Familial Analysis of Patients with Hypertension in Jatinangor, West Java, Indonesia

Keumala Hayati,[1] Yulia Sofiatin,[2] Sri Endah Rahayuningsih,[3] Rully M.A. Roesli[4]
[1]Faculty of Medicine Universitas Padjadjaran, [2]Department of Public Health Faculty of Medicine, Universitas Padjadjaran, [3]Department of Child Health Faculty of Medicine Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital,Bandung, [4]Department of Internal Medicine Faculty of Medicine Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital Bandung

Abstract

Background: Hypertension is a disease that is influenced by genetic factors, although the single gene affecting the occurrence of the disease has not been yet discovered. Genetic analysis and familial analysis on hypertension are needed to be done but genetic analysis needs substantial fund, and familial analysis on hypertension has been never done in community. Besides sharing the genetic factors, family also shares similar environment and life style. Latest study showed that the association between genetic and environmental factors can affect the phenotype of chronic disease suchas hypertension. The study was aimed to explore the family history contribution of patients with hypertension in Jatinangor.

Methods: This was a descriptive-quantitave study. The subjects were 283 hypertensive patients in Jatinangor with complete data of family history. The data was retrospectively obtained from secondary data of a previous study conducted in Community Health and Well-ness Study Center, Faculty of Medicine, Universitas Padjadjaran titled Epidemiology of Hypertension and Albuminuria in Jatinangor 2014. Familial analysis conducted in this study was modified trios analysis.

Results: In this modified trios analysis, there was only 20% of total patients with hypertension who have history of hypertension in two generations of their family. The proportion of patients with hypertension who have history of hypertension in one generation of their family was greater. More than 45% from the total 283 patients with hypertension analyzed in this study have family history of hypertension.

Conclusions: Familial analysis using modified trios analysis showed similar results with the study conducted using other genetical analysis.

Keywords: Familial analysis, hypertension, modified trios

Introduction

Hypertension is one of the most commonly found disease in the primary health care setting.[1] Prevalence of hypertension in the age of ≥18 years old is 25.8%.[2,3] West Java is in the fourth place with the prevalence of 29.4%.[3] A study conducted by Study Center of Community Health and Fitness at Faculty of Medicine Universitas Padjadjaran in 2014 which prevailed the prevalence of hypertension and its complications in Jatinangor stated that prevalence of hypertension in Jatinangor was considered high, which was 38%.[2] This national prevalence of hypertension in Indonesia is 25.8%.

There are risk factors that contribute to the development of hypertension in an individual, they are the genetical and environmental factor.[4-6] Genetic analysis and familial analysis are conducted to discover the genetic factor. Medical history of family members and relatives including the previous illness is needed in order to construct a proper familial analysis. The most common family members chosen as source for familial analysis are parents, siblings, and children.[7]

Familial relationship, or kinship, is a relationship in a family consisted of parents, siblings, and children.[3] Kinship in a family has a lot of inherited similarity. Some of them are genes, environment, and lifestyle.[8-10] Genetic

Correspondence: Keumala Hayati, Faculty of Medicine, Universitas Padjadjaran, Jalan Raya Bandung-Sumedang Km.21, Jatinangor, Sumedang, Indonesia, Email: hkeumala@outlook.com

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factor is one of the inherited similarities in a kinship which may lead to medical disorders.[4,10] Recent study stated that combination of genetic factor, environment and lifestyle might influence the fenotypic manifestation in chronic disease such as hypertension.[4,6,8]

Based on the previous analytical study conducted in Europe, it was found that fraction of blood pressure influenced by genetic factor and controlled by hereditary mechanism varied among the range of 30—50%, and the risk of developing hypertension in an individual who had hypertensive sibling increased 2.5-3.5 times (relative risk).[11]

The aim of this study was to find the proportion of hypertensive patients who have family members with hypertension among hypertensive patients in Jatinangor.

Methods

A descriptive-quantitative study was conducted with the study population of all hypertensive patients in Jatinangor. The data was collected from secondary data obtained previously by The Study Center of Community Health and Fitness at Faculty of Medicine Universitas Padjadjaran in the study entitled "Epidemiology of Hypertension and Albuminuria in Jatinangor" in the year of 2014.[2] Minimum sample size was 97, taken using the sampling method of total sampling technique. The total of all hypertensive respondents in Jatinangor was 475, but 30% of these respondents do not have proper familial record so tracing back the familial history was difficult. Three hundred thirteen respondents aged ≥18 years were collected and followed by data analysis. From 313 hypertensive respondents, 30 were excluded because of the incomplete familial record, which were only consisted of one generation record. In the end, the total respondents of this study was 283. Data collection had been approved by the Health Research Ethics Committee of Faculty of Medicine Universitas Padjadjaran (1119/UN6.C1.3.2/KEPK/PN/2016).

Analytical method used in this study was familial association study. Familial association

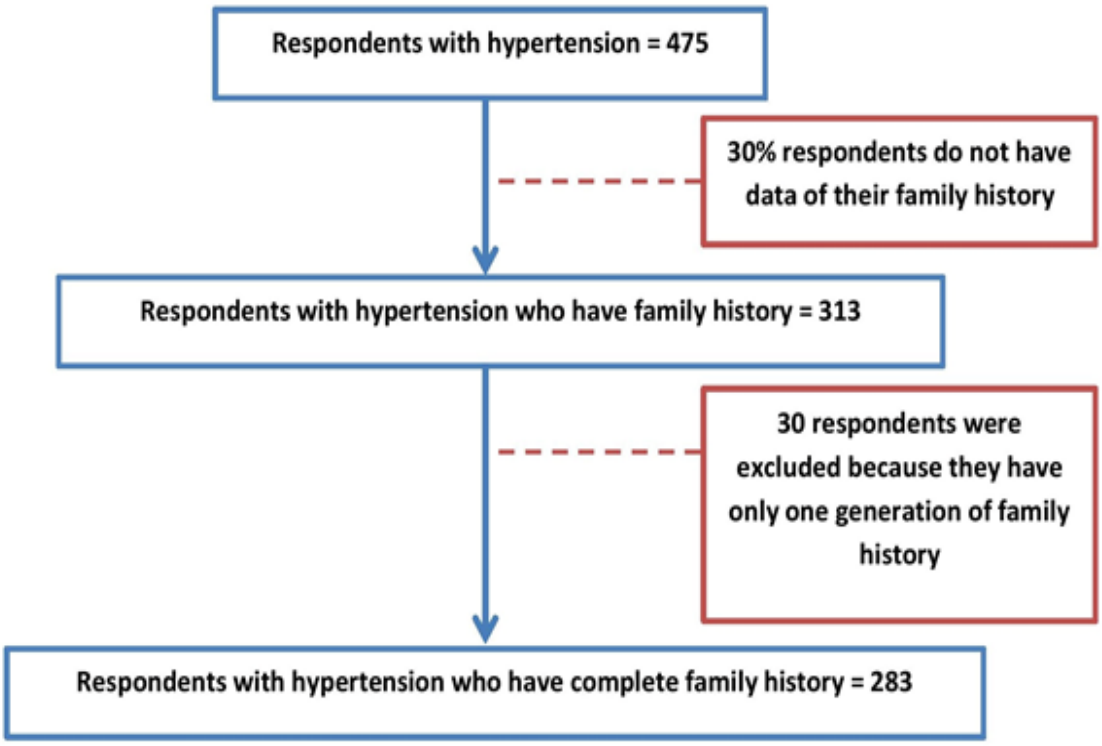

Figure 1 Sampling method

study is a method used for examining the existence of hereditary genetic factor in a familial or relative association.[7] Familial association study could be conducted using various methods, such as analysis of aggregation, heritability, segregation, trios, and sibling-study.[7]

Method of familial analysis used in this study was modified trios method, because epigenetic study approach has never been used in the familial association before. Trios method was considered stronger compared to sibling study or twin study because of its three-genotype involvement in the genetic process (genotypes of father, mother, and child) and the two-genotype involvement in the sibling and twin study.[7] This study adopted trios method for its emphasize in the family and environment built inside the family. Nevertheless, this study was not fully similar with the trios method because this study also analyzed the possibility of association with the family outside the respondent and their parents only, which included association pattern of respondents with their siblings and their children.

Hypertension was diagnosed based form the result of blood pressure measurement. Measurement was conducted two times with the interval of two minutes among each measurements. During the measurement, patient sat upright position, upper arm lied above the table paralleled to the shoulder. The measurement was preceded 5-minutes rest for the patient,do not smoke and/or drink caffeine 30 minutes before the measurement.[12] Respondent was diagnosed as having hypertension if the systolic blood pressure was ≥140 mmHg and diastolic blood pressure was ≥90 mmHg.[5] After that, the respondents were classified as stadium 1 and stadium 2 hypertension based on the classification written in the Eighth Report of the Joint National Committee (JNC 8).[5] This was applied only for patients aged ≥18years old.

Record of hypertension in family member was obtained from interview not from direct measurement. Respondents were asked whether their family members had hypertension or not. Family members who were asked in the interview were parents, siblings, and children (adopted children was not included). If one of the siblings or children was known for having hypertension, then it

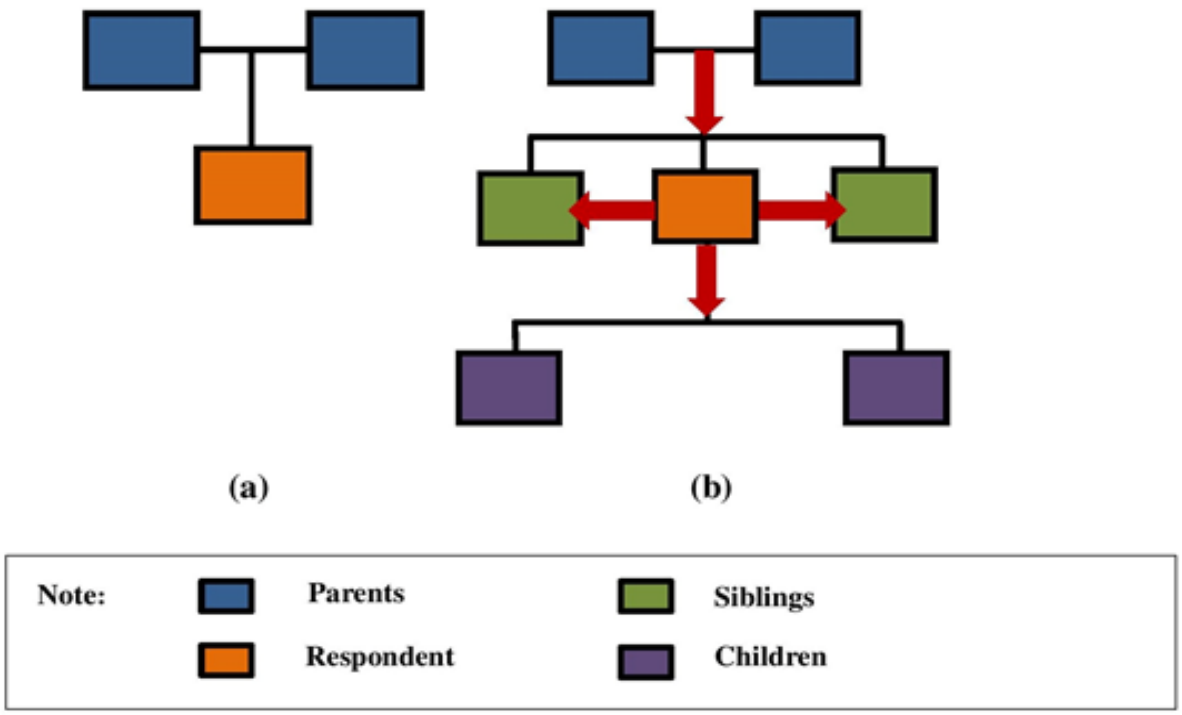

Figure 2 (a) Model of trios analysis,7 (b) Model of modified trios analysis

Table 1 Basic Characteristic of the Data

Characteristic		Frequency
Gender	Male	86
	Female	197
Age (years old)	18–39	29
	40–59	135
	≥60	91
Diagnosis	Stage 1 Hypertension	154
	Stage 2 Hypertension	129

was concluded that 'sibling' or 'children' had the history of hypertension. The answers of respondent consisted of three kinds of answer: 'yes', 'no', and 'unknown'. For the purpose of analysis, the 'unknown' answer was excluded because the failure might occur if this answer was included. Respondents who know the hypertension history only less than 2 family members were also excluded because the criteria for modified trios method would not be met in this condition.

Results

This study, discovered that female with hypertension was more frequent compared to male, while there were only a slight difference between the frequency of patient with stage 1 hypertension (158 patients) compared to patient with stage 2 hypertension (165 patients).

From the 3 familial category, which were parents, siblings, and children, it was shown that most of the complete data was regarding the hypertensive history of siblings, followed by parents and children. Proportion of 'unknown' answer in 'parents' category was higher compared to siblings and children, while the proportion of negative answer in the siblings category was found to be the highest among others (Figure 3, Figure 4).

The comparison of proportion between patients with stage 1 and stage 2 hypertension which were previously analyzed using modified trios method showed that the history of hypertension in two related generations only appeared in the pairing of parents-siblings only, while in the data pairing of siblings-children, most of them had no history of hypertension in both data (Figure 5).

In the stage 1 hypertension group, data

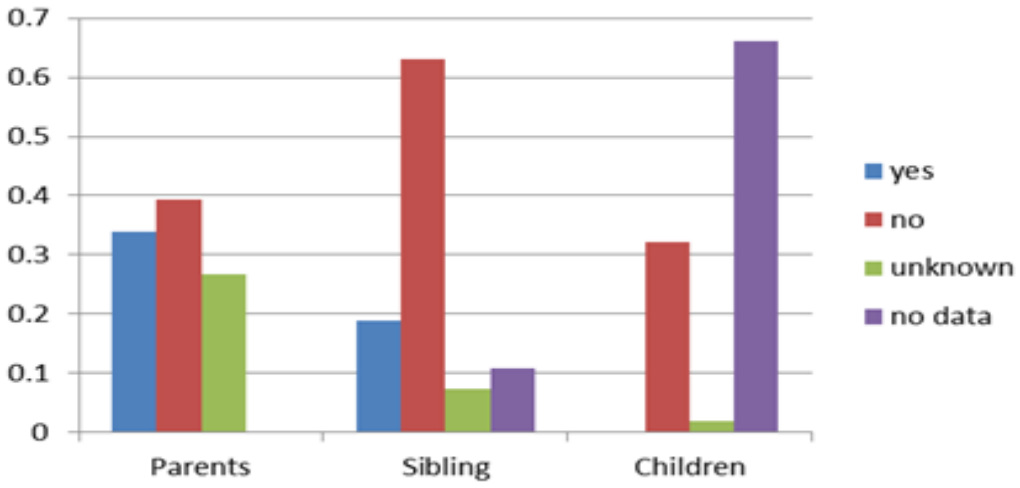

Figure 3 Proportion of Family History in Respondents with Stage 1-Hypertension

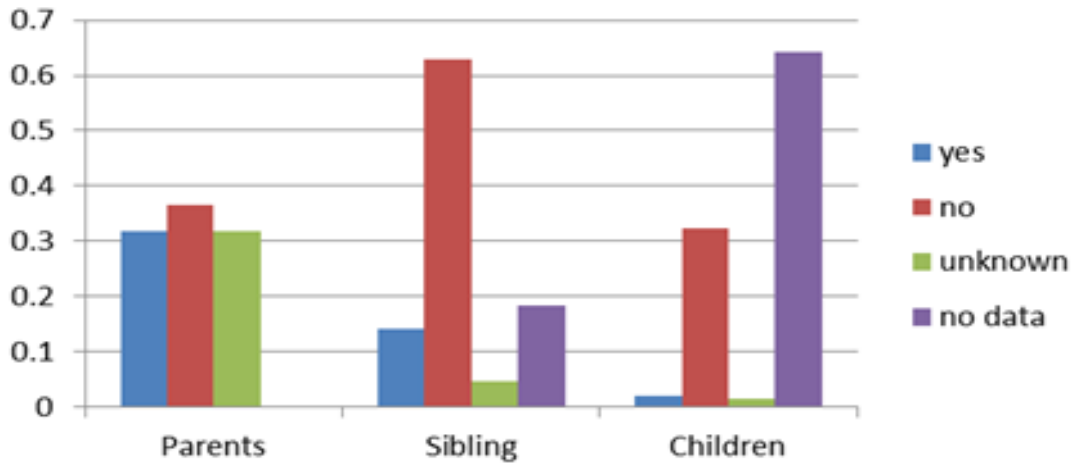

Figure 4 Proportion of Family History in Respondents with Stage 2-Hypertension

pairing of parents-children showed the highest proportion in the 'parents-children have no hypertension' category. On the other hand, in the stage 2 hypertension group, the proportion of 'one of them have hypertension' was the highest. There were no respondents having the history of hypertension in three generation for all at once. Approximately 10% of the respondents had history of hypertension in two generations.

Discussion

Primary hypertension is a multifactorial disease.[4] There are a lot of factors other than genetic factors influencing the development

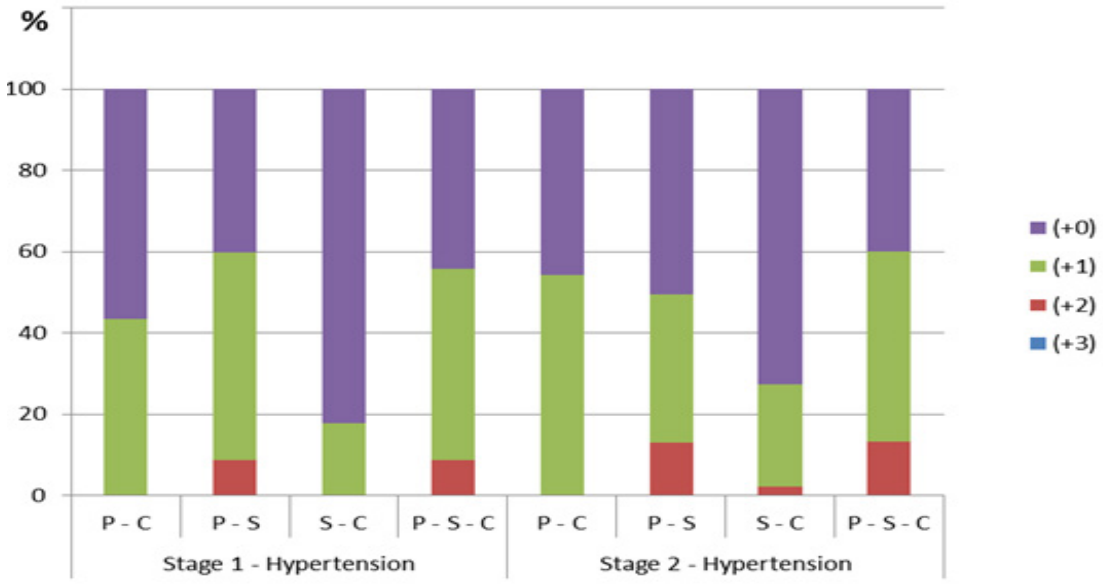

Figure 5 Comparison between the Proportion of Family History in Respondents with Hypertension stage-1 and Hypertension stage-2

Note: P=parents, S=sibling, C=children, (+0)=no positive result in three generations, (+1)=positive result in one generation, (+2)=positive result in two generation, (+3)=positive result in three generation.

of hypertension, and one of them was environmental factor.[4,6,10,15] A complex interaction among these factors has given a large influence for the increase in blood pressure.[4,14] In this condition, epigenetic has a largeinfluential role. Epigenetic is a science of molecular changing in epigenomic level and correlates with fenotypes inherited in the familial relationship, either from mitosis or meiosis.[4] Epigenom is a chemical compounds and proteins which attached to nucleotide chain and able to alter its fenotype manifestation by altering the end product of protein synthesis in the cell, but not converting the nucleotide chain itself.[4]

Familial association study has strong relationship with epigenetic issue, especially in hypertension disease.[4,7] Epigenomic changes which induce the appearance of hypertensive fenotype are able to be inherited from the parents to their children.[4] This might happen because of the similarity in behavior pattern exemplified by the parents to their children, such as physical activity, diet, and food preferences.[9] These behaviors have large influence in epigenomic changes which may induce the fenotype manifestation leading to clinical manifestation of hypertension.[4] In other words, if an individual has a family member who developed primary hypertension, then this individual also has possibility of having the same disease.[8,9,15]

In the study of familial association, the most commonly used method is the trios method,[7,16] but this method is unable to be conducted in Jatinangor due to the difficulty to conduct genetic examination because most of patients with hypertension were more than 45 years old[17-19] died, or live in different place. Considering this condition, modified trios method was chosen by converting the DNA examination with fenotype (hypertension) examination, and hypertension in family member was based on the history only. Limitation of this modified method was overcome by adding the information from the siblings or biological children of the respondents, so the information from 3 generations was obtained.

Most of the respondents in this study were female. Males were excluded because of their different environmental condition. Similar with the previous study, it was stated that this might happen because of most of the male residence of Jatinangor have their jobs outside the Jatinangor area.[2]

This study presented that 1/3 of the respondents had history of hypertension. Only 2% of the respondents with stage 2 hypertension had a hypertensive children. The occurence of hypertension increases in accordance with age,[17-19] thus the possibility of having a child with hypertension was low. Previous study also stated that 30% of patients with hypertension had parents with hypertension.[11] Genetical study also reported that the fraction of blood pressure variance influenced by genetic factor was approximately 30—50%.[11]

Approximately 1/3 of the repondents did not know the blood pressure of their parents. Most of the respondents who answered 'unknown' were elderly. This might be caused by the minimal access to health care facility.. More than 60% of the respondents who had no children aged more than 18 years old were included in this study.

In the two generations analysis, it was shown that hypertension in two generations mostly appeared in stage 2 hypertension, which consisted of parents-sibling and children-sibling pairings. This was probably caused by the elderly age of the respondents that lead to more severe disease and have more children, or might be caused by a lot of excluded data because of 'unknown' answer. The reason of this phenomena is remained unknown.

In the analysis of three generations, there were 20% of respondents who had history of hypertension in two generations, and this finding is smaller than previous studies.[11] This is probably caused by the possibility of environmental suppression of the fenotype, or might also be clouded by the number of respondents excluded because of their 'unknown' answer. Previous study conducted in Jatinangor stated that 1/3 of patients with hypertension were not aware of their hypertension disease.[20] It was also found in this study that 1/3 of the repondents did not know whether their parents had hypertension or not. There were possibilities that these 'unknown' patient were actually had hypertension, and so it might be revealed that the hypertension history in two generations were higher than this finding.

Limitation of this study was the source of information regarding to hypertension in family member only relying on history taking. Although 'unknown' choice was given in order to prevent the feeling of obligation in choosing between 'yes' or 'no', the risk of giving the wrong answer still remained. Previous study stated that 36% patients with hypertension were not aware of their disease,[20] so they might

inform that they were not having hypertension although they were apparently having it. Other than that, fenotype was actually a good paramater as a basis for epigenomic study in community setting, but the accuracy of the data is also matters.

The conclusion from this familial analysis using modified trios analysis showed that similar results with the study conducted using other genetical analysis. Suggestion for the next study is to conduct measurement for all the subjects and is not just rely on history taking. More accurate study is needed to prove the familial association in disease development. Medical record might be one of the accurate source of the fenotype data, which is also needed a good access to health facility and a good screening program. Analytical study using case-control design has to be encouraged for genetical study on patients with hypertension.

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