Proceedings of the 2nd International Conference on Modern Medicine and Global Health
DOI: 10.54254/2753-8818/45/20240781

Transmission of X-linked recessive inheritance in the population

Jiarui Feng

Capital Normal University High School, Beijing,100080, China

fengjiarui2023@163.com

Abstract. X-linked recessive inheritance refers to diseases caused by X-chromosome recessive disease-causing genes. Specific examples include genetic diseases such as human red-green color blindness and hemophilia. The current rate of red-green color blindness: 8% males 0.5% females. This study is based on the SIR model for the conversion of concomitant x recessive genetic disorders in the total population. We theoretically derive the disease-free equilibrium of the proposed dynamic system, as well as the basic reproduction number. Based on the derived basic reproduction number, further, discuss the impact of the transmission rate of the companion x genetic disease and the transmission rate of the disease gene in the population. The results have implications for controlling the emergence of genetic diseases in the population.

Keywords: Mathematic modeling, Reproduction number, Genetic diseases.

1. Introduction

1.1. X-linked recessive inheritance

X-linked recessive inheritance is a specific pattern of inheritance where a genetic mutation occurring in a gene located on the X chromosome results in the consistent manifestation of the corresponding phenotype in males. This is due to the fact that males have one X and one Y chromosome, making them hemizygous for the gene mutation. In females, the phenotype is expressed when they are homozygous for the gene mutation, meaning they carry two copies of the mutated gene. It is important to consider zygosity when analyzing the expression of the phenotype. Females who possess only one copy of the mutated gene are called carriers [1-3]. X-linked recessive inheritance refers to transmitting a genetic trait or disorder from parent to offspring due to mutations in a gene on the X chromosome. For males who possess only one X chromosome, the presence of a mutated gene on their singular X chromosome manifests the condition. In contrast, females with two X chromosomes must have mutations on both chromosomes to be affected by the disorder. Typically, when the father or mother carries the mutated X-linked gene, their daughters remain unaffected and are considered carriers; they possess one mutated X chromosome and one normal X chromosome. Sons, on the other hand, will exhibit the condition if they inherit the mutated X-linked gene from their mother. It's important to note that fathers are unable to transmit X-linked recessive disorders to their sons [4]. The process is shown in Table 1.

DOI: 10.54254/2753-8818/45/20240781

Table 1. Punnett squares for each combination of parents' color vision status, giving probabilities of their offspring's status; A superscript 'c' denotes a chromosome with an affected gene.

		Normal father		Patient father	
		x	Y	x^{Q}	Y
Normal mother	X	Xx	XY	Xx^{Q}	XY
	X	Xx	XY	Xx^{Q}	XY
Carrier mother	X	Xx	XY	Xx^{Q}	XY
	X^{Q}	$X^{Q}x$	$X^{Q}Y$	$X^{Q}x^{Q}$	$X^{Q}Y$
Patient mother	X^{Q}	$X^{Q}x$	$X^{Q}Y$	$X^{Q}x^{Q}$	$X^{Q}Y$
	X^{Q}	$X^{Q}x$	$X^{Q}Y$	$X^{Q}x^{Q}$	$X^{Q}Y$
		daughter	son	daughter	son

1.2. Genetics of red-green color blindness

The most prevalent form of colorblindness is congenital red-green color blindness, also known as Daltonism, which encompasses protanopia/protanomaly and deuteranopia/deuteranomaly. These conditions are influenced by the OPN1LW and OPN1MW genes, respectively, located on the X chromosome. In the case of colorblindness, the "affected" gene is either absent (as in Protanopia and Deuteranopia - Dichromacy) or exists as a hybrid gene (as in Protanomaly and Deuteranomaly) [5]. Since the OPN1LW and OPN1MW genes are situated on the X chromosome, they are considered sex-linked, resulting in a disproportionate impact on males and females. Due to the recessive nature of the "affected" alleles responsible for color blindness, this condition predominantly follows X-linked recessive inheritance. Males possess only one X chromosome (XY), while females have two (XX). As a result, if a male inherits an affected gene, he will be colorblind due to having only one gene copy. On the other hand, since females possess two alleles of each gene (one on each X chromosome), if only one gene is affected, the dominant normal alleles will prevail over the recessive affected allele, resulting in normal color vision for the female. However, if a female inherits two mutated alleles, she will still experience colorblindness. This discrepancy explains the higher prevalence of colorblindness in males, with approximately 8% of males exhibiting colorblindness compared to around 0.5% of females [6].

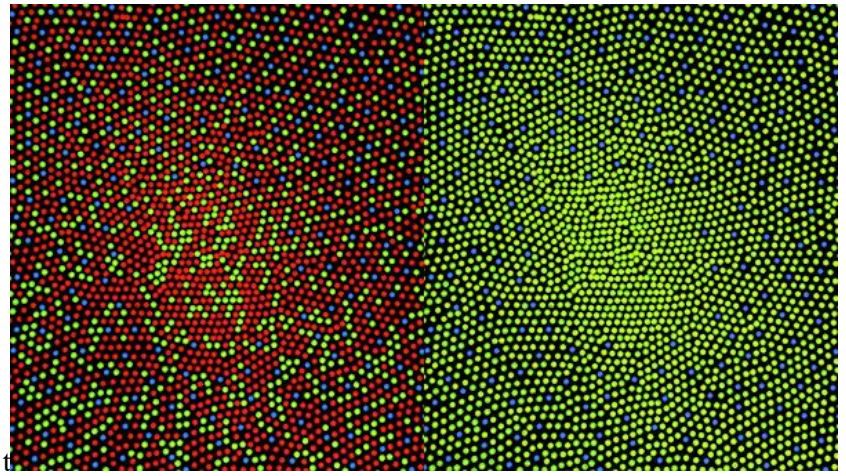

Figure 1. Retinal mosaic in the fovea of an individual with normal color vision (left), and protanopia (right). The protanope is complete missing red cones and is, therefore a dichromat [7].

1.3. Compartmental models

Compartmental models are a very general modelling technique. They are often applied to the mathematical modelling of infectious diseases. The population is assigned to compartments with labels. Models try to predict things such as how a disease spreads, the total number infected, or the duration of

DOI: 10.54254/2753-8818/45/20240781

an epidemic, and to estimate various epidemiological parameters. People may progress between compartments (see Table 2).

Table 2. Parameter description.

Parameter	Interpretation
b(N)	number of people born
N	Total population
d	Death rate
β_1	The probability that a male who did not carry the disease gene comes into contact with a female who developed the disease and gives birth to a male infant who developed the disease
β_2	The probability that a male who did not carry the disease gene comes into contact with a female who carried the disease gene and gives birth to a male infant who developed the disease
β_3	The probability that a male who developed the disease comes into contact with a female who did not carry the disease gene and gives birth to a female infant who carried the disease gene
β_4	The probability that a male who developed the disease comes into contact with an female who carries the disease gene and gives birth to a female infant who developed the disease

2. Model

In this paper, we use compartmental models to analyze the nature of the transmission of companion X diseases in the population. according to the previous background, the model consists of three compartments.

S: The number of people who do not have the disease-causing gene in their X sex chromosome. S Individuals will come into contact with diseased(I) individuals and carriers(C) and produce diseased or carrier infants. We consider this situation as a transmission from S individuals to carriers(C) and diseased(I) individuals.

C: The number of people with the disease-causing gene in the X sex chromosome who do not develop the disease. C individuals may come into contact with diseased(I) individuals and carriers(C) and have diseased(I) infants. We consider this situation as a switch from C to diseased(I) individuals. C individuals only exist in women

I: The number of people with the disease-causing gene in their X chromosome and who develop the disease. Because it is a genetic disease, even if the disease symptoms of individual I disappear under modern medical treatment, the genotype of individual I remains unchanged, so there is no transmission of individual I to other types of individuals.

For simplicity, we make the following assumption.

(i) The ratio of male to female births is one to one

(ii) Excluding the case of specific mutations in genes

Based on the inheritance characteristics of the associated x-chromosome disorder itself we divided the total population into males S_m (i.e., genotype is XY) who did not carry the disease gene(q is a disease-causing gene), females S_f (i.e., genotype is XX) who did not carry the disease gene, females C_f (i.e., genotype is X^QX) who carried the disease gene, males I_m (i.e., genotype is X^QY) who developed the disease, and females I_f (i.e., genotype is X^QX^Q) who developed the disease. Because of the nature of the genetic disease itself, which is inherently incurable, the status of recovered individuals R is not considered in this paper. The increase in the population of carriers and pathogens can only be increased by the birth of newborns, which we consider as a switch from the S or C population. For S_m population, $\frac{1}{2}$ b (N) is considered as the number of births in the total male population, $\frac{\beta_1 S_m I_f}{N}$ is seen as $S_m(\mathrm{i.e.,genotype\ is\ XY})$having a birth with I_f $(\mathrm{i.e.,genotype\ is}\ X^QX^Q)$and having a male baby with

DOI: 10.54254/2753-8818/45/20240781

genotype X^QY and is treated as converting a S_m individual to I_m individual. $\frac{\beta_2 S_m C_f}{N}$ is seen as S_m (i.e., genotype is XY)having a birth with C_f (i.e., genotype is X^QX)and having a male baby with genotype X^QY and is treated as converting a S_m individual to I_m individual. For S_f population, is considered as the number of births in the total female population. $\frac{\beta_3 S_f I_m}{N}$ is seen as S_f(i.e., genotype is XX)having a birth with I_m (i.e., genotype is X^QY)and having a female baby with genotype X^QX , this situation is treated as converting a S_f individual to C_f individual. For C_f population, $\frac{\beta_4 C_f I_m}{N}$ is seen as C_f (i.e., genotype is X^QX) having a birth with I_m (i.e., genotype is X^QY)and having a female baby with genotype X^QX^Q , this situation is treated as converting a C_f individual to I_f individual. The whole process is showed in Figure 1.

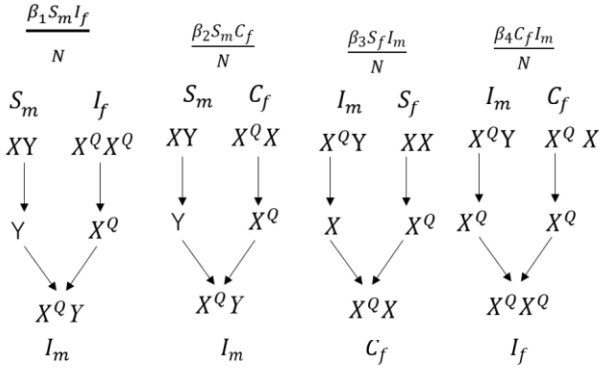

Figure 2. The transmission process between compartments.

Based on the following discussion and flowchart in Figure 2, the model is formulated as follows in Figure 3.

$$\begin{cases} \dfrac{dC_f}{d_t} = \dfrac{\beta_3 S_f I_m}{N} - C_f d \\ \dfrac{dI_m}{d_t} = \dfrac{\beta_1 S_m I_f}{N} + \dfrac{\beta_2 S_m C_f}{N} - I_m d \\ \dfrac{dI_f}{d_t} = \dfrac{\beta_4 C_f I_m}{N} - I_f d \\ \dfrac{dS_m}{d_t} = \dfrac{1}{2} b(N) - \dfrac{\beta_1 S_m I_f}{N} - \dfrac{\beta_2 S_m C_f}{N} - S_m d \\ \dfrac{dS_f}{d_t} = \dfrac{1}{2} b(N) - \dfrac{\beta_3 S_f I_m}{N} - S_f d \end{cases} \tag{1}$$

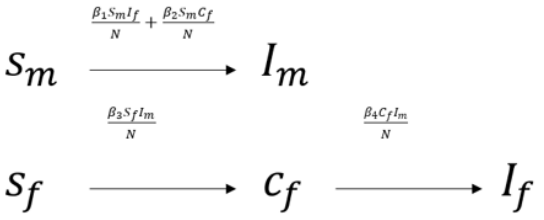

Figure 3. Flowchart of X-linked recessive inheritance transmission.

DOI: 10.54254/2753-8818/45/20240781

3. Result

3.1. Basic reproduction number

The disease-free equilibrium is $E_0 = (0,0,0,S_m,S_f)$, let

$$\mathcal{F} = \begin{pmatrix} \frac{\beta_3 S_f I_m}{N} \\ \frac{\beta_1 S_m I_f}{N} - \frac{\beta_2 S_m C_f}{N} \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{2}$$

$$\mathcal{V} = \begin{pmatrix} -\frac{\beta_3 S_f I_m}{N} + C_f d \\ I_m d \\ I_f d \\ -b(N) + \frac{\beta_1 S_m I_f}{N} + \frac{\beta_2 S_m C_f}{N} + S_m d \\ -b(N) + \frac{\beta_3 S_f I_m}{N} + S_f d \end{pmatrix} \tag{3}$$

Then, the linearization of system (2,1) at $E_0$is given by

$$D\mathcal{F}(E_0) - D\mathcal{V}(E_0) = \begin{pmatrix} F - V & 0 \\ -J_3 & -J_4 \end{pmatrix} \tag{4}$$

Where J_3 and J_4 are 3×3 matrices, and

$$F = \begin{pmatrix} 0 & \beta_3 & 0 \\ \beta_2 & 0 & \beta_1 \\ 0 & 0 & 0 \end{pmatrix} \tag{5}$$

$$V = \begin{pmatrix} d & \beta_3 & 0 \\ 0 & d & 0 \\ 0 & 0 & d \end{pmatrix} \tag{6}$$

Since all eigenvalues of J_4 have positive real parts, the stability of E_0 is determined by the eigenvalues of matrix F-V. Moreover, it follows from the results in Diekmann et al. (2010) and van den Driessche and Watmough that all eigenvalues of F-V have negative real parts if and only if $\rho(FV^{-1}) < 1$.[8,9]. Where $\rho(A)$ denotes the snectral radius of a matrix A. One can compute FV^{-1} ,called the generation matrix, that is,

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\beta_3}{d} & 0 \\ \frac{\beta_2}{d} & \frac{\beta_3\beta_2}{d} & \frac{\beta_1}{d} \\ 0 & 0 & 0 \end{pmatrix} \tag{7}$$

Which has eigenvalues

$\lambda_1=0$

$$\lambda_{2,3} \frac{\beta_3\beta_2 \pm \sqrt{4d^2\beta_3\beta_2 + (\beta_3\beta_2)^2}}{2d^2} \tag{8}$$

Thus, the basic reproduction is

DOI: 10.54254/2753-8818/45/20240781

$$\mathscr{R}_0 = \frac{\beta_3\beta_2 + \sqrt{4d^2\beta_3\beta_2 + (\beta_3\beta_2)^2}}{2d^2} \tag{9}$$

3.2. Sensitivity analyzation

The real meaning of $\mathcal{R}_0$ is the basic regeneration number, when it is greater than 1 it means that the disease will continue to spread until all people are infected. And when it is less than 1, it means that the disease will eventually disappear and all the people will be positive [10]. According to the formula we can conclude that $\mathcal{R}_0$ is proportional to β_3 and β_2, which means that $\mathcal{R}_0$ increases with the probability that a male who does not carry the gene for the disease comes into contact with a female who carries the gene for the disease and gives birth to a male baby with the disease and the probability that a male who carries the disease gene is in contact with a female who carries the disease gene and has a male infant with the disease. $\mathcal{R}_0$ simultaneously increases as the mortality rate d becomes smaller. Also, we can conclude that the value of $\mathcal{R}_0$ is independent of β_1, i.e., it is independent of the proportion of sick babies born to normal males and sick females.

4. Conclusion

In this paper, we introduce a model for the transmission of a companion x chromosome genetic disorder based on its characteristics, and then derive the formula for its basic regeneration number and its properties based on the model. Human beings are currently facing many difficulties in treating genetic diseases, so it is more important to focus on preconception testing of pregnant women in order to control the spread of genetic diseases. In this paper, we have constructed a model for the transmission of genetic diseases in the population, which will be helpful in controlling the transmission of genetic diseases in medicine.

References

[1] "History of Bleeding Disorders". National Hemophilia Foundation. 2014-03-04

[2] OMIM Color Blindness, Deutan Series; CBD". nih.gov. Archived from the original on 29 September 2009. Retrieved 3 May 2018.

[3] Jais JP, Knebelmann B, Giatras I, De Marchi M, Rizzoni G, Renieri A, et al. (2003). "X-linked Alport syndrome: natural history and genotype-phenotype correlations in girls and women belonging to 195 families: a "European Community Alport Syndrome Concerted Action" study". Journal of the American Society of Nephrology. 14 (10): 2603–10.

[4] Dobyns, William B.; Filauro, Allison; Tomson, Brett N.; Chan, April S.; Ho, Allen W.; Ting, Nicholas T.; Oosterwijk, Jan C.; Ober, Carole (2004). "Inheritance of most X-linked traits is not dominant or recessive, just X-linked". American Journal of Medical Genetics. 129A (2): 136–43.

[5] "Facts About Color Blindness". NEI. February 2015. Archived from the original on 28 July 2016. Retrieved 29 July 2016.

[6] Neitz, J; Neitz, M (2011). "The genetics of normal and defective color vision". Vision Res. 51 (7): 633–651.

[7] Mark Fairchild.(2010) http://rit-mcsl.org/fairchild/WhyIsColor/images/ConeMosaics.jpg

[8] Van den Driessche, P.; Watmough, James (2002). "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission". Mathematical Biosciences. 180 (1): 29–48

[9] Diekmann,O., Heesterbeek,J.A.P.,Roberts,M.G.,(2010).The construction of nextg eneration matrices for compartmental epidemic models. J. R. Soc. Interface 7,873-885.

[10] Fine, P.; Eames, K.; Heymann, D. L. (2011). "'Herd Immunity': A Rough Guide". Clinical Infectious Diseases. 52 (7): 911–916.