## Characteristics of myocardial infarction in young patients at Dr. Cipto Mangunkusumo Hospital, Jakarta

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#### Abstrak

Penyakit jantung koroner (PJK) merupakan penyebab kematian tertinggi di negara industri. Di negara berkembang, termasuk Indonesia, terjadi peningkatan frekwensi PJK. Prevalensi IM (infark miokard) pada laki-laki usia < 45 tahun menurut studi Framingham, adalah 75 per 1000 dibandingkan pada umur > 65 tahun sebesar 212 per 1000 dalam 8 tahun. Faktor-faktor yang umumnya menonjol pada pasien IM usia muda adalah merokok, riwayat penyakit keluarga, dan dislipidemia, Lp (a). Metode dan cara kerja :Penelitian retrospektif pada semua pasien IMA yang dirawat di ICCU, RSUPN Dr Cipto Mangunkusumo, Jakarta dari tanggal 1 Januari 1990 sampai 31 Desember 1994 sejumlah 642 orang. Hasil penelitian : dari 642 kasus didapatkan laki-laki sebanyak 531 orang (82,7%) dengan umur rata-rata 53,98±10,66 dan wanita sebanyak 111 (17,3%) dengan umur rata-rata 61,40±10,97 tahun. Jumlah pasien berusia di bawah 45 tahun seluruhnya 94 orang (14,6%) dengan umur rata-rata 38,54±5,63 tahun. Dari jumlah ini didapatkan laki-laki sebanyak 88 orang (93,6%) dan wanita 6 orang (6,4%). Faktor risiko pada usia < 45 tahun adalah sebagai berikut : merokok, faktor keturunan, stress. Kesimpulan : Pasien IMA usia muda didapatkan lebih banyak pada laki-laki daripada wanita dengan perbandingan 93,6% : 6,4%. Faktor risiko yang ditemukan terutama adalah merokok dan stress.

#### Abstract

Coronary artery disease (CAD) is the most frequent cause of death in the industrialized countries. In developing countries, such as Indonesia, CAD showed an increase. According to Framingham's study, the prevalence of myocardial infarction (MI) in the last 8 years in males under 45 years of age was 75 per 1000 people, compared to those above 65 years of age with a ratio of 212 per 1000 people. The important risk factors in the young MI patients were smoking, family history of CAD and dyslipidemia, Lp (a). Materials and Methods: A retrospective study was done on all MI patients of the ICCU of Dr Cipto Mangunkusumo Hospital, from January 1, 1990 to December 31, 1994, with a total of 642 cases. Results : Of the 642 cases, the number of male patients was found to be 531 (82.7%) with average age of  $53.98\pm10.66$ , and 111 females (17.3%) with average age of  $61.40\pm10.97$ . The number of patients under 45 years was 94 (14.6%), with average age of  $38.54\pm5.63$ . Of this number, 88 patients (93.6%) were males and 6 females (6.4%). The risk factors of CAD in the age below 45 years were smoking, hereditary factor and stress. Conclusions: Young MI patients were found more in the male group than in female, with the ratio of 93.6 : 6.4%. The risk factors identified were mainly smoking and stress.

Keywords : Myocardial infarction, young people, risk factor

Coronary artery disease (CAD) is the most important cause of death in industrialized countries. In the USA, 46 % of all deaths in 1986 were caused by CAD.<sup>1</sup> In Asian countries, CAD also became a major cause of death. In Singapore, for instance, deaths due to CAD had doubled in two decades since 1959. The same phenomenon was also found in Latin America.<sup>2</sup> In Japan the increased frequency of CAD was assumed to be due to changes in dietary pattern. In the past, the incidence of myocardial infarction in Japan was much lower than in the western countries. Between 1975 and 1979 in Tokai, Tokyo, there was only one myocardial infarction patient under 40 years of age and this number is increased to 3 between 1980 to 1985.<sup>3</sup>

According to the 1985/1986 Household Health Survey, in Indonesia CAD was the second most common cause of death (9.9%), but in the 1992 survey it has doubled to 16.6 %.<sup>4</sup> Of 523,000 subjects involved in the Monica Project conducted in the municipality of Jakarta in 1990, 2073 were randomly selected to take part in the study. Abnormal ECG was found in 2.7% of the population studied.<sup>5</sup> An epidemiological study conducted in 1993 by the Division of Endocrinology, Faculty of Medicine University of Indonesia in Kayu

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Putih village, Jakarta, showed a 5.7%.<sup>6</sup> Suyono predicted an increase in CAD incidence because of the change in dietary pattern, particularly in the big cities, from high fiber diet to a diet high in carbohydrate, protein and fat.<sup>7</sup>

In the USA, multiple CAD risk factor intervention initiated in the 1970s, has succeeded in sharply reducing CAD mortality rate to 3% annually.<sup>1</sup> From 1971 to 1982 there was also a decline in the incidence of myocardial infarction, being 24% in man and 37% in women. Patients under 45 years of age showed twice as much as reduction in the incidence of myocardial infarction than those of over 45 years old.<sup>8</sup>

The prevalence of myocardial infarction in the young was relatively lower compared to the older population. The reported prevalence of myocardial infarction in patients below 45 years of age ranged from 3% to 10% in males and 0.3% to 2% in female.<sup>9-14</sup> Framingham's study showed that the likelihood of myocardial infarction within 8 years in male subjects aged under 45 years was 75 in 1.000, whilst in those aged above 65 years it was 212 in 1000.<sup>14</sup>

In the National Cardiac Center, Jakarta, Hanafiah reported an increase in the incidence of myocardial infarction in patients under 45 years, from 7 % in 1985 to 17% in 1989.<sup>11</sup>

The principal risk factors of myocardial infarction in the young patients were smoking,  $^{9,10,,12, 13, 31}$  positive family history,  $^{9,12, 13, 32, 33, 34}$  dyslipidemia, and Lp (a). Hypertension was not so prevalent in older people, ranging from 16.7 to 29 %, diabetes mellitus in the young was also less frequently found, being in the range of 3% to 6.3%. One should take note, that in the literature "young age" was defined differently, i.e., from age below 35 years to below 60 years, while the mean value ranged from 40 to 45 years.

## MATERIALS AND METHODS

#### **Population and sample**

A retrospective study was undertaken in all patients with acute myocardial infarction admitted at the ICCU, Dr. Cipto Mangunkusumo Hospital, Jakarta from January 1, 1990 to December 31, 1994.

## Statistical tests

For quantitative data, mean and standard error of the mean (SEM) and standard deviation (SD) were measured. Statistical significance was set at a p value of <0.05.

## RESULTS

### Age and sex

There were 642 myocardial infarction patients. Their ages ranged from 14 to 85 years with mean age of 55.26 years (SEM  $\pm$  0.44 year, SD  $\pm$  11.06 year) and median age of 55 years. Of them, 531 (82.7%) were males, with age ranging from 14 to 85 years, mean age was 53.98 years (SEM  $\pm$  0.46, SD  $\pm$  10.66) and median age 53 years, while the number of females was 111 (17.3%) patients with age ranging from 35 to 85 years, mean age was 61.40 years (SEM  $\pm$  1.04 years, SD  $\pm$  10.97) and median age 60 years. Males were significantly younger than females, being 53.98 years (SD  $\pm$  10.66) vs 61.40 years respectively (SD  $\pm$  10.79 years) p=0.000001.

#### Patients below 45 years old

Ninety-four (14.6%) patients were below 45 years old, their mean age was 39,54 years (SEM $\pm$  0.58 years SD  $\pm$  5.63 years) and median age was 40 years. Eighty-eight (93.8%) patients were males and 6(6.4%) were females. Mean age of male patients was 38.48 years (SEM $\pm$  0.617 years, SD $\pm$  5,79 year) and median age 40 years. The youngest male patient was 14 years old. Mean age of female patients was 39.50 years (SEM $\pm$  1.057 years, SD $\pm$  2.59 years) and median age 40.5 years. The youngest female patient was 35 years old.

#### Patients over 45 years old

The number of patients above 45 years old was 548 (85.4%). The oldest patient was 85 years old. Mean age was 58.12 years (SEM  $\pm$  0.39 years, SD  $\pm$  9.04 years) and median age 45 years. Four hundred and forty-three (80.8%) patients were males, the oldest was 85 year of age, their mean age was 57.05 years (SEM  $\pm$  0.40 year, SD  $\pm$  8.50 years) and median age 56 years. The number of female patients was 105 (19.2%), the oldest was 85 years old, their mean age was 62.69 years (SEM  $\pm$  0.93 years SD  $\pm$  9.50 years) and median age 65 years. The female-to-male ratio in the group of

## Occupation

Occupational data were obtained from 564 (87.85 %) patients. Occupation was classified into: civil servants such as: member of parliament, bank official, lecturer, school teacher, judge, medical doctor, and nurse; private sector employee such as trader, entrepreneur, journalist, stock broker, retired people, blue-collar worker i.e. driver, brick layer, laborer; and unemployed people. The most common occupation was private sector employee (32.3%), followed by civil servants (19.1%), retired people (17%), unemployed people (15.6%) and blue collar workers (16%).

## Time of onset

Four hundred and eighty-seven patients (75.86%) were admitted with a time of onset of less than 24 hours.

#### **Risk factors**

The most common risk factor was smoking (66.2 %), followed by hypertension (47.2 %), personality trait (48,2%), stress ( 46.1 %), history of diabetes mellitus (37.7 %), obesity (28.1 %), dyslipidemia (13.7%), and genetic factor (10.7%).

Table 1 showed the difference in % of risk factors between patients aged less than 45 versus those above 45 years of age.

## **CLINICAL PRESENTATIONS**

#### **Chief complaints**

The most common complaints were chest pain, i.e., specific chest pain - anginal pain (86%), followed by breathlessness (5.6%), epigastric pain (4%), severe condition (3.1%), and miscellaneous complaints (1.1%).

Table 1. Risk factors between AMI < 45 years vs  $\ge$  45 year subgroups

Risk factors	< 45 years		≥ 45 years		10.1		
	Ν	n	%	Ν	n	%	p
Hypertension	94	29	30.9	548	274	50	0.0005
History of DM	89	12	13.5	515	117	22.7	0.049
Glucose tolerance	94	24	25.5	548	214	39.1	p-0.012
Dyslipidemia	72	9	12.5	440	56	12.7	NS
Smoking	94	75	79.7	9545	348	63.9	0.002
Obesity	94	33	35.1	535	144	26.9	NS
Family history	98	16	16.3	524	50	9.5	0.03
Stress	86	55	64	477	205	43	0.0003
Personality A	11	6	54.6	72	34	47.2	NS

#### Table 2. Chief complaints

Chief complaints	All n=642	< 45 years n=94	$\geq$ 45 years n=598	р
Chest pain	553 (86.1%)	86 (91.5%)	467 (85.2%)	NS
Shortness of breath	36 (5.6%)	3 (3.2%)	33 (6.0%)	NS
Epigastric pain	26 (4.0%)	3 (3.2%)	24 (4.4%)	NS
severe condition*	20 (3.1%)	1 (1.1)	19 (3.5 %)	NS
Miscellaneous	7 (1.1%)	1 (1.1%)	19 (3.5%)	NS

\* severe conditions include : faint, fatigue, severely ill, shock, feet cyanosis

Miscellaneous: palpitation, diarrhea, cold sweat, post-PTCA, no complaint.

Chief complaints between patients aged > 45 years and those aged < 45 years did not differ significantly.

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In the USA, multiple CAD risk factor intervention initiated in the 1970s, has succeeded in sharply reducing CAD mortality rate to 3% annually.<sup>1</sup> From 1971 to 1982 there was also a decline in the incidence of myocardial infarction, being 24% in man and 37% in women. Patients under 45 years of age showed twice as much as reduction in the incidence of myocardial infarction than those of over 45 years old.<sup>8</sup>

The prevalence of myocardial infarction in the young was relatively lower compared to the older population. The reported prevalence of myocardial infarction in patients below 45 years of age ranged from 3% to 10% in males and 0.3% to 2% in female.<sup>9-14</sup> Framingham's study showed that the likelihood of myocardial infarction within 8 years in male subjects aged under 45 years was 75 in 1.000, whilst in those aged above 65 years it was 212 in 1000.<sup>14</sup>

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## **Characteristics of chest pain**

There were 26 different characteristics of chest pain noted in 520 patients.

The most frequent chest pains were sensation of pressure (36.5%), stabbing (26.2%), burning (9.0%), crushing (5.4%), squeezing (5%), and nonspecific chest pain (18.1%). Nature of chest pain in the young age group compared to the older group was not statistically different.

## LABORATORY INVESTIGATION

#### **Chest x-ray**

Data were collected from 368 patients. Cardiothoracic ratio (CTR) greater than 50% was found in 166 subjects (45.1%), while 202 patients (54.9%) had CTR of less than 50%. The difference between both groups was not significant (p=0.1816).

#### Peak creatinine kinase (CK) value

Four hundred and seventy-one patients had their peak CK values analyzed. The mean value was 925.33 µl (SD  $\pm$  1127.33 µl). Peak value in patients under 45 years of age was 1083.56 µl (SD  $\pm$  1082.24 µl). Whereas in patients aged over 45 years, peak value was 895.36 µl (SD $\pm$  1134.52 µl). The difference between the two groups was statistically significant (p < 0.05).

# Peak creatinine kinase muscle-brain (CKMB) value

There were 465 subjects whose CKMB value could be analyzed. The mean was  $81.82 \ \mu l \ (SD \pm 176.96 \ \mu l)$ . Peak value in patients below 45 years of age was

Characteristics	All n =52	< 45 years n= 78	$\geq$ 45 years n=44	р
pressure	189 (36.4%)	31 (39.74%)	158 (35.7%)	ns
stabbing	136 (26.2%)	21 (26.92%)	115 (26%)	ns
burning	47 (9.0%)	8 (10.25%)	39 ( 8.8%)	ns
crushing	28 (5.4%)	2 ( 2.56%)	26 ( 5.9%)	ns
squeezing	26 (5%)	4 ( 5.12%)	22 ( 5%)	ns
typical*	17 (3.3%)	4 ( 5.13%)	13 ( 2.9%)	ns
pain*	15 (2.9 %)	1 ( 1.28%)	14 ( 3.2%)	ns
miscellaneous	94 (18.1%)	12 ( 15.4%)	82 (18.6%)	ns

Table 3. Characteristics of chest pain

\* the characteristic of pain was not described in the records.

\*\* with each frequency of < 1.5 % : a sense of being ripped, tingling sensation, suffocation, dull pain, a sense of beaten, a sense of fullness, breathlessness.

88.88  $\mu$ l (SD ± 118.94  $\mu$ l), while those aged over 45 years was 80.48  $\mu$ l (SD ± 186.01  $\mu$ l). The difference between both of groups was statistically significant (p < 0.05).

## Leucocyte count

Leucocyte count could be analyzed in 438 patients. Mean leucocyte count was  $12385.3/\mu$ l (SD± 5265.6/ $\mu$ l). In patients under 45 years of age the mean leucocyte was  $13341/\mu$ l (SD ± 5618.7/ $\mu$ l), while in patients of over 45 years old the mean count was 12209.5/ $\mu$ l (SD+5187  $\mu$ l), both groups differed significantly (p < 0.05).

Mean leucocyte count in nonsurviving patients was  $13218.2/\mu l$  (SD  $\pm$  4834.2/ $\mu l$ ), while the mean in surviving patients was  $122239.7/\mu l$  (SD  $\pm$  4435.3/ $\mu l$ . The difference between the two group did not reach statistical significance (p=0.31).

#### DISCUSSION

#### Age and sex

In the males, the youngest patient was 14 years old. The prevalence increased by age and the highest prevalence was in age group of 45-54 years old. The youngest female patient 35 years old. The highest frequency was in the age group of 60-64 years and decreased from age of 55.26 years. The highest incidence took place in the group of 50-60 years old. In the Framingham's study,<sup>26</sup> in which a population of 35-85 years old was followed-up for 26 year, the incidence of myocardial infarction was found to increase with aging. The highest incidence was in the age group of 75-85 years in both genders. Male-to-female ratio in this study was 82.7% : 17.3%. The similar ratios were reported by other investigators. Zimmerman et al<sup>11</sup> reported a ratio of 84.9%:15.1% among 8839 cases of acute myocardial infarction in 1974-1979 in the USA, while Holt et al<sup>8</sup> found a ratio of 73.8%:26.14% among 2643 cases studied in 1968-1983 in the USA and Canada. In Framingham's study<sup>26</sup> in a course of 26 years follow-up, the incidence of acute myocardial infarction among the males was tripled as compared to that of the females. In a study conducted at the National Cardiac Center in Jakarta, 1988-1989, Hanafiah reported a male-to-female rates of 99,1% to 0.1 %.<sup>10</sup> Our study confirmed the abovementioned reports, that the incidence of myocardial infarction was higher in the males with a male-tofemale ratio ranging from 3 to 5, although a much higher ratio was observed in Hanafiah's study.

The prevalence of acute myocardial infarction patients under 45 years of age in this study was 14.6%. Holt<sup>8</sup> reported a prevalence of 8% in patients under 45 years of age. A value of 1-8% was reported by Jakuwick in patients under 35 years of age. Hanafiah<sup>10</sup> reported a prevalence of 10.17% in patients under 45 years of age. In the age group of under 45 years of age, the male-to-female ratio was 93.6% : 6.4% as compared to a ratio of 83.8% : 19.2 % in the age group above 45 years. This lower prevalence of females attacked by acute myocardial infarction in the younger group showed a moderately significant statistical difference.

In Framingham's study in males aged 35-45 years old, the incidence of coronary heart disease was 1.2/1000 population while in the age group of 75-85 years it increased to 46.8/1000 population. The incidence of coronary heart disease rose after the age of 45 years. In the females suffering from CHD the increase was less frequent in comparison with that of premenopausal age.<sup>26</sup>

## Occupation

In this study, it was found that private sector employee had the highest prevalence of acute myocardial infarction (32.3 %), far exceeding those with the other kinds of occupation. However, our study was not designed to answer this issue.

In a study performed by Morris comprising 18.000 civil servants in England, those who used their leisure times with physical activities > 7.5 cal/m for over 8 years life span, had a 50% decrease of relative risk of acute myocardial infarction.<sup>27</sup>

#### Time of onset

Acute myocardial infarction has circadian variability. In our study in which patients with time of onset less than 24 hours were analyzed, we found the peak incidence of acute myocardial infarction at approximately 09.00 a.m. This pattern was similar to TRIMM<sup>29</sup> and GiISSI studies.<sup>30</sup>

The TRIMM study (Trigger and Mechanism of Myocardial Infarction)<sup>29</sup> reported a significantly higher prevalence of acute myocardial infarction between 06.00 to 09.00 a.m. The time of onset was defined as the time of the most severe symptom experienced for the first time by the patient. After adjustment with time of wake-up was made, the study showed that in three hours after wake-up the heart rate increased 1.8 to 2.4 times. In ISSI study,<sup>30</sup> involving only patients with onset less than 6 hours, there was an increase in the frequency of anginal attacks in the morning and during the day. Fiquras and Lidon reported<sup>31</sup> that these attacks occurred most frequently on 07.00-10.00 and on 19.00 - 22.00.

In this study, the principal risk factors in the male patients were smoking and stress, whereas in the females these factors included history of diabetes mellitus, glucose intolerance, hypertension and obesity. In Framingham's study,<sup>26</sup> the most important risk factor for the males was smoking and for the females diabetes mellitus. This result was different from that of the present study in which hypertension was more prevalent in female acute myocardial infarction.

#### Risk factors in patients under 45 years of age

In this study, the most common risk factors in patients under 45 years old were smoking, positive family history and stress, while hypertension and diabetes mellitus were not as frequent as in older patients. This result confirmed the studies of Holt,<sup>8</sup> Zimmerman<sup>11</sup> and Barbash<sup>12</sup> where smoking was found as the most frequent risk factor in patients under 45 years of age. Barbash<sup>12</sup> found that a positive family history was the second most important risk factor after smoking.

Some investigators found a positive family history as the principal risk factor in young age. Hanafiah encountered that stress was more prevalent in young acute myocardial infarction patients than in older patients.<sup>10</sup> Hypertension and diabetes mellitus in young age were less important than in the older patients.

#### **Clinical manifestations**

In this study, chest pain was the most frequent complaint (86.1%), but there were other complaints that also deserved attention such as breathlessness (5.6%), epigastric pain (4.0%), "severe conditions" (fainting, fatigue, severe illness, convulsion, shock, feet cyanosis) (3.1%), and other miscellaneous complaint (palpitation, diarrhea, cold sweat, post-PTCA and without complaint) of 1.1%. In their study, Harun et al<sup>35</sup> found substernal chest pain as the chief complaint in 89 % of their patients.

## Peak values of CK and CKMB enzymes

Peak values of creatinine kinase (CK) and creatinine kinase muscle brain (CK-MB) enzymes correlated with the extent of myocardial damage.<sup>36</sup> This study encountered a peak value of CK enzyme of 925.33  $\mu$ l (SD ± 1127.33  $\mu$ l), while peak value of CKMB enzyme was 81.821  $\mu$ l (SD ± 176.96  $\mu$ l). The trend of peak values of CK and CKMB enzymes in patients under 45 years of age was higher than that of the older age. Statistically, this was not significant. Holt in his study found a peak value of CK in age group of under 45 years old to be higher than that in those above 45 years old, i.e., 1064 (+816) : 826 (+655), (P=0.001).

#### Leucocyte

As body responded to acute myocardial infarction, the leucocyte count would increase. The magnitude of response was correlated with the extent of the inflammatory process and myocardial necrosis.<sup>37</sup> Elevated periphery leucocyte count is associated with ventricular arrhythmia in initial phase of acute myocardial infarction. In this study, we found leucocytosis with a mean count of 12385  $\mu$ l (SD ± 5618/ $\mu$ l). The mean leucocyte count of nonsurviving patients was higher than that of surviving patients, being 13.218/ $\mu$ l (SD± 4835/ $\mu$ l) compared with 12.2239/ $\mu$ l (SD± 4435/ $\mu$ l). However the difference was not statistically significant.

## Annual trend of acute myocardial infarction

In the observation period from 1990 to 1994, we did not find an increasing trend of acute myocardial infarction cases in patients under 45 years vs those above 45 years. Hanafiah reported a trend towards increasing age from 7% in 1985 to 17% in 1989.<sup>10</sup> For the whole sample: the ages of male patients with acute myocardial infarction ranged from 14 to 85 years, (mean age  $53.98 \pm 10.66$  years), whereas in the female patient ranged from 35 to 85 years, (mean age  $61.40 \pm 11.06$  years). Mean age of all patients was 55.26 years. Female patients were fewer than male patients, with a ratio of 17%: 83%.

In the young age: the most prevalent risk factors in patients under 45 years of age were : smoking and stress, whereas risk factors of diabetes mellitus and hypertension were less common in the young than in the older age.

Conventional risk factors were: hypertension (30.9%), history of diabetes mellitus (13.5%), glucose intolerance (25.5%), smoking 79,8%, history of dys-lipidemia (12.5%), positive family history (16.3%). Non-conventional factors were obesity (35.1%). stress (64%), and type A personality (54.6%).

Chief complaints were: chest pain (91.5%), breathlessness (3.2%), epigastric pain (3.2%), severe general conditions (1.1%). Characteristics of chest pains were: pressure sensation (39.7%), stabbing sensation (26.9%), burning sensation (10.3%), feeling of being squeeze (5.1%).

There was no difference in the male-to-female ratio in patients under 45 years vs that of above 45 years from 1990 to 1994.

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