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Mathematical Modeling of Sickle Cell Anaemia in Nigeria with Cartesian Product of Sets and Relations

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ABSTRACT

Sickle cell disease (SCD) is the commonest monogenetic disease worldwide and its greatest burden found in Sub-Saharan Africa especially Nigeria. Genotype test before contracting marriages has become very imperative because of the danger it poses on the couples, the offspring and in fact the society at large. This work used Cartesian product of sets and relations on sets, to explain how sickle cell anaemia can easily be spread fast, if measures are not taken. Finally we gave suggestions on how to overcome the menace.

Key words: Sickle cell anaemia, Cartesian product of sets, Genotype Test

INTRODUCTION

Sickle cell anaemia, the first genetic disease to be described in terms of a gene mutation, is one of the most common genetic causes of illness and death in the world (Makani *et al*, 2013). The mutation changes the molecule haemoglobin, causing the red blood cells (RBC's) to become stiff and sometimes sickle – shaped when they release oxygen to the body tissues. The sickled cells tend to get stuck in narrow blood vessels, blocking the flow of blood. As a result, those with

sickle cell disease suffer painful 'crises' in their joints and bones. They may suffer strokes, blindness, or damage to lungs, kidneys or heart. They, most often, are hospitalized for blood transfusions and are at risk for a life threatening complication called acute chest syndrome. Although many sufferers of sickle cell disease die before the age of 20, modern medical treatments can sometimes prolong these individuals' lives into their 40s and 50's (Nuffield Foundation, 2008).

There are two versions or alleles of gene important for the inheritance of sickle cell anaemia: A and S individuals with two A's alleles (AA) have normal haemoglobin, and therefore normal RBC's. Those with two S's alleles (SS) develop sickle cell anaemia and have completely abnormal haemoglobin. Those who are heterozygous for the sickle cell allele (AS) produce both normal and abnormal haemoglobin. Heterozygous individuals are usually healthy, but they may suffer some symptoms of sickle cell anaemia under conditions of low blood oxygen, such as high altitudes or during exercise. Heterozygous (AS) individual are said to be carriers of the sickle cell gene. Both forms of haemoglobin are made in the AS heterozygotes (this is different from the situation with the more common dominant and recessives genes where either the

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dominant and recessive characteristics is expressed) Heterozygotes are said to have sickle cell trait.

Sickle cell disease (SCD) is the commonest monogenetic disease worldwide and its greatest burden found in Sub-Saharan Africa especially Nigeria (Weatherall, et al., 2002; Modell et al., 2008). In most parts of West Africa, the prevalence of sickle cell trait ranges between 10 and 40% of the population (WHO, 2013). However, in some areas in Uganda, prevalence has been reported to be as high as 45% while in Nigeria about 20 to 30% of the population are trait carriers (Serjeant, et al, 2001). Sickle cell disease (SCD) has also been shown to be associated with a very high rate (50 to 90%) of childhood mortality (Serjeant, 2005).

Our attitudes towards certain alleles seen in the context of our 21st century environment are strongly influenced by current social and economic factors. The sickle cell allele or cystic fibrosis alleles that were once an advantage in some areas may now have nothing but a negative effect on the quality of human life. Today we have the technology to artificially remove such alleles from the population, for example by ante-natal genetic screening Parents from families with these are faced with decisions about whether it is 'right' to allow children with two copies of the allele to be born, when the technology exists to detect and abort such embryos.

The aim of this paper is to use Cartesian product of set and relation to ascertain the rate at which sickle cell anaemia can spread in Nigerian society, with intention to present effective and definite preventive measures so that we can achieve the desired genotype.

The term "Cartesian" is borrowed from coordinate geometry, where a point in the plane is represented by an ordered pair of real numbers (x, y) called its Cartesian coordinates. The Cartesian product $R \times R$ is then the set of Cartesian coordinates of all points in the plane. The Cartesian product of two sets is a set, and elements of that set are ordered pairs. In each ordered pair the first component is an element of A and the second component is an element of B.

If A_1, A_2, \dots, A_n are nonempty sets, then the Cartesian product of them is the set of all ordered m-tuples (a_1, a_2, \dots, a_m) where $a_i \in A_i$ where $i=1, 2, \dots, m$

Denotes $A_1 \times A_2 \times \dots \times A_m = \{ (a_1, a_2, \dots, a_m) / a_i \in A_i \text{ and } i=1, 2, \dots, m \}$

Subsets of the Cartesian Product

Many of the results of the operations of the sets produce subsets of the Cartesian Products set

Example of Cartesian Product

If $A = (1, 2, 3)$ and $B = (a, b, c)$, find $A \times B$

$A \times B = (1,a), (1,b), (1,c), (2,a), (2,b), (2,c), (3,a), (3,b), (3,c)$

To define Relations, Let A and B be two sets, A relation R from A to B is a Subset of the Cartesian

product $A \times B$. A relation R is a subset of a Cartesian product that uses a definition to state whether an m-tuple is a member of the subset or not. If $(a,b) \in R$, then it is also denoted by aRb means $(a,b) \in R$.

Relation Across same set: Relations may be from one set to the same kind of set, thus $A=B$. Terminology Relation R on A. Such that $R: A \times A$

METHODOLOGY

A relation is a set of ordered pairs. There need be no relationship between the components of ordered pairs: any set of ordered pairs is a relation. Usually, however, we choose which ordered pairs belong to the relation so that components are related in some way. So we think of a relation as somehow representing the connection for example $A = \{Pam, Tsok, Dung\}$ and $B = \{Vou, Mary, Yop\}$ Where A is a set of Male and B a set of female folks then $R = \{(Pam, Vou), (Tsok, Mary), (Dung, Yop)\}$ is a relation from A to B that pairs each male in Set A and his spouse extension in set B.

Matrix of a Relation

We can represent a relation between two finite sets with a matrix

$$M_R = [M_{ij}]$$

$$\text{where } M_{ij} = \begin{cases} 1 & \text{if } (a_i, b_j) \in R \\ 0 & \text{if } (a_i, b_j) \notin R \end{cases}$$

Using Matrices to Denote Cartesian product

For Cartesian product of two sets, you can use a matrix to find the sets.

Example

Assume $A = (1,2,3)$ and $B = (a, b, c)$ The table below represents $A \times B$

X	A	B	C
1	(1,a)	(1,b)	(1,c)
2	(2,a)	(2,b)	(2,c)
3	(3,a)	(3,b)	(3,c)

Theorem 1

For any set A, we have $A \times \Phi = \Phi$ (and $\Phi \times A = \Phi$)

Proof

If $(a,b) \in A \times \Phi$, then $a \in A$ and $b \in \Phi$, this is impossible. End of proof.

Some useful Definitions

Definition 1. The Cartesian product (or cross product) of any sets A and B, denote by $A \times B$, is the set $A \times B = \{(a,b) | a \in A \text{ and } b \in B\}$

1. The elements (a, b) of $A \times B$ are ordered pairs
2. For pairs (a, b), (c, d) we have $(a, b) = (c, d) \leftrightarrow a = c \text{ and } b = d$

Definition 2. The n-fold product of sets A_1, A_2, \dots, A_n is the set of n-tuples $A_1 \times A_2 \times \dots \times A_n = \{ (a_1, a_2, \dots, a_n) | a_i \in A_i \text{ for all } 1 \leq i \leq n \}$

Definition 3. A (binary) relation from a set A to a set B is a subset of $A \times B$.

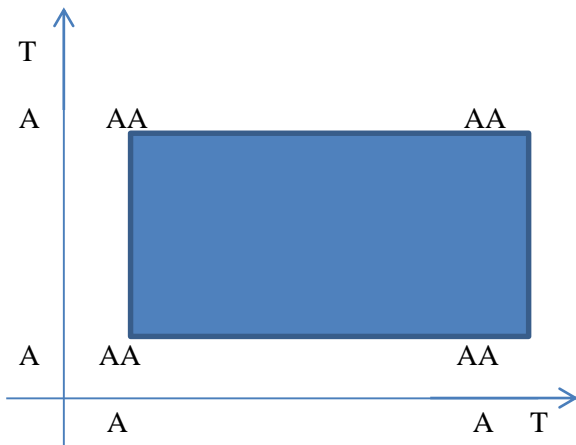
Definition 4. A (binary) relation on A is a subset of $A \times A$.

RESULTS

Throughout this work, the following letters shall be considered as Sets $T = \{AA\}$, $I = \{AS\}$ and $Z = \{SS\}$ which stand for the different genotype. Let $G = \{T, I, Z\}$ represents the universal set of all the genotypes which also stand for both male and female first phyla generation.

Note : The set T is free from sickle cell (The desired genotype) The set I is a carrier of sickle cell (at moderate risk) The set Z is at the highest risk of sickle cell.

A. A relation $R = \{ (AA), (AA), (AA), (AA) \in T \times T \}$
This is the Cartesian product of the set T by T



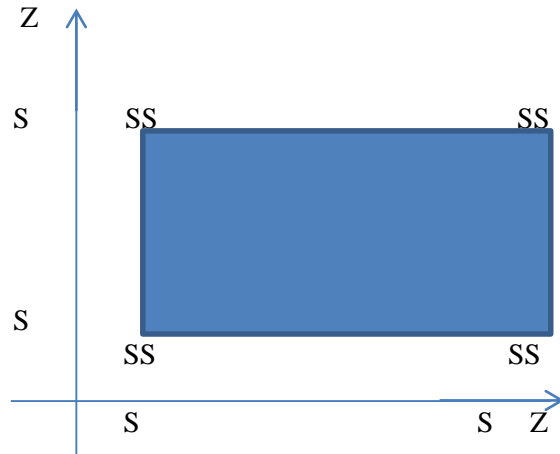
$T \times T = \{ (AA), (AA), (AA), (AA) \}$ as the subset which is the relation R from T to T.

B. A relation $R = \{ (AA), (AS), (AS), (SS) \in I \times I \}$ This is the Cartesian product of the set I by I



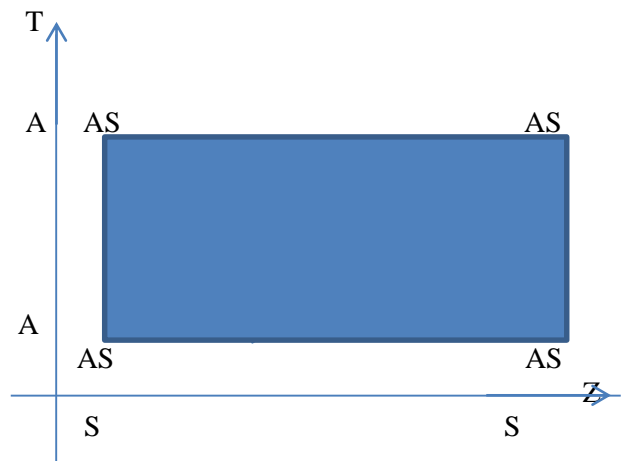
$I \times I = \{ (AA), (AS), (AS), (SS) \}$ as the subset which is the relation R from I to I.

C. A relation $R = \{ (SS), (SS), (SS), (SS) \in Z \times Z \}$ This is the Cartesian product of the set Z by Z



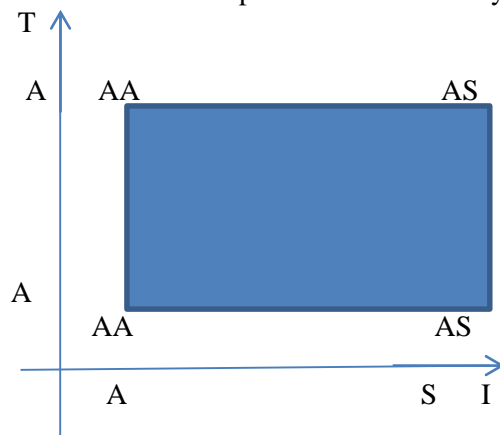
$Z \times Z = \{ (SS), (SS), (SS), (SS) \}$ as the subset which is the relation R from Z to Z.

D. A relation $R = \{ (AS), (AS), (AS), (AS) \in T \times Z \}$
This is the Cartesian product of the set T by Z



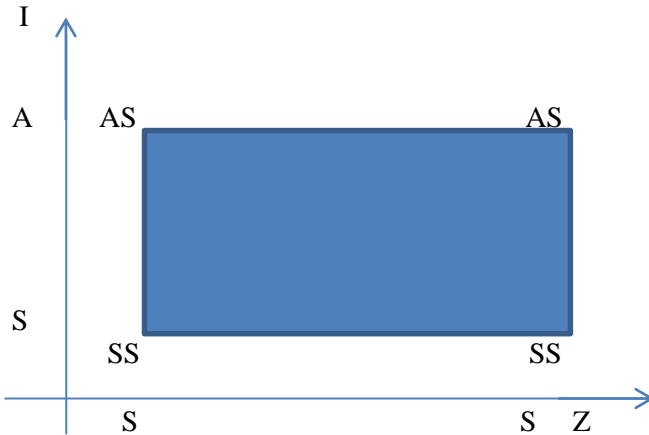
$T \times Z = \{ (AS), (AS), (AS), (AS) \}$ as the subset which is the relation R from T to Z.

E. A relation $R = \{ (AA), (AS), (AA), (AS) \in T \times I \}$
This is the Cartesian product of the set T by I



$T \times I = \{ (AA), (AS), (AA), (AS) \}$ as the subset of which is the relation R from T to I

F. A relation $R = \{ (AS), (AS), (SS), (SS) \in I \times Z \}$ This is the Cartesian product of the set I by Z



$I \times Z = \{ (AS), (AS), (SS), (SS) \}$ as the subset which is the relation R. from I to Z.

Using Matrices to denote Cartesian Products of the set $G = \{ T, I, Z \}$ The table of the Cartesian product $G \times G$ is the table of first phyla generation of nine different families.

X	T			I			Z		
T	AA, AA, AA, AA	AA, AA, AA, AA	AA, AA, AA, AA	AA, AA, AS, AS	AA, AA, AS, AS	AA, AA, AS, AS	AS, AS, AS, AS	AS, AS, AS, AS	AS, AS, AS, AS
I	AA, AA, AS, AS	AA, AA, AS, AS	AA, AA, AS, AS	AA, AS, AS, SS	AA, AS, AS, SS	AA, AS, AS, SS	AS, AS, AS, SS	AS, AS, AS, SS	AS, AS, AS, SS
Z	AS, AS, AS, AS	AS, AS, AS, AS	AS, AS, AS, AS	AS, AS, AS, SS	AS, AS, AS, SS	AS, AS, AS, SS	SS, SS, SS, SS	SS, SS, SS, SS	SS, SS, SS, SS

The interpretation of the results

The interpretation of the Cartesian product on the graph as in A, B, C, D, E and F which is summarize by the table above.

From A. The Cartesian product $T \times T = \{ (AA), (AA), (AA), (AA) \}$ which clearly represents when two persons both with genotype AA got married, their chance of having offspring with AA is sure and the probability of the offspring having AA is 1.
 Probability of the offspring having AS is 0
 Probability of the offspring having SS is 0
 The two A's alleles (AA) have normal haemoglobin, and therefore normal RBC's. When contracting

marriages the two couples having both A's alleles should be encouraged. This kind of union is the best and desired one, because the society will be free from sickle cell anaemia.

From B. The Cartesian product $I \times I = \{ (AA), (AS), (AS), (SS) \}$ this represents two couples with both genotype AS when married their chance of having offspring is observed as below.

Probability of the offspring having AA is $\frac{1}{4}$

Probability of the offspring having AS is $\frac{1}{2}$

Probability of the offspring having SS is $\frac{1}{4}$

The union here produce half chance with moderate risk, while the chances of desired genotype and the genotype with the highest risk, are both one-quarter each. Therefore this can cause serious problem to the society. If only one-quarter of the society are free from sickle cell, one can imagine the kind of challenge that the three- quarter of the society will be faced with. Therefore when contracting marriages, couples who are both heterozygous should be discourage of such union by the appropriate bodies (Churches, Mosques, Traditional, Courts and etc.) contracting such marriage.

From C. The Cartesian product $Z \times Z = \{ (SS), (SS), (SS), (SS) \}$ this represents two couples with both genotype SS when married their chance of having offspring.

Probability of the offspring having AA is 0

Probability of the offspring having AS is 0

Probability of the offspring having SS is 1

Those with S's alleles (SS) develop sickle cell anaemia and have completely abnormal haemoglobin. With this kind of union the society is at the highest risk of sickle cell anaemia. This union should highly be discouraged. Imagine a society that is full with only critically ill people, with no healthy person to help the others.

From D. The Cartesian product $T \times Z = \{ (AS), (AS), (AS), (AS) \}$ this Stand for two couples with one having genotype AA and the other SS when married their chance of having offspring.

Probability of the offspring having AA is 0

Probability of the offspring having AS is 1

Probability of the offspring having SS is 0

This Union can cause moderate risk to the society. If any person with the S's (SS) alleles need to married the only option is for that person's partner be one with A's (AA) alleles. This union also is not advisable, except when it becomes necessary for the person with the S's (SS) alleles to marry.

From E. The Cartesian product $T \times I = \{ (AA), (AS), (AA), (AS) \}$ this represents two couples with one

having genotype AA and the other AS when married their chance of having offspring.

Probability of the offspring having AA is $\frac{1}{2}$

Probability of the offspring having AS is $\frac{1}{2}$

Probability of the offspring having SS is 0

This union can be more acceptable than the cases of B, C, D and F in the absence of case A.

From F. The Cartesian product $I \times Z = \{(AS), (AS), (SS), (SS)\}$ this set represents the offspring of two couples which one of them having genotype AS and the other SS when married, their chance of having offspring has the following observations.

Probability of the offspring having AA is 0

Probability of the offspring having AS is $\frac{1}{2}$

Probability of the offspring having SS is $\frac{1}{2}$

Such union can only pose more danger to the society so it should be discouraged.

The analysis of the table GXG

$G \times G = \{T \times T, I \times I, Z \times Z, T \times Z, T \times I, I \times Z\}$

The table of $G \times G$ which considered the first phyla generation of nine different families' shows that the Cartesian product of all the genotypes has a total 36, at their first phyla generation.

The first column and the first row stand for males and females respectively while their product is their offspring. Thus when contracted marriages they produce offspring which share their genotype as it appear on the table.

The total of the genotype AA after the Cartesian product of all the genotype is 9

The probability of AA is $\frac{9}{36} = \frac{1}{4}$

The total of the genotype AS after the Cartesian product of all the genotypes is 18

The probability of AS is $\frac{18}{36} = \frac{1}{2}$

The total of the genotype SS after the Cartesian product of all the genotypes is 9

The probability of SS is $\frac{9}{36} = \frac{1}{4}$

The above analysis shows that there is more chance of having the risk of many carriers in the society. The table shows that out of these nine different families first phyla generation produces 36 different offspring. The analysis shows that only one-quarter of the offspring will have the AA alleles, which is the desired genotype expected to be attended. Whereas the heterozygous offspring AS alleles will produce half of the entire offspring reproduced at that first phyla generation, while the SS alleles were discovered to take one-quarter of the entire offspring. These clearly suggest that three-quarter of the total population will either be trait carriers or completely at the highest risk of sickle cell disease (Crisis situation of the sickle cell). If

precautions are not taken, the entire society may be affected within short period of time.

DISCUSSION

The Cartesian product of sets as appeared in the interpretation of results. **A** shows that when two couples both with genotype AA, got married, their chance of having offspring with AA is certain and that of AS and SS is zero. When contracting marriages the two couples having both A's alleles should be encouraged. This kind of union is the best and desired one, because the society will be free from sickle cell anaemia. **B** represents two couples both with genotype AS when married their chance of having normal offspring AA is just one-quarter, while three-quarter of the chances is affected.

The union here produces half chance with moderate risk, while the chances of desired genotype and the genotype with the highest risk, are both one-quarter each. Therefore this can cause serious problem to the society. If only one-quarter of the society are free from sickle cell, one can imagine the kind of challenge that the three-quarter of the society will be faced with. Therefore when contracting marriages, couples who are both heterozygous should be discouraged of such union by the appropriate bodies contracting such marriage. **C** stands for two couples both with genotype SS when married. Their chance of having offspring AA and AS is zero while the chance of having offspring SS is certain.

Those with S's alleles (SS) develop sickle cell anaemia and have completely abnormal haemoglobin. With this kind of union the society is at the highest risk of sickle cell anaemia. This union should highly be discouraged. Imagine a society that is full with only critically ill people, with no healthy person to help the others.

D represents the union of two couples with genotype AA and SS when married the chance of having offspring AA and AS is zero, while the chance of having offspring AS is certain. This Union can cause moderate risk to the society. If any person with the S's (SS) alleles need to married the only option is for that person's partner be one with A's (AA) alleles. This union also is not advisable, except when it becomes necessary for the person with the S's (SS) alleles to marry. **E** is a relation of set which represents two couples with genotype AA and AS, when married their chance of having offspring SS is zero while that of AA and AS is one-half. This union can be more acceptable than the cases of B, C, D and F in the absence of case A. **F** shows when two couples with genotype AS and SS when married, their chance of having offspring AA is zero and that of offspring AS and SS is one-half.

Such union can only poise more danger to the society so it should be discourage.

The table GXG is one that shows the first phyla generation of nine different families which reveal that the Cartesian product of all the couples with different genotype has a total of 36 at the first phyla generation. The analysis on table shows that there is more chance of having high risk of many carriers in the society.

The table shows that out of these nine different families first phyla generation produces 36 different offspring. These reveal that only one-quarter of the offspring will have the AA alleles, which is the desired genotype expected to be attended. Whereas the heterozygous offspring AS alleles will produce half of the entire offspring reproduced at that first phyla generation while the SS alleles were discovered to take one-quarter of the entire offspring. These clearly suggest that three-quarter of the total population will either be trait carriers or completely at the highest risk of sickle cell disease (Crisis situation of the sickle cell).

If definite control measures are not taken when contracting marriages, the entire society may be affected within shortest period of time. We just work on the first phyla generation of nine different families which marriages was contracted without any precautions. We observed that three-quarter of the population was affected.

In conclusion, considering the results of this findings, which suggest to us that if strict control measures taken, the entire society will be affected after a period of time, this is dangerous to the next generation. This paper therefore have the following recommendation to make, if adhere to, will enable Nigerian society to achieve the desired Genotype:

1. Government should impose laws for a compulsory genotype test for all students as part of entry requirement from secondary and all tertiary institution of higher learning and as well at the pre-marital stage
2. All religious leaders should ensure that they make a law for intending couples to undergo genotype test before contracting them into marriages.
3. Proper legislation is necessary to define conditions of contracting marriages in order to avoid the prevalence of this disease.
4. Government agencies should organise awareness campaigns on the danger of this disease in order to safeguard the coming generation.

5. Media outfits on their part should organise media chats and programmes that could bring awareness on sickle cell disease, what causes it, and how to avoid it.

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