomes, and different of mutant alleles of each clade will become fixed in each population such as the ethno-geographic groups defined later on in this thesis.

It is the hypothesis of this thesis that the phenomena mentioned above may be operative here in Ethiopia and can best be scientifically tested among the various Population Categories found in Harari Region, the smallest administrative region in Ethiopia, where communities composed of different ethnic origins are found living side by side in an area with relatively reduced environmental variation (for example, geographical variation).

The general and specific objectives of this research can be summarized as follows:

1. General objectives:

A) Human disease traits:

- To sample hospital inpatient populations in Harari Region of Ethiopia and estimate the RFD of some human disease traits the etiology and/or prognosis of which have been described by several previous independent scientific studies as being partially or wholly determined by genetic risk factors.
- To compare the estimated RFD of genetically determined diseases among the sampled hospital inpatient populations from different Population Categories using disease group, age group (generation), and sex stratified statistical analysis.
- To infer whether or not the sampled populations are significantly variable, i.e., whether or not the sampled populations from the different Population Categories could have been drawn from the same general population, with respect to each of the selected disease trait groups and, by extension, exposures to the epidemiological determinant factor(s) - genetic and/or environmental factors - that play a role in their causal spectrum.

B) Polymorphic ABO locus:

- To estimate the phenotypic frequency distribution of the ABO/Rh blood groups among volunteers from the normal/healthy population of Harar.
- To estimate the allelic frequency distribution of the ABO/Rh blood group locus among volunteers from the normal/healthy population of Harar.
- To statistically test the estimated phenotypic and allelic frequency distributions of the ABO locus among the different ethnic groups in Harar and see whether or not the sampled populations are:
    - Phenotypically homogenous/heterogeneous.
    - In genetic equilibrium (HWE).

2. Specific objectives:

- To infer the degree to which the RFD of specific disease groups are affected by ethno-geographic variations associated with the different Population Categories.
- To characterize the relative genetic-epidemiological profiles of the different Population Categories, each with their own unique ethnic composition, inter-ethnic interactions, and environmental circumstances:
    - The degree of similarity/dissimilarity (homogeneity/heterogeneity gradient) between the various compared PCs based on the average consistency levels of significant variations in the RFD of specific disease traits.
    - The degree of similarity/dissimilarity (homogeneity/heterogeneity gradient) between the various compared PCs based on the total average consistency level of significant variations.
- To estimate the level of homogeneity/heterogeneity of the sampled populations and infer the existence of non-randomly mating genetic-substructures, if any, along ethnic lines based on the allelic and phenotypic frequencies of the ABO locus in the sampled populations.

## *III. MATERIALS AND METHODS*

### *1. SELECTION OF HUMAN TRAITS OF INTEREST*

After a careful review of the available literature, human traits or conditions, which have been established by several previous studies as having genetic factors in their causal-spectrum (to varying degrees), were selected for analysis:

- Genetically determined diseases.
- ABO/Rh blood groups.

### *2. SELECTION OF STUDY SITE*

Harari Region was chosen as data source by virtue of the fact that it conveniently fulfills the following genetic-epidemiological requirements:

- The existence of communities (Population Categories) composed of people with different ethnic backgrounds living side by side in a relatively small geographical area with naturally and socially reduced environmental variation.
- The existence of a particular PC, the Harari ethnic group, which possesses attributes amenable to genetic-epidemiological studies:
    - A relatively small sized population, historically characterized by endogamy or inbreeding.
    - Geographically localized in a well-defined space or homeland established by themselves centuries ago.
    - The presence of health centers or hospitals capable of diagnosing the selected disease conditions.

### *3. DATA COLLECTION*

#### *3.1. Data on the Spectrum, Frequency, and distribution of Diseases*

The inpatient lists of all departments (wards) in two hospitals, Misrak Arbegnoch and Hiwot Fana, were obtained and all recorded cases of the selected disease conditions in WHO codes were scored along with inpatient attributes- sex, age, and address. Ethnicity was not recorded

because not even a single list contained such data although a space is provided in the standard formats. A total sample of more than 15,000 cases of the selected disease conditions were collected from all available medical data of ten years (from 1984 to 1994 E.C.).

### *3.1.1. Data Categorization*

Data categorizations were necessary in order to make sure that statistical comparisons are made between equivalent or similar groups of inpatient data (sex, age, and disease group) that differ only in their Population Category membership. The collected data were categorized for statistical analysis as follows:

*A) Medical Data Categorization*

*i) Dxgroups- Disease or Diagnosis Groups (in Dxcodes)-* the disease traits or conditions were selected and categorized exactly as they are specified and grouped in the Ethiopian Ministry of Health's (MOH) "List of Causes for Tabulation of Morbidity and Mortality" (See Appendix-1 for disease synopsis):

- Dxgroup-1: Malaria (the only 'Infective and Parasitic' disease sampled since its manifestation or prognosis has for long been known to be affected by the presence/absence of specific genetic factors in the genetic milieu of the infected person)
    - Dxcode-037.1: Vivax Malaria
    - Dxcode-037.2: Malarial Malaria
    - Dxcode-037.3: Falciparum Malaria
    - Dxcode-037.4: Unspecified Malaria
- Dxgroup-2: Neoplasms
    - Dxcode-044: Malignant Neoplasms of Buccal cavity and Pharynx
    - Dxcode-045: Malignant Neoplasms of Esophagus
    - Dxcode-046: Malignant Neoplasms of Stomach
    - Dxcode-047: Malignant Neoplasms of Intestine, Except Rectum
    - Dxcode-048: Malignant neoplasms of Rectum
    - Dxcode-049: Malignant Neoplasms of Larynx
    - Dxcode-050: Malignant Neoplasms of Trachea, Bronchus, and Lung

- Dxcode-051: Malignant Neoplasm of Breast
- Dxcode-052: Malignant Neoplasm of Cervix-Uteri
- Dxcode-054: Malignant neoplasm of Prostate
- Dxcode-055.1: Malignant Neoplasm of Skin of Leg
- Dxcode-055.2: Malignant Neoplasm of Skin Other Than Leg
- Dxcode-056.1: Malignant Neoplasm of Jaw
- Dxcode-056.2: Malignant Neoplasm of Other Bone and Connective Tissue
- Dxcode-057.1: Malignant Neoplasm of Liver (Primary)
- Dxcode-057.2: Malignant Neoplasm of Ovary
- Dxcode-057.3: Malignant Neopplasm of Penis
- Dxcode-057.4: Malignant Neoplasm of Other Unspecified Sites
- Dxcode-058: Leukaemia and Aleukaemia
- Dxcode-059: Lymphosarcoma and Other Neoplasms of Lymphatic and Haematopoitic System
- Dxcode-060.1: Benign Neoplasm of Breast
- Dxcode-060.2: Uterine Pybnomayoma
- Dxcode-060.3: benign Neoplasm of Ovary
- Dxcode-060.4: Other Benign and Unspecified Neoplasms

- Dxgroup-3: Deficiency Diseases
  - Dxcode-063.1: Diabetes Mellitus
  - Dxcode-063.2: Diabetes Insipidus
- Dxgroup-4: Deficiency Diseases
  - Dxcode-065.1: Pernicious Anemia
  - Dxcode-065.2: Iron Deficiency Anemias (Hypochromic Anemias)
  - Dxcode-065.3: Sickel Cell Anemia
  - Dxcode-065.4: Other Unspecified Anemias
- Dxgroup-5: Mental, Psychoneurotic, and Personality Disorders
  - Dxcode-067: Psychosis
  - Dxcode-068: Psychoneurosis and Disorders of Personality
  - Dxcode-069: Mental Deficiency
- Dxgroup-6: Diseases of the Nervous System and Sense Organs

- Dxcode-073: Epilepsy
- Dxcode-075: Cataract
- Dxcode-076: Glaucoma

- Dxgroup-7: Diseases of the Circulatory System
  - Dxcode-079: Rheumatic Fever
  - Dxcode-080: Chronic Rheumatic Heart Disease
  - Dxcode-081: Arteriosclatoic and Degenerative heart Disease
  - Dxcode-082.2: Endomyocardial Fibrosis
  - Dxcode-82.3: Other Diseases of Heart
  - Dxcode-083: Hypertension With Heart Disease
  - Dxcode-084: Hypertension Without Mention of Heart
- Dxgroup-9: Diseases of the Digestive System
  - Dxcode-102: Appendicitis
  - Dxcode-103.1: Hernia of Abdominal Cavity Without Obstruction
  - Dxcode-103.2: Hernia of Abdominal Cavity With Obstruction
  - Dxcode-103.3: Intussusception
  - Dxcode-103.4: Volvulus
  - Dxcode-104: Gastro- Enterities and Colitis
  - Dxcode-105.1: Cirrhosis of Liver
  - Dxcode-105.2: Cholelithiasis and Cholelicystitis
  - Dxcode-107.1: Necrosis of the Liver
- Dxgroup-10: Diseases of the Genito-Urinary System
  - Dxcode-108: Acute Nephritis
  - Dxcode-109: Chronic and Other Unspecified Nephritis
  - Dxcode-112: Hyperplasia of Prostate
  - Dxcode-113; Diseases of Breast
  - Dxcode-114.1: Strictures of Urethra
  - Dxcode-114.2: Hydrocele
  - Dxcode-114.3: Disorders of Menstruation
  - Dxcode-114.4: Sterility of Female
- Dxgroup-11: Diseases Asociated with pregnancy, Child Birth, and the Puerperium

- Dxcode-115: Sepsis of pregnancy, Childbirth, and the Puerperium
- Dxcode-116.1: Pre-Eclamptic Toxaemia
- Dxcode-116.2: Eclamptic Toxaemia
- Dxcode-116.3: Other Toxaemia of Pregnancy and Childbirth (Ante-Natal)
- Dxcode-117.1: Haemorrhage of Pregnancy and Childbirth

- Dxgroup-12: Diseases of Skin, Cellular Tissues, Bones, and Organs of Movement
  - Dxcode-122: Arthritis and Spondylitis
  - Dxcode-123: Muscular Rheumatism and Rheumatism Unspecified
  - Dxcode-124: Osteomyelitis and Periostitis
- Dxgroup-13: Cogenital Malformations (Including Spontaneous Abortions)
  - Dxcode-118: Abortion Without Mention of Sepsis or Toxaemia
  - Dxcode-129: All Congenital Malformations

[Note: Spontaneous abortions and congenital malformations were grouped together because those born congenitally malformed can be considered as those who escaped being aborted earlier in embryogenesis.]

*ii) Disease Types (Dxtypes) and Age Groups (Generations)*- Based on the recognition that certain diseases are sex and/or age dependent (specific) the diseases listed above were further subdivided and categorized as follows:

- Disease Types (Dxtypes):
  - Dxtype-1: Congenital Malformations and Spontaneously Aborted Fetuses (both males and females).
  - Dxtype-2: those diseases affecting males.
  - Dxtype-3: those diseases affecting females.
  - Dxtype-4: those diseases related to pregnancy and childbirth.
- Age Groups:
  - First generation- all ages less than or equal to 25.
  - Second generation- age 26 up to 49 years of age.
  - Third generation- all ages greater than or equal to 50.

*B) Population Categorization*

Based on the recognition that population settlement patterns are not random, Population Categories (PCs) were constructed in order to delineate and define inpatients based on their recorded addresses (regions, woredas, kebeles, and farmers associations). Each Population Category is characterized by its local geographic area, unique ethnic composition, and intra/inter-ethnic interactions. Although the primary or ideal aim was to identify and define inpatients of separate ethnic entities whatever their addresses may be, the formation of compound categories that denote the ethnic composition and geographical location [Local Ethno-Geographic-Categories (EGCs)] was necessitated by:

- The complete absence of information about the ethnic identities from literally all of the available medical history of inpatients.
- The failure of serious attempts made to ascertain the ethnic identity of inpatients by consulting the registrar offices of kebeles.

Therefore, refuge was taken in the historical population settlement patterns and current administrative boundaries of Harari Region, which are presumed to be based on ethnicity. The historical reality of human settlements to closely follow ethnic denominations and thus reflect the ethnic identities of their residents is especially true of Djegol, the homeland of the Harari ethnic group, which is one of the main reference categories in this research.

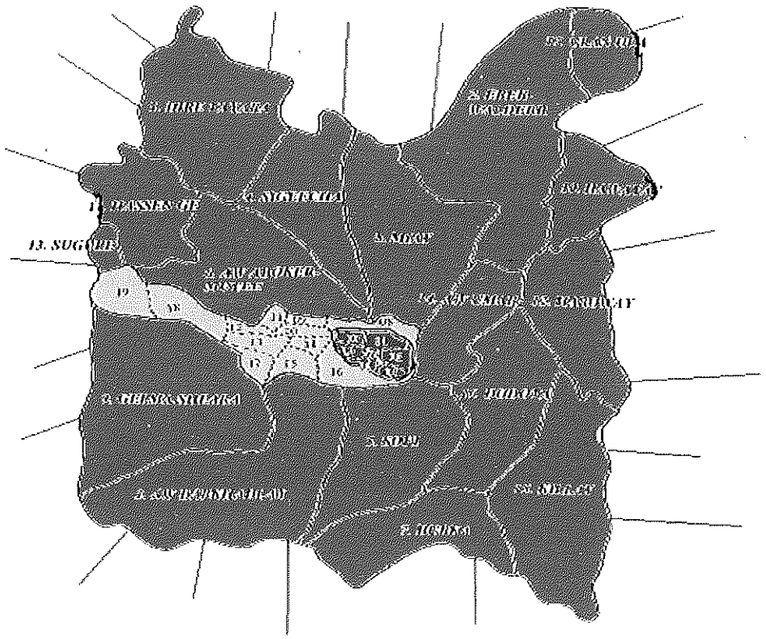
Accordingly, 4 basic Population Categories (PCs) were identified as follows based on inpatient addresses (Map-1):

- PC-1: Inpatients from Woreda-1 consisting of Kebeles 1-7 (Djegol- the Old Walled City of Harar)-Red Colored.
- PC-2: Inpatients from Woreda-2 and 3 consisting of Kebeles 8-19 (The New City) - Yellow Colored.
- PC-3: Inpatients from Hundene consisting of 17 Peasant Associations surrounding the city of Harrar - Green Colored.
- PC-4: Migrant inpatients from the neighboring regions of Harar and the rest of Ethiopia (non-residents of Region-13) - Blue Lines.

For all intents and purposes of this research, the major reference PCs can be ethno-geographically characterized as follows:

- The urban populations of PC-1 and PC-2 are similar in their ethnic composition consisting of representatives of all ethnic groups present in Harar except for the almost exclusive concentration of the Harari in the former category.
- The rural population of PC-3 is almost entirely composed of the Oromo people, closely approximating the perfect "Population Category or Local Ethno-Geographic Category".
- The migrant populations of PC-4 are composed of representatives of "Multi-Ethnic Ethiopia" especially from the neighboring regions of Harar.

***Fig. 2. Map of Population Categories (Local Ethno-Geographic Categories) in Harari Region (Adapted from: Map of Region-13, Regional Bureau, Harari People National Regional State, Ethiopia)***



As stated earlier, since the 4 basic PCs outlined were based on historical population settlement patterns and current administrative boundaries, there is a possibility of exclusion and/or overlapping of some segments of populations to varying degrees both in terms of ethnic composition and general environmental factors related to geographical location. Hence, to minimize or account for the effect of such uncertainties in Population Category membership, the 4 basic PC were combined in pairs of twos and threes to create other categories (local ethno-geographic strata) with which the 4 major PCs can be compared: PCs– 12, 13, 14, 23, 24, 34, 123, 124, 134, and 234.

### *3.2. Data on the Phenotypic and Allelic Frequency Distribution of the ABO Blood Group*

Upon the approval and recommendation of the Health and Education Bureaus of Region-13, students of Harar Junior and Secondary School (grade 9⊴2) were asked to be informed volunteers in providing samples of their blood to be typed. Two hundred and seventy nine (279) students came forward whose blood group and ethnicities were recorded (certificates of the blood-typing results and gratitude awarded to each volunteer to take home).

The blood samples were collected and typed by a qualified laboratory technician in the presence of the volunteers who were thereby notified of their blood types.

## *4. STATISTICAL ANALYSES*

### *4.1. The Spectrum and Relative Frequency Distribution of Diseases*

The statistical comparisons between the various PCs were made based on the proportional or relative frequency distribution (RFD) values of the selected diseases in each PC estimated from the total combined data. The RFD for each PC was calculated within each disease type, disease group, and for each generation of inpatients admitted to all hospitals. The statistical analysis itself was done by a computer statistical software known as SPSS and the objective was to see if the RFD of the diseases within each disease group were significantly different between any of the various compared PC using the F-test (Leven's Test for the Equality of Variance) at the $\alpha$=0.05 level of significance (95% confidence level).

### *4.2. The Phenotypic and Allelic Frequency Distribution of the ABO Blood Group*

Both phenotypic and allelic frequencies of the ABO and Rh blood groups were estimated from the collected blood samples of each ethnic group as well from the variously combined data. Statistical tests for phenotypic heterogeneity and for genetic equilibrium were performed using the chi-square test. The objectives of the tests were to find whether the population were homogenous (phenotype frequency) and/or in genetic equilibrium.

In general, the research methodology was designed to, as far as possible, safely conclude that any results obtained could be attributed more to genetic determinants of phenotypes since:

- Firstly, the selection of disease/health conditions to be surveyed were limited to those non-communicable, genetically determined traits;
- Secondly, the study site was selected primarily because the prevailing environmental variations are naturally and socially reduced to a minimum.

Therefore, the analysis of the spectrum and relative frequency distribution of genetically determined human traits observed in the present study can be safely assumed to reflect the additive effects of those factors involved in their causal spectrum such as the unique history of inter-ethnic interactions, population dynamics, and overall ethno-geographic backgrounds which, to varying degrees, determine the health/disease states of the people of Harari Region, Ethiopia.

## *IV. RESULTS AND DISCUSSION*

The findings of the study would be best presented in two parts: Part-I deals with the spectrum, frequency and distribution of diseases; and Part-II deals with the phenotypic and allelic frequency of the ABO blood groups.

### *Part-1. THE SPECTRUM AND RELATIVE FREQUENCY DISTRIBUTION OF DISEASES*

The spectrum (types) and relative frequency distribution (RFD) of the diseases in the consolidated data collected from the only two civilian hospitals in Harar is as presented in Appenix-2.

The age, sex, and Dxgroup stratified statistical analyses were performed on the raw data presented in Appenix-2 the results of which are outlined in Appenix-3 at two levels: Level-I and Level-II.

- Level-I: Depicts the entire statistical outcome regardless of the significance values, i.e., actual $p$ values for each test of the equality of variance (F-test) based on the RFD of diseases in the compared PCs. Significant values, at the 95% level, are italicized; '.' indicates where no statistics could be computed (Tables: 12-23). The advantage of listing the statistical data in this manner is that, first, it enables to outline the detailed sex, age, and Dxgroup specific results and, second, it is possible to modify the significance levels so as to test the hypothesis at different levels of significance if necessary. Nevertheless, it is difficult from this presentation alone to draw an overall picture of, and discuss, the nature of the relationships between the various PCs beyond pair-wise comparisons. In other words, from the results presented in Level-I, it is possible only to tell which of the compared PCs significantly differ or not, for which Dxgroup, sex, and generation (at any specified level of significance). Therefore, it is necessary, to find another option, Level-II.
- Level-II: Depicts a summary of all statistical results in a manner that transcends details so that a general picture emerges which describes the status of each PC relative to the other compared categories. This objective can be attained by outlining the consistency level or

pattern, if any, of a given significantly different result across the age and sex group variables for each Dxgroup.

It is clear from the results presented in Appendix-3 that the spectrum and RFD of most of the disease phenotypes surveyed are significantly variable among the majority of the compared PC pairs albeit to varying degrees of consistency.

The general interpretation of significant differences is that, even if the actual causes of diseases were unknown, their spectrum and RFD is not uniform among the compared PCs and thus the local ethno-geographic background of a person is an epidemiological determinant factor. Epidemiologic determinant factors are defined as those factors (intrinsic personal attributes and/or environmental factors) that determine the liability of an individual and, by extension, the whole population of which he/she is a member, to be exposed to health risk factors or, when exposed, to actually develop the particular disease phenotype(s).

Therefore, results of significant differences indicate that the epidemiological determinants responsible for pathogenesis and distribution are not uniformly distributed, i.e., the populations of the various PCs are not exposed to the same type and degree of genetic and/or environmental health risk factors. That is why either one or the other of the compared pair of PC is more or less affected than the other. In simple terms, wherever a significant difference is observed it indicates that the samples compared did not come from the same population.

On the other hand, a non-significant result does not necessarily indicate that the ethno-geographic background of a person is not an epidemiological determinant factor. Rather, it only means that there is no sufficient statistical evidence to conclude that the factors responsible for disease pathogenesis and distribution are not uniformly distributed.

The results also indicate that the spectrum and RFD of most of the diseases are not only significantly variable among the various compared PCs, but the variations are Dxgroup, age group, sex, and PC specific as well (Level-I). These observed variations of results are not unexpected since the epidemiological patterns (incidence/prevalence) of diseases are dependent on factors that affect the natural history of each disease, which includes the personal characteristics of those at risk such as:

• Age

- Different diseases arise at different stages of development in life (for example, there are early or late onset diseases depending on the anatomical and immunological states of a person)
- The period of time a person has lived determines the duration of exposure to causative environmental factors
- The prevalence (absence, presence, and distribution) of environmental agents can differ in time or from generation to generation
- Socio-economic activities, migratory tendencies, mating behaviors such as inter-ethnic marriages and the population dynamics of a region differ in time

• Sex

- Males and females differ in their genetic, physiological, and anatomical (physical) make up as well as their socio-economic activity that can differentially affect their susceptibility to different diseases

• Population Category (Local Ethno-Geographic Category)

- It comprises a combination of inherent factors (biological or genetic variations related to ethnic genealogy) and external conditions (variations related to social, cultural, religious, economic as well as environmental factors) closely associated with Population Category membership and that can all affect disease etiology and distribution.

Based on the total consistency values of significant differences scored by each reference PC for each Dxgroup, it is possible to conveniently classify and order the results as presented in Level-II, which depicts the consistency level or average occurrences of significant variations in the RFD of diseases among a pair of compared PC. These figures are obtained by summing up and averaging the number of times a significant difference is scored by a particular PC out of all age, sex, and PC stratified statistical comparisons made for a given Dxgroup. For example, for each Dxgroup, PC-1 is compared with 7 other PCs (PCs- 2, 3, 4, 23, 24, 34, and 234) each stratified into 3 age groups (Generations- 1, 2, and 3) and 2 sex groups (females and males) except Dxgrs-

13 which is analyzed without regard to sex (since it is impossible to know the sex of the spontaneous abortus and cases of female or male congenital malformations occur because the conditions were not sever enough to be spontaneously aborted earlier during pregnancy).

The advantage of the consistency level value emanates from the fact that its estimation takes account of all statistical analysis performed under each and every condition or epidemiological variables (under different sex, age, and ethno-geographic circumstances) and seeks for a pattern or consistency of results, in this case results indicating significant variations between a pair of PCs in their RFD of the diseases within a specific Dxgroup (Table-6).

Furthermore, one can justifiably infer that the higher the consistency level of any statistical outcome, the more unlikely it is to be due to some constant error or fallacy that somehow permeates every statistical inquiry undertaken.

Accordingly, by summarizing the age and sex specific statistical results into average consistency levels of significant variations, a consolidated picture of the total degree of similarity or difference (homogeneity/heterogeneity) between the various compared PCs can be obtained. As such, the average consistency level of significant variations can be indicative of not only the relative prevalence and distribution of the disease traits themselves, but also of the epidemiological determinant factors (variations in genetic and/or environmental factors) which affect their causal spectrum such as:

- The incidence/prevalence of specific pathogenic mutations in the genetic pool.
- Prevalence of genetically predisposing factors in the genetic mileu.
- Prevalence of agents causing mutations (mutagens, carcinogens, teratogens, haplogens, etc.).
- Socio-economic activity and status, cultural and religious tendencies (e.g., dietary preferences), and
- Mating patterns (or the degree of genetic admixture) between populations of the various Population Categories.

***Table- 6. Representation of a Stratified Statistical Analyses of the RFD of Disease Traits***

| *Compared PCs* | | *Females* | | | *Males* | | | *Consistency of Sig. Var.* |
|---|---|---|---|---|---|---|---|---|
| | | *Gen.-1* | *Gen.-2* | *Gen.-3* | *Gen.-1* | *Gen.-2* | *Gen.-3* | |
| *PC-1* | *PC-2* | *F-test Values:*<br>*Significant Variation ($p < 0.05$) = 1*<br>*Non-Significant variation ($p > 0.05$) = 0* | | | | | | |
| | *PC-3* | | | | | | | |
| | *PC-4* | | | | | | | |
| | *PC-23* | | | | | | | |
| | *PC-24* | | | | | | | |
| | *PC-34* | | | | | | | |
| | *PC-234* | | | | | | | |
| *Consistency of Sig. Var.* | | | | | | | | *Overall Consistency of Sig. Var.* |

The following Homogeneity/Heterogeneity Gradients, on a scale of '0' to '1', are discernible for each Dxgroup where '0' and '1' indicate total homogeneity and total heterogeneity, respectively (Fig. 3-13).

Fig. 3- Homogeneity/Heterogeneity Gradient: Dxgr-1,9,11

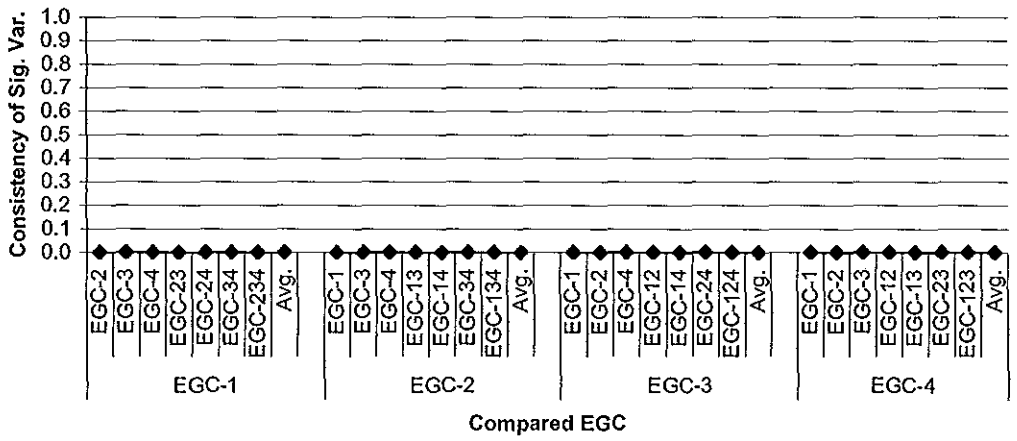



Fig. 4- Homogeneity/Heterogeneity Gradient: Dxgr-2

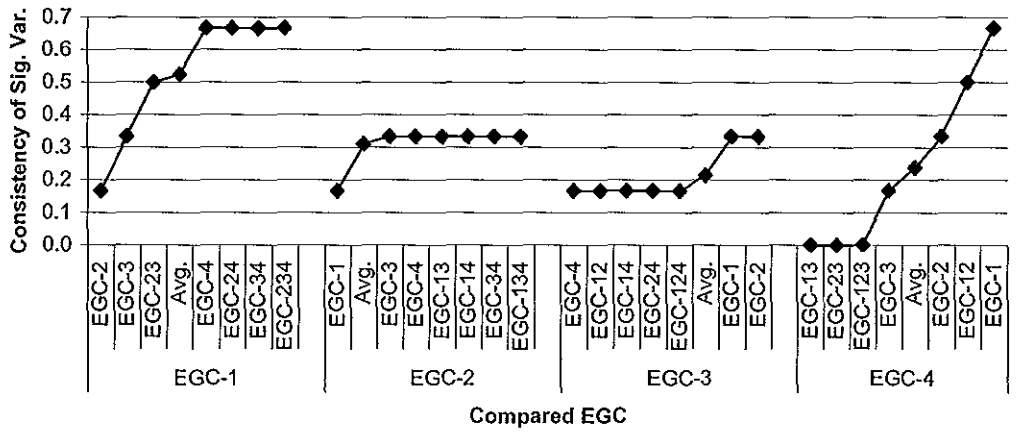



Fig. 5- Homogeneity/Heterogeneity Gradient: Dxgr-3

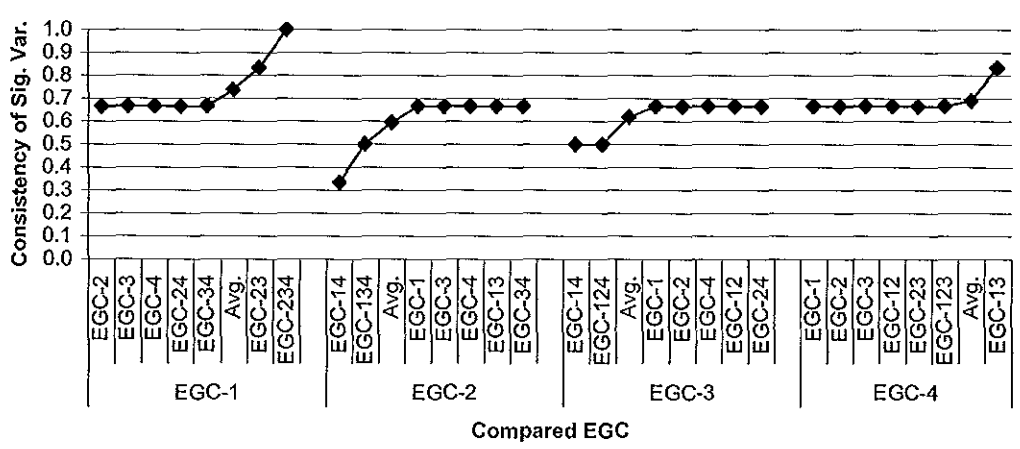


Fig. 6- Homogeneity/Heterogeneity Gradient: Dxgr-4

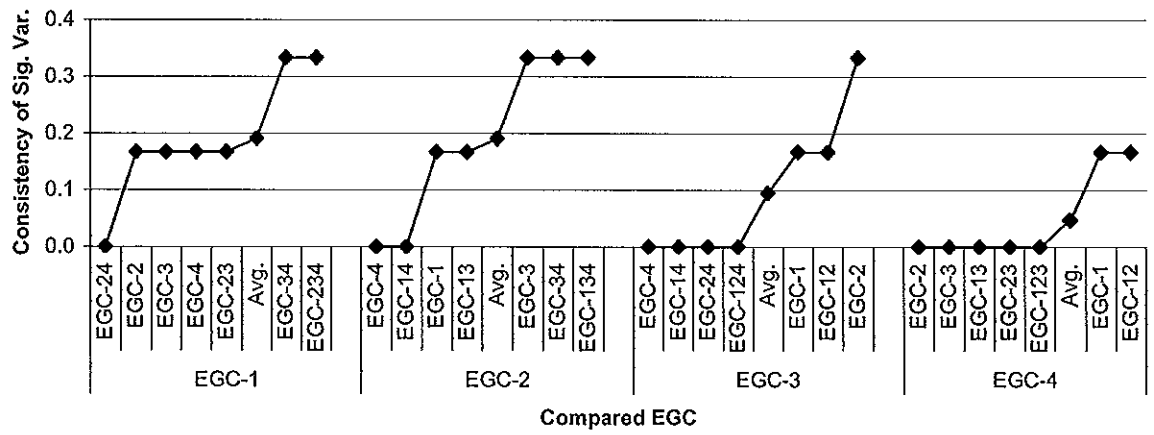



Fig. 7- Homogeneity/Heterogeneity Gradient: Dxgr-5

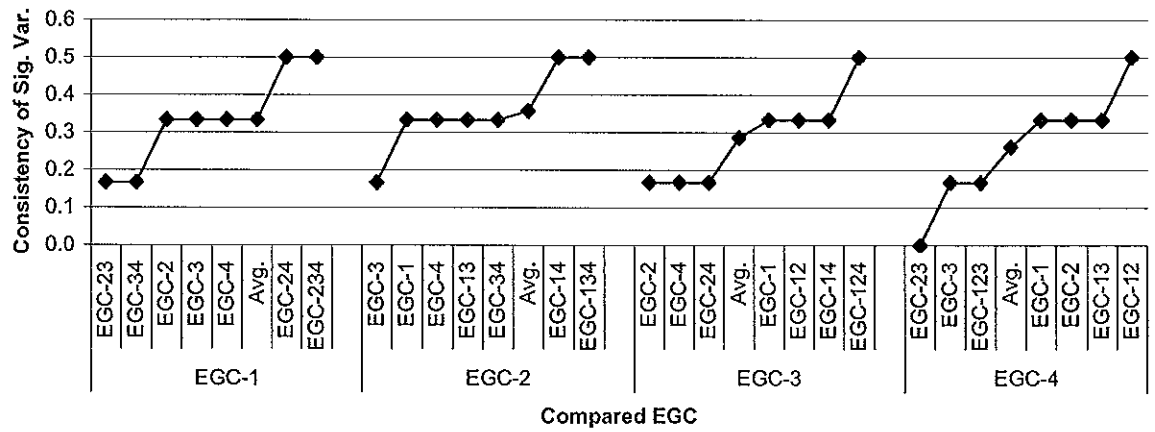



Fig. 8- Homogeneity/Heterogeneity Gradient: Dxgr-6

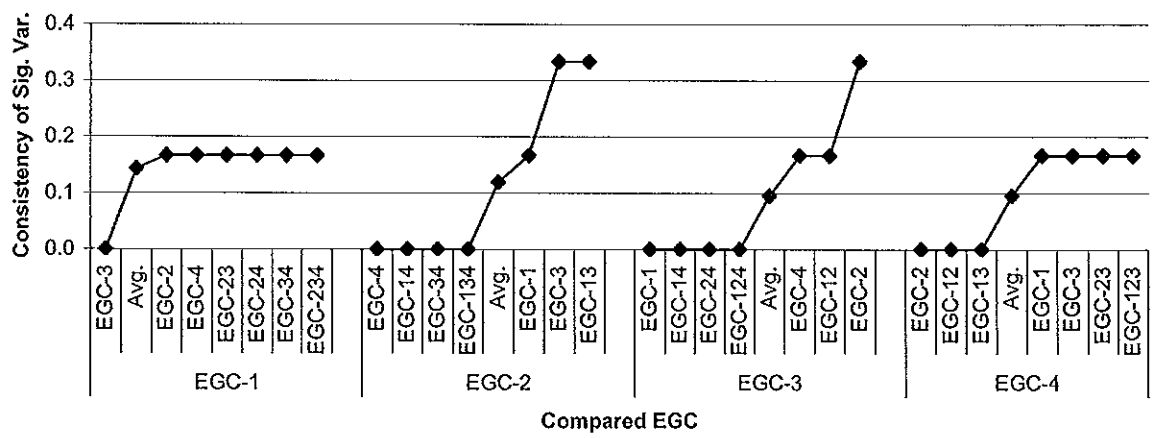


Fig. 9- Homogenity/Heterogenelty Gradient: Dxgr-7

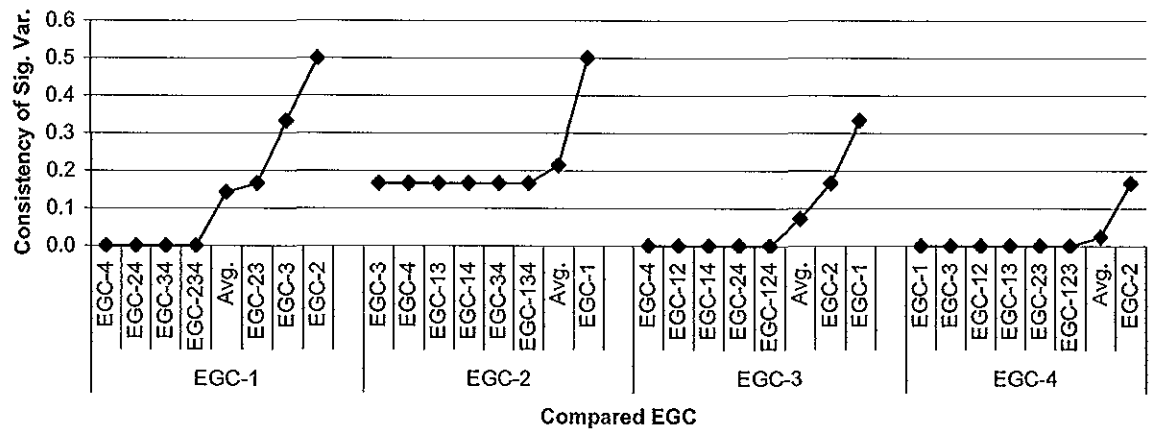



Fig. 10- Homogeneity/Heterogeneity Gradient: Dxgr-10

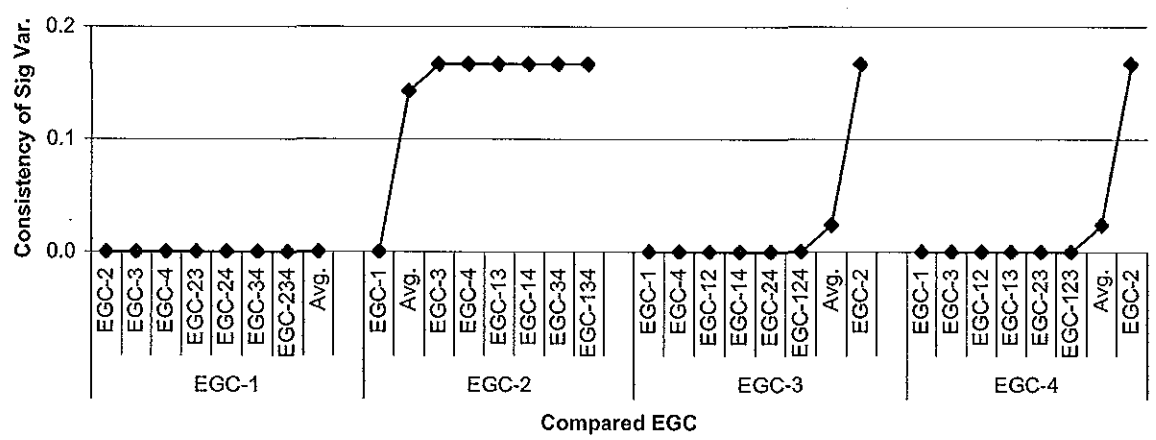



Fig. 11- Homogeneity/Heterogeneity Gradient: Dxgr-12

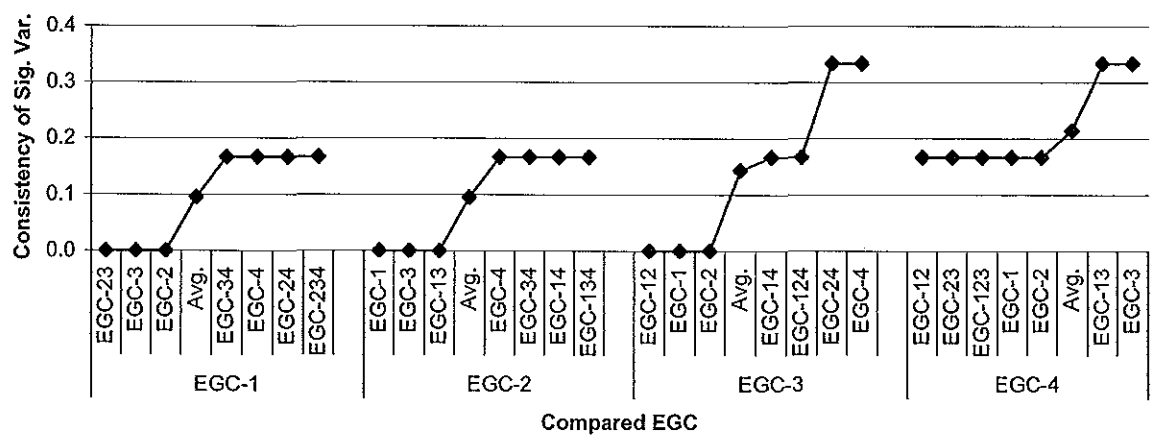


**Fig. 12- Homogeneity/Heterogeneity Gradient: Dxgr-13**

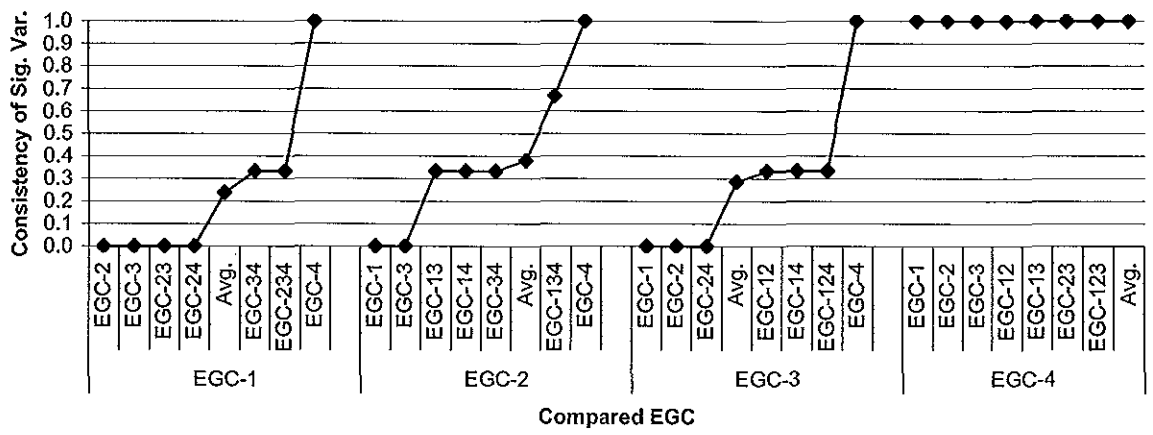
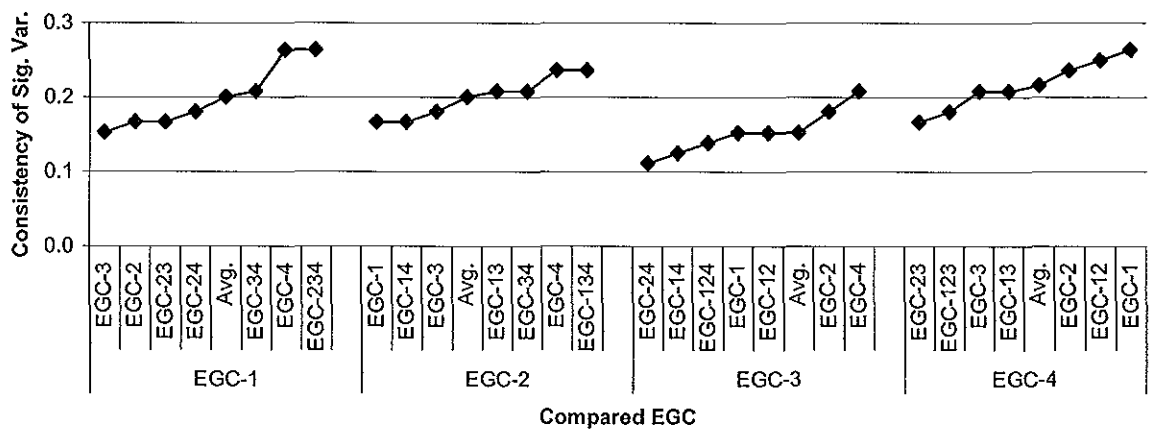



**Fig. 13- Overall Homogeneity/Heterogeneity Gradient: All Dxgrs**



There are two major features of the results presented above (Fig. 3-13):

- Not all compared PCs show significant variation in the RFD of all disease groups.
- The consistency level of significant variation in the RFD of a given disease group is not uniform among all compared PCs.
- Most of the homogeneity/heterogeneity gradient patterns are Dxgroup specific as well as being distinguishable between the major PCs.

Such differential occurrences of significant variations in the RFD of diseases among the compared PCs may be reflections of:

- The degree of homogeneity/heterogeneity of distribution or prevalence of the epidemiological risk factors that play a role in the causal spectrum of diseases.
- The homogeneity/heterogeneity of ethnic group composition or distribution.
- The level of historical inter-ethnic interactions or admixtures.
- The unique evolutionary history of populations with differing ethno-geographic origins with respect to the genetic determinants of disease epidemiology.

Therefore, the lower/higher the observed consistency level of significant variation in the RFD of a given disease group between any two compared PCs, the higher/lower the degree of similarity/dissimilarity between their respective populations.

Moreover, the homogeneity/heterogeneity gradient of significant variation, i.e., the range from the lowest to the highest consistency level of significant variation, is an indication of the extent of shared ethnic diversity, ways of life, and environmental circumstances between the populations making up the compared PCs.

The following is an outline of the salient features of the research results within the context of the overall degree of similarity/dissimilarity between the compared PCs, which can be ordered starting from the least heterogeneous (most homogenous) pairs of PCs to the most heterogeneous (least homogenous) pairs as shown below:

*PC-1 and PC-3 (15.3%) < PC-1 and PC-2 (16.7%) < PC-2 and PC-3 (18.1%) < PC-3 and PC-4 (20.8%) < PC-2 and PC-4 (23.6%) < PC-1 and PC-4 (26.4%).*

It is apparent that the population of PC-1 uniquely occupies the extremes of both sides of the overall homogeneity/heterogeneity gradient, i.e., PC-1 vs. PC-3 and PC-1 vs. PC-4 were found to be the least heterogeneous (most homogenous) and the most heterogeneous (lest homogenous) pairs in the study respectively. These particular results can be used to illustrate the effects of both genetic (e.g. ethnic composition) and environmental (e.g. geographic location) factors on disease epidemiology.

The relationship between PC-1 and PC-3 is consistent with the close relationship of the two populations. Particularly it may reflect the historical fact that the Harari and Oromo ethnic groups, which make up sizeable proportions of the two PCs respectively, have relatively been the closest interacting populations starting from the earliest foundation of Harar by virtue of their:

- spatially and temporally adjacent/overlapping settlement patterns
- religious affinity (Islamic)
- economic dependency

These conditions provide ample opportunities for gene-flow or exchange between the two populations thereby reducing overall genetic variation.

On the other extreme, the highest heterogeneity score found between PC-1 and PC-4 may be a reflection of the cumulative or additive effects of their numerous individual ethnic groups' differences, the two PCs representing the most ethnically diverse populations in the study. Such additive effects of variations due to each individual ethnic group member of the two populations, however small, can contribute to the observed relatively high level of total average consistency of significant variation in the RFD of diseases.

Moreover, it must be pointed out that, being 'outsiders', members of the population of PC-4 have the least chance of all to penetrate and intermingle with the people of Region-13 as a whole and particularly with its innermost inhabitants, PC-1, which is dominated by the relatively closed or conservative Hararis. It is also important to note that PC-1 and PC-4 are the most environmentally distant or varied categories in the study.

In general, the unique ethnic compositions and relationships between the populations of the various compared PCs, i.e., some close relationships and some distant, affect the average consistency level of significant variation by accentuating or modifying the heterogeneity gradient

range/stretch either on one or both sides or extremes of variation. For example, PC-1 exhibited the lowest total average consistency level of significant variation in the study with PC-3, which is the most ethnically homogenous category in Region-13 composed as it is of 95% Oromo people, i.e., the relative homogeneity of the population of PC-3 reduced the possible additive effect of ethnic diversity on the average consistency level of significant variation. On the other end, PC-1 and PC-4 exhibited the highest average consistency level of significant variation in the study. This can be attributed to the fact that both are highly ethnically diverse and thus have increased levels of total genetic variation. Specifically, first, PC-1 is a category composed of most of the different ethnic groups in Region -13, each with their own distinctive genetic-pool, and exceptional in that it contains virtually all members of a relatively inbreeding population, i.e., 97% of the Harari people; second, PC-4 is composed of migrant populations from all over Ethiopia probably representing many ethnic groups in Ethiopia. However, such individual or limited number of individuals representing each group is not a genomic representation.

Modification of the heterogeneity gradient range/stretch is the least noticeable in PC-2, which exhibited the smallest gradient range consistent with the fact that, as an urban center, it's population approximates a microcosm of life in Region-13.

The logic of the discussion presented above can also be applied to the rest of the PC pairs that exhibited intermediate consistency levels of significant variations. The main point, however, is that genetic and/or environmental variations have a bearing on disease epidemiology in such a way that different populations making up the various PCs are differentially predisposed (susceptible) or resistant to pathogenesis, which can also be interpreted as indicative of the fact that agents or factors that play a role in the causal spectrum of each of the various disease phenotypes (pathogenic genes and/or environmental elements) are different as well as being differentially distributed across the various PCs.

The results of the study can also be viewed and interpreted from the standpoint of the diseases themselves. It is possible that the higher the total average consistency level of significant differences observed, the higher the probability that either one or both of the epidemiological determinant factors (genetic and/or environmental elements) are involved or operating to a higher degree in disease pathogenesis as well as distribution.

Based on this assumption, and although the cut-points are arbitrary or subjective, it is possible to conveniently classify and order the results according to the total average (%) consistency levels of significant variations in the RFD of each Dxgroup scored by the major reference PCs (Table-24):

- Those disease groups that showed total homogeneity or no significant variation at all: 0% consistency level (Dxgroups-1, 9, and 11).
- Those disease groups that showed a low-level heterogeneity: 0% < 25% consistency of significant differences (Dxgroups-4, 6, 7, 10, and 12).
- Those disease groups that showed a medium-level heterogeneity: 25% < 50% consistency of significant differences (Dxgroups-13, 2, and 5).
- Those disease groups that showed a high-level heterogeneity: ≥ 50% consistency of significant differences (Dxgroup-3).

***Table-7. Overall Comparative Genetic-Epidemiological Health Profile of the Major PCs Based on the Percentage Consistency Levels of Significant Variations.***

| Disease Group | Consistency of Sig. Var. | | Order of Consistency Level |
|---|---|---|---|
| Dxgr-3 | *High Level Heterogeneity* | *66.1%* | *PC-1 (73.8%) > PC-4 (69.0%) > PC-3 (61.9%) > PC-2 (59.5%)* |
| Dxgr-13 | *Medium Level Heterogeneity* | *47.6%* | *PC-4 (100.0%) > PC-2 (38.1%) > PC-3 (28.6%) > PC-1 (23.8%)* |
| Dxgr-2 | | *32.2%* | *PC-1 (52.4%) > PC-2 (31.0%) > PC-4 (23.8%) > PC-3 (21.4%)* |
| Dxgr-5 | | *31.0%* | *PC-2 (35.7%) > PC-1 (33.3%) > PC-3 (28.6%) > PC-4 (26.2%)* |
| Dxgr-12 | *Low Level Heterogeneity* | *13.7%* | *PC-4 (21.4%) > PC-3 (14.3%) > PC-1 (9.5%) = PC-2 (9.5%)* |
| Dxgr-4 | | *13.1%* | *PC-1 (19.0%) = PC-2 (19.0%) > PC-3 (9.5%) > PC-4 (4.8%)* |
| Dxgr-6 | | *11.3%* | *PC-1 (14.3%) > PC-2 (11.9%) > PC-3 (9.5%) = PC-4 (9.5%)* |
| Dxgr-7 | | *11.3%* | *PC-2 (21.4%) > PC-1 (14.3%) > PC-3 (7.1%) > PC-4 (2.4%)* |
| Dxgr-10 | | *4.7%* | *PC-2 (14.3%) > PC-3 (2.4%) = PC-4 (2.4%) > PC-1 (0.0%)* |
| Dxgr-1 | *Total Homogeneity* | *0.0%* | *NO SIGNIFICANT VARIATION (0.0%)* |
| Dxgr-9 | | *0.0%* | |
| Dxgr-11 | | *0.0%* | |

It is clear that the spectrum and RFD of diseases in Dxgroups 1, 9, and 11 are the least affected by ethno-geographic epidemiological factors prevailing in Harar and its surroundings, which may be an indication that these factors are more or less uniformly distributed among all PCs. The RFD of disease conditions grouped in Dxgroups 3 and 13 are affected the most by ethno-

geographic background variations while the RFD of diseases in Dxgroups 4, 6, 7,10,12 and Dxgroups 2 and 5 are affected from low to medium levels, respectively.

In general, such variations could be associated with the natural history of each disease group in as much as the pathological processes that result in the onset or expression of each disease-state requires the fulfillment of its own specific combination of factors involved in its causal spectrum. This results in each disease group exhibiting its own 'clonal' epidemiological pattern in each PC, which, however, could be similar to other closely related PC's pattern.

A closer analysis of the results might reveal a more detailed relative genetic-epidemiological landscape in terms of both the similarities or differences of PCs and the natural history of diseases. However, the one major drawback that makes it difficult to do so is the constraint imposed by the nature of the available data, especially problems associated with the absence of individual inpatient attributes which made it impossible to ascertain the exact ethnic identity of cases beyond their geographic locations, i.e., addresses. The interpretation of the statistical results is therefore somewhat limited in such a way that one can not discriminate between or estimate the relative effects or contributions of genetic (ethnic) and environmental (geographic) risk factors on the spectrum and RFD of diseases. In other words, one can not be entirely sure to which of the two major epidemiological factors any of the significant variations found be attributed to. However, the analysis of the mere existence or absence of variation is justification enough for this kind of study since it can provide a firm ground for further better-designed investigations.

It must also be realized, on the other hand, that the aim of this study was not to investigate whether or not diseases are affected by either the genetic or environmental background of people (i.e., not to ask "Are genes and environmental elements risk factors?" although one hopes that it may eventually contribute more in this regard) since almost all human traits, upon closer inspection, are so affected.

On the contrary, it was precisely in anticipation of the aforementioned uncertainties in the interpretation of statistical results that the following strategies were incorporated in the design of the research:

1) Selection of disease conditions the etiology and prognosis of which have for long been described as being genetically influenced, i.e., disease phenotypes that are wholly or in part determined by the genetic make up of a person.

2) Identification of a study site where communities composed of people of different ethnic backgrounds live side by side under circumstances where geographic, and hence, environmental variations, are naturally reduced due to the small area coverage of the region.

3) Identification and delineation of communities, populations, or ethnic groups in the study site which posses properly definable geographical locations, i.e., Population categories. The construction of such PCs is based on by the recognition of the historical reality or tendency of human beings all over the world to establish settlements based on some common denominator of the inhabitants, such as shared ethnic identity, cultural value, etc.

It was in accordance with the above strategies that the diseases were selected, Harari Region was chosen as the study site, and the major PCs identified or constructed as the primary reference communities to be compared with one another, each with their own unique ethnic composition, inter-ethnic interactions, and geographic location.

Furthermore, while it is a world wide fact that human population settlement patterns closely follow and reflect the ethnic composition and overall social interactions of the inhabitants, for centuries this has been particularly true of the historic city of Djegol (PC-1) in Harar which is the homeland of the Harari and a special interest of this research.

Djegol was delineated as PC-1, one of the primary reference communities of this research, not only because it represents the only self-defined enclave of the Harari people, but also because it is unique among the PCs in that it contains virtually all members of a particular ethnic group (97% of all Hararis living in Region-13) wherein they probably constitute the largest single ethnic group (35%) while the rest of the population (65%) represents all other ethnic groups in Harar.

Based on these proportional figures alone one might expect PC-1 to be the least differing category of all since its population is an amalgam of all ethnic groups present in Region-13. However, high ethnic diversity in a given locality does not necessarily lead to homogenization through random inter-ethnic reproductive mating (panmictic) between the members. Rather, it is possible, as several studies citied in the literature review section indicate, that some ethnic group members or communities, especially the Harari ethnic group, may engage in preferential inter-ethnic reproductive relations to varying degrees or never at all. And if this hypothesis holds true, there is a chance that the implications or consequences of such reproductive preferences (reproductive isolation) could permeate in time down to the distinctive genetic pools (genetic variation) of the respective populations and eventually be reflected in their specific and/or overall differential health profiles (phenotypic variation).

For example, the hospital inpatient population of PC-1 stands out from the rest by demonstrating the highest consistency levels of statistically significant variations in the RFD of the following three Dxgroups:

* Dxgr-3: Diabetes (Diabetes Mellitus and Diabetes Insipidus) scoring a 73.8% average consistency level of significant variation.

* Dxgr-2: Neoplasms (both malignant and benign types) scoring a 52.4% average consistency level of significant variation.

* Dxgr-6: Diseases of the Nervous System and Sense Organs (Epilepsy, Glaucoma, and Cataract) scoring a 14.3% average consistency level of significant variation.

The observed differential health profiles also depend on several factors besides inter-ethnic reproductive behavior, related to the original or starting genetic pool (founder effect) of the various ethnic groups, population dynamics (immigration or migration), the role of environmental factors, etc. This research does not presume to account for all these factors but attempts only to make sense of what is called the 'natural experiment" in which all of these factors and others interact and are manifested through the spectrum and frequency distribution of diseases among hospital inpatient populations with differing ethno-geographic backgrounds.

*Table-8. Level of Homogeneity/Heterogeneity Gradient Between PC-1 and All Other PCs*

| Dxgroup | Average Homogeneity/Heterogeneity Gradient | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | .1 | .2 | .3 | .4 | .5 | .6 | .7 | .8 | .9 | 1 |
| 3 (73.8%) | | | | | | | | PC-2 PC-3 PC-4 | | | |
| | | | | | | | | PC-24 PC-34 | PC-23 | | |
| | | | | | | | | | | | PC-234 |
| 2 (52.4%) | | | PC-2 | PC-3 | | | | PC-4 | | | |
| | | | | | | PC-23 | | PC-24 PC-34 | | | |
| | | | | | | | | PC-234 | | | |
| 5 (33.3%) | | | | PC-2 PC-3 PC-4 | | | | | | | |
| | | | PC-23 PC-34 | | | PC-24 | | | | | |
| | | | | | | PC-234 | | | | | |
| 13 (28.6%) | PC-2 PC-3 | | | | | | | | | | PC-4 |
| | PC-23 PC-24 | | | PC-34 | | | | | | | |
| | | | | PC-234 | | | | | | | |
| 4 (19.0%) | | | PC-2 PC-3 PC-4 | | | | | | | | |
| | PC-24 | | PC-23 | PC-34 | | | | | | | |
| | | | | PC-234 | | | | | | | |
| 6 (14.3%) | PC-3 | | PC-2 PC-4 | | | | | | | | |
| | | | RGC-23 PC-24 PC-34 | | | | | | | | |
| | | | PC-234 | | | | | | | | |
| 7 (14.3%) | PC-4 | | | PC-3 | | PC-2 | | | | | |
| | PC-24 PC-34 | | PC-23 | | | | | | | | |
| | PC-234 | | | | | | | | | | |
| 12 (9.5%) | PC-2 PC-3 | | PC-4 | | | | | | | | |
| | PC-23 | | PC-24 PC-34 | | | | | | | | |
| | | | PC-234 | | | | | | | | |
| 1,9,10,11 (0.0%) | PC-2 PC-3 PC-4 | | | | | | | | | | |
| | PC-23 PC-24 PC-34 | | | | | | | | | | |
| | PC-234 | | | | | | | | | | |

Accordingly, it is within the above-mentioned contexts that the degrees of similarities or differences (homogeneity/heterogeneity gradients) between PC-1 and the various PCs should be

understood. Table-25 depicts homogeneity/heterogeneity gradients between PC-1 and the various PCs on a scale of '0' to '1' (rounded up to one decimal place), where '0' indicates complete heterogeneity and '1' indicates complete heterogeneity.

In general, the Homogeneity/Heterogeneity Gradient table presented above can be regarded as an indicator of both specific and overall genetic health profiles of the different populations in Region-13 relative to the population of Djegol (PC-1). By some stretch of the imagination, the table is also indicative of historical relationships, social interactions, migration, marriage (reproduction), shared elements of the environment, and micro-evolutionary trends of their respective populations.

### *Part-2. THE PHENOTYPIC AND ALLELIC FREQUENCIES OF THE ABO BLOOD GROUP*

The allelic and phenotypic frequency parameters of the ABO blood group data collected from informed volunteers of the Oromo, Amhara, and Harari ethnic group members living in Harar were estimated from each of the single entries as well as from the totals of different combinations of the entries (Table-26).

The estimated parameters were then statistically analyzed for:

- Phenotypic heterogeneity- calculated by the contingency Chi-square test for independence.
- Genetic equilibrium- calculated on the basis of the deviations between the phenotypic raw data and the expected frequencies based on the calculated gene frequencies.

Both tests were performed on the following combinations of ethnic groups (genetic-equilibrium tests were also carried out within each ethnic group):

- Oromo, Amhara, and Harari
- Oromo and Amhara
- Oromo and Harari
- Amhara and Harari

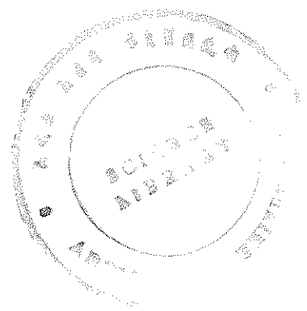


*Table- 9. Phenotypic and Allelic Frequencies of the ABO Locus*

| | Ethnic Groups | Number | % Phenotypic Frequencies | | | | Allelic Frequencies | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | O | A | B | AB | $I^A$ | $I^B$ | i |
| | Oromo | 123 | 51.220 | 23.577 | 18.699 | 6.504 | 0.16382 | 0.13515 | 0.71568 |
| | Amhara | 99 | 39.394 | 35.354 | 19.192 | 6.061 | 0.23459 | 0.13543 | 0.62765 |
| | Harari | 57 | 52.632 | 29.825 | 14.035 | 3.509 | 0.18350 | 0.09194 | 0.72548 |
| 1 | Tot. | 279 | 47.312 | 29.032 | 17.921 | 5.735 | 0.19233 | 0.12625 | 0.68784 |
| | Oromo | 123 | 51.220 | 23.577 | 18.699 | 6.504 | | | |
| | Amhara | 99 | 39.394 | 35.354 | 19.192 | 6.061 | | | |
| 2 | Tot. | 222 | 45.946 | 28.829 | 18.919 | 6.306 | 0.19461 | 0.13527 | 0.67783 |
| | Oromo | 123 | 51.220 | 23.577 | 18.699 | 6.504 | | | |
| | Harari | 57 | 52.632 | 29.825 | 14.035 | 3.509 | | | |
| 3 | Tot. | 180 | 51.667 | 25.556 | 17.222 | 5.556 | 0.12123 | 0.17001 | 0.71880 |
| | Amhara | 99 | 39.394 | 35.354 | 19.192 | 6.061 | | | |
| | Harari | 57 | 52.632 | 29.825 | 14.035 | 3.509 | | | |
| 4 | Tot. | 156 | 44.231 | 33.334 | 17.308 | 5.129 | 0.11929 | 0.21553 | 0.66506 |

The results of the statistical analyses show that (Table- 27):

A- *Phenotypic heterogeneity test*

The total chi-square for homogeneity among the entries in ethnic-group-combination 1 (Oromo, Amhara, and Harari) and 2 (Oromo and Amhara) were both non-significant (Chi-square=5.932 and 4.332 respectively; $p>0.05$).

[Note: The same test could not be performed for ethnic-group-combinations 3 and 4 because the sample size of the Harari ethnic group was too small to satisfy the chi-square test criteria.]

These non-significant results of the chi-square test for the independence of ABO-blood group (phenotype) distribution and ethnicity indicate that the ABO-blood types are distributed uniformly or proportionally across the compared ethnic groups, which are thus phenotypically homogenous.

B- *Genetic equilibrium test*

i) Intra-ethnic test

The chi-square test on the Oromo and Amhara ethnic group entries were non-significant (Chi-square=1.860 and 0.025, respectively; $p>0.05$).

[Note: The same test could not be performed on the Harari ethnic group because enough volunteers were not available].

The non-significant results indicate that there is random intra-ethnic mating within the Oromo and Amhara ethnic groups to the extent of reaching genetic equilibrium.

ii) Inter-ethnic test

The Chi-square test on the total data of ethnic-group-combination 1 (Oromo, Amhara, and Harari) and 2 (Oromo and Amhara) were non-significant (Chi-square=0.719 and 0.761 respectively; $p>0.05$) while the Chi-square test on the total data of ethnic-group-combination 3 (Oromo and Harari) and 4 (Amhara and Harari) were significant (Chi-square=11.849 and 35.221 respectively, $p<0.05$).

Non-significant results indicate that there is random inter-ethnic mating among the sampled populations to the extent of reaching genetic equilibrium while the significant results indicate to the contrary.

***Table-10. Phenotypic Heterogeneity and Genetic Equilibrium Test Results***

| | Ethnic Groups | Phenotypic Heterogeneity Test (Chi-square Values) | | | | | | Genetic Equilibrium Test (Chi-square Values) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | A | B | AB | O | Tot. | Sig. | A | B | AB | O | Tot. | Sig. |
| | Oromo | 1.261 | 0.042 | 0.127 | 0.397 | 1.827 | | 0.307 | 0.355 | 1.197 | 0.000 | 1.859 | NS |
| | Amhara | 1.360 | 0.089 | 0.018 | 1.312 | 2.779 | | 0.005 | 0.007 | 0.013 | 0.000 | 0.025 | NS |
| | Harari | 0.012 | 0.480 | 0.493 | 0.341 | 1.326 | | 0.001 | 0.001 | 0.003 | *0.000* | 0.005 | ? |
| 1 | Tot. | 2.633 | 0.611 | 0.638 | 2.050 | 5.932 | NS | 0.117 | 0.159 | 0.443 | 0.000 | 0.719 | NS |
| | Oromo | 1.177 | 0.003 | 0.008 | 0.744 | 1.932 | | | | | | | |
| | Amhara | 1.462 | 0.004 | 0.009 | 0.925 | 2.400 | | | | | | | |
| 2 | Tot. | 2.639 | 0.007 | 0.017 | 1.669 | 4.332 | NS | 0.132 | 0.172 | 0.457 | 0.000 | 0.761 | NS |
| | Oromo | 0.188 | 0.156 | 0.199 | 0.005 | 0.548 | | | | | | | |
| | Harari | 0.406 | 0.336 | *0.430* | 0.010 | 1.182 | | | | | | | |
| 3 | Tot. | 0.594 | 0.492 | 0.629 | 0.015 | 1.730 | ? | 4.222 | 6.73 | 0.897 | 0.000 | 11.849 | S |
| | Amhara | 0.121 | 0.200 | 0.168 | 0.524 | 1.013 | | | | | | | |
| | Harari | 0.211 | 0.353 | *0.291* | 0.909 | 1.764 | | | | | | | |
| 4 | Tot. | 0.332 | 0.553 | 0.459 | 1.433 | 2.777 | ? | 23.224 | 11.997 | 0.000 | 0.000 | 35.221 | S |

The non-significant results found in this research seem to fly in the face of common knowledge about the inter-ethnic reproductive interactions of the people of Harar in general, and the endogamous Harari ethnic group in particular. It is also in sharp contrast to the highly significant result found in another large-scale study conducted elsewhere in Ethiopia, Addis Ababa, where

the population may be presumed to be relatively more randomly mating, and yet was found to be far from genetic equilibrium (Seifu and Kifle, 1985).

It is possible that the non-significant results, particularly in ethnic-group-combination 1, may not necessarily indicate the existence of random mating between the sampled major ethnic groups in Harar since the same result can be obtained from pooled samples taken even from populations that are known to be reproductively isolated as long as each population is randomly mating within itself (at genetic equilibrium) and all have similar allelic frequencies of the ABO locus. In other words, the chi-square test for genetic equilibrium is more useful in disproving a hypothesis of random mating than otherwise.

The most probable explanation for the non-significant result in ethnic-group-combination 1 is a statistical bias towards the largest ethnic groups in the otherwise fundamentally heterogeneous population of Harari Region. Such bias can occur particularly when the data size is as small as this one (N = 279) and even more so when two of the largest ethnic groups in the sample (Oromo 40% and Amhara 32%) are each found to be in genetic equilibrium within themselves.

The later speculation is lent more credence by the findings of significant chi-square test values for genetic equilibrium on the total data of ethnic-group-combinations 3 (Oromo and Harari) and 4 (Amhara and Harari) (Chi-square=11.849 and 35.220, respectively; $p<0.05$). These results suggest that the total population of Harar is fundamentally genetically heterogeneous with a differential level of genetic relatedness among the various ethnic groups. For example, it is clear that the Harari ethnic group does not engage in reproductive mating with neither the Oromo nor the Amhara, at least not to the extent of reaching genetic equilibrium; it also shows that the Harari are genetically closer to the Oromo than to the Amhara. These results are possible consequences of the relative historical, cultural, and religious characteristics as well as migration and settelment patterns of the different ethnic groups inhabiting the eastern region of Ethiopia.

The findings of the present research that indicate genetic heterogeneity among some the population groups of Harari Region are consistent with another genetic-epidemiological study, which suggested the existence of genetic sub-structures in Ethiopian populations along ethnic lines (De Stefano *et al.*, 1998). The researchers, which sought to investigate and characterize the

genetic structure of the Oromo and Amhara people, the two main groups inhabiting not only Region-13 but the country as a whole, analyzed samples of these groups for three RFLPs of the COL1A2 gene (Type-I collagen). To better define the genetic relationship between the Oromo and Amhara, genetic distances between the two populations were estimated using the COL1A2 allele and haplotype frequencies, and the allele frequencies of 16 additional classical markers. The results of Chi-square analysis applied to the COL1A2 allele and haplotype frequencies were reported to show a small but statistically significant degree of differentiation/heterogeneity between the two Ethiopian populations, which the present result failed to show.

Generally, therefore, it can be concluded that the present statistical tests performed with regard to the polymorphic ABO locus indicate that while the population of Harar is probably phenotypically homogenous and some ethnic groups are in genetic equilibrium within themselves, the occurrence of random inter-ethnic reproductive admixture can not be definitely proved. Another informative aspect of the homogeneity test is that since the ABO blood group frequencies have been found by several previous studies to vary widely even within small geographic areas (whilst the frequencies of other blood groups vary only over much longer continental distances), which has been interpreted as indicating that the genes at the ABO-blood group locus are susceptible to variations in environmental agents (*Mourant, 1980*), the non-significant results of this research are additional indications that Harari Region, from which all the samples were collected, was probably a well chosen study site where environmental variations are reduced to a minimum.

## *V. CONCLUSIONS AND RECOMMENDATIONS*

Most of the accumulated knowledge about the genetic determination of various human traits of interest is the result of interdisciplinary investigations based on their variable manifestation, frequency, and distribution among different sections of human populations, i.e., genetic-epidemiology. The present study can be taken as a preliminary effort towards the genetic-epidemiological characterization of some segments of the Ethiopian population.

The first part of the present comparative genetic-epidemiological study, which is based on the relative frequency distribution (RFD) of some selected diseases, has shown that diseases which are genetically determined are not uncommon in Ethiopia with significantly variable incidence/prevalence that are age, sex, and ethno-geography specific. The consistency of significant variations across the stratified statistical comparisons exhibit distinctive homogeneity/heterogeneity gradients that can be interpreted as showing the degree of similarity/dissimilarity between the compared ethno-geographic population categories in terms of their genetic and phenotypic characteristics.

The other part of the current study, which dealt with the ABO blood group, indicated the existence of genetic heterogeneity, despite overall phenotypic homogeneity, among the population of Harari Region as evidenced by the differential levels of genetic equilibrium among the sampled ethnic groups. Observations of such variable levels of genetic interrelations are possible results of the historical practice of preferential or non-random inter-ethnic reproductive mating in the region.

The overall or conclusive picture that emerges from the present study is that of a gradient of phenotypic and genetic heterogeneity that may indicate the existence of sub-structures among the population of Harari Region of Ethiopia along ethno-geographic and/or ethnic lines.

The precise nature or reasons behind such genetic-epidemiological variations should be further investigated especially for those human traits that exhibited relatively high consistency levels of significant variations (for example, Diabetes).

The possible implications of such genetic-epidemiological variations in multi-ethnic Ethiopia, with various ethnic groups showing differential levels of genetic relatedness, should also be given serious attention and be assessed more precisely (for example, on large-scale, more polished or ascertainable data) than the present humble, preliminary attempt.

It can be said that there are very few previous genetic-epidemiological studies in Ethiopia, disease related or not, which may illustrate the lack of knowledge about the role that genetics plays in human life. Nevertheless, the mere fact that there are some 'studies', albeit almost entirely being concerned with presenting case reports of individual patients afflicted by long-established or classical genetic ailments and who present themselves for medical attention, can be regarded as hopeful indications that the 'lack' of knowledge is not despairingly 'complete'.

It is hoped that this work lifts the veil and more Ethiopian scholars will be drawn into the field of genetic-epidemiology and perform population based studies. Neither should anyone feel obliged to apologize for such studies, as one member of the medical profession did in his presentation in the Ethiopian Medical Journal on the rather high observed incidence of some congenital malformations among Ethiopian children admitted to surgical wards. Rather, one should realize and focus on the fact that genetic-epidemiology is rapidly becoming the way forward in the betterment of health care: it can provide scientific knowledge that enables us to take informed health care measures both in the prevention or treatment of diseases.

The role of Health Institutions in Ethiopia is crucial in this regard. They should initiate mechanisms or procedures that enable the development and application of genetic-epidemiological approaches to disease prevention and treatment. These objectives can be achieved only when appropriate patients' data are recorded in a standardized manner, maintained, and made available in formats amenable for genetic-epidemiological surveys. This is a prerequisite, especially in a country such as ours where it can be very difficult to carry out individual or population-wide genetic screenings and the only plausible alternative is to rely on the 'natural experiment', i.e., properly classified and recorded medical histories of patients presenting themselves to health centers.

Such standardized procedures would help to minimize the problems encountered in the current and other genetic-epidemiological investigations associated with unsuitable of medical history record formats such as:

- Variation in diagnostic and/or classification criteria.
- Absence of records of individual patient's attributes, especially the age and ethnicity of patients.
- Inconsistency in medical data presentation.
- Difficulties in ascertainment of cases.
- Etc.

Finally, education about human genetics for Ethiopian health care professionals and the public at large should also be given more than cursory attention. General practitioners will need to incorporate genetic knowledge into clinical practice if patients are to benefit from scientific advances. They will also require training to deliver proper genetic counseling to patients and those at risk.

Ethiopia, as a member state, should take advantage of its partnerships with the works of WHO in the field of human genetics which is supported by a wide network of international organizations, non-governmental collaborating centers, and research programmes. A good example of such collaboration between countries is the Human Genome Project, a global initiative to map and sequence the entire human genome. The project's most important outcome will be increased understanding of the ways in which genes interact with each other and with the environment to generate normal (and pathological) structure and function. Current trends in genetic approaches to disease prevention and control are strongly linked with the progress of this project.

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## *VII. APPENDIX*

### *Appendix-1: Disease Synopses*

The following are generalized descriptions of the disease traits surveyed in this research. The notes were taken from several resources listed in the Reference section (earmarked '*').

*Neoplasm (044.0-060.4)*

*Neoplasms (cancers or tumors, benign or malignant) are diseases in which cells continually undergo uncontrolled growth and division eventually interfering with one or more vital biological functions. There are neoplasms of various kinds, their classification depending on their site of origin, cell type, morphology, differentiation metastatic ability, and on whether they are benign or malignant, unilateral or bilateral, location, etc.*

*Anything that can interfere with the normal cell growth and division may lead to neoplasm of one kind or another. The causal spectrum of neoplasm incorporates both environmental and genetic factors to varying degrees. The consolidated data on the causes of neoplasm have led to a model, which explains certain observations of the involvement of genetic mechanisms that may be heritable in the development of neoplasia. According to this model (The Kuddson Model), cancer is proposed to arise as a two-step process each requiring a mutation. The first mutation may be either germinal (inherited) or somatic (acquired). The second mutation is almost always somatic. The model explains observations that Mendelian tumors [for instance, Retinoblastoma, an autosomal dominant trait, del (13) (q14)] not only are usually bilateral but also develop earlier in life than do non-Mendelian tumors. All cells in individuals with a gene for Mendelian tumors are assumed to have accomplished step one as a result of being born with the mutant gene(s). Conversely, a person born without the germinal mutation could develop a histologically similar tumor only as a result of oncogenic agents sequentially producing two somatic mutations. Naturally, this latter circumstance would arise less often because not a single event but two independent mutational events are necessary.*

*Although neoplasms have traditionally been thought of as qualitative (presence/ absence) traits, their complexity has all the characteristics that typify polygenic/miltifactorial traits. This is because the genes involved in neoplasm are those involved in the machinery of the cell-cycle,*

*and if abnormally expressed either lead to decreased cell-growth control, altered cellular structures, biochemistry, or cellular interactions. These genes include oncogens, suppressor genes, hormone and growth-factor genes and their receptor genes, as well as genes for intracellular message transduction and nuclear-DNA binding proteins.*

*The genetic basis and heritability potential of neoplasms is supported by several genetic-epidemiological studies that reveal not all individuals families, races or ethnic groups are equally vulnerable or predisposed to develop the various neoplasms. Although environmental risk factors (carcinogens, both natural and man-made, and some oncogens or viruses) can be involved in the causation of neoplasms, there are evidences that show such factors may select among a much higher prevalence of susceptible individuals who are vulnerable to them. In other words, there is a distribution of susceptibility genotypes in populations. Furthermore, there are strong evidences that chromosomal changes are etiologically important in the genesis of neoplasia. For instance, first several congenital disorders are associated with different cancers, second, various chromosomal aberrations occur associated with increased risk of neoplasia, third, specific chromosomal regions appear preferentially altered in specific neoplasms.*

*Overall, the current opinion is that some neoplasms, or susceptibility to them, are inherited according to specific genetic principles, some are caused by the interplay of specific genes and environmental agents, and it is possible to identify specific chromosomes and/or genes involved in the transformation of human cells into cancer cells. There are now increasing long lists of neoplasms categorized according to their transmission patterns either as autosomal dominant recessive, x-linked, sex-linked, or polygenic/ multifactiorial, and specific recurrence risks worked out based on diagnosis, family history, ethnicity, and exposure to carcinogens, as well as age, sex, socioeconomic status, or occupation.*

*To conclude, although neoplasms are genetic diseases, selection may have prevented them from being directly heritable. Neoplasms also demonstrate the important effects that somatic mutations can have in that they reflect 'evolution in a microcosm', occurring among our own cells, during our own life time rather than among the individuals in a population over evolutionary time. Neoplasm age-patterns also reflect the time required for somatic mutations to produce their complex cellular phenotypes.*

*Diabetes Mellitus (063.1)*

*Diabetes Mellitus (DM) is a chemical disorder characterized by hyperglycemia, and as such, it is very likely that under the diagnosis of DM, disorders of different pathological physiology are included (heterogeneity). Most classifications distinguish between at least three types: - Juvenile Onset, Insulin- Dependent (IDDM), or Type-I DM; Maturity Onset, non-insulin-dependent, or Type-II DM (NIDDM); and, Maturity Onset Diabetes of Youth (MODY). Others classify DM broadly into two categories: - IDDM and NIDDM.*

*DM pathogenesis involves many possible genetic defects such as defective regulatory mechanisms for insulin secretion; decreased out-put of biologically normal insulin either due to defective synthesis, storage or release; abnormal synthesis of molecular insulin; abnormalities in insulin transport; increased destruction of circulating insulin; and defective cellular response to the effect of insulin, either due to an intrinsic end-organ resistance or a modification of the insulin effect by circulating antagonists Obviously, inheritance is not involved when diabetes arises from other acquired disease processes resulting in the destruction of the β-cells of the pancreas, pancreatitis, pancreactomy, etc.*

*There has for long been a general agreement a that genetic factors are important in the etiology of DM. Familial aggregations in the form of higher prevalence of DM among relatives of patients than in the relatives of healthy control subjects, have been significantly observed irrespective of age of onset or severity of the condition. The hereditary nature of DM is also indicated by the higher concordance among MZ twins than among DZ twins. The age-adjusted concordance among MZ twins is nearly 100% and the disease tends to develop within similar ages. Another evidence of the pivotal role of genetic factors is that DM is one of several features of some 30 different genetic malformations, suggesting that DM can result from gene mutations at different loci. Variation in susceptibility and expression between different ethnic groups and the relative uniformity of the disease pattern (age- and sex- specific incidences) among specific populations are phenomena that have not been well explained on the basis of environmental differences alone and suggest that DM may also be a genetically clonal disease.*

*However, there is no unanimous agreement about the mode of DM inheritance. Pedigrees suggesting x-linked recessive to autosomal dominant have been reported. The frequent tendency for DM to skip generations, nevertheless, has led to the prevailing opinion that DM may be inherited as autosomal recessive trait with clinical expression occuring in the homozygous state at anytime during life. Another tendency of DM, that of females being more often affected than males, though inconsistent with simple autosomal recessive inheritance, could be explained if variable penterance is assumed. On the other hand, some investigators believe that the evidence available is compatible with multifactiorial/polygenic inheritance, and genetic heterogeneity is suggested to explain the clinical variability of patients with DM.*

*Type-I and Type-II DM are suggested to be separate conditions, however, in that environmental factors appear far more significant in the former than the latter. MZ twin concordance is less in Type-I than Type-II DM, and certain HLA's are observed to be more associated with type I DM than type- II DM. The likelihood that offerings of parents with Type-I and Type-II DM will be similarly affected is also different.*

*Overall, although there is a general consensus that at least the susceptibility to develop DM is inherited, the clinical expression of the disorder seems to depend on other associated genetic factors (eg. variable penetrance and heterogeneity), compensatory mechanisms, and environmental factors (phenotype amplification). Age, sex, diet. Infection, obesity, excessive secretion of growth hormones, gluccorticoids, aldosterone catecholamines, glucagon, and pregnancy are well-known diabetogenic factors.*

*Diabetes Insipidus*

*Diabetes Insipidus (DI) is a clinical syndrome characterized by the inability of the patient of form concentrated urine with consequent polyuria, increased thrist, polydipsia, and in the absence of a sufficient intake of water, dehydration and increased osmolality of the body fluids. The disorder may arise from an absence or deficiency of vasopressin formation or release from the hypothalmic-neuro-hypophyseal system, which is piteressin-sensitive (Pituitary-type DI) or from the lack of response to pitressin by the renal tubes (Nephrogenic type DI). The prtressin-sensitive Pituitary-type DI can be idiopathic, familial, or secondary to a variety of disorders.*

*Pitressin-resistant nephrogenic-type DI can occur as an x-linked inherited disorder and may be associated with various other renal diseases. Familial vasopressin deficient DI has been reported to be inherited in an autosomal dominant and x-linked manner.*

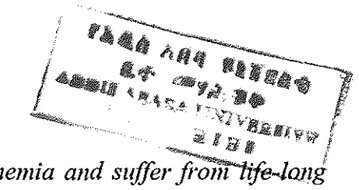
*Pernicious Anemia (065.1)*

*There are several hereditary anemias broadly classified as those due to decreased erythrocyte production and those due to increased erythrocyte destruction. Pernicious anemia (PA) belongs to the former. PA is primarily a gastric disease characterized by atrophy of the mucosa and reduced secretion of the intrinsic-factor (IF) needed for absorption of alimentary vitamin B12, which is necessary for normal hematopoiesis. Patients have antibodies against gastric parietal cells and against the IF itself.*

*The hereditary basis of PA is indicated by the documentation of familial aggregations, the concordant occurrence of PA in MZ twins, and the demonstration of decreased absorption of vitamin B-12 even in the asymptomatic relatives of PA patients. The disease occurs most commonly in adults and is rare in infancy and childhood which is attributed to the homozygous inheritance of the gene regulating IF secretion, and there has been evidence of consanguinity consistent with this hypothesis in cases of juvenile PA. Antibodies against IF and parietal cells which have been found in the serum of patients also suggest a genetically determined auto-immune disorder. PA is more common in whites than non-whites but has been described in all races. There is a significant association with blood group-A, and an increased incidence of HLA-B7 in PA patients and their relatives, which is taken as an evidence of gene-linkage.*

*Sickle-Cell Anemia (065.3)*

*Sickle-cell Anemia is one of the best understood hemoglobinopathies caused by a mutation at the hemoglobin coding locus resulting in the production of hemoglobin-s a state commonly referred to as sickle-cell (Hb-S) trait, which could exist both in the hetero- and homo-zygous states. The constituents of hemoglobin are coded for by the $\alpha$- globin gene cluster on chromosome-11 and the $\beta$- globin gene cluster on chromosome-16. Hemoglobin made dysfunctional by mutations lead to various forms of anemia. Usage varies, but 'Thalassemia' is the commonly used term for mutations that alter the functional efficiency of the gene product.*



*Patients homozygous for Hb-s gene or allele have sickle-cell anemia and suffer from life-long complications with many cardio-vascular manifestations, in part due to the markedly shortened life span of their red blood cells that may lead to death. In the heterozygous sickle-cell states, clumping of 'sickled' erythrocytes can result in similar but less severe complications besides the anemic manifestations. There are several variants of sickle-cell gene in different populations, i.e., it can be clonal in origin. DNA analysis for the sickle gene is possible. Thalassemia mutations are also important because such the mutation confer resistance to various forms of malaria across regions of the world where malaria is endemic.*

*Epilepsy (073)*

*Epilepsy is one of those health disorders for which it has been difficult to draw a universally accepted classification due to the existence of several types of seizures (which is one of its major symptoms), their often obscure etiology, and the negative social connotations of such disorders, and hence, the complications in clinical research and evaluation of their genetic aspects. There are different epileptic seizures like Centro-cephalic epilepsy, photically induced epilepsy, reading epilepsy, and those induced by the 'startle phenomena', in all of which cases familial aggregations have been reported with a high risk of developing epilepsy in the close relatives of probands. Epileptic seizures could also be manifestations of a more general inherited metabolic disorder with an overall reduced threshold, or just unusual responses to environmental factors and trauma. However, although patients are usually reassured during counseling that epileptic seizures are not hereditary, individuals are found with unequivocal family history without other associated health conditions.*

*Cataract (075)*

*Cataract is a disorder affecting vision, one of the hundreds of inheritable diseases of the local ocular areas as well as those affecting vision by distorting the general body condition. There are several cataract types and sub-types such as congenital, juvenile, presenile, senile, mixed forms, etc. Cataracts are also found in many syndromes that present as mental retardation and those which appear as isolated genetic disturbances even in cases where environmental causes are emphasized. However, although anyone may develop senile cataract if one lives long*

*enough, individuals with a family history of cataract develop senile cataract earlier (pre-senile cataract, which might be a case of anticipation) and more consistently, than individuals form unaffected background and, moreover, develop exactly the same type of cataract. Different inheritance patterns of cataract have been proposed with variable penetrance.*

*Glaucoma (076)*

*Glaucoma or hydrophtalmia is a malformation of the eyeball accompanied to differing degrees, by an increase in ocular tension and in the dimensions of the eye. There are different types of Glaucoma such as congenital or juvenile, open or closed angle, etc. Several studies have established the hereditary nature of glaucoma with high degrees of twin concordance and different members of the same sib-ship showing symptoms of the disease at the same age, with fairly consistent clinical pictures, the same evolution or prognosis, the same errors of refraction, and the same response to treatment. Transmission is mainly through recessive heredity. The genetic nature of glaucoma does not, however, rule out environmental influences, particularly in closed-angle glaucoma.*

*Diseases of the Circulatory System (080, 081, 083, 084)*

*Except for a few uncommon genetic syndromes, diseases of the circulatory system, especially of the cardiovascular system, do not appear to be monogenic. The role of heredity in such systemic disorders is difficult to determine owing to the high frequency or common occurrence of the disorder in some populations, particularly in the western world, due to the numerous factors which may be involved in the disease etiology (cholesterol and triglyceride levels, clotting factors, anatomical defects, vascular pressure, sex, age, body weight, diet, emotional stress, exercise habits, occupation, smoking habits, etc). The results of family and population studies, which have been the main genetic venues employed, when coupled with other approaches (e.g., pharmacogenetic and statistical) have provided insights into the genetics of diseases of the circulatory system proving the influence of heredity indisputable Much of the information regarding to the underlying genetic basis of circulatory diseases, especially that of coronary artery diseases (080, 081, 083, 084), comes from the study of the involvement of lipoproteins which carry cholesterol in the blood, and the lipid system in general.*

*The lipid system is strongly associated with cardiovascular diseases, mainly heart attacks, atherosclerosis and other conditions associated with arterial function. For instance circulatory lipids can be deposited as fatty atherosclerotic plaque on the interior of the arteries eventually closing the arteries and/or leading to roughened surfaces or other characteristics that can trigger blood-clotting reactions that clog blood vessels. The steps in the lipid physiology are dependent on gene products such as the apolipoproteins, enzymes, and cell surface receptors involved in the lipid system, which is interactive and homeostatic with several feedback loops. Allelic variants of the apolipoproteins that transport lipids exist and affect the level, and other functional features, of the lipoproteins.*

*Coronary heart diseases (CHD) have been shown to aggregate in families although the CHD risks do not segregate in a neat Mendelian way except for the severe, low-density-lipoprotein receptor (LDL- receptor) mutations in Familial Hypercholesterolemia (FH). The LDL- receptor locus defects cause FH, a codominant disorder leading to early heart attacks and other associated problems which are gene dose dependent, i.e , can be heterozygous or homozygous states. However, there is considerable variation as cholesterol levels are affected by other loci as well. Phenotype amplification by environmental risk factors also exists relative to the primary effects of the loci, i.e., polygenic/multifactorial causation.*

*The study of hypertension has also provided valuable information into the nature of the circulatory system and its disorders. Although the investigation of hypertension is subject to difficulties arising from the variable nature of blood pressure measurements, most studies have documented familial aggregations. For instance, it has been demonstrated that by 2 years of age there is already a significant familial correlation for blood pressure. Twin studies further support the role of genetic factors on arterial blood pressure and hypertension with MZ twins showing higher correlation than other relatives. Approximate estimates of heritability attribute 60% of blood-pressure variability to genetic components. There is no unanimity concerning the mode (s) of inheritance, however. Perhaps in some populations, a major-gene effect is principally responsible for hypertension, whereas in others polygenic/multifactorial causes are responsible. More likely hypertension is a genetically heterogeneous quantitative trait.*

*Diseases of the Digestive System (102,103.1, 103.2, 103.3, 104.3, 105.1, 106.1)*

*The analysis of the genetic aspects of diseases of the digestive or gastrointestinal (GI) system exemplify the difficulties inherent in disentangling the various environmental influences in disease etiology from the genetic causal spectrum particularly in common diseases the Genetic component of Gl diseases have been sought in familial aggregations, HLA or immunologic associations, ethnic variations or associations with other well established genetic or heritable disorders.*

*Appendictis (102), Abdominal Hernia (103.1, 103.2,) Intussuception (103.3)*

*Appendictis, particularly acute appendictis, has been shwn to demonstrate definite associations with HLA-B12, while not all Gl diseases are associated with HLA. Abdominal Hernia is included here, not because there has been found any particular reference in the literature to the genetic aspect of Adbominal Hernia perse, rather because other hernias such as, Diaphramatic Hernia, Inguinal Hernia, and Umbilical Hernia have been described as having genetic components in their causal spectrum and categorized along with polygenic/multifactorial disorders. The same general comments apply to Intussuception, which is also grouped under the polygenic/ multifactorial malformations.*

*Cirrhosis of Liver (105.1)*

*There are several genetically determined disorders with associated liver disease. Cirrhosis of liver has been reported as familial where by inheritance affects the ability of the liver to withstand exogenous insults such as exposure to hepatotoxins and alcohol. It is well known that the liver is main organ in drug metabolism or disposition and inherited alterations may involve enzymes that participate in such processes. Several of these enzymes are also hepatic enzymes that are genetically controlled.*

*Cholelithiasis and Cholelcystitis (106.1)*

*Cholelithiasis or gallstones are concentrations or depositions of insoluble material from bile in the biliary tract and mostly found in the gallbladder. The study of cholelithiasis has taken advantage of the availability of relatively homogenous populations with very high or very low frequencies of gallstone diseases, i.e., marked racial differences exist in the analysis of*

*geographical pathology which have not been well explained on the basis of environmental differences alone. Famillial aggregations have also been found, not only in terms of susceptibility to produce concentrated bile (lithogenicity), but also in terms of the gallstone composition itself although the preponderance is towards cholestrole. The predisposition to gallstone formation is generally considered polygenic/ multifactorial.*

*Diseases of the Geneito-Urinary System*

*Acute Nephritis (108), Chronic, Other and Unspecified Nephritis (109)*

*That renal disorders, functional or anatomical, may be hereditary has been known for long. In great measure, this is so because abnormalities of renal function can be studied by quantitative techniques. The hereditary nature of some of these conditions, especially, the functional abnormalities of the kidney, was pointed out when they were included (eg. Cystinuria) in the initial list of "Inborn Errors of Metabolism". Several of the hereditary renal diseases are reported to be x-linked, exhibit increased severity in males, and variable expression in females, which are the expected clinical variations for an x-linked trait. Renal disorders also show syndrome associations with ear and eye disorders, which, together, comprise almost half the diseases of man that have been accepted as x-linked. Hereditary chronic nephritis has been reported as a possible partial x-linked or a preferentially segregating trait. Autosomal renal diseases also occur such as the hereditary Glomerulonephritis which is an autosomal dominant trait with variable penetrance. Other factors may exacerbate nephritis such as pregnancy which may cause development of either preeclampsia or the nephritic syndrome.*

*Diseases Associated with Pregnancy, Childbirth, and the Puerperium (115-120.5)*

*Abortion without Mention of Sepsis or Toxemia (118)*

*That not all conceptions result in a live born infant is well known. Among conceptions that are clinically recognized, 12% to 15% are lost during the first trimester. Additional losses occur later in pregnancy. There are many potential explanations for both preclinical and clinically recognized spontaneous abortions, but the one proven explanation is a genetic abnormality in early embryos, which can cause death and resorbption or abortion of the embryo before term.*

*Obstetricians inform couples experiencing spontaneous abortion concerning the frequency of fetal wastage (12% to 15% of clinically recognized pregnancies), its usual causes (at least 50% cytogenic), and provide estimates of recurrence risks. The cytogenetic abnormalities include polyploidy, particularly autosomal trisomies, which are the largest (53%) single-class of chromosomal complements in cytogenetically abnormal spontaneous abortions; monosomy-x which is the single most common chromosomal abnormality in spontaneous abortions (20% to 25%), structural chromosomal rearrangement (1-5%) mostbeing translocations (60% reciprocal and 40% Robertsonian), and Neural Tube defects and other polygenic/multifactorial traits. Maternal age is also positively correlated with spontaneous abortion rates.*

*In general, the more altered the genome of a zygote, the more severe will the normal progress of its development be disrupted, and the greater its risk of death at any age. Therefore, those carrying the most altered chromosomal complements are the ones that die sooner following fertilization as is shown by 50% to 60% of first trimester spontaneous abortions and 5% of still-births associated with gross chromosomal abnormalities. Moreover, frequencies of autosomal aberrations detected by amniocentesis are even higher for any given maternal age group than the frequencies found in newborns. This difference results from many of these abnormal fetuses being lost as late abortions or stillbirths. Embryo and fetal death can be thought of as one of the stark realities of natural selection, a process by which the errors in gamete and zygote formation are eliminated.*

*Diseases of Skin, Cellular Tissue, Bones, and Organs of Movement*

*Arthritis and Spondylitis (122)*

*Arthritis is classified as an autoimmune diseases in which there is evidence of immunologcal hyperactivity directed against the individual's own body constituents. There is an increase of upto six-fold in the incidence of arthritis in relative of patients with this diseases as compared to control series, although it is estimated that only 50% of patients who are genetically predisposed actually develop the disease.*

*Spondylitis is an inflammatory diseases of joints and connective tissue, It is one of the strongest HLA associated diseases world-wide; for instance, over 90% of patients with Ankilosing*

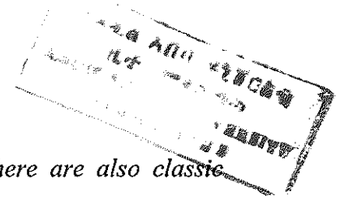
*Spondylitis are HLA-B27$^{+}$, compared with only 6% to 8% of the normal population. It is an autosomal dominant trait, albeit influenced by other factors.*

*Familial clustering of Rheumatoid Arthritis and Ankylosing Spondylitis exists, with the frequency of the diseases in relatives of probands reported to be much greater than in suitable controls.*

*Congenital Malformations (127-129)*

*Approximately 1 of every 160 live born infant has been reported to have a demonstrable chromosomal abnormality at least half of which leads to conditions (malformations or anomalies) requiring medical intervention. The frequency of congenital malformations would have been greater if any of the abnormal fetuses were not lost as late abortions or stillbirths. Congenital malformations, most of which are characterized by deficiencies of the genetic material include, mental retardation, intrauterine and/or postnatal growth retardations, and anomalies of many organ systems, such as the cranio-facial, skeletal, cardiac, and genitourinary systems. In particular, abnormal facies, low set or malformed ears, and certain digital anomalies, suggest autosomal imbalance, even more so if they are part of a spectrum of anomalies. It should be pointed out that any chromosomal aberration sufficiently gross to be, for example, visible with the light microscope, most probably contains a good deal of genetic material and therefore would be expected to have a profound effect upon the developmental pattern of its bearer. Recurrence risks depend on whether the chromosomal aberration is numerical or structural, on factors that increase the risk of non-disjunction, parental mosaicism, or aneuploidy, a previous trisomic offspring, and increased parental age. Sporadic (de novo) structural rearrangements are believed to have a low risk of recurrence. If a familial structural rearrangement exists, however, the risk of having offspring with chromosomal imbalance is increased the magnitude varying according to the specific rearrangement.*

*The most common polygenic/multifactorial birth defects encountered by obstetricians and gynecologists are the Neural Tube Defects (NTD'S) Hydrocephaly, Facial Clefts (cleft-lip with or without cleft-palate), cardiac anomalies, tracheoesophageal and other fistulas, Intussusceptions, various hernias, uretral and bladder anomalies, imperforate anus,*



*cryptochidism, hip dislocation, and limb reduction defects. However, there are also classic Mendelian congenital malformations too many to list here.*

***Apendix-2: Relative Frequency Distributions***

***The following tables show the absolute count and relative frequency of diseases under different categories.***

***Table-1. Total Count and Relative Frequency Distributions (%) of Diseases in Dxtype-1***

| *Hiwot Fana and Misrak Arbegnoch Hospitals* | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Dxtype-1* | | *Generation* | | | | | | | | | | | |
| | | *1* | | | | *2* | | | | *3* | | | |
| | | *PC* | | | | *PC* | | | | *PC* | | | |
| *Dxgr* | *Dx* | *1* | *2* | *3* | *4* | *1* | *2* | *3* | *4* | *1* | *2* | *3* | *4* |
| *11* | *118* | 96.774 | 100.000 | 100.000 | 93.467 | 100.000 | 100.000 | 100.000 | 98.633 | 100.000 | 100.000 | 100.000 | 94.118 |
| *13* | *129* | 3.226 | | | 6.533 | | | | 1.367 | | | | 5.882 |
| *Total count* | | 62 | 53 | 78 | 199 | 143 | 127 | 146 | 512 | 6 | 2 | 1 | 17 |

***Table-2. Total Count and Relative Frequency Distributions (%) of Diseases in Dxtype-2.***

| *Hiwot Fana and Misrak Arbegnoch Hospitals* | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Dxtype-2* | | *Generation* | | | | | | | | | | | |
| | | *1* | | | | *2* | | | | *3* | | | |
| | | *PC* | | | | *PC* | | | | *PC* | | | |
| *Dxgr* | *Dx* | *1* | *2* | *3* | *4* | *1* | *2* | *3* | *4* | *1* | *2* | *3* | *4* |
| *1* | *37.1* | 2.817 | 5.882 | 1.310 | 1.329 | 0.840 | 1.754 | 1.509 | 1.037 | | | 0.483 | 0.360 |
| | *37.2* | 7.042 | | 4.367 | 1.772 | | | 0.755 | 0.080 | | | | |
| | *37.3* | 30.986 | 31.373 | 39.301 | 19.823 | 40.336 | 20.175 | 30.189 | 12.041 | 9.901 | 3.774 | 5.797 | 3.357 |
| | *37.4* | 5.634 | 7.843 | 3.057 | 3.987 | 5.042 | 3.509 | 2.642 | 3.429 | 0.990 | | 0.966 | 1.319 |
| 2 | *44* | | | 0.437 | 0.111 | | | | 0.159 | | | | 0.240 |
| | *45* | | | | 0.111 | | | | 0.159 | | | | 0.240 |
| | *46* | | | | 0.221 | | 0.877 | | 0.080 | | 1.887 | | 0.240 |
| | *47* | | | | | 0.840 | | | 0.159 | | | | 0.240 |
| | *48* | | | | | | | | 0.080 | 0.990 | | | |
| | *50* | | | | | | | | 0.159 | | | | 0.120 |
| | *51* | | | | | | | | 0.080 | 0.990 | | | 0.120 |
| | *54* | | | 0.437 | 0.111 | | | | | 0.990 | 3.774 | | 0.839 |
| | *55.1* | | | | 0.111 | | | | 0.239 | | | | 0.120 |
| | *56.1* | | | 0.437 | 0.111 | | | | 0.080 | | | | 0.120 |
| | *56.2* | | | | | | | | 0.080 | | | | 0.240 |
| | *57.1* | | | | 0.221 | | 0.877 | 0.377 | | | | | |
| | *57.3* | | | | | | | | 0.080 | | | | 0.120 |
| | *57.4* | | | | 0.111 | | | | 0.080 | | | | 0.360 |
| | *58* | | | | | | | | 0.159 | | | | |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *59* | | | | 0.221 | | | 0.377 | 0.399 | 0.990 | | | 0.480 |
| | *60.1* | | 1.961 | | 0.111 | | | | | | | | 0.120 |
| | *60.4* | | | | 0.554 | | | | 0.478 | | | | 0.480 |
| *3* | *63.1* | 1.408 | 1.961 | 4.367 | 6.977 | 5.042 | 7.018 | 5.283 | 7.656 | 7.921 | 3.774 | 11.594 | 7.314 |
| | *63.2* | | | | 0.221 | | | 0.377 | 0.159 | 0.990 | | | |
| *4* | *65.1* | | | | 0.221 | | | 0.377 | 0.080 | | | 0.483 | 0.240 |
| | *65.2* | 4.225 | 1.961 | 6.987 | 7.530 | 0.840 | 0.877 | 1.132 | 0.558 | | | | 0.240 |
| | *65.3* | | | 0.437 | | | | | | | | | |
| | *65.4* | 1.408 | 1.961 | 2.183 | 1.993 | 0.840 | 1.754 | 0.377 | 0.718 | 0.990 | | | 0.360 |
| *5* | *67* | | | 0.437 | 0.443 | 0.840 | 2.632 | 0.377 | 0.478 | | 1.887 | | 0.120 |
| | *68* | 1.408 | 3.922 | | | | 0.877 | 0.377 | 0.159 | | | 0.966 | |
| | *69* | | | | 0.332 | | | | 0.080 | | | | |
| *6* | *73* | | | 0.437 | 0.664 | 0.840 | 0.877 | 0.755 | 0.638 | | | | |
| | *75* | 2.817 | 1.961 | 0.873 | 2.547 | 0.840 | 0.877 | 0.755 | 2.791 | 10.891 | 18.868 | 9.662 | 17.626 |
| | *76* | 1.408 | 1.961 | 0.437 | 0.997 | 1.681 | 3.509 | 1.132 | 0.957 | 0.990 | 1.887 | 0.483 | 1.439 |
| *7* | *79* | | | | | | | | 0.159 | | | | |
| | *80* | 4.225 | | 2.183 | 3.654 | 1.681 | | 2.642 | 1.037 | 6.931 | | 4.348 | 1.319 |
| | *81* | | | | | | | | 0.239 | | | | |
| | *82.2* | 1.408 | 1.961 | 0.437 | 1.661 | | | | | | | | |
| | *82.3* | | | 0.437 | 0.221 | | | | | | | | 0.120 |
| | *83* | | | 0.437 | 0.221 | 0.840 | 2.632 | 0.377 | 0.558 | 1.980 | 1.887 | | 0.480 |
| | *84* | 2.817 | | 0.437 | 1.218 | 0.840 | 2.632 | 3.019 | 2.153 | 13.861 | 9.434 | 17.874 | 7.314 |
| *9* | *102* | 9.859 | 5.882 | 5.677 | 8.084 | 12.605 | 7.018 | 8.679 | 10.048 | 0.990 | 1.887 | 3.382 | 5.276 |
| | *101.3* | 4.225 | 3.922 | 2.183 | 3.101 | 4.202 | 0.877 | 1.509 | 3.429 | 6.931 | 3.774 | 1.449 | 5.516 |
| | *103.2* | | 1.961 | | 0.332 | | 0.877 | 0.377 | 0.399 | 0.990 | 1.887 | 0.483 | 0.959 |
| | *103.3* | | | | 0.997 | | 2.632 | 0.377 | 1.037 | | | | 0.719 |
| | *103.4* | | | | 0.443 | | | | 0.957 | | | | 0.240 |
| | *104* | 2.817 | 11.765 | 3.493 | 8.970 | 6.723 | 12.281 | 10.943 | 21.531 | 5.941 | 7.547 | 7.729 | 14.269 |
| | *105.1* | 4.225 | 3.922 | 6.987 | 8.195 | 8.403 | 12.281 | 16.604 | 12.360 | 6.931 | 11.321 | 21.256 | 9.233 |
| | *106.1* | | | 0.873 | 0.554 | | 0.877 | 0.377 | 0.797 | 0.990 | 1.887 | 0.966 | 0.480 |
| | *107.1* | | | | 0.332 | | | 0.755 | 0.239 | | | | 0.360 |
| *10* | *108* | 5.634 | 1.961 | 8.297 | 6.202 | 4.202 | 4.386 | 4.528 | 4.705 | 8.911 | 9.434 | 4.831 | 3.957 |
| | *109* | | 1.961 | 0.437 | 1.329 | 0.840 | | 0.377 | 0.239 | 0.990 | | 0.483 | 0.600 |
| | *112* | | | | | | 0.877 | | 0.319 | 4.950 | 5.660 | 1.449 | 3.357 |
| | *113* | | | | 0.221 | | | | | | | | |
| | *114.1* | | | 0.437 | 0.775 | | 0.877 | 0.377 | 1.276 | 1.980 | | | 3.357 |
| | *114.2* | 1.408 | | | 0.221 | | | 1.132 | 1.196 | | 7.547 | 2.415 | 4.077 |
| *12* | *122* | 4.225 | | | 0.221 | 1.681 | 1.754 | 0.377 | 0.478 | | | 1.932 | 0.240 |
| | *123* | | 3.922 | 0.437 | | | 0.877 | | 0.239 | | 1.887 | | 0.120 |
| | *124* | | 1.961 | 1.747 | 2.215 | | 3.509 | 0.755 | 3.270 | 0.990 | | 0.966 | 1.559 |
| *Total count* | | 71 | 51 | 229 | 903 | 119 | 114 | 265 | 1254 | 101 | 53 | 207 | 834 |

***Table-3. Count and Relative Frequency Distributions (%) of Diseases in Dxtype-3.***

*Hiwot Fana and Misrak Arbegnoch Hospitals*

| *Dxtype-3* | | *Generation* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *1* | | | | *2* | | | | *3* | | | |
| | | *PC* | | | | *PC* | | | | *PC* | | | |
| *Dxgr* | *Dx* | *1* | *2* | *3* | *4* | *1* | *2* | *3* | *4* | *1* | *2* | *3* | *4* |
| *1* | *37.1* | | | 3.067 | 2.529 | 1.031 | 1.667 | | 0.789 | | | 1.613 | 0.567 |
| | *37.2* | 6.329 | 3.030 | 1.840 | 2.724 | | | | 0.395 | | | | |
| | *37.3* | 32.911 | 33.333 | 36.810 | 20.039 | 15.464 | 8.333 | 32.124 | 11.184 | 7.965 | 3.226 | 8.871 | 6.516 |
| | *37.4* | 7.595 | 3.030 | 4.908 | 4.669 | 3.093 | 1.667 | 3.109 | 2.632 | 1.770 | 3.226 | 2.419 | 0.567 |
| *2* | *44* | | | | | | | | 0.263 | | | | |
| | *45* | | | | 0.195 | | | | 0.263 | | | | |
| | *46* | | | 1.227 | 0.389 | | 1.667 | | 0.395 | | | | 1.133 |
| | *47* | | | | 0.195 | | 1.667 | | 0.263 | | | | |
| | *48* | | | | | | | | 0.132 | 0.885 | | | 0.283 |
| | *49* | | | | | 1.031 | | | | | | | |
| | *51* | | | | | 2.062 | 1.667 | 0.518 | 1.053 | 0.885 | | | 0.283 |
| | *52* | | | | 0.584 | 1.031 | 5.000 | 1.036 | 0.789 | | 3.226 | 2.419 | 1.416 |
| | *55.1* | | 3.030 | | 0.195 | | | | 0.132 | | | | 0.283 |
| | *55.2* | | | | | | | | | | | | |
| | *56.1* | | | | 0.195 | | | | 0.263 | | | | |
| | *56.2* | | | | 0.195 | | | | 0.132 | | | | |
| | *57.1* | | | | 0.389 | | | | 0.395 | | | | 0.283 |
| | *57.2* | | | | 0.584 | | | 0.518 | 0.263 | | | | 0.567 |
| | *57.4* | 1.266 | | 1.227 | | | 1.667 | | 0.132 | | | | |
| | *58* | | | | | | | | 0.263 | | | | |
| | *59* | 1.266 | | | 0.389 | 2.062 | | 0.518 | 0.395 | 0.885 | | 0.806 | 0.567 |
| | *60.1* | | | | 0.778 | | | | 0.526 | 0.885 | | | |
| | *60.2* | 1.266 | | 0.613 | 0.584 | 3.093 | 5.000 | 1.036 | 2.237 | | | 0.806 | 0.567 |
| | *60.3* | 1.266 | | 0.613 | 0.973 | 1.031 | | 2.591 | 0.789 | | | | 0.283 |
| | *60.4* | 1.266 | 3.030 | | 0.973 | | | 0.518 | 0.789 | | | | 0.283 |
| *3* | *63.1* | 3.797 | 3.030 | 1.840 | 6.420 | 4.124 | 5.000 | 6.736 | 5.658 | 12.389 | 12.903 | 7.258 | 5.382 |
| | *63.2* | 1.266 | 3.030 | | | | | | 0.132 | 0.885 | 3.226 | | |
| *4* | *65.1* | | | 0.613 | 0.389 | 4.124 | | 1.554 | 0.395 | | | | 0.283 |
| | *65.2* | 8.861 | 9.091 | 6.748 | 6.615 | 2.062 | | 1.036 | 1.316 | | | 0.806 | 0.283 |
| | *65.3* | | | 0.613 | | 1.031 | | | | | | | |
| | *65.4* | 2.532 | | 1.840 | 2.724 | | 3.333 | 2.073 | 1.447 | | | 3.226 | |
| *5* | *67* | | | | 0.584 | | 1.667 | 1.036 | 0.526 | | | | |
| | *68* | | | | 0.195 | 1.031 | | | 0.395 | 0.885 | | | |
| | *69* | | | | | | | | | | | | |
| *6* | *73* | | 3.030 | 0.613 | 0.778 | 1.031 | | | 0.526 | 0.885 | | | |
| | *75* | | | 1.227 | 3.307 | 1.031 | 1.667 | 2.073 | 2.368 | 9.735 | 16.129 | 19.355 | 27.762 |
| | *76* | | 3.030 | | 0.584 | | | | 1.579 | 0.885 | | | 3.399 |
| *7* | *79* | | | 0.613 | 0.195 | 2.062 | 1.667 | | | | | | 0.567 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *80* | 5.063 | | 3.681 | 5.058 | 3.093 | 5.000 | 5.181 | 2.763 | 2.655 | 3.226 | 7.258 | 1.416 |
| | *81* | | | | 0.195 | | | 0.518 | 0.132 | | | 0.806 | 0.283 |
| | *82.2* | | | 1.227 | 0.973 | | | | | | | | 0.283 |
| | *82.3* | | | | 0.195 | | 1.667 | | 0.132 | | | | |
| | *83* | | | 1.227 | 1.167 | 2.062 | 1.667 | 1.554 | 0.395 | 4.425 | | 1.613 | 1.133 |
| | *84* | 1.266 | | 0.613 | 0.584 | 4.124 | 15.000 | 4.145 | 2.895 | 22.124 | 25.806 | 14.516 | 7.932 |
| *9* | *102* | 10.127 | 9.091 | 4.908 | 5.837 | 5.155 | 3.333 | 3.627 | 5.132 | 3.540 | | | 1.700 |
| | *103.1* | | 3.030 | 1.227 | 1.167 | 1.031 | 1.667 | 0.518 | 3.158 | 0.885 | | 0.806 | 3.116 |
| | *103.2* | | | | 0.195 | | | | 0.395 | | | | 0.283 |
| | *103.3* | | | | 0.389 | | | | 0.263 | | | | |
| | *103.4* | | | 0.613 | 0.389 | | | | | | | | 0.283 |
| | *104* | 2.532 | 6.061 | 4.294 | 3.696 | 3.093 | 1.667 | 2.073 | 7.763 | 5.310 | 3.226 | 1.613 | 6.516 |
| | *105.1* | 1.266 | 6.061 | 2.454 | 5.058 | 4.124 | 5.000 | 9.326 | 12.500 | 10.619 | 6.452 | 11.290 | 8.499 |
| | *106.1* | | | | 1.556 | 4.124 | 5.000 | 0.518 | 3.553 | 0.885 | 6.452 | | 3.683 |
| | *107.1* | | 3.030 | | 0.778 | 1.031 | 1.667 | 0.518 | 0.395 | | | | 1.416 |
| *10* | *108* | 6.329 | 3.030 | 7.362 | 7.782 | 17.526 | 8.333 | 8.290 | 6.447 | 7.080 | 9.677 | 12.903 | 5.666 |
| | *109* | 1.266 | | 2.454 | 0.584 | 1.031 | 1.667 | 1.554 | 0.789 | 0.885 | | | 0.850 |
| | *113* | | | 1.227 | 0.195 | | 1.667 | 1.036 | 1.579 | 1.770 | 3.226 | 0.806 | 0.567 |
| | *114.1* | 1.266 | | | 0.195 | 1.031 | | | 0.132 | | | 0.806 | |
| | *114.2* | | | | | | | | | | | | |
| | *114.3* | | | 0.613 | 1.362 | 5.155 | 1.667 | 2.073 | 8.684 | 0.885 | | | 1.983 |
| | *114.4* | | | 0.613 | 0.584 | 1.031 | 3.333 | 1.036 | 2.237 | | | | 0.283 |
| *12* | *122* | | | 1.227 | 0.778 | | | 1.036 | 0.526 | | | | 0.567 |
| | *123* | | | | 0.195 | | | 0.518 | 0.132 | | | | |
| | *124* | 1.266 | 3.030 | 1.840 | 2.724 | | | | 1.184 | | | | 2.266 |
| *Total count* | | 79 | 33 | 163 | 514 | 97 | 60 | 193 | 760 | 113 | 31 | 124 | 353 |

***Table-4. Total Count and Relative Frequency Distributions (%) of Diseases in Dxtype-4***

| *Hiwot Fana and Misrak Arbegnoch Hospitals* | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Dxtype-4* | | *Generation* | | | | | | | | | | | |
| | | *1* | | | | *2* | | | | *3* | | | |
| | | *PC* | | | | *PC* | | | | *PC* | | | |
| *Dxgr* | *Dx* | *1* | *2* | *3* | *4* | *1* | *2* | *3* | *4* | *1* | *2* | *3* | *4* |
| *11* | *115* | 3.268 | 2.609 | 4.737 | 4.288 | 1.163 | 1.661 | 3.590 | 2.458 | | | | 1.724 |
| | *116.1* | 1.961 | 3.478 | 2.105 | 1.991 | 4.651 | 2.658 | 2.564 | 1.621 | 8.333 | | | |
| | *116.2* | 1.961 | | 1.053 | 3.063 | 0.581 | 0.664 | 0.769 | 0.994 | | 10.000 | | |
| | *116.3* | | 1.739 | 0.526 | 0.613 | 1.744 | 0.332 | 0.256 | 0.994 | | | | 1.724 |
| | *117.1* | 6.536 | 6.087 | 3.158 | 3.063 | 3.488 | 4.651 | 3.846 | 4.393 | 16.667 | | 14.286 | |
| | *118* | 39.216 | 46.087 | 41.053 | 28.484 | 41.570 | 42.193 | 37.436 | 26.412 | 50.000 | 20.000 | 14.286 | 27.586 |
| | *120.1* | 3.268 | 1.739 | 1.579 | 0.613 | 1.453 | 1.661 | 1.538 | 0.941 | | | 14.286 | |
| | *120.2* | 6.536 | 5.217 | 5.263 | 8.729 | 5.233 | 8.306 | 9.487 | 9.362 | | 10.000 | | 3.448 |
| | *120.3* | 3.268 | 2.609 | 4.737 | 4.135 | 2.326 | 2.658 | 3.846 | 5.492 | | | | 5.172 |
| | *120.4* | 0.654 | 0.870 | | 2.144 | | | 1.538 | 3.400 | | | | 3.448 |
| | *121.5* | 33.333 | 29.565 | 35.789 | 42.879 | 37.791 | 35.216 | 35.128 | 43.933 | 25.000 | 60.000 | 57.143 | 56.897 |
| *Total count* | | 153 | 115 | 190 | 653 | 344 | 301 | 390 | 1912 | 12 | 10 | 7 | 58 |

*Appendix-3: Analysis of Variation*

***The following tables show the statistical figures obtained by analyses of variations***

***Table-1. Results of Leven's Test for the Equality of Variance- Dxgroup-1***

| Compared PCs. | | Level-1 | | | | | |
|---|---|---|---|---|---|---|---|
| | | Sig. (Females- p value) | | | Sig. (Males- p value) | | |
| | | Gene.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 |
| 1 | 2 | 0.94425 | 0.22115 | 0.1473 | 0.84457 | 0.26963 | 0.29809 |
| | 3 | 0.51152 | 0.56761 | 0.2983 | 0.74348 | 0.19549 | 0.97028 |
| | 4 | 0.46677 | 0.08861 | 0.09966 | 0.36901 | 0.52116 | 0.72888 |
| | 23 | 0.56856 | 0.44349 | 0.26017 | 0.7593 | 0.29899 | 0.81258 |
| | 24 | 0.49647 | 0.09579 | 0.1002 | 0.40941 | 0.49946 | 0.6582 |
| | 34 | 0.70665 | 0.12811 | 0.12338 | 0.57318 | 0.98787 | 0.81144 |
| | 234 | 0.72237 | 0.13323 | 0.12415 | 0.60036 | 0.96666 | 0.75332 |
| | Avg. Level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 1 | 0.94425 | 0.22115 | 0.1473 | 0.84457 | 0.26963 | 0.29809 |
| | 3 | 0.56588 | 0.41344 | 0.51648 | 0.8906 | 0.07048 | 0.3001 |
| | 4 | 0.45356 | 0.33674 | 0.6148 | 0.27195 | 0.56474 | 0.41048 |
| | 13 | 0.6569 | 0.33047 | 0.30562 | 0.97448 | 0.09148 | 0.29368 |
| | 14 | 0.48569 | 0.51831 | 0.90035 | 0.331 | 0.5128 | 0.36818 |
| | 34 | 0.67048 | 0.57757 | 0.80156 | 0.43998 | 0.25901 | 0.36616 |
| | 134 | 0.68661 | 0.7382 | 0.96847 | 0.47845 | 0.25988 | 0.34623 |
| | Avg. Level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 1 | 0.51152 | 0.56761 | 0.2983 | 0.74348 | 0.19549 | 0.97028 |
| | 2 | 0.56588 | 0.41344 | 0.51648 | 0.8906 | 0.07048 | 0.3001 |
| | 4 | 0.2147 | 0.13275 | 0.30328 | 0.23299 | 0.10571 | 0.70695 |
| | 12 | 0.52672 | 0.99672 | 0.50047 | 0.7855 | 0.13319 | 0.74582 |
| | 14 | 0.23045 | 0.1942 | 0.46875 | 0.28259 | 0.11351 | 0.77209 |
| | 24 | 0.22788 | 0.14736 | 0.30514 | 0.25988 | 0.10255 | 0.63947 |
| | 124 | 0.24248 | 0.20688 | 0.47008 | 0.30647 | 0.10996 | 0.71581 |
| | Avg. Level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | 1 | 0.46677 | 0.08861 | 0.09966 | 0.36901 | 0.52116 | 0.72888 |
| | 2 | 0.45356 | 0.33674 | 0.6148 | 0.27195 | 0.56474 | 0.41048 |
| | 3 | 0.2147 | 0.13275 | 0.30328 | 0.23299 | 0.10571 | 0.70695 |
| | 12 | 0.44497 | 0.13912 | 0.1438 | 0.33507 | 0.78329 | 0.97335 |
| | 13 | 0.25096 | 0.11339 | 0.18533 | 0.26339 | 0.14926 | 0.71503 |
| | 23 | 0.23647 | 0.16502 | 0.34151 | 0.23783 | 0.14748 | 0.92742 |
| | 123 | 0.26622 | 0.13506 | 0.20969 | 0.2641 | 0.19101 | 0.83955 |
| | Avg. Level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 |

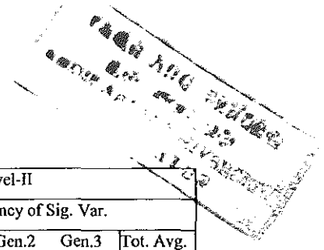


***Table-2. Results of Leven's Test for the Equality of Variance- Dxgroup-2***

| Compared PCs. | Level-I | | | | | | Level-II | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sig. (Females- p value) | | | Sig. (Mates- p value) | | | Avg. Consistency of Sig. Var. | | | | | |
| | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | F | M | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 2 | 0.0414 | 0.21089 | 0.28796 | 0.73913 | 0.095 | 0.90698 | 0.333 | 0.000 | 0.500 | 0.000 | 0.000 | 0.167 |
| 3 | 7.00E-05 | 0.78406 | 1.00E-06 | 0.05102 | 0.08333 | 0.6197 | 0.667 | 0.000 | 0.500 | 0.000 | 0.500 | 0.333 |
| 4 | 0.0002 | 0.76672 | 0.0127 | 0.019 | 0.0148 | 0.92423 | 0.667 | 0.667 | 1.000 | 0.500 | 0.500 | 0.667 |
| 23 | 1.00E-06 | 0.82462 | 0.0021 | 0.0249 | 0.16055 | 0.71913 | 0.667 | 0.333 | 1.000 | 0.000 | 0.500 | 0.500 |
| 124 | 8.00E-05 | 0.96815 | 0.0251 | 0.0166 | 0.0282 | 0.97071 | 0.667 | 0.667 | 1.000 | 0.500 | 0.500 | 0.667 |
| 34 | 4.00E-06 | 0.95916 | 0.0024 | 0.0033 | 0.0139 | 0.94692 | 0.667 | 0.667 | 1.000 | 0.500 | 0.500 | 0.667 |
| 234 | 6.00E-07 | 0.82062 | 0.0052 | 0.0027 | 0.0231 | 0.97363 | 0.667 | 0.667 | 1.000 | 0.500 | 0.500 | 0.667 |
| Avg. Level of Sig. Var. | 1 | 0 | 0.857 | 0.714 | 0.571 | 0 | 0.619 | 0.429 | 0.857 | 0.286 | 0.429 | 0.524 |
| 1 | 0.0414 | 0.21089 | 0.28796 | 0.73913 | 0.095 | 0.90698 | 0.333 | 0.000 | 0.500 | 0.000 | 0.000 | 0.167 |
| 3 | 0.41911 | 0.0952 | 0.0048 | 0.17767 | 0.006 | 0.82417 | 0.333 | 0.333 | 0.000 | 0.500 | 0.500 | 0.333 |
| 4 | 0.29464 | 0.21604 | 0.0459 | 0.15037 | 0.0017 | 0.94802 | 0.333 | 0.333 | 0.000 | 0.500 | 0.500 | 0.333 |
| 13 | 0.269 | 0.07826 | 0.023 | 0.22405 | 0.0089 | 0.83891 | 0.333 | 0.333 | 0.000 | 0.500 | 0.500 | 0.333 |
| 214 | 0.26175 | 0.18592 | 0.0393 | 0.14188 | 0.0023 | 0.74847 | 0.333 | 0.333 | 0.000 | 0.500 | 0.500 | 0.333 |
| 34 | 0.2669 | 0.12661 | 0.0302 | 0.09007 | 0.0016 | 0.9388 | 0.333 | 0.333 | 0.000 | 0.500 | 0.500 | 0.333 |
| 134 | 0.24335 | 0.11406 | 0.0274 | 0.10176 | 0.0022 | 0.76964 | 0.333 | 0.333 | 0.000 | 0.500 | 0.500 | 0.333 |
| Avg. Level of Sig. Var. | 0.143 | 0 | 0.857 | 0 | 0.857 | 0 | 0.333 | 0.286 | 0.071 | 0.429 | 0.429 | 0.310 |
| 1 | 7.00E-05 | 0.78406 | 1.00E-06 | 0.05102 | 0.08333 | 0.6197 | 0.667 | 0.000 | 0.500 | 0.000 | 0.500 | 0.333 |
| 2 | 0.41911 | 0.0952 | 0.0048 | 0.17767 | 0.006 | 0.82417 | 0.333 | 0.333 | 0.000 | 0.500 | 0.500 | 0.333 |
| 4 | 0.5179 | 0.39042 | 2.00E-05 | 0.91928 | 0.46171 | 0.68049 | 0.333 | 0.000 | 0.000 | 0.000 | 0.500 | 0.167 |
| 12 | 0.45723 | 0.20519 | 5.00E-05 | 0.09826 | 0.14293 | 0.47821 | 0.333 | 0.000 | 0.000 | 0.000 | 0.500 | 0.167 |
| 314 | 0.38621 | 0.44179 | 0.0002 | 0.85587 | 0.58196 | 0.43526 | 0.333 | 0.000 | 0.000 | 0.000 | 0.500 | 0.167 |
| 24 | 0.50474 | 0.61967 | 0.0001 | 0.84067 | 0.61819 | 0.62392 | 0.333 | 0.000 | 0.000 | 0.000 | 0.500 | 0.167 |
| 124 | 0.37917 | 0.68215 | 0.0005 | 0.75855 | 0.69086 | 0.4294 | 0.333 | 0.000 | 0.000 | 0.000 | 0.500 | 0.167 |
| Avg. Level of Sig. Var. | 0.143 | 0 | 1 | 0 | 0.143 | 0 | 0.381 | 0.048 | 0.071 | 0.071 | 0.500 | 0.214 |
| 1 | 0.0002 | 0.76672 | 0.0127 | 0.019 | 0.0148 | 0.92423 | 0.667 | 0.667 | 1.000 | 0.500 | 0.500 | 0.667 |
| 2 | 0.29464 | 0.21604 | 0.0459 | 0.15037 | 0.0017 | 0.94802 | 0.333 | 0.333 | 0.000 | 0.500 | 0.500 | 0.333 |
| 3 | 0.5179 | 0.39042 | 2.00E-05 | 0.91928 | 0.46171 | 0.68049 | 0.333 | 0.000 | 0.000 | 0.000 | 0.500 | 0.167 |
| 12 | 0.78385 | 0.59062 | 0.0254 | 0.0421 | 0.0428 | 0.69436 | 0.333 | 0.667 | 0.500 | 0.500 | 0.500 | 0.500 |
| 413 | 0.87194 | 0.29012 | 0.18777 | 0.5719 | 0.24082 | 0.79399 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 23 | 0.40719 | 0.92615 | 0.3067 | 0.95707 | 0.30564 | 0.7755 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 123 | 0.95665 | 0.63267 | 0.87902 | 0.62157 | 0.14489 | 0.76571 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Avg. Level of Sig. Var. | 0.143 | 0 | 0.571 | 0.286 | 0.429 | 0 | 0.238 | 0.238 | 0.214 | 0.214 | 0.286 | 0.238 |

***Table-3. Results of Leven's Test for the Equality of Variance- Dxgroup-3***

| Compared PCs. | | Level-I | | | | | | Level-II | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Sig. (Females- p value) | | | Sig. (Males- p value) | | | Avg. Consistency of Sig. Var. | | | | | |
| | | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | F | M | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 1 | 2 | . | . | 2.00E-16 | 0 | 3.00E-15 | 2.00E-15 | 0.333 | 1.000 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 3 | 1.00E-16 | . | 2.00E-16 | 2.00E-16 | 1.00E-16 | . | 0.667 | 0.667 | 1.000 | 0.500 | 0.500 | 0.667 |
| | 4 | . | . | 3.00E-14 | 2.00E-16 | 2.00E-16 | 0 | 0.333 | 1.000 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 23 | . | 8.00E-15 | 1.00E-15 | 0 | 1.00E-16 | 1.00E-16 | 0.667 | 1.000 | 0.500 | 1.000 | 1.000 | 0.833 |
| | 24 | . | . | 2.00E-13 | 0 | 1.00E-15 | 0 | 0.333 | 1.000 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 34 | . | 9.00E-16 | 2.00E-15 | 0 | 2.00E-16 | . | 0.667 | 0.667 | 0.500 | 1.000 | 0.500 | 0.667 |
| | 234 | 0 | 0 | 2.00E-15 | 0 | 1.00E-15 | 0 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| | Avg. Level of Sig. Var. | 0.286 | 0.429 | 1 | 1 | 1 | 0.714 | 0.571 | 0.905 | 0.643 | 0.714 | 0.857 | 0.738 |
| 2 | 1 | . | . | 2.00E-16 | 0 | 3.00E-15 | 2.00E-15 | 0.333 | 1.000 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 3 | 2.00E-16 | . | 0 | . | 7.00E-16 | 9.00E-16 | 0.667 | 0.667 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 4 | . | . | 2.00E-16 | 1.00E-16 | 8.00E-15 | 3.00E-16 | 0.333 | 1.000 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 13 | . | 0 | . | 0 | 5.00E-15 | 8.00E-14 | 0.333 | 1.000 | 0.500 | 1.000 | 0.500 | 0.667 |
| | 14 | . | . | . | . | 2.00E-14 | 7.00E-16 | 0.000 | 0.667 | 0.000 | 0.500 | 0.500 | 0.333 |
| | 34 | . | 5.00E-12 | 0 | . | 4.00E-15 | 3.00E-16 | 0.667 | 0.667 | 0.000 | 1.000 | 1.000 | 0.667 |
| | 134 | . | . | 0 | . | 7.00E-15 | 7.00E-16 | 0.333 | 0.667 | 0.000 | 0.500 | 1.000 | 0.500 |
| | Avg. Level of Sig. Var. | 0.143 | 0.286 | 0.714 | 0.429 | 1 | 1 | 0.381 | 0.810 | 0.286 | 0.643 | 0.857 | 0.595 |
| 3 | 1 | 1.00E-16 | . | 2.00E-16 | 2.00E-16 | 1.00E-16 | . | 0.667 | 0.667 | 1.000 | 0.500 | 0.500 | 0.667 |
| | 2 | 2.00E-16 | . | 0 | . | 7.00E-16 | 9.00E-16 | 0.667 | 0.667 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 4 | 2.00E-16 | . | 3.00E-16 | 2.00E-16 | . | 4.00E-16 | 0.667 | 0.667 | 1.000 | 0.000 | 1.000 | 0.667 |
| | 12 | 2.00E-16 | . | 1.00E-16 | 9.00E-14 | . | 1.00E-16 | 0.667 | 0.667 | 1.000 | 0.000 | 1.000 | 0.667 |
| | 14 | 2.00E-16 | . | 2.00E-16 | . | 0 | . | 0.667 | 0.333 | 0.500 | 0.500 | 0.500 | 0.500 |
| | 24 | 2.00E-16 | . | 3.00E-16 | . | 9.00E-16 | 0 | 0.667 | 0.667 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 124 | 9.00E-16 | . | 2.00E-16 | . | 2.00E-16 | . | 0.667 | 0.333 | 0.500 | 0.500 | 0.500 | 0.500 |
| | Avg. Level of Sig. Var. | 1 | 0 | 1 | 0.429 | 0.714 | 0.571 | 0.667 | 0.571 | 0.714 | 0.357 | 0.786 | 0.619 |
| 4 | 1 | . | . | 3.00E-14 | 2.00E-16 | 2.00E-16 | 0 | 0.333 | 1.000 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 2 | . | . | 2.00E-16 | 1.00E-16 | 8.00E-15 | 3.00E-16 | 0.333 | 1.000 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 3 | 2.00E-16 | . | 3.00E-16 | 2.00E-16 | . | 4.00E-16 | 0.667 | 0.667 | 1.000 | 0.000 | 1.000 | 0.667 |
| | 12 | 0 | . | 1.00E-15 | 2.00E-16 | . | 1.00E-16 | 0.667 | 0.667 | 1.000 | 0.000 | 1.000 | 0.667 |
| | 13 | . | 0 | 3.00E-16 | 2.00E-16 | 1.00E-14 | 0 | 0.667 | 1.000 | 0.500 | 1.000 | 1.000 | 0.833 |
| | 23 | . | 0 | 2.00E-15 | 2.00E-16 | . | 0 | 0.667 | 0.667 | 0.500 | 0.500 | 1.000 | 0.667 |
| | 123 | . | . | 1.00E-15 | 2.00E-16 | 9.00E-15 | 1.00E-16 | 0.333 | 1.000 | 0.500 | 0.500 | 1.000 | 0.667 |
| | Avg. Level of Sig. Var. | 0.286 | 0.286 | 1 | 1 | 0.571 | 1 | 0.524 | 0.857 | 0.643 | 0.429 | 1.000 | 0.690 |

***Table-4. Results of Leven's Test for the Equality of Variance- Dxgroup-4***

| Compared PCs. | | Level-I | | | | | | Level-II | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Sig. (Females- p value) | | | Sig. (Males- p value) | | | Avg. Consistency of Sig. Var. | | | | | |
| | | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | F | M | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 1 | *2* | 0.48473 | 0.23257 | *0.024* | 0.81289 | 0.95295 | . | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *3* | 0.43877 | 0.54834 | 0.21661 | 0.56162 | 0.26925 | *0.0371* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *4* | 0.34785 | *0.0158* | 0.08954 | 0.60599 | 0.19544 | . | *0.333* | *0.000* | *0.000* | *0.500* | *0.000* | *0.167* |
| | *23* | 0.59462 | 0.75966 | 0.1381 | 0.66641 | 0.32201 | *0.0371* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *24* | 0.38213 | 0.10137 | 0.0822 | 0.61589 | 0.20884 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *34* | 0.36362 | *0.0037* | 0.07829 | 0.5705 | 0.1844 | *0.0338* | *0.333* | *0.333* | *0.000* | *0.500* | *0.500* | *0.333* |
| | *234* | 0.39187 | *0.0124* | 0.07355 | 0.58569 | 0.19639 | *0.0338* | *0.333* | *0.333* | *0.000* | *0.500* | *0.500* | *0.333* |
| | *Avg. Level of Sig. Var.* | 0 | *0.429* | 0 | 0 | 0 | *0.571* | *0.190* | *0.190* | *0.000* | *0.214* | *0.357* | *0.190* |
| 2 | *1* | 0.48473 | 0.23257 | *0.024* | 0.81289 | 0.95295 | . | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *3* | 0.19427 | 0.20105 | *0.024* | 0.39377 | 0.2554 | *0.0371* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| | *4* | 0.15347 | 0.09716 | 0.05837 | 0.43115 | 0.1728 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *13* | 0.22759 | 0.17294 | . | 0.5233 | 0.20282 | *0.0371* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *14* | 0.16199 | 0.1043 | 0.13397 | 0.47381 | 0.11511 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *34* | 0.15991 | 0.09277 | *0.0498* | 0.40556 | 0.16379 | *0.0338* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| | *134* | 0.1669 | 0.09897 | *0.0338* | 0.44045 | 0.11928 | *0.0338* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| | *Avg. Level of Sig. Var.* | 0 | 0 | *0.571* | 0 | 0 | *0.571* | *0.190* | *0.190* | *0.000* | *0.000* | *0.571* | *0.190* |
| 3 | *1* | 0.43877 | 0.54834 | 0.21661 | 0.56162 | 0.26925 | *0.0371* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *2* | 0.19427 | 0.20105 | *0.024* | 0.39377 | 0.2554 | *0.0371* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| | *4* | 0.85281 | 0.83825 | 0.35029 | 0.93796 | 0.83234 | 0.05887 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *12* | 0.30979 | 0.26145 | 0.56035 | 0.50016 | 0.7971 | *0.0371* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *14* | 0.89884 | 0.8917 | 0.42324 | 0.88714 | 0.47742 | 0.05259 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *24* | 0.9145 | 0.99362 | 0.3058 | 0.93903 | 0.88843 | 0.0567 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *124* | 0.95597 | 0.96868 | 0.37816 | 0.89235 | 0.52428 | 0.05145 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *Avg. Level of Sig. Var.* | 0 | 0 | 0.143 | 0 | 0 | 0.429 | *0.048* | *0.143* | *0.000* | *0.000* | *0.286* | *0.095* |
| 4 | *1* | 0.34785 | *0.0158* | 0.08954 | 0.60599 | 0.19544 | . | *0.333* | *0.000* | *0.000* | *0.500* | *0.000* | *0.167* |
| | *2* | 0.15347 | 0.09716 | 0.05837 | 0.43115 | 0.1728 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *3* | 0.85281 | 0.83825 | 0.35029 | 0.93796 | 0.83234 | 0.05887 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *12* | 0.24223 | *0.0463* | 0.1859 | 0.54335 | 0.89536 | . | *0.333* | *0.000* | *0.000* | *0.500* | *0.000* | *0.167* |
| | *13* | 0.72595 | 0.83839 | 0.24875 | 0.87934 | 0.81748 | 0.09033 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *23* | 0.65807 | 0.29546 | 0.57216 | 0.91847 | 0.75359 | 0.06617 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *123* | 0.59024 | 0.18467 | 0.48329 | 0.80818 | 0.92221 | 0.10165 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *Avg. Level of Sig. Var.* | 0 | *0.286* | 0 | 0 | 0 | 0 | *0.095* | *0.000* | *0.000* | *0.143* | *0.000* | *0.048* |

***Table-5. Results of Leven's Test for the Equality of Variance- Dxgroup-5***

| Compared PCs. | Level-I | | | | | | Level-II | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sig. (Females- p value) | | | Sig. (Males- p value) | | | Avg. Consistency of Sig. Var. | | | | | |
| | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | F | M | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 1 2 | 0.07336 | 0.1736 | *0.0161* | . | 0.2642 | *0.0161* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| 1 3 | 0.05782 | 0.11475 | *0.0161* | . | 0.98904 | *0.0161* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| 1 4 | 0.05177 | 0.109 | *0.0161* | 0.05015 | 0.12524 | *0.0161* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| 1 23 | 0.1198 | 0.91855 | 0.11611 | . | 0.71356 | *0.0161* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| 1 24 | *0.0256* | 0.2806 | *0.0161* | 0.05015 | 0.17123 | *0.0161* | *0.667* | *0.333* | *0.500* | *0.000* | *1.000* | *0.500* |
| 1 34 | 0.05027 | 0.10151 | 0.11612 | 0.05015 | 0.18516 | *0.0161* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| 1 234 | *0.0293* | 0.22741 | *0.0161* | 0.05015 | 0.23467 | *0.0161* | *0.667* | *0.333* | *0.500* | *0.000* | *1.000* | *0.500* |
| 1 *Avg. Level of Sig. Var.* | *0.286* | 0 | *0.714* | 0 | 0 | *1* | *0.333* | *0.333* | *0.143* | *0.000* | *0.857* | *0.333* |
| 2 1 | 0.07336 | 0.1736 | *0.0161* | . | 0.2642 | *0.0161* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| 2 3 | *0.0242* | 0.08478 | 0.15736 | . | 0.2682 | . | *0.333* | *0.000* | *0.500* | *0.000* | *0.000* | *0.167* |
| 2 4 | *0.0232* | 0.08294 | *0.0202* | 0.05015 | 0.05206 | . | *0.667* | *0.000* | *0.500* | *0.000* | *0.500* | *0.333* |
| 2 13 | *0.0218* | 0.09132 | 0.06817 | . | 0.07905 | *0.0161* | *0.333* | *0.333* | *0.500* | *0.000* | *0.500* | *0.333* |
| 2 14 | *0.0204* | 0.08814 | *0.0197* | 0.05015 | 0.05017 | *0.0161* | *0.667* | *0.333* | *0.500* | *0.000* | *1.000* | *0.500* |
| 2 34 | *0.0227* | 0.08016 | *0.0217* | 0.05015 | 0.06718 | . | *0.667* | *0.000* | *0.500* | *0.000* | *0.500* | *0.333* |
| 2 134 | *0.0206* | 0.08445 | *0.0211* | 0.05015 | 0.05748 | *0.0161* | *0.667* | *0.333* | *0.500* | *0.000* | *1.000* | *0.500* |
| 2 *Avg. Level of Sig. Var.* | *0.857* | 0 | *0.714* | 0 | 0 | *0.571* | *0.524* | *0.190* | *0.429* | *0.000* | *0.643* | *0.357* |
| 3 1 | 0.05782 | 0.11475 | *0.0161* | . | 0.98904 | *0.0161* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| 3 2 | *0.0242* | 0.08478 | 0.15736 | . | 0.2682 | . | *0.333* | *0.000* | *0.500* | *0.000* | *0.000* | *0.167* |
| 3 4 | 0.77798 | 0.9013 | *0.0254* | 0.05015 | 0.12375 | . | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| 3 12 | *0.0317* | 0.07788 | 0.3375 | . | 0.25938 | *0.0161* | *0.333* | *0.333* | *0.500* | *0.000* | *0.500* | *0.333* |
| 3 14 | 0.27691 | 0.88093 | *0.0241* | 0.05015 | 0.11553 | *0.0161* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| 3 24 | 0.10637 | 0.50831 | *0.0405* | 0.05015 | 0.16904 | . | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| 3 124 | *0.0387* | 0.43667 | *0.0364* | 0.05015 | 0.13838 | *0.0161* | *0.667* | *0.333* | *0.500* | *0.000* | *1.000* | *0.500* |
| 3 *Avg. Level of Sig. Var.* | *0.429* | 0 | *0.714* | 0 | 0 | *0.571* | *0.381* | *0.190* | *0.214* | *0.000* | *0.643* | *0.286* |
| 4 1 | 0.05177 | 0.109 | *0.0161* | 0.05015 | 0.12524 | *0.0161* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| 4 2 | *0.0232* | 0.08294 | *0.0202* | 0.05015 | 0.05206 | . | *0.667* | *0.000* | *0.500* | *0.000* | *0.500* | *0.333* |
| 4 3 | 0.77798 | 0.9013 | *0.0254* | 0.05015 | 0.12375 | . | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| 4 12 | *0.0298* | 0.07544 | *0.0327* | 0.05015 | 0.4566 | *0.0161* | *0.667* | *0.333* | *0.500* | *0.000* | *1.000* | *0.500* |
| 4 13 | 0.7301 | 0.89268 | *0.0327* | 0.05015 | 0.85725 | *0.0161* | *0.333* | *0.333* | *0.000* | *0.000* | *1.000* | *0.333* |
| 4 23 | 0.64064 | 0.34985 | 0.19018 | 0.05015 | 0.09241 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| 4 123 | 0.31638 | 0.26733 | 0.23181 | 0.05015 | 0.43785 | *0.0161* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| 4 *Avg. Level of Sig. Var.* | *0.286* | 0 | *0.714* | 0 | 0 | 0.571 | *0.333* | *0.190* | *0.143* | *0.000* | *0.643* | *0.262* |

***Table-6. Results of Leven's Test for the Equality of Variance- Dxgroup-6***

| Compared PCs. | | Level-I | | | | | | Level-II | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Sig. (Females- p value) | | | Sig. (Males- p value) | | | Avg. Consistency of Sig. Var. | | | | | |
| | | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | F | M | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 1 | 2 | 0.90252 | 0.06045 | 0.23298 | *0.0161* | 0.2642 | 0.18865 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | 3 | 0.18966 | 0.11475 | 0.79866 | 0.11611 | 0.14625 | 0.11955 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 4 | 0.74998 | 0.11729 | 0.27002 | *0.0171* | 0.57253 | 0.07583 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | 23 | 0.22143 | 0.55834 | 0.85533 | *0.0161* | 0.16504 | 0.1294 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | 24 | 0.7283 | 0.20627 | 0.2675 | *0.0173* | 0.62601 | 0.07878 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | 34 | 0.59338 | 0.19895 | 0.35117 | *0.0194* | 0.56856 | 0.0813 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | 234 | 0.58438 | 0.33516 | 0.34346 | *0.0199* | 0.54618 | 0.0838 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | Avg. Level of Sig. Var. | 0 | 0 | 0 | *0.857* | 0 | 0 | *0.000* | *0.286* | *0.429* | *0.000* | *0.000* | *0.143* |
| 2 | 1 | 0.90252 | 0.06045 | 0.23298 | *0.0161* | 0.2642 | 0.18865 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | 3 | *0.0386* | *0.0275* | 0.17848 | 0.07594 | 0.57456 | 0.63553 | *0.667* | *0.000* | *0.500* | *0.500* | *0.000* | *0.333* |
| | 4 | 0.73987 | 0.49513 | 0.88039 | 0.70983 | 0.78543 | 0.28086 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 13 | 0.12142 | *0.0346* | 0.19485 | *0.0422* | 0.86011 | 0.75767 | *0.333* | *0.333* | *0.500* | *0.500* | *0.000* | *0.333* |
| | 14 | 0.77625 | 0.36477 | 0.796 | 0.47362 | 0.58334 | 0.45686 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 34 | 0.4722 | 0.27222 | 0.70177 | 0.44299 | 0.81208 | 0.33485 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 134 | 0.51635 | 0.21373 | 0.64964 | 0.31975 | 0.70128 | 0.48615 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | Avg. Level of Sig. Var. | 0.143 | 0.286 | 0 | 0.286 | 0 | 0 | *0.143* | *0.095* | *0.214* | *0.143* | *0.000* | *0.119* |
| 3 | 1 | 0.18966 | 0.11475 | 0.79866 | 0.11611 | 0.14625 | 0.11955 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 2 | *0.0386* | *0.0275* | 0.17848 | 0.07594 | 0.57456 | 0.63553 | *0.667* | *0.000* | *0.500* | *0.500* | *0.000* | *0.333* |
| | 4 | 0.06016 | *0.042* | 0.20409 | 0.10341 | 0.48522 | 0.46983 | *0.333* | *0.000* | *0.000* | *0.500* | *0.000* | *0.167* |
| | 12 | 0.097 | *0.0381* | 0.43453 | 0.95986 | 0.18811 | 0.17915 | *0.333* | *0.000* | *0.000* | *0.500* | *0.000* | *0.167* |
| | 14 | 0.06658 | 0.05195 | 0.22907 | 0.14077 | 0.3505 | 0.75229 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 24 | 0.07245 | 0.07182 | 0.20234 | 0.14011 | 0.4677 | 0.51176 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 124 | 0.07925 | 0.09185 | 0.22572 | 0.19206 | 0.35473 | 0.78366 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | Avg. Level of Sig. Var. | 0.143 | 0.429 | 0 | 0 | 0 | 0 | *0.190* | *0.000* | *0.071* | *0.214* | *0.000* | *0.095* |
| 4 | 1 | 0.74998 | 0.11729 | 0.27002 | *0.0171* | 0.57253 | 0.07583 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | 2 | 0.73987 | 0.49513 | 0.88039 | 0.70983 | 0.78543 | 0.28086 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 3 | 0.06016 | *0.042* | 0.20409 | 0.10341 | 0.48522 | 0.46983 | *0.333* | *0.000* | *0.000* | *0.500* | *0.000* | *0.167* |
| | 12 | 0.72498 | 0.70857 | 0.51373 | 0.06975 | 0.56661 | 0.10055 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 13 | 0.19404 | 0.05683 | 0.22389 | 0.05284 | 0.89888 | 0.20552 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 23 | 0.09831 | 0.1934 | 0.32847 | *0.0359* | 0.54405 | 0.42671 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | 123 | 0.25117 | 0.17175 | 0.31114 | *0.0285* | 0.87876 | 0.21322 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | Avg. Level of Sig. Var.. | 0 | 0.143 | 0 | 0.429 | 0 | 0 | *0.048* | *0.143* | *0.214* | *0.071* | *0.000* | *0.095* |

***Table-7. Results of Leven's Test for the Equality of Variance- Dxgroup-7***

| Compared PCs. | | Level-I | | | | | | Level-II | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Sig. (Females- p value) | | | Sig. (Males- p value) | | | Avg. Consistency of Sig. Var. | | | | | |
| | | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | F | M | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 1 | *2* | *0.0338* | *0.0457* | 0.25027 | *0.0205* | 0.119 | 0.77817 | *0.667* | *0.333* | *1.000* | *0.500* | *0.000* | *0.500* |
| | *3* | *0.0328* | *0.0421* | 0.829 | 0.46561 | 0.49865 | 0.70867 | *0.667* | *0.000* | *0.500* | *0.500* | *0.000* | *0.333* |
| | *4* | 0.4112 | 0.91097 | 0.10402 | 0.78831 | 0.43071 | 0.17067 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *23* | *0.0191* | 0.11841 | 0.95588 | 0.31391 | 0.18045 | 0.8184 | *0.333* | *0.000* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *24* | 0.35299 | 0.85552 | 0.10954 | 0.70822 | 0.80215 | 0.22572 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *34* | 0.26595 | 0.58159 | 0.23986 | 0.69361 | 0.67719 | 0.25793 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *234* | 0.23356 | 0.64517 | 0.23537 | 0.63571 | 0.97115 | 0.30249 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *Avg. Level of Sig. Var.* | 0.429 | 0.286 | 0 | 0.143 | 0 | 0 | *0.238* | *0.048* | *0.286* | *0.143* | *0.000* | *0.143* |
| 2 | *1* | *0.0338* | *0.0457* | 0.25027 | *0.0205* | 0.119 | 0.77817 | *0.667* | *0.333* | *1.000* | *0.500* | *0.000* | *0.500* |
| | *3* | 0.95463 | 0.87323 | 0.27767 | *0.0231* | 0.1896 | 0.51071 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *4* | 0.15797 | 0.09298 | 0.62522 | *0.0415* | 0.08105 | 0.13321 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *13* | 0.61628 | 0.58149 | 0.26446 | *0.0443* | 0.15152 | 0.59105 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *14* | 0.13727 | 0.07903 | 0.7832 | *0.0396* | 0.0817 | 0.23191 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *34* | 0.25784 | 0.1678 | 0.97855 | *0.0419* | 0.09665 | 0.19287 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *134* | 0.22571 | 0.14445 | 0.9274 | *0.0416* | 0.09569 | 0.26278 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *Avg. Level of Sig. Var.* | 0.143 | 0.143 | 0 | *1* | 0 | 0 | *0.095* | *0.333* | *0.571* | *0.071* | *0.000* | *0.214* |
| 3 | *1* | *0.0328* | *0.0421* | 0.829 | 0.46561 | 0.49865 | 0.70867 | *0.667* | *0.000* | *0.500* | *0.500* | *0.000* | *0.333* |
| | *2* | 0.95463 | 0.87323 | 0.27767 | *0.0231* | 0.1896 | 0.51071 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *4* | 0.15117 | 0.08129 | 0.15682 | 0.67322 | 0.19921 | 0.10404 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *12* | 0.07088 | 0.123 | 0.55134 | 0.90163 | 0.65571 | 0.67427 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *14* | 0.13149 | 0.06968 | 0.19788 | 0.65944 | 0.20484 | 0.32894 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *24* | 0.16067 | 0.08798 | 0.16194 | 0.74575 | 0.38474 | 0.18188 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *124* | 0.13907 | 0.07699 | 0.19771 | 0.72208 | 0.36973 | 0.41418 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *Avg. Level of Sig. Var.* | 0.143 | 0.143 | 0 | 0.143 | 0 | 0 | *0.095* | *0.048* | *0.143* | *0.071* | *0.000* | *0.071* |
| 4 | *1* | 0.4112 | 0.91097 | 0.10402 | 0.78831 | 0.43071 | 0.17067 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *2* | 0.15797 | 0.09298 | 0.62522 | *0.0415* | 0.08105 | 0.13321 | *0.000* | *0.333* | *0.500* | *0.000* | *0.000* | *0.167* |
| | *3* | 0.15117 | 0.08129 | 0.15682 | 0.67322 | 0.19921 | 0.10404 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *12* | 0.81352 | 0.56038 | 0.25623 | 0.75038 | 0.19654 | 0.16764 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *13* | 0.33967 | 0.21728 | 0.13665 | 0.74334 | 0.28776 | 0.18125 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *23* | 0.09923 | 0.1994 | 0.22051 | 0.48939 | 0.0662 | 0.11416 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *123* | 0.23756 | 0.26981 | 0.18244 | 0.60502 | 0.13722 | 0.17703 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *Avg. Level of Sig. Var.* | 0 | 0 | 0 | 0.143 | 0 | 0 | *0.000* | *0.048* | *0.071* | *0.000* | *0.000* | *0.024* |

***Table-8. Results of Leven's Test for the Equality of Variance- Dxgroup-9***

| | | Level-I | | | | | |
|---|---|---|---|---|---|---|---|
| | | Sig. Dif. (F)-p value | | | Sig. Dif. (M)-p value | | |
| Comp.PC. | | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 |
| 1 | 2 | 0.74039 | 0.75123 | 0.80133 | 0.58511 | 0.59491 | 0.66859 |
| | 3 | 0.59417 | 0.34198 | 0.25043 | 0.55202 | 0.70818 | 0.6449 |
| | 4 | 0.40323 | 0.18645 | 0.20965 | 0.74199 | 0.14422 | 0.64495 |
| | 23 | 0.70263 | 0.42648 | 0.29953 | 0.69997 | 0.97912 | 0.52275 |
| | 24 | 0.42451 | 0.20208 | 0.23014 | 0.78681 | 0.17084 | 0.61978 |
| | 34 | 0.56174 | 0.181 | 0.21747 | 0.69052 | 0.18811 | 0.55196 |
| | 234 | 0.57361 | 0.1964 | 0.23747 | 0.72719 | 0.22634 | 0.55026 |
| | Avg. level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 1 | 0.74039 | 0.75123 | 0.80133 | 0.58511 | 0.59491 | 0.66859 |
| | 3 | 0.40998 | 0.50904 | 0.34101 | 0.12776 | 0.52433 | 0.85256 |
| | 4 | 0.70704 | 0.27424 | 0.39372 | 0.22725 | 0.10533 | 0.93251 |
| | 13 | 0.46716 | 0.70498 | 0.59568 | 0.22738 | 0.68793 | 0.95445 |
| | 14 | 0.77051 | 0.30072 | 0.45748 | 0.25444 | 0.11608 | 0.85055 |
| | 34 | 0.89083 | 0.2771 | 0.39648 | 0.19048 | 0.13585 | 0.77743 |
| | 134 | 0.93527 | 0.3024 | 0.44761 | 0.21477 | 0.15702 | 0.80037 |
| | Avg. level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 1 | 0.59417 | 0.34198 | 0.25043 | 0.55202 | 0.70818 | 0.6449 |
| | 2 | 0.40998 | 0.50904 | 0.34101 | 0.12776 | 0.52433 | 0.85256 |
| | 4 | 0.11623 | 0.58816 | 0.69392 | 0.60592 | 0.34167 | 0.90194 |
| | 12 | 0.37515 | 0.34348 | 0.2735 | 0.41469 | 0.60011 | 0.8843 |
| | 14 | 0.14066 | 0.65338 | 0.62234 | 0.58074 | 0.39858 | 0.96544 |
| | 24 | 0.1272 | 0.63929 | 0.66215 | 0.53534 | 0.39686 | 0.9205 |
| | 124 | 0.15062 | 0.70162 | 0.59843 | 0.52525 | 0.43657 | 0.95854 |
| | Avg. level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | 1 | 0.40323 | 0.18645 | 0.20965 | 0.74199 | 0.14422 | 0.64495 |
| | 2 | 0.70704 | 0.27424 | 0.39372 | 0.22725 | 0.10533 | 0.93251 |
| | 3 | 0.11623 | 0.58816 | 0.69392 | 0.60592 | 0.34167 | 0.90194 |
| | 12 | 0.41279 | 0.18494 | 0.25257 | 0.60208 | 0.1181 | 0.96738 |
| | 13 | 0.14092 | 0.4009 | 0.87971 | 0.87931 | 0.20562 | 0.99657 |
| | 23 | 0.13281 | 0.47623 | 0.83808 | 0.91065 | 0.2107 | 0.76824 |
| | 123 | 0.15077 | 0.36211 | 0.80356 | 0.95989 | 0.16785 | 0.91304 |
| | Avg. level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 |

***Table-9. Results of Leven's Test for the Equality of Variance- Dxgroup-10.***

| | Compared PCs. | Level-I | | | | | | Level-II | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Sig. (Females- p value) | | | Sig. (Males- p value) | | | Avg. Consistency of Sig. Var. | | | | | |
| | | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | F | M | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 1 | 2 | 0.2855 | 0.9995 | 0.2728 | 0.3433 | 0.1968 | 0.3957 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 3 | 0.539 | 0.938 | 0.1447 | 0.7056 | 0.1784 | 0.3472 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 4 | 0.9859 | 0.9795 | 0.1443 | 0.7393 | 0.3519 | 0.7815 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 23 | 0.7219 | 0.9732 | 0.3279 | 0.8619 | 0.1718 | 0.3876 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 24 | 0.9601 | 0.981 | 0.1694 | 0.7816 | 0.3248 | 0.8087 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 34 | 0.8725 | 0.9765 | 0.1162 | 0.7688 | 0.2964 | 0.9546 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 234 | 0.917 | 0.978 | 0.1367 | 0.8012 | 0.2808 | 0.9306 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | Avg. Level of Sig. Var. | 0 | 0 | 0 | 0 | 0 | 0 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| 2 | 1 | 0.2855 | 0.9995 | 0.2728 | 0.3433 | 0.1968 | 0.3957 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 3 | 0.162 | 0.9393 | *0.005* | 0.1705 | 0.8883 | 0.7729 | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | 4 | 0.319 | 0.9802 | *0.002* | 0.2287 | 0.4675 | 0.2505 | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | 13 | 0.1845 | 0.9746 | *0.017* | 0.2077 | 0.5934 | 0.8499 | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | 14 | 0.3181 | 0.9818 | *0.003* | 0.2365 | 0.355 | 0.2629 | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | 34 | 0.2683 | 0.9773 | *0.002* | 0.2381 | 0.5586 | 0.439 | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | 134 | 0.2703 | 0.9788 | *0.003* | 0.2441 | 0.4519 | 0.4242 | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | Avg. Level of Sig. Var. | 0 | 0 | *0.857* | 0 | 0 | 0 | *0.286* | *0.000* | *0.000* | *0.000* | *0.429* | *0.143* |
| 3 | 1 | 0.539 | 0.938 | 0.1447 | 0.7056 | 0.1784 | 0.3472 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 2 | 0.162 | 0.9393 | *0.005* | 0.1705 | 0.8883 | 0.7729 | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | 4 | 0.5611 | 0.9604 | 0.8368 | 0.9874 | 0.406 | 0.2523 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 12 | 0.2599 | 0.9375 | 0.1712 | 0.5205 | 0.3576 | 0.4251 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 14 | 0.5556 | 0.9583 | 0.8362 | 0.9515 | 0.3089 | 0.2587 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 24 | 0.5222 | 0.9585 | 0.7591 | 0.9373 | 0.4442 | 0.2644 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 124 | 0.5195 | 0.9567 | 0.7698 | 0.9085 | 0.346 | 0.2682 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | Avg. Level of Sig. Var. | 0 | 0 | 0.143 | 0 | 0 | 0 | *0.048* | *0.000* | *0.000* | *0.000* | *0.071* | *0.024* |
| 4 | 1 | 0.9859 | 0.9795 | 0.1443 | 0.7393 | 0.3519 | 0.7815 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 2 | 0.319 | 0.9802 | *0.002* | 0.2287 | 0.4675 | 0.2505 | *0.333* | *0.000* | *0.000* | *0.000* | *0.500* | *0.167* |
| | 3 | 0.5611 | 0.9604 | 0.8368 | 0.9874 | 0.406 | 0.2523 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 12 | 0.5201 | 0.9795 | 0.1737 | 0.569 | 0.6994 | 0.6169 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 13 | 0.653 | 0.9951 | 0.8559 | 0.9215 | 0.9828 | 0.4112 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 23 | 0.7439 | 0.9946 | 0.5248 | 0.8538 | 0.3844 | 0.2811 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | 123 | 0.8026 | 0.9992 | 0.6114 | 0.8184 | 0.8524 | 0.4183 | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | Avg. Level of Sig. Var. | 0 | 0 | 0.143 | 0 | 0 | 0 | *0.048* | *0.000* | *0.000* | *0.000* | *0.071* | *0.024* |

*Table-10. Results of Leven's Test for the Equality of Variance- Dxgroup-11*

| Comp.PC. | | Level-I<br>Sig. Dif. (F)-p value<br>Gen.1 | Gen.2 | Gen.3 |
|---|---|---|---|---|
| 1 | 3 | 0.84404 | 0.7728 | 0.97747 |
| | 4 | 0.95605 | 0.70147 | 0.94388 |
| | 23 | 0.86068 | 0.83598 | 0.82871 |
| | 24 | 0.97955 | 0.72628 | 0.96341 |
| | 34 | 0.99817 | 0.71092 | 0.9852 |
| | 234 | 0.98436 | 0.73177 | 0.99733 |
| | Avg. Level of Sig Var. | 0 | 0 | 0 |
| 2 | 1 | 0.88972 | 0.93291 | 0.97877 |
| | 3 | 0.9588 | 0.84029 | 1 |
| | 4 | 0.85058 | 0.76491 | 0.93108 |
| | 13 | 0.97452 | 0.94142 | 0.95707 |
| | 14 | 0.85647 | 0.8013 | 0.97183 |
| | 34 | 0.89244 | 0.77549 | 0.96734 |
| | 134 | 0.89144 | 0.80405 | 1 |
| | Avg. Level of Sig Var. | 0 | 0 | 0 |
| 3 | 1 | 0.84404 | 0.7728 | 0.97747 |
| | 2 | 0.9588 | 0.84029 | 1 |
| | 4 | 0.80525 | 0.91369 | 0.92753 |
| | 12 | 0.89405 | 0.80372 | 0.86296 |
| | 14 | 0.81054 | 0.95403 | 0.97022 |
| | 24 | 0.82536 | 0.94327 | 0.94561 |
| | 124 | 0.82745 | 0.97873 | 0.98059 |
| | Avg. Level of Sig Var. | 0 | 0 | 0 |
| 4 | 1 | 0.95605 | 0.70147 | 0.94388 |
| | 2 | 0.85058 | 0.76491 | 0.93108 |
| | 3 | 0.80525 | 0.91369 | 0.92753 |
| | 12 | 0.90869 | 0.73037 | 0.78652 |
| | 13 | 0.87055 | 0.81689 | 0.87075 |
| | 23 | 0.82154 | 0.85446 | 0.79337 |
| | 123 | 0.86486 | 0.80128 | 0.78173 |
| | Avg. Level of Sig Var. | 0 | 0 | 0 |

***Table-11. Results of Leven's Test for the Equality of Variance- Dxgroup-12***

| Compared PCs. | | Level-I | | | | | | Level-II | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Sig. (Females- p value) | | | Sig. (Males- p value) | | | Avg. Consistency of Sig. Var. | | | | | |
| | | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | F | M | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 1 | *2* | 0.51733 | 0.59784 | 0.1676 | 0.09808 | . | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *3* | 0.08044 | 0.09263 | 0.58105 | 0.69573 | 0.11611 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *4* | 0.14893 | 0.22344 | 0.41849 | 0.2628 | 0.06252 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *23* | 0.08152 | 0.35836 | 0.94975 | 0.76517 | 0.11611 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *24* | 0.12834 | 0.24011 | 0.56275 | 0.24247 | 0.06251 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *34* | 0.12807 | 0.34786 | 0.82468 | 0.39264 | 0.08237 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *234* | 0.11566 | 0.36054 | 0.97287 | 0.36189 | 0.08237 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *Avg. Level of Sig. Var.* | 0 | 0 | 0 | 0 | 0 | *0.571* | *0.000* | *0.190* | *0.000* | *0.000* | *0.286* | *0.095* |
| 2 | *1* | 0.51733 | 0.59784 | 0.1676 | 0.09808 | . | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *3* | 0.41241 | 0.12477 | 0.63947 | 0.18581 | 0.11611 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *4* | 0.62183 | 0.54473 | 0.43744 | 0.47838 | 0.06252 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *13* | 0.23291 | 0.13491 | 0.27207 | 0.14133 | 0.11612 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *14* | 0.50728 | 0.72704 | 0.39844 | 0.39972 | 0.06251 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *34* | 0.57249 | 0.7778 | 0.28186 | 0.36963 | 0.08237 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *134* | 0.48331 | 0.95066 | 0.26717 | 0.32586 | 0.08237 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *Avg. level of Sig. Var.* | 0 | 0 | 0 | 0 | 0 | *0.571* | *0.000* | *0.190* | *0.000* | *0.000* | *0.286* | *0.095* |
| 3 | *1* | 0.08044 | 0.09263 | 0.58105 | 0.69573 | 0.11611 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *2* | 0.41241 | 0.12477 | 0.63947 | 0.18581 | 0.11611 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *4* | 0.47089 | *0.0422* | 0.93463 | 0.46551 | 0.88628 | *0.0325* | *0.333* | *0.333* | *0.000* | *0.500* | *0.500* | *0.333* |
| | *12* | 0.72022 | 0.16759 | 0.34202 | 0.74084 | 0.11611 | . | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* | *0.000* |
| | *14* | 0.73334 | 0.05334 | 0.89521 | 0.52786 | 0.97124 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *24* | 0.53806 | *0.0445* | 0.80385 | 0.43706 | 0.97663 | *0.0325* | *0.333* | *0.333* | *0.000* | *0.500* | *0.500* | *0.333* |
| | *124* | 0.80173 | 0.05605 | 0.78002 | 0.49607 | 0.89296 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *Avg. Level of Sig. Var.* | 0 | 0.286 | 0 | 0 | 0 | *0.571* | *0.095* | *0.190* | *0.000* | *0.143* | *0.286* | *0.143* |
| 4 | *1* | 0.14893 | 0.22344 | 0.41849 | 0.2628 | 0.06252 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *2* | 0.62183 | 0.54473 | 0.43744 | 0.47838 | 0.06252 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *3* | 0.47089 | *0.0422* | 0.93463 | 0.46551 | 0.88628 | *0.0325* | *0.333* | *0.333* | *0.000* | *0.500* | *0.500* | *0.333* |
| | *12* | 0.34719 | 0.11584 | 0.13392 | 0.60679 | 0.06252 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *13* | 0.11082 | *0.0443* | 0.65305 | 0.33773 | 0.46831 | *0.0325* | *0.333* | *0.333* | *0.000* | *0.500* | *0.500* | *0.333* |
| | *23* | 0.44604 | 0.09737 | 0.44667 | 0.52686 | 0.58833 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *123* | 0.05287 | 0.06361 | 0.18788 | 0.434 | 0.34266 | *0.0325* | *0.000* | *0.333* | *0.000* | *0.000* | *0.500* | *0.167* |
| | *Avg. Level of Sig. Var.* | 0 | 0.286 | 0 | 0 | 0 | 1 | *0.095* | *0.333* | *0.000* | *0.143* | *0.500* | *0.214* |

***Table-12. Results of leven's Test for the Equality of Variance: Dxgroup-13***

| | | Level-I | | | Level-II | | | |
|---|---|---|---|---|---|---|---|---|
| | | Sig. (Female & Male-p value) | | | Avg. Consistency of Sig. Var. | | | |
| Comp.PC. | | Gen.1 | Gen.2 | Gen.3 | Gen.1 | Gen.2 | Gen.3 | Tot. Avg. |
| 1 | 2 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 3 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 4 | 6.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 23 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 24 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 34 | 3.00E-14 | . | . | 1.000 | 0.000 | 0.000 | 0.333 |
| | 234 | . | 9.00E-14 | . | 0.000 | 1.000 | 0.000 | 0.333 |
| | Avg. Level of Sig. Var. | 0.286 | 2.86E-01 | 0.143 | 0.286 | 0.286 | 0.143 | 0.238 |
| 2 | 1 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 3 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 4 | 2.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 13 | 3.00E-14 | . | . | 1.000 | 0.000 | 0.000 | 0.333 |
| | 14 | . | . | 6.00E-15 | 0.000 | 0.000 | 1.000 | 0.333 |
| | 34 | 3.00E-15 | . | . | 1.000 | 0.000 | 0.000 | 0.333 |
| | 134 | 4.00E-15 | . | 3.00E-15 | 1.000 | 0.000 | 1.000 | 0.667 |
| | Avg. Level of Sig. Var. | 5.71E-01 | 0.143 | 4.29E-01 | 0.571 | 0.143 | 0.429 | 0.381 |
| 3 | 1 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 2 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 4 | 2.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 12 | 3.00E-14 | . | . | 1.000 | 0.000 | 0.000 | 0.333 |
| | 14 | . | . | 6.00E-15 | 0.000 | 0.000 | 1.000 | 0.333 |
| | 24 | . | . | . | 0.000 | 0.000 | 0.000 | 0.000 |
| | 124 | 1.00E-15 | . | . | 1.000 | 0.000 | 0.000 | 0.333 |
| | Avg. Level of Sig. Var.. | 4.29E-01 | 0.143 | 0.286 | 0.429 | 0.143 | 0.286 | 0.286 |
| 4 | 1 | 6.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 2 | 2.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 3 | 2.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 12 | 7.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 13 | 5.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 23 | 2.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | 123 | 3.00E-15 | 9.00E-15 | 3.00E-15 | 1.000 | 1.000 | 1.000 | 1.000 |
| | Avg. Level of Sig. Var. | 1 | 1 | 1 | 1.000 | 1.000 | 1.000 | 1.000 |