Application of Tree in Finding Inherited Genetical Diseases Using Genogram

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***Abstract*—Genogram is a representation of a family tree that displays detailed data among individuals. It goes beyond traditional family tree, for it contains additional data that may include education, occupation, and in this case, inherited medical conditions of each member of the family. Therefore, with the knowledge gain from genogram, it is expected that a family member infected with a genetic disease can inform other family members who may be at risk.**

***Keywords*—diseases, family tree, genetics, genogram.**

I. Introduction

As time goes by, technology develops. Along with the development of technology, the environment changes and this leads to the emergence of some medical conditions which begin to exist in the present days.

Some of these medical conditions are caused by the mutation of the DNA that are either inherited from the parents or acquired during a person's life. These kind of medical conditions are often called as genetic disease.

Some genetic diseases can be caused by the mutation of a single gene, multiple genes, a damage to the chromosome, or interaction between genes and the environment.

Genetic diseases are typically acquired through inheritance of a mutated gene. Each cell in the body of a human contains 23 pairs of chromosomes and each pair is inherited from their parents. The appearance of a person is the result of the dominant gene in their DNA.

Genetic conditions can be inherited through three ways, the first one is called *autosomal recessive inheritance* where a child must have inherited both copy of the faulty gene to be affected by the disease. The second condition is called *autosomal dominant inheritance*, where a child inherit one normal gene and one faulty gene and has a 50:50 chance to be affected. The last condition is called the *sex-linked recessive inheritance*. It occurs when a parent has an affected X chromosome and passes it down to their child. In this case, the daughter will most likely be normal for she still has another X chromosome which is able to 'neutralize' the mutated chromosome. But for the son, he will almost certainly be affected since he only has one X chromosome.

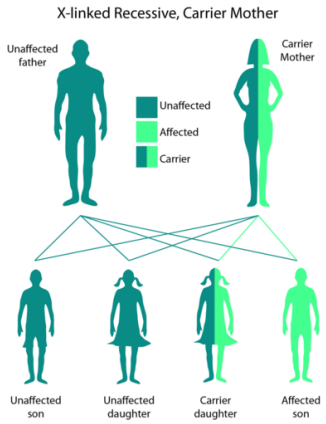

Figure 1.1 The inheritance of the genes
Source: https://www.ck12.org/biology/mendelian-inheritance/lesson/Mendelian-Inheritance-in-Humans-BIO/ accessed 8th of December 2018

Despite the fact that some diseases can jump over a generation, that results in the child being a carrier only, the genes containing the cause of the disease will always be passed down.

Luckily, the development in genetics researches these days has allowed a person to learn about their possibility of being infected by inheriting genetic diseases.

One of the methods is to generate a family tree that contains the history of genetic disease running in the family. It is expected that, with the knowledge obtained from the family tree, if a person in the family is affected, they will notify others who may be at risk of having the same genes. Therefore, further risk can be reduced and any threats in the upcoming future can be handled early.

II. Basic Theories

A. Graph

A graph is a diagram that contains a specific information. It is used in daily life to visualize objects so that it will be easier to understand.

Each diagram consists of objects (square, circle, and so on) to represent something and it also contains lines to connect those objects. Graph can be directed or undirected. A directed graph is usually used if the relationship between the objects drawn are important. A graph can also have a circuit, which means that in said graph we can go from one vertex and pass every other

vertex to go back to the starting vertex. A graph is said to be a connected graph if there exists a path from one vertex to another.

B. Trees

Tree is a specialized form of a graph, which is a connected graph that has no circuit and is undirected. The term 'tree' has been used since 1857 when an English mathematician used it to count chemical compounds. Since then, trees have been used to solved a lot of problems in many different aspects. In Fig. 2.1, G_3 and G_4 are not trees. G_3 is not tree for that it has circuit and G_4 is not tree because it is not connected.

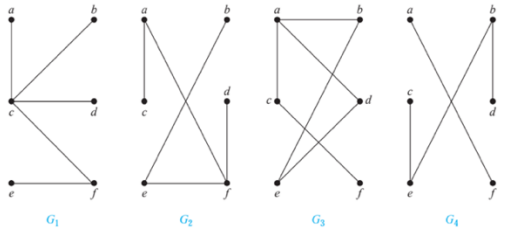

Fig. 2.1 Example of trees and not trees
Source: Discrete Mathematics and Its Application

Because of the fact that the definition of tree is derived from one of graph, it is safe to say that tree can only have one vertex. Or, if it is said by *G(V, E)*, *V* must be at least one and *E* can be zero. Whereas something is being defined as a forest if it is a group of tree which are detached between one and another.

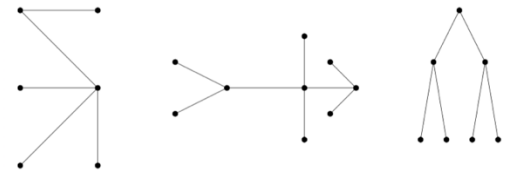

Fig. 2.2 An example of a forest
Source: http://informatika.stei.itb.ac.id/~rinaldi.munir/Matdis/2013-2014/Pohon%20(2013).pdf, Accessed on 7th of December 2018.

C. Properties of Trees

Let's say *G(V, E)* is a way to declare a tree with *n* vertex, then these statements below are equivalent:

1. *G* is a tree.
2. Every couple vertex in *G* is connected by a single path.
3. *G* has *n-1* edges.
4. An addition of an edge of *G* will result in addition of one circuit to the tree.
5. *G* is connected, and a removal to one of the edges will cause G to be separated to two components.

D. Spanning Tree

Let *G(V, E)* be a graph that has several circuits. *G* can be transformed to a tree $T(V_1, E_1)$ by removing some circuits on *G,* so that *T* is a subgraph of *G* which contains every vertex of *G* and every edges of *T* are part of edges of *G*.

E. Rooted Tree

Some trees are regarded as *free tree* and some others as *rooted tree.* On some literature, trees which are defined in part A are defined as free tree. Whereas a tree is defined as a rooted tree when one of the vertex is specialized from the rest of the vertices and said vertex is designated as the *root* of the tree, the edges from the vertex are directed away from the root. With that being said, choosing a different vertex to be the root of the tree will generate a different rooted tree. It is common to remove the arrow on the edges of the tree.

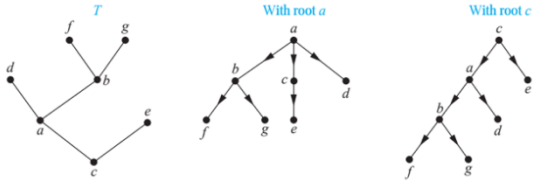

Fig. 2.3 A tree T and example of rooted tree
Source: Discrete Mathematics and Its Implementation

F. Terminology for Rooted Tree

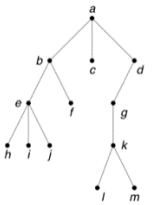

Fig. 2.4 A rooted tree *A*
Source: http://informatika.stei.itb.ac.id/~rinaldi.munir/Matdis/2013-2014/Pohon%20(2013).pdf, Accessed on 7th of December 2018.

- Children and Parent

Let's say *u* and *v* is vertices in a rooted tree. If there exist a directed edge from *u* to *v*, then *u* is called the parent and *v* is called the child. In Fig. 2.4, *a* is a parent of *b*, *c*, and *d*.

- Path

Let *u* be a vertex in a rooted tree. A path is a series of vertex that *u* go through if it wants to reach some other vertex. In Fig. 2.4, the path from vertex *a* to *m* are *a*, *d*, *g*, *k*, and *m*. The length of a path is the total amount of vertices that *a* go through to reach *m*, which is four.

- Descendant and Ancestor

Let *u* and *v* be vertices from a rooted tree. If there is a path from *u* to *v*, then *u* is said to be the ancestor of *v* whereas *v* is said to be the descendant of *u*. In Fig. 2.4, *a* is an ancestor of *m*.

- Sibling

A vertex which has the same parents as other vertex are said to be siblings to each other. In Fig. 2.4*, b, c*, and *d* are siblings but *g* is not their siblings for they do not have the same parents.

- Subtree

If *a* is a vertex in a tree, then a subtree *T'* of a tree *T* is a subgraph consisting of *a* as its root, every descendants of *a*, and all edges incident to those descendants.

- Degree

A degree of a vertex in a rooted tree is the total amount of children or subtree of the vertex in the tree. The maximum degree of all vertex is said to be the degree of the tree itself. In Fig. 2.4, the degree of *b* is two whereas the degree of the tree is three.

- Leaf

A vertex is said to be a leaf if the mentioned vertex has no children. In Fig. 2.4, the leaves of the tree are *h, i, j, l,* and *m*.

- Internal Node

An internal node is a vertex that has children. Unless it is the only vertex in the tree, which will be a leaf, the root is also defined to be an internal node. In Fig. 2.4, the internal nodes of the tree are *b, e, g,* and *k*.

- Level

The level of a vertex *u* in a rooted tree is the amount of line between that said vertex to the root.

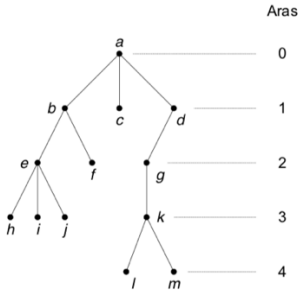

Fig. 2.5 A tree and the level of each vertex
Source: http://informatika.stei.itb.ac.id/~rinaldi.munir/Matdis/2013-2014/Pohon%20(2013).pdf, Accessed on 8th of December 2018.

- Height or Depth

Height or depth is the maximum level of a tree. The only difference between height and depth, is that height is measured from above (the root) and depth is measured from below (the leaves). In Fig. 2.4, the height or depth of the tree is four.

G. Ordered Rooted Tree

An ordered rooted tree is a tree where the order of the children of each vertices matters and are in order from left to right.

H. M-ary Tree

A *m-ary* tree is a tree consisting maximum *m* children between each vertex. A *m-ary* tree is said to be a full tree if each vertex has exactly *m* children. Therefore, a family tree is made of a *m-ary* tree, because of the fact that each family member does not always have the same amount of child.

I. Binary Tree

A tree is defined as a binary tree due to the fact that its vertices has two children at most. Because a binary tree can only have two children at most, in an ordered binary tree, the first child of the vertex is called the left child and the tree rooted to the left child is said to be the left subtree of the tree. Whereas the second child of the vertex is called the right child and the tree rooted to the right child is said to be the right subtree of the tree.

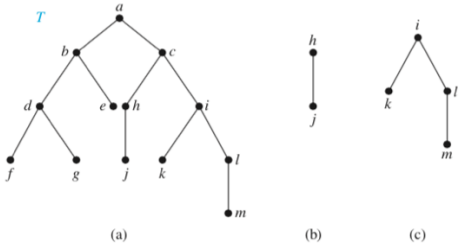

Fig. 2.6 A binary tree T and the left subtree and right subtree of vertex *c*
Source: Discrete Mathematics and Its Implementation

In Fig. 2.6, (b) is said to be the left subtree of subtree *c* and (c) is the right subtree of the subtree *c*.

III. GENOGRAM

A. Genogram

A genogram (pronounced: *jen-uh-gram*) is one representation of a family tree that portrays detailed data among each individual. That said, data are the basics data, along the lines of name, gender, date of birth, and date of death, and the additional data such as education, occupation, emotional relationship among individuals, social relationship among individuals, and disorders—may it be genetic or not. It was first invented by a clinical psychologist in 1985. Since then, it has been used as a tool by psychologist and other experts to help finding the cause of some disorders, traits, and so on in a client. Genograms can vary, for it does not have any limitation to what type of data that must be included.

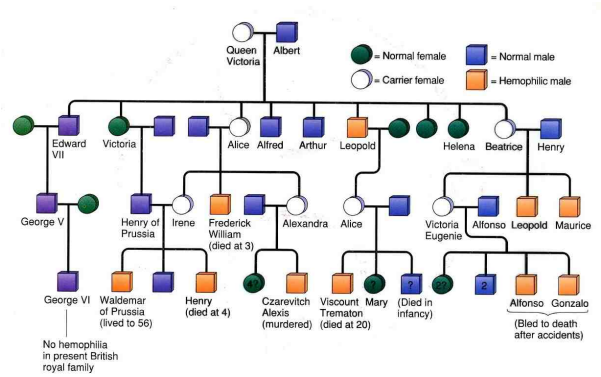

Fig. 3.1 Queen Victoria's well-known genogram
Source: http://www.biology-pages.info/Q/Queen_Victoria.html Accessed on 8th of December 2018.

The male in the family is defined by squares whereas the female is defined as circles. To make it clear, below are the basic genogram symbols.

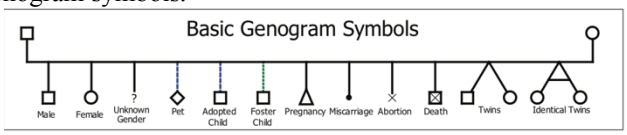

Fig. 3.2 Basic Genogram Symbols
Source: https://www.genopro.com/genogram/Genogram-Basic-Symbols.pdf. Accessed 9th of December 2018.

In the genogram, every vertex is symbolized based on the condition of every person. So the vertex portraying a normal person and the vertex portraying a carrier or an affected person is displayed differently.

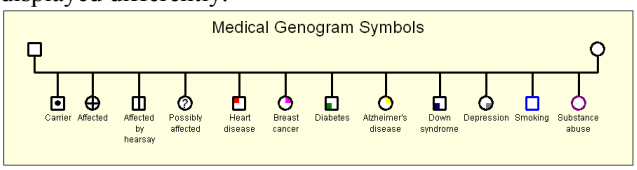

Fig. 3.3 An example of symbols of the vertex in a genogram
Source: https://upload.wikimedia.org/wikipedia/commons/d/da/Genogramma_medico.png. Accessed 8th of December 2018.

The relationship among the family members is also symbolized. By relationship, it does not necessarily have to be paternal. Friends, acquaintances, adoptive children, and a mistress could also be included in a genogram.

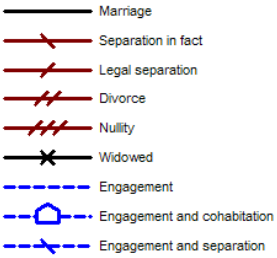

Figure 3.4 Some family relationships in genogram
Source: https://www.genopro.com/genogram/family-relationships/ with some changes.
Accessed 9th of December 2018

B. The Importance of Genogram

It is of the uttermost important to generate a family tree, especially the ones like a genogram.

Based on Mendel's Law of Inheritance, if a person carries a mutated gene, whether they are infected or not, there is a chance that their child will be affected too. The chances are getting bigger once they marry someone who is also a carrier. By making a genogram, a person can find out about their chance of getting infected by a genetical disease. This will allow them to reduce the risks by doing routine check-up, for instance.

On some cases, there are also people who get divorced due to an abusive partner. Usually, a person copies what they went through as a child. So if there is an abusive person, there is a high possibility that it is because their parents are abusive and that their grandparents are too. By generating a genogram, or at least knowing the history of your partner, you could see the potential of your marriage. May it be your children carrying a mutated gene or not, or psychological traits that may be carried by you or your partner that could affect the marriage.

Generally, a person uses a genogram as a tool to help notify a family member should his/her relative get infected by a genetical disease.

IV. Application of Tree in Finding Inherited Genetical Diseases Using Genogram

Like the usual tree, a genogram consists of root and its children. Since a family tree is basically a combination of two or more tree, representing a couple that marry, the root of the tree will be more than one.

Before making a genogram, one has to be aware of the reason why they want to make a genogram and what kind of genogram do they want to make. It is due to the fact that generating a genogram is not always easy, and it takes time to research the information needed. For instance, one desires to generate a genogram that is focused on the issue of inherited genetical disease for preparation of their future.

The first thing that needs to be done to generate a genogram is deciding how many generations should be in the genogram. Ideally, a genogram that is used to check the inheritance of a genetical disease consists of three or four generations. The more generations included in a genogram, the easier it is to see the pattern of the inheritance.

The preceding step is to research one's family history. For starter, ask the questions about who the first generations are (whom we will call *grandparents* from now on) and do they have any genetical disease? An answer to this can be obtained through basic information that one has or through an interview with the relatives. But one has to be careful if they choose to do the second option, for some people might consider this upsetting.

The way to know how a person inherit a mutated gene is by predicting it using Mendel's Law of Inheritance.

For instance, we want to know who inherit a hemophilia in the family.

Hemophilia is a rare disorder in which blood does not clot normally. A hemophilia is a condition that can not be cured. It is an extremely dangerous condition, in which an affected will continuously bleeding even to a small cut. Hemophilia usually occurs in males.

First thing first, we need to learn on how to use the Mendel's Law of Inheritance. First, symbolize the affected gene with superscript h and normal gene with superscript H. Therefore, we symbolize *normal female* with X^HX^H, *normal male* with X^HY, *affected female* with X^hX^h, *affected male* with X^hY, and *carrier female* with X^HX^h for she only has one mutated gene.

Thus, from the marriage of a carrier female (X^HX^h) and a normal male (X^HY) we will obtain:

Table I. Application of Mendel's Law of Inheritance

	X^H	X^h
X^H	$X^H X^H$	$X^H X^h$
Y	X^HY	X^hY

To be noted, the first row and the first column could be traded. For instance, X^h could be in the row three and column one while Y takes place in the first row and third column. From Table 4.1, it can be concluded that the couple will possibly have a normal female child, a normal male child, a female carrier of hemophilia, or a hemophilia-affected male.

From the explanation above, we can predict who in the family tree has hemophilia or might carry a hemophilia gene.

As an addition, in Mendel's Law of Inheritance, the symbol used to symbolized the chromosomes are different depending on the genetical disease. For instance, in the case of hemophilia we use the symbol as explained above. In the case of sickle cell anemia, SS is used to represent a person who has sickle cells anemia, Ss is used to represent a carrier and ss is used to represent a normal person. Whereas in the case of albino, the symbols Aa (represents a carrier), AA (represents a normal), and aa (represents an albino) are used. So, it does not have to be X's or Y's—depending on the genetical disease.

What we need to do now is to look around for our grandparents in the first generation that have signs of hemophilia. If we cannot find any, that does not mean they do not inherit the gene.

But if none shows the symptomps of a hemophilia, or if both grandparents are deceased, proceed to the next step which is to research the second generations of the family.

Now, the question to ask is does any of the children of one's grandparents have hemophilia? If some of them have it, then it is very likely that either of the grandparents (or probably the both of them) is a carrier or maybe even affected and the rest of the children could either be a normal or a carrier.

At this point, we mark those who has hemophilia in our notes and those who does not show any sign of hemophilia needs further research by looking at the next generation.

The next step is look at who the children of the grandparents (whom we will call *parents* from now on) is marrying to. If the parents marry to another carrier or affected, then at least one of the children from the third generation will be a carrier or an affected. The risk of getting affected is getting bigger once a carrier marries an affected or an affected marries an affected. This shows in the children. If a couple's child is 100% hemophilic, it is certain that the couple themselves are hemophilic. We are able to predict the percentage based on the Mendel's Law of Inheritance as explained above.

The data received from the research is better to be written in table to make it easier to read.

The example below are the data obtained from a family that inherits color-blind gene.

A color-blind is a condition where one can not see certain colors. Some people can not see red and green properly, some others can not see blue and yellows. A complete absence of color vision, or a total color-blind, is a rare condition. It is a condition which is usually genetically inherited, although there are some cases in which the affected has color-blind from another disease like diabetes.

Now we try to predict the inheritance of color-blind gene using Mendel's Law of Inheritance. X^+ is a symbol for *dominant* gene, X^C is a *recessive* gene that caused a color-blind. A normal male is symbolized by X^+Y, an affected male is symbolized by X^CY, an affected female is symbolized by X^CX^C, and a carrier female is symbolized by X^+X^C while a normal female is symbolized by X^+X^+. Since a male only has one X chromosome and color-blind is passed through X chromosome, a male cannot be a carrier of a color-blind gene.

Table II. Possible genes of a family

Name	Possible Genes
First Generation	
Alfredo	X^+Y
Helena	X^+X^C
Second Generation	
James	X^CY
Sophie (Wife of James)	X^+X^+
Gonzalo	X^+Y
Anne (Wife of Gonzalo)	X^+X^C
Tatiana	X^+X^C
John (Ex-husband of Tatiana)	X^CY
Anthony (Husband of Tatiana)	X^+Y
Marie	X^+X^+
Sebastian (Husband of Marie)	X^+Y
Third Generation	
Catherine (child of James)	X^CX^+
Philip (child of James)	X^+Y
Alice (wife of Philips)	X^+X^+
Eugenie (child of Gonzalo)	X^+X^+
Leopold (child of Gonzalo)	X^+Y
Beatrice (child of Gonzalo)	X^CX^+
George (child of Gonzalo)	X^+Y
Alice (child of Tatiana)	X^CX^+
Anna (child of Tatiana)	X^CX^C
William (child of Tatiana)	X^CY
Hans (child of Tatiana)	X^+Y
Peter (child of Tatiana)	X^CY
Donald (child of Marie)	X^+Y
Elizabeth (child of Marie)	X^+X^+
Fourth Generation	
Charlotte (child of Philip)	X^+X^+

A genogram is a family tree. Therefore, it has the properties of a tree. It is also directed from root to leaves, representing the oldest generation to the latest generation. A root in the tree does not necessarily mean that the person represented by the root does not have parents. It simply means, in this family tree, said root is the eldest of the family.

After acquiring the data needed, the next step is to build a genogram. Since genogram is a family tree, generating a genogram means generating a family tree. The difference is in the symbol of the vertices used.

In starting a genogram, we need to generate a tree that represents level zero of the tree or known as the first generation of the family. Based on Table 4.2, the first generations are Alfonso who is a normal person and Helena who carries a color-blind gene. We portray them both using symbols like in Fig. 3.2 and Fig. 3.3.

Figure 4.1 Level 0 of a family tree

The next step is to draw the descendants of Helena and Alfonso, which is their children and their grandchildren. Based on Table 4.1, the children of Helena and Alfonso are James, Gonzalo, Tatiana, and Marie. James later marries Sophie, Gonzalo later marries Anne, Tatiana married John and has children with him before she got divorced and later marries Anthony, lastly Marie marries Sebastian. All of them become the internal nodes of the tree, due to the fact that they all have children. They make level one of the tree.

Figure 4.2 Level 1 of a family tree

To draw the third generation of de Villa's family, we need to pay attention to the second generation first.

James and Sophie's marriage gave birth to two children, whom one of them is a carrier of the color-blind gene. Whereas Gonzalo and Anne have four children, and one of them is

affected with color-blind. Since Tatiana is a carrier of color-blind gene and John is a color-blind, two of their four children are also color blind. After Tatiana marries Anthony, the child still possesses the risks of getting affected to be a color-blind. That is why it is not much of a shock to find that their child is a color-blind. Lastly, Marie and Sebastian have two children and both of them are normal. The children of Alfonso and Helena make level two of the tree.

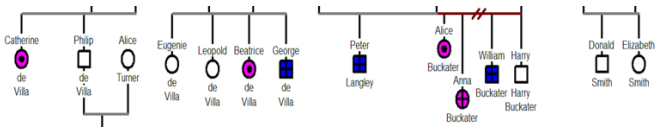

Figure 4.3 Level 2 of the family tree

Philip, son of James and Sophie, is married to Alice. Thus, since their child is the youngest in the family and has not yet marry, their child is being put in the last level of the family tree which is level three. Since she obviously does not have any children yet, it makes Charlotte a part of the leaves too.

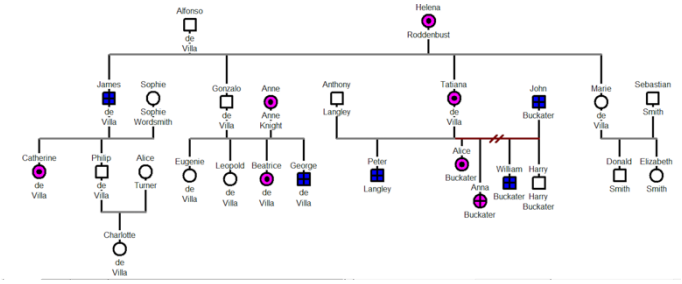

Figure 4.4 The family tree of de Villa's family

Finally, the desired family tree is finished. And from the family tree, we are able to see that the height of the tree is three, since the highest level is three.

It is also known from the family tree, when a carrier marries an affected color-blind, 75% of their children will carry a color-blind gene. While if a normal person marries an affected color-blind, the chance will be 50:50 to have a color-blind child.

V. Conclusion

From the explanation on above, it can be concluded that the presence of a genogram, or simply the knowledge of history of your family is important. For instance, in other cases like Tatiana's case on above explanation, some couple get divorced due to the fact that there is a lot of fight going on regarding their child. If only they had the knowledge before marriage, they might be able to reduce the risks (in case of other disease that could be treated early) or they might find the solution before the problem occurs. Other than that, a genogram is useful in a treatment of a patient since knowing the history would make it easier to find the solution and also it could warn others in the family member to be careful.

VI. Acknowledgment

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PERNYATAAN

Dengan ini saya menyatakan bahwa makalah yang saya tulis ini adalah tulisan saya sendiri, bukan saduran, atau terjemahan dari makalah orang lain, dan bukan plagiasi.

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