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An Overview of Human Genetic Disorders with Special Reference to African Americans

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Introduction

Genetic disorders are the harmful effects on an individual caused by inherited genetic diseases. Racial disparities exist and a variety of factors, including genetics, seem to play a role. Usually genetic disorders are recessive, so they are expressed only in a small percentage of the population. When expressed in the homozygous recessive individual, they often code for the wrong protein or amino acid sequence. There are many genetic disorders for African Americans and they are cardiovascular disease, diabetes, HIV/AIDS, sickle cell disease, cancer, and vitamin D deficiency. Genes definitely play a role, so does the environment where the people live and the socioeconomic status. Usually genetic disorders are recessive, so they are expressed only in a small percentage of the population.

Diabetes

Diabetes among African Americans is twice as likely to be diagnosed compared to general population. Approximately 13% of the U.S. adults have type-2 diabetes. African Americans also suffer more from comorbidities of diabetes, such as high blood pressure (hypertension) and high cholesterol (hyperlipidaemia). Along with genetics, obesity is the major risk factors for diabetes as it affects the African American community. Among patients with diabetes, African Americans have higher overall incidence rates of End Stage Renal Disease (ESRD), diabetic neuropathy, retinopathy, and Chronic Glomerulonephritis (CGN). African American diabetic patients exhibit a particular lipid profile that is different from the rest of the population: low HDLs (High Density Lipoproteins), high LDLs (Low-Density Lipoproteins), or increased levels of triglycerides (fats in blood) are all risk factors for heart disease, obesity, and stroke. Type 2 diabetes is more common in African American women than men. The genome-wide admixture scans identified two potential loci for diabetes at 9p21, 12p13.31 and 13q14.3 [1].

Hypertension

It is known for many years that in the United States people of African descent are more likely to develop hypertension. Blood pressure is measured with a sphygmomanometer, which gives a reading of two numbers: systolic and diastolic pressure. The systolic reading indicates the maximum pressure exerted by the blood on the arterial walls, this high point occurs when the left ventricle of the heart contracts, forcing blood through the arteries. Diastolic pressure is a measure of the lowest pressure on the blood vessel walls and happens when the left ventricle relaxes and refills with blood. When blood pressure consistently above 140/90 (normal blood pressure systolic 120 and diastolic 80), physicians diagnose hypertension. The Renin-Angiotensin-Aldosterone System (RAAS), intricate series of chemical reactions has the net effect of controlling the amount of the protein angiotensin II (present in the blood stream). The RAAS performs a range of functions, e.g., prompting the constriction of blood vessels which causes a rise in blood pressure, and triggering the release of another crucial chemical, aldosterone, which induces an increase in the reuptake of sodium by the kidneys. Some of the risk factors for hypertension might promote the disorder by elevating levels of angiotensinogen in the blood. Obesity, in particular, may contribute to chronic high blood pressure. Researchers reported that two alleles of the angiotensinogen gene viz., 235T and 174M are related with high levels of circulating angiotensinogen. The 235T allele is twice as common among African Americans. Recent Genome-Wide Association Studies (GWAS) of common genetic variants found 13 Single Nucleotide Polymorphisms (SNPs) or variants in systolic and 20 for diastolic blood pressure readings representing different genes and genetic heterogeneity. Hypertension is the second leading cause of kidney failure, which needs dialysis or a kidney transplant in order to live [2].

Pancreatic Cancer

Pancreatitis is an inflammatory disease of the pancreas. Pancreatitis may either be acute (sudden and severe) or chronic (long-standing). Individuals that have had repeated attacks of acute pancreatitis can develop chronic pancreatitis [3]. The risk of pancreatic cancer is elevated in all patients with pancreatitis and African Americans are at the highest risk of developing pancreatitis of any racial group. Pancreatic cancer is the fourth leading cause of cancer death in the United States. The incidence is 50-90% higher in African American than any other racial group in the United States. The environmental and socioeconomic factors are responsible for high incidence of the disease. Cigarette smoking is one of the main causes for the disease. Other risk factors for pancreatic cancer include diabetes mellitus, pancreatitis, and being overweight. Type 2 diabetes (associated with obesity and lack of exercise) doubles the risk of pancreatic cancer. Highly frequent mutational changes affecting the DPC4 gene, p16 gene, and p53 gene has also been reported. K-ras gene mutations are known to be common in pancreatic cancer [4].

Prostate Cancer

Prostate cancer occurs more often in African American men than in men of other races. African American men are also more than twice as likely to die of prostate cancer as white men. Prostate cancer seems to

run in some families. Researchers at National Human Genome Research Institute (NHGRI), John Hopkins Medical Institutions, The Cleveland Clinic and their collaborators have identified a specific gene called ribonuclease L (RNASEL) in the Hereditary Prostate Cancer on chromosome 1 (HPC1) region that contains mutations associated with prostate cancer in some families with a history of the disease. Scientists mapped prostate cancer susceptibility genes to chromosomes 1, 17, 20 and X. Having a father or brother with prostate cancer more than doubles a man's risk of developing this disease. Inherited mutations in particular genes, such as BRCA1, BRCA2, and HOXB13, account for some cases of hereditary prostate cancer. Mutations in these genes may also increase prostate cancer risk in men. Men with hereditary non-polyposis colorectal cancer (HNPCC or Lynch syndrome) caused by inherited gene changes, have an increased risk for a number of cancers, including prostate cancer. The development and progression of prostate cancer involve testosterone and other androgens (or male hormones). The gene, CYP3A4 is involved in the metabolism of testosterone. It is reported that the people carry the genetic variant AGGGCAGGAG (instead of normal AGGGCAAGAG) has higher stage tumors and higher Gleason scores than the men who do not carry the genetic variant. Researchers hypothesized that if the genes no longer metabolize testosterone properly, the genetic variant could lead to the development of prostate cancer [5-8].

Alzheimer's Disease

Alzheimer disease is a degenerative disease of the brain that causes dementia, which is a gradual loss of memory, judgment, and ability to function. Alzheimer disease currently affects an estimated 2.4 million to 4.5 million Americans. Researchers have found that this form of the disorder can result from mutations in one of three genes: APP, PSEN1, or PSEN2. A gene called APOE has been studied extensively as a risk factor for the disease. In particular, a variant of this gene called the e4 allele seems to increase an individual's risk for developing late-onset Alzheimer disease. Variants in the ATP-binding cassette transporter (ABCA7) and the apolipoprotein E (APOE-e4) alleles are major genetic risk factors for late onset Alzheimer's disease among African Americans. Researchers were able to identify genes linked to *tau* protein which develops in the brain of Alzheimer's patients as the disease slowly progresses [9-11].

Sickle Cell Disease

Sickle Cell Disease (SCD) describes a group of inherited red blood cell (erythrocytes) disorders. People with SCD have abnormal haemoglobin, called haemoglobin S or sickle haemoglobin, in their red blood cells. SCD is a serious blood disorder that affects the red blood cells, which use a protein called haemoglobin to transport oxygen from the lungs to the rest of the body. Mutations in the haemoglobin gene cause sickle cell disease. SCD is the most common genetic disorder in the United States with higher frequency in African Americans when compared to other populations. About one in 500 African American babies are born with sickle cell anaemia and one in 12 African American people carry the gene for this trait or disease. About 100,000 Americans are thought to be living with SCD, and every year another 1,000 babies are born with the disease. Approximately 3 million Americans including 10% of African American population carry one gene for SCD (i.e., sickle cell trait). SCD has several recognized forms including sickle cell anaemia, sickle cell haemoglobin C disease and sickle cell thalassemia disease. The red blood cells of patients with SCD don't live as long as healthy red blood cells. So people with this disorder often have low red blood cell counts (anaemia), which is why this disease is commonly referred to as sickle cell anaemia. Affected patients characteristically are asymptomatic until approximately 4 to 6 months of age. The median age at death is approximately 42 years for men and 48 years for women.

Patients with sickle cell disease have a mutation in a gene on chromosome 11 that codes for the beta subunit of the haemoglobin protein. As a result, haemoglobin molecules don't form properly, causing red blood cells to be rigid and have a concave shape (like a sickle used to cut wheat). People are born with SCD, it does not develop in adulthood, and it is not contagious. SCD is inherited in an autosomal recessive pattern. This means that a child will not inherit the disease unless both parents pass down a defective copy of the gene. People who inherit one good copy of the gene (A) and one mutated copy (S) are carriers (always more A than S). They are clinically normal, but can still pass the defective gene to their children (corresponding change in codon 6 of the beta-globin gene GAG to GTG). While most people with sickle cell trait are unaffected carriers who don't experience SCD symptoms or complications, a very small number can develop problems when they are exposed to factors viz., high altitude, yellow eyes or jaundice, increased atmospheric pressure, low oxygen, early gallstones, lung blockage, delayed growth, eye damage, kidney damage, priapism (painful erection in men), sequestration (blood blockage in spleen or liver), and severe dehydration [12,13].

Kidney Disease

Black Americans are three times more likely than white Americans to develop kidney disease. The most common causes of kidney disease in the black population are diabetes and high blood pressure. The high risk genetic variant in a gene called Apolipoprotein L1 (APOL1), speed up kidney disease progression and substantially increase the risk of developing kidney failure. In fact, more than 1 in 3 kidney failure patients living in the United States is African American which is over 150,000 people. One copy of the APOL1 gene risk variant provides protection from the parasite (*Trypanosoma brucei rhodesience*) that causes African American sleeping sickness, a disease transmitted by the tse-tse fly. When individuals inherit two copies of the APOL1 risk variant, their risk of kidney disease increases seven to ten fold. About 70 percent of African Americans with non-diabetic forms of kidney disease have the newly isolated MYH9 gene on chromosome 22 [14-16].

Inflammatory Bowel Disease

Although the risk is slightly lower than that of white Americans, African Americans are at significant risk for Inflammatory Bowel Disease (IBD). Crohn's disease and ulcerative colitis are chronic autoimmune diseases that affect as many as 1.6 million Americans. Patients with IBD have immune systems that attack their own intestines, resulting in inflammation. The researchers at Emory University School of Medicine, John Hopkins Meyerhoff Inflammatory Bowel Disease Center and Cedars-Sinai found the gene variants within three of the most highly associated regions for Crohn's disease-NOD2, interleukin 23 receptor (IL23R), and a region on chromosome 5 known as 5p15.1. Identifying specific regions of the African American genome, the researchers found evidence for regions on four of the 22 autosomal chromosomes 10, 15, 16 and 17 (viz., STAT3 and STAT5) as causative for IBD [17].

AIDS

The people of African descent are much more likely to have a genetic trait that makes them more susceptible to infection with the HIV virus. Human Immunodeficiency Virus (HIV), like all viruses, can't make new copies of itself without help. It needs to enter cells and use their machinery to reproduce and spread throughout the body. HIV can only enter certain cells by special proteins, called receptors. Receptors sit on the outside of cells to receive messages and transmit them into the cell. HIV grabs onto cells that have a receptor (cell surface molecule) called CD^{4+}. Cells with the CD^{4+} receptor are an important part of the body's system for fighting all diseases (our immune system). HIV gradually destroys these cells and cripples the immune system. It turns out that CD^{4+} isn't enough. Another protein called, chemokine receptor gene (CCR5) is needed as well. CCR5, called a co-receptor because it works with CD^{4+}, is the door that opens to allow HIV to enter the cell. Many people who are resistant to HIV have a mutation in the CCR5 gene called CCR5-delta32. The CCR5-delta32 mutation results in a smaller protein that isn't on the outside of the cell anymore. Most forms of HIV cannot infect cells if there is no CCR5 on the surface [18-21].

Sarcoidosis

Sarcoidosis is a disease that causes inflammation of the body's tissues. It affects multiple systems (predominantly lungs and lymphatic system) and is characterized by the formation of granulomas (small lumps). The age-adjusted incidence rate for African Americans is over three times that of Caucasians. A scan of the entire genome among African American families identified chromosome 5 as a potential home for the gene that could be related to sarcoidosis risk [22].

Discussion

Of all minority groups, African Americans have the most, and many times the largest, differences in health risks when compared to other minority groups. African Americans have more disease, disability, and early death as well. The onset of diabetes can be prevented through diet and lifestyle changes. Keeping blood glucose (blood sugar), blood pressure, and cholesterol levels in the recommended target range are the keys to prevent, reduce or significantly delay the chance of getting diabetes. The hypertension can generally be managed with the help of special diets, exercise regimens, and medication. Further understanding of the genetics of hypertension will require the use of advances in bioinformatics tools and genetic technology [e.g., SNP, exon and noncoding (micro) RNA arrays]. There are steps (maintain a healthy weight, eating healthy diet, being physically active, take medicine as directed, limit alcohol and avoid tobacco) to help prevent or control high blood pressure and protect kidneys from permanent and progressive damage. There are tests viz., a blood test for creatinine to determine estimated Glomerular Filtration Rate (eGFR; normal is 60) which shows how well the kidneys are filtering wastes from the blood and urine test to see the amount of albumin can tell how well the kidney are working. Men who eat a lot of red meat or high-fat dairy products appear to have a slightly higher chance of getting prostate cancer. Most currently licensed HIV drugs target proteins using the virus's genetic material. The introduction of the CCR5 inhibitor maraviroc (Celsentri) changes this picture. This drug targets human proteins, so genetic variation could possibly affect response to treatment. The researchers have identified a gene known as CCL3L1, has the most immunity to HIV. RNA repair may be appropriate genetic approach to treat sickle cell disease though the efficacy of beta-globin RNA repair does not have to be 100% to benefit patients. At present, it is of great importance to figure out why these disorders differ across populations.

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References

1. Cheng CY, Reich D, Haiman CA, Tandon A, Patterson N, et al. (2012) African ancestry and its correlation to type 2 diabetes in African Americans: a genetic admixture analysis in three U.S. population cohorts. PLoS One 7: e32840.
2. Stanford News (2005) Genetics key to African-Americans' hypertension. Stanford University.
3. John Hopkins Medicine (2015) Specific to African American Population.
4. John Hopkins Medicine (2009) The Genetics of Pancreatic Cancer.
5. American Cancer Society (2015) What are the risk factors for prostate cancer?
6. Harvard Medical School (2011) Prostate Cancer Risk in African Americans.
7. National Human Genome Research Institute (2002) Researchers Link Gene to Hereditary Form of Prostate Cancer.
8. Genetics Home Reference (2015) Prostate Cancer. National Library of Medicine, National Institute of Health.
9. University of Miami Health System (2015) Researchers Identify new gene associated with Alzheimer's disease in African Americans.
10. Medical News Today (2013) Alzheimer's Gene Doubles Risk in African Americans.
11. Genetics Home Reference (2015) Alzheimer's Disease. National Library of Medicine, National Institute of Health.
12. Online Mendelian Inheritance in Man (2015) Sickle Cell Anemia.
13. Infoplease (2004) Human Disorders and Gene Therapy.
14. John Hopkins School of Medicine, News Report (2013) Gene Puts African Americans at Higher Risk for Kidney Failure.
15. Wake Forest Baptist Medical Center (2015) APOL1 Gene Discovery: New Pathways to Cure Kidney Disease.
16. Huffpost Healthy Living (2014) Silent Epidemic: Kidney Disease in African American Population.
17. Emory News Center (2015) Study Describes Genetic Risks for Inflammatory Bowel Disease in African Americans.
18. The Washington Post (2008) Genetic Trait Boosts AIDS Risks in Blacks.
19. The Tech Museum of Innovation, Stanford University (2013) The Evolving Genetics of HIV. Can genes stop HIV?
20. AIDSMAP (2015) Genes, Genetics and Inheritance.
21. WIRED (2005) Genetic HIV Resistance Deciphered.
22. American Lung Association (2015) Sarcoidosis.