e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.iipcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(11); 723-728

Original Research Article

Factors Influencing Pre-Hospital Delay in Acute Myocardial Infarction **Patients**

Nikhil Shah¹, Kinjal Patel², Purvi Patel³, Dipesh Patel^{4*}

- ¹Assistant Professor, Department of General Medicine, Namo Medical Education and Research Institute, Silvassa, India
- ²Assistant Professor, Department of General Medicine, Namo Medical Education and Research Institute, Vinoba Bhave Hospital, Silvassa, India
- ³Assistant Professor, Department of General Medicine, Namo Medical Education and Research Institute, Silvassa, India
- ⁴Associate Professor, Department of General Medicine, Namo Medical Education and Research Institute, Silvassa, India

Received: 25-08-2023 / Revised: 18-10-2023 / Accepted: 17-11-2023

Corresponding Author: Dr Dipesh Patel

Conflict of interest: Nil

Abstract

Introduction: Acute Myocardial Infarction (AMI), or a heart attack, remains a major global health concern. Timely medical care during an AMI is vital, as every moment can impact patient outcomes. Pre-hospital delay, the time from symptom onset to treatment initiation, is a critical period. Despite efforts to reduce delays, challenges persist. This study explores the multifaceted factors contributing to pre-hospital delay in our region, with a focus on socio-demographic, clinical, situational, and cognitive influences.

Material and Methods: This 12-month prospective observational cross-sectional study, conducted from February 2022 to January 2023 in Silvassa tertiary care center, aimed to investigate pre-hospital delay factors in Acute Myocardial Infarction (AMI) patients. A total of 150 AMI patients aged 18 or older were included, with exclusion criteria for severe communicative impairments. The AMI diagnosis considered medical history, electrocardiographic criteria, and elevated cardiac biomarkers. Data collection employed a structured questionnaire covering sociodemographics, clinical details, situational factors, and cognitive factors. Interviews and medical record reviews were conducted, following informed consent. Descriptive statistics, normality checks, univariate comparisons, and logistic regression analysis were performed using SPSS 20.1.1 to assess factors contributing to pre-hospital delay.

Results: In our study of 150 AMI patients, the mean age was 49.9 years. Most patients were \leq 60 years old (60.6%) and male (74.7%). The majority was married (88%), belonged to the upper-middle class (52%), and resided in urban areas (59.3%). The median pre-hospital delay was 2.5 hours, with a mean delay of 6.5 hours (±14.54 hours). Gender significantly influenced delay, with males seeking medical attention sooner than females (p = 0.01). Marital status also played a notable role, with married individuals having shorter delays compared to unmarried counterparts (p = 0.04). Socioeconomic status and education levels showed significant associations, with higher classes and education linked to shorter delays (p = 0.03 and p = 0.04, respectively). Urban residents reached medical care more promptly than rural residents (p = 0.02). The origin and seriousness of symptoms, as well as the mode of transport, showed significant associations with delay (p = 0.03, p = 0.02, and p = 0.001, respectively). Conclusion: In conclusion, our study identifies several critical factors that significantly influence pre-hospital delay in acute myocardial infarction (AMI) patients. The delay is significantly influenced by demographic and psychosocial factors that emphasize the need for targeted interventions to expedite access to medical care for AMI patients, ultimately enhancing their outcomes.

Keywords: AMI, pre-hospital delay, socio-demographic factors.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Shah et al.

Acute Myocardial Infarction (AMI), colloquially known as a heart attack, stands as a formidable global health challenge, persistently claiming its status as a leading cause of morbidity and mortality. [1] In an era marked by remarkable strides in medical science and healthcare infrastructure, the

timely delivery of medical intervention has emerged as a pivotal factor in shaping the destiny of AMI patients. [2] At the heart of this critical juncture lies the concept of pre-hospital delay, an interval that stretches from the onset of symptoms to the commencement of medical treatment. It is within

this temporal realm that the fate of AMI patients hangs in the balance.[3]

In the intense arena of AMI management, every passing minute holds significant importance. Extensive research has underscored that the earlier a patient receives medical attention, the more favorable their odds of survival, and the less extensive the myocardial damage incurred. [4] However, despite concerted efforts to expedite care, pre-hospital delays continue to persist as a formidable challenge. Thus, it becomes imperative to delve into the multifaceted factors that conspire to lengthen these delays, both to appreciate the intricacies of AMI care and to identify tangible avenues for improvement. [5] Although extensive studies on pre-hospital delays have been conducted worldwide, the variations in healthcare systems, sociodemographic factors, and cultural contexts necessitate region-specific research to effectively address this pressing issue.[6–8]

This prospective observational study aims to illuminate the factors contributing to pre-hospital among patients experiencing Myocardial Infarction in our region. By examining the intricate interplay of socio-demographic, clinical, situational, and cognitive factors in the decision-making process of individuals during AMI symptoms, we seek to provide vital insights into areas where intervention may be most effective. Our research endeavors to bridge existing knowledge gaps, allowing healthcare providers to tailor educational strategies and interventions that empower individuals to accurately recognize AMI symptoms and understand the urgency of seeking early medical treatment.

Material and Methods

This prospective study was conducted at the Department of Medicine in our tertiary care center in Silvassa, with a primary objective to investigate the factors contributing to pre-hospital delay in patients diagnosed with Acute Myocardial Infarction (AMI). The study was conducted over a 12-month period, from February 2022 to January 2023, and adopted a cross-sectional research design.

A total of 150 patients who were diagnosed with Acute Myocardial Infarction and presented for treatment at our tertiary care center were included in the study. Inclusion criteria required participants to exhibit symptoms of AMI, be aged 18 years or older, and express a willingness to participate in the study. Exclusion criteria were applied to patients with severe communicative issues, such as hearing and cognitive disorders.

The diagnosis of Acute Myocardial Infarction was established based on a comprehensive evaluation, taking into account the patient's medical history, electrocardiographic criteria, which included ST-

segment elevation (> 0.1 mV) in ≥ 2 contiguous precordial or adjacent limb leads or the presence of a new left bundle branch block, along with elevated serum cardiac biomarkers.

e-ISSN: 0975-1556, p-ISSN: 2820-2643

Data collection relied on a questionnaire developed specifically for this study, drawing inspiration from previous research in the field. The questionnaire encompassed four key domains: socio-demographic information, clinical details, situational factors, and cognitive factors. Socio-demographic data included age, gender, marital status, job status, educational level, living area, monthly income, and health insurance status. Clinical details encompassed pain intensity, prior history of myocardial infarction, diabetes, smoking habits, symptoms, type of onset, duration of pain, symptom hospitalization. Situational factors examined mode of transport, place of symptom onset, time of acute symptom initiation, distance to the hospital, and admission day. Cognitive factors probed the interpretation of symptoms, perception of symptom seriousness, and anxiety associated with the symptoms. The severity of pain or discomfort was quantified on a numeric pain intensity scale ranging from 0 (indicating no pain) to 10 (representing the worst possible pain.

Data collection for the study involved structured interviews conducted by our research team and a review of the medical records of the participating patients. Written informed consent was obtained from all patients prior to their inclusion in the study. The study protocol was approved by the Ethical Committee of our tertiary care center in Silvassa.

The data analysis involved calculating descriptive statistics, including means and standard deviations, while normality was checked using Kolmogorov-Smirnov test. The analysis was **SPSS** 20.1.1.Univariate performed using comparisons were then conducted to examine relationships between independent variables and pre-hospital delay. Statistical significance was set at p < 0.05. Variables with significance below this threshold underwent stepwise Logistic regression analysis. This analysis used pre-hospital delay (categorized as ≤ 2 hours and > 2 hours) as the dependent variable, with gender, marital status, education level, monthly income, living area, mode of transport, type of symptom onset, admission day, interpretation of symptoms, perception of symptom seriousness, and anxiety as independent variables.

Results

In present study of 150 participants, the mean age of the participants was 49.9±14.3 years with most of patients were younger than 60 years, which is a crucial demographic for our study. The majority were married, belonged to the upper-middle class, and were male, factors that may impact pre-hospital delay. Additionally, the high percentage of non-

smokers and urban residents might have implications for our analysis. Conversely, there were fewer participants who were older, unmarried, from lower socioeconomic classes, smokers, and had co-morbidities, and a substantial portion lived in rural areas, which could also influence pre-hospital delay.

e-ISSN: 0975-1556, p-ISSN: 2820-2643

Table 1: Socio demographic characteristics

Variable		n (%) out of 150	Variable		n (%) out of 150
AGE	≤60 years	91 (60.6%)	Sex	Male	112 (74.7%)
	>60 years	59 (39.4%)		Female	38 (25.3%)
Marital status	Married	132 (88%)	Smoker	Yes	63 (42%)
	Unmarried	18 (12%)		No	87 (58%)
Socio economi-	Upper	12 (8%)	Co-morbidities	Yes	41 (27.3%)
cal class	Upper middle	78 (52%)		No	109 (72.7%)
	Lower middle	34 (22.7%)	Locality	Urban	89 (59.3%)
	Lower	26 (17.3%)		Rural	61 (40.7%)

In our study, the majority experienced abrupt pain onset (65.33%), while a substantial portion used ambulance transport (30.67%) and were hospitalized (76.67%). A significant number experienced acute symptoms from 6 AM to 12 PM (34%), with most reporting cardiac-origin pain

(76%) and considering their symptoms serious (75.33%). It's important to highlight the relatively high percentage of participants experiencing anxiety (71.33%). These factors may significantly influence pre-hospital delay in AMI patients.

Table 2: Factors Related to Pre-Hospital Delay in AMI Patients

Variable		n (%) out of 150	Variable		n (%) out of 150
Onset of pain	Abrupt	98 (65.33%)	Symptoms other	None	35 (23.33%)
symptoms	Gradual	52 (34.67)	than pain	1-2	76 (50.67%)
Duration of pain	<30mins	39 (26%)		<u>≥</u> 3	39 (26%)
(mins)	≥30mins	111 74%)	Site of infarction	Anterior MI	69 (46%)
Mode of	Ambulance	46 (30.67%)		Inferior MI	41 (27.33%)
transport	Own vehicle	38 25.33%)	=	Other	40 (26.67%)
	Public trans.	66 44%)	History of MI	Yes	17 (11.33%)
Hospitalization	Yes	115 76.67%)		No	133 (88.67%)
	No	35 (23.33%)	History of DM	Yes	41 (27.33%)
Time of acute	0-6 AM	51 (34%)		No	109 (72.67%)
symptoms onset	6-12AM	43 (28.67%)	History of HTN	Yes	39 (26%)
	12-6PM	38 (25.33%)		No	111 (74%)
	6-12PM	18 (12%)	Distance to hos-	≤10km	137 (91.33%)
Origin of Pain	Cardiac	114 (76%)	pital (km)	>10km	13 (8.67%)
	Non cardiac	36 (24%)	Anxiety	Present	107 (71.33%)
Seriousness of	Non serious	37 (24.67%)		Absent	43 (28.67%)
symptoms	Serious	113 (75.33%)			

Table 3 investigates pre-hospital delay in AMI patients and its association with different factors.

In our study, the median of pre-hospital delay was 2.5 hours, with a mean delay of 6.5 hours (± 14.54 hours). The result reveals that gender significantly influences delay, with males seeking medical attention sooner than females (p = 0.01). Marital status plays a notable role, where married individuals exhibit shorter delays compared to their unmarried counterparts (p = 0.04). Socioeconomic status and education levels are also significant, with

higher classes and education linked to shorter delays (p = 0.03 and p = 0.04, respectively). Urban residents tend to reach medical care more promptly than their rural counterparts (p = 0.02). The origin and seriousness of symptoms, as well as the mode of transport, show significant associations with delay (p = 0.03, p = 0.02, and p = 0.001, respectively). Overall, these results highlight the substantial impact of various factors on pre-hospital delay in AMI patients, underscoring the need for tailored interventions to reduce delays.

Table 3: Pre-Hospital Delay in AMI Patients and Associated Factors

Variables	•	Pre-hospital delay (hours) (mean ± SD)	P	
			values	
Sex	Male	6.4±9.59	0.01	
	Female	8.59±14.51]	
Marital status	Married	7.78±12.13	0.04	
	Unmarried	6.46±15.04		
Socio economical sta-	Upper	2.37±5.46	0.03	
tus	Upper middle	3.31±4.74	1	
	Lower middle	7.32±7.39		
	Lower	8.42±9.59		
Education	Illiterate	7.13±18.64	0.04	
	Primary	6.32±16.07	-	
	Secondary	5.74±3.61]	
	Graduate	1.65±0.98]	
Locality	Urban	5.02±16.08	0.02	
	Rural	8.01±16.63]	
Mode of transport	Ambulance	7.25±14.87	0.06	
	Others	8.12±22.02		
Type of symptoms	Acute abrupt	6.70±11.43	0.03	
	Gradual	9.44±19.36		
Symptoms origin	Cardiac	5.32±9.42	0.02	
	Non cardiac	Non cardiac 9.46±21.95		
Seriousness of symp-	Serious	5.58±11.31	0.001	
toms	Non serious	Von serious 11.39±12.41		
Anxiety	Yes	7.54±11.92		
•	No	7.67±15.45	1	

Discussion

In the realm of healthcare, time often stands as a defining factor between life and death, and nowhere is this more apparent than in the management of Acute Myocardial Infarction (AMI), commonly known as a heart attack. The timely delivery of medical care during an AMI is not just a matter of medical urgency; it's a matter of life-altering consequences. Every minute that slips away before a patient receives medical intervention can significantly impact their chances of survival and the extent of cardiac damage incurred. In the face of this sobering reality, our study delves into the intricate domain of pre-hospital delay, a pivotal period that stretches from the onset of AMI symptoms to the initiation of medical treatment. This critical interval is where the destiny of AMI patients teeters on the precipice, and it is the focus of our research.

In our study of 150 participants, the mean age was 49.9±14.3 years, with 60.6% aged 60 or younger and 74.7% males. Comparing to other studies, Chowdhury et al. [7] reported a mean age of 53.8±11.2 years with 67.6% males while in Nilsson et al. [9], the mean patient age was 68.1 years. Yoon et al. [10] found significant age differences between acute ischemic stroke (AIS) and acute myocardial infarction (AMI) patients, and Khan et al. [11] studied STEMI patients with a mixed gender population. These variations highlight age and gender disparities among AMI patients in different

studies, likely influenced by diverse study populations and settings, which could impact prehospital delay in acute myocardial infarction patients.

e-ISSN: 0975-1556, p-ISSN: 2820-2643

In our study, the median pre-hospital delay was 2.5 hours, with a mean delay of 6.5 hours (± 14.54 hours). Comparing these findings to other studies, Khan et al.¹¹ found that only 17% of patients could reach the hospital in less than 2 hours, and 25% reached between 2 to 4 hours after symptom onset. G.S. Youssef et al. [12] reported a mean pre-hospital delay of 8.7 hours. Mussi et al. [13] observed geometric means of 1.13 hours for men and 0.74 hours for women in the time of decision (TD) to seek medical care, with 1.74 hours for men and 1.47 hours for women in the time of arrival (TA) at the health service. Khaled et al. [14] studied factors responsible for prehospital delay in patients with acute coronary syndrome in Bangladesh. Mujtaba et al. [15] noted a median pre-hospital time of 120 minutes (IQR 229), with 33.3% of patients arriving within one hour of symptom onset. Bates et al. [16] observed a median total pre-hospital delay of 5.1 hours, with patient and transport delays of 1.5 and 2.1 hours, respectively. These findings highlight the considerable variability in pre-hospital delay times different studies, reflecting diverse among healthcare systems and patient behaviors in different regions.

In our study of 150 AMI patients, we explored prehospital delay, a critical aspect of acute myocardial infarction management. Our findings highlighted key factors influencing this delay. The mean prehospital delay was 6.5 hours, with a median of 2.5 hours. Notably, gender played a significant role, with males experiencing shorter delays (mean 6.4 hours) compared to females (mean 8.59 hours, p=0.01). Marital status also mattered, as married individuals faced longer delays (mean 7.78 hours) than unmarried counterparts (mean 6.46 hours, p=0.04). Socioeconomic status and education were linked to shorter delays (p=0.03 and p=0.04, respectively).

Our study's findings are consistent with other studies [8,11,16] that have delved into pre-hospital delay in AMI patients. Chowdhury et al. [7] reported that nearly half of their patients presented to the hospital more than 12 hours after symptom onset, with factors such as typical chest pain, diabetes, residence distance from the nearest hospital, socioeconomic status significantly affecting prehospital delays. Nilsson et al. [9] highlighted the importance of the first medical contact, with primary care visits and telephone counseling contributing to prolonged delays. Additionally, symptom type, chest pain in particular, played a pivotal role in influencing the delay. Yoon et al. [10] observed significant age disparities, with older patients exhibiting longer delays, and the use of emergency medical services (EMS) emerging as a critical determinant.

Furthermore, Rafi et al. [17] identified factors such as age, family income, distance from primary care centers, symptom interpretation, and referral from primary care centers as significant determinants of pre-hospital delays in AMI patients. Khan et al. also transportation underscored problems misinterpretation of symptoms as major contributors to delayed presentation. Ogushi et al. [18] emphasized age, diabetes, and the time of symptom onset as positively associated with longer prehospital delays. Youssef et al. [12] provided an indepth analysis of pre-hospital and hospital delays and observed that patient-related causes accounted for a significant portion of pre-hospital delay time, with 66% of the time being attributed to patients. Additionally, transportation contributed to 34% of the pre-hospital delay time.

The study by Khaled et al. [11] from Bangladesh revealed an array of factors contributing to pre-hospital delay, including age, residence, income, and several symptom and care-related factors. In Russia, Bates et al. [16] noted that delays were longer than recommended, highlighting the need to reduce patient delays, as transport delays were inevitably protracted in many regions. Li et al. [19] also delved into the psychology of delay, emphasizing the significance of perceived barriers

to care-seeking as a major predictor of longer prehospital delays in AMI patients, alongside genderrelated variations.

e-ISSN: 0975-1556, p-ISSN: 2820-2643

The cumulative findings of these studies [14,20] emphasize the complexity of pre-hospital delay in AMI patients. These delays are influenced by a multitude of factors, including demographic, socioeconomic, and healthcare system-related elements, underlining the multifaceted nature of this critical aspect of acute myocardial infarction management. Understanding these dynamics is paramount in formulating targeted interventions to reduce pre-hospital delay, thereby improving patient outcomes and reducing the burden of AMI.

A limitation of our study is the relatively small sample size of 150 participants, which may restrict the generalizability of our findings. Additionally, the data are based on retrospective analysis, which could introduce recall bias, and may not capture the full spectrum of factors influencing pre-hospital delay in acute myocardial infarction patients. Furthermore, the study was conducted in a specific geographic region, potentially limiting the applicability of our results to more diverse populations with varying healthcare systems and cultural factors.

Conclusion

In our study, we found that certain demographic and clinical factors significantly influence pre-hospital delay in Acute Myocardial Infarction (AMI) patients. Notably, being male, married, having higher socioeconomic status and education, and residing in urban areas were associated with shorter pre-hospital delays. On the other hand, being female, unmarried, having lower socioeconomic status and education, and living in rural areas were linked to longer delays. The type and seriousness of symptoms, as well as the mode of transport, also played a significant role in influencing delay. Our study underscores the importance of understanding these factors to develop targeted interventions that reduce pre-hospital delay and improve outcomes for AMI patients.

Bibliography

- 1. Johansson S, Rosengren A, Young K, Jennings E. Mortality and morbidity trends after the first year in survivors of acute myocardial infarction: a systematic review. BMC cardiovascular disorders. 2017;17:1–8.
- 2. Bradley EH, Herrin J, Wang Y, Barton BA, Webster TR, Mattera JA, et al. Strategies for reducing the door-to-balloon time in acute myocardial infarction. New England Journal of Medicine. 2006;355(22):2308–20.
- 3. Saceleanu VM, Toader C, Ples H, Covache-Busuioc RA, Costin HP, Bratu BG, et al. Integrative Approaches in Acute Ischemic Stroke:

- From Symptom Recognition to Future Innovations. Biomedicines. 2023;11(10):2617.
- Authors/Task Force Members, Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. European heart journal. 2008; 29(23):2909–45.
- Chhabra S, Eagles D, Kwok ES, Perry JJ. Interventions to reduce emergency department door-to-electrocardiogram times: a systematic review. Canadian Journal of Emergency Medicine. 2019;21(5):607–17.
- Wechkunanukul K, Grantham H, Clark RA. Global review of delay time in seeking medical care for chest pain: An integrative literature review. Australian Critical Care. 2017;30(1): 13– 20.
- 7. Chowdhury IZ, Amin MN, Chowdhury MZ, Rahman SM, Ahmed M, Cader FA. Pre hospital delay and its associated factors in acute myocardial infarction in a developing country. Plos one. 2021;16(11):e0259979.
- 8. Ruffin F, Van Horn E, Letvak S, Kennedy-Malone L. Exploration of pre-hospital patient delays in seeking care for symptoms of bacteremia and sepsis: A qualitative study. Nursing Open. 2023;
- Nilsson G, Mooe T, Söderström L, Samuelsson E. Pre-hospital delay in patients with first time myocardial infarction: an observational study in a northern Swedish population. BMC cardiovascular disorders. 2016;16:1–10.
- Yoon CW, Oh H, Lee J, Rha J, Woo S, Lee WK, et al. Comparisons of prehospital delay and related factors between acute ischemic stroke and acute myocardial infarction. Journal of the American Heart Association. 2022; 11 (9):e023214.
- 11. Khan A, Phadke M, Lokhandwala YY, Nathani PJ. A study of prehospital delay patterns in acute myocardial infarction in an urban tertiary care institute in Mumbai. J Assoc Physicians India. 2017;65(5):24–7.
- 12. Youssef G, Kassem H, Ameen O, Al Taaban H, Rizk H. Pre-hospital and hospital delay in

patients with non-ST elevation acute coronary syndromes in tertiary care. The Egyptian Heart Journal. 2017;69(3):177–81.

e-ISSN: 0975-1556, p-ISSN: 2820-2643

- 13. Mussi FC, Mendes AS, Queiroz TL de, Costa ALS, Pereira Á, Caramelli B. Pre-hospital delay in acute myocardial infarction: judgement of symptoms and resistance to pain. Revista da Associação Médica Brasileira. 2014;60:63–9.
- Khaled MFI, Adhikary DK, Islam MM, Alam MM, Rahman MW, Chowdhury MT, et al. Factors Responsible for Prehospital Delay in Patients with Acute Coronary Syndrome in Bangladesh. Medicina. 2022;58(9):1206.
- 15. Mujtaba SF, Sohail H, Ram J, Waqas M, Hassan M, Sial JA, et al. Pre-hospital delay and its reasons in patients with acute myocardial infarction presenting to a primary percutaneous coronary intervention-capable center. Cureus. 2021;13(1).
- 16. Bates K, Schirmer H, Kontsevaya A, Bobrova N, Leon DA, McKee M. Pre-Hospital Delays among Patients with Acute Coronary Syndrome in the Russian Federation: a multicentre prospective observational cohort study (the AMIR Study). Frontiers in Disaster and Emergency Medicine. 2023;1.
- 17. Rafi A, Sayeed Z, Sultana P, Aik S, Hossain G. Pre-hospital delay in patients with myocardial infarction: an observational study in a tertiary care hospital of northern Bangladesh. BMC health services research. 2020;20(1):1–12.
- 18. Ogushi A, Hikoso S, Kitamura T, Nakatani D, Mizuno H, Suna S, et al. Factors Associated With Prehospital Delay Among Patients With Acute Myocardial Infarction in the Era of Percutaneous Coronary Intervention—Insights From the OACIS Registry—. Circulation Journal. 2022;86(4):600–8.
- 19. Li PW, Yu DS. Predictors of pre-hospital delay in Hong Kong Chinese patients with acute myocardial infarction. European Journal of Cardiovascular Nursing. 2018;17(1):75–84.
- 20. Lee SH, Kim HK, Jeong MH, Lee JM, Gwon HC, Chae SC, et al. Pre-hospital delay and emergency medical services in acute myocardial infarction. The Korean journal of internal medicine. 2020;35(1):119.