A STUDY OF CLINICAL PROFILE OF UNRECOGNISED MYOCARDIAL INFARCTION

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ABSTRACT

BACKGROUND

Atypical and silent myocardial infarctions were grouped together as unrecognised myocardial infarction. The prognosis for patients with unrecognised myocardial infarction is as serious as that of recognised myocardial infarction. It is difficult to choose methods by which to identify these patients and to take decisions about secondary prevention and medical treatment. Detailed knowledge about this disease entity is therefore important and must include a thorough understanding of which patient subgroups are especially vulnerable.

The aim of the study is to study the presenting symptoms listed as those of unrecognised myocardial infarction in patients attending NRMCH with no chest pain.

MATERIALS AND METHODS

Twenty-two patients over the age of 40 years with these symptoms were studied. All investigations including serial ECG, cardiac enzymes and echocardiogram were done and the outcome assessed.

RESULTS

Females dominated the study. Out of 22 patients, 50% presented with breathlessness, 45.45% with sweating, 36.36% with abdominal pain, 31.82% with cough and expectoration, 27.27% with fever, 22.73% with nausea and vomiting, 13.64% with oedema, 18.18% with loose stools, 9.09% each with palpitation and hemiplegia, 4.55% each with giddiness, bleeding per rectum and coma. Four died during the study period.

CONCLUSION

It is recommended that an ECG and cardiac enzymes at least be a part of clinical workup offered to all patients with any symptom, however, atypical that might indicate a myocardial infarction.

KEYWORDS

Silent Myocardial Infarction, Unrecognised Myocardial Infarction, Atypical Myocardial Infarction.

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BACKGROUND

The aim of this study was to evaluate the presenting symptoms listed as those of unrecognised myocardial infarction in patients admitted to the medical wards in NRMCH.

MATERIALS AND METHODS

Study Place- NRI Medical College and Hospital, Chinakakani, Guntur district.

Period of Study- Two years.

Study Design

All cases above age of 40 years with complaints listed as symptoms of unrecognised myocardial infarction were taken into study. A detailed history with special reference to risk factors for myocardial infarction was taken. A complete detailed physical examination was done and the patient progress in hospital was followed until discharge. All investigations including serial ECG, cardiac enzymes, echocardiogram with special reference to risk factor profile was done. The outcome of patients were studied.

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Inclusion Criteria

All cases above age of 40 years admitted in the ward, ICU with complaints listed as symptoms of unrecognised myocardial infarction, i.e. breathlessness, cough, fatigue, abdominal or epigastric pain, nausea and vomiting, syncope or giddiness or coma, palpitation, typical changes of acute myocardial infarction and raised cardiac enzymes.

Exclusion Criteria

- Cases with previous history of ischaemic heart disease.
- Cases presenting with typical or atypical angina.

Sample Size

All cases above age of 40 years who satisfy inclusion criteria getting admitted in ward/ICU during the study period.

Manoeuvres

All the following details will be obtained from patients who satisfy the inclusion criteria.

Presenting Complaints

- Chest pain, breathlessness.
- Sweating, palpitation.
- Nausea and vomiting.
- Abdominal pain, diarrhoea.
- Giddiness, syncope, coma.

Past History

- Diabetes mellitus, hypertension.

- Tuberculosis, ischaemic heart disease.
- Rheumatic heart disease.

Family History

- Diabetes mellitus, hypertension.
- Sudden death.

Personal History

- Tobacco consumption, alcohol consumption.
- Drug consumption, sleep pattern.

Clinical Examination

Pulse rate, respiratory rate, blood pressure and temperature during admission.

- General examination.
- Systemic examination.
- Investigations.
- Haemogram, urinalyses, blood sugar.
- Renal function tests, electrolytes.
- Cardiac enzymes, lipid profiles.
- ECG, echocardiogram.
- Outcome.
- Observation, total number of cases.
- Age group, mean age.
- Personal history, family history.
- Incidence of symptoms.
- Analysis of risk factors.
- Analysis of general examination.
- Analysis of vitals.
- Analysis of investigations.
- Analysis of clinical diagnosis.
- Analysis of mortality.

REVIEW OF LITERATURE

Acute Myocardial Infarction

It is defined as a clinical syndrome with characteristic symptoms, serial electrocardiographic changes, increase in the level of cardiac enzymes and pathological myocardial damage.

Acute myocardial infarction is a serious complication of atherosclerotic coronary artery disease. It usually results from the formation of a thrombus on an atheromatous plaque in an infarct-related artery. Coronary artery occlusion leads to myocardial ischaemia and late myocardial necrosis sets in. Progression of the atherosclerotic lesion to the point where thrombus formation occurs is a complex process related to vascular injury. The injury is produced and facilitated by the factors such as smoking, hypertension and lipid accumulation.

Unrecognised Myocardial Infarction

While most acute myocardial infarctions are characterised by significant and often severe symptoms, a substantial minority are accompanied by minimal or no discomfort. Consequently, many affected patients may not seek medical attention and the diagnosis maybe delayed for months or years. These patients are unaware of any history of myocardial infarction, but are ultimately identified clinically when electrocardiography shows diagnostic Q waves.

Such events, termed "unrecognised myocardial infarctions," were first described by Herrick in 1912.⁽¹⁾

Subsequent studies have demonstrated that unrecognised myocardial infarctions represent a significant proportion of all infarctions and that they may therefore represent a significant public health problem. Moreover, since available analyses have focused primarily on infarctions with persistent significant Q waves, the true prevalence of undetected infarctions maybe even greater than available estimates.

Pathophysiology of Unrecognised Myocardial Infarction

The Notion of a Defective Anginal Warning System. The specific course of events that leads to unrecognised myocardial infarction is not known; however, as in the case of recognised infarction, the process presumably begins with atherosclerotic plaque rupture and occlusion of a thrombotic coronary artery. According to this hypothesis, unrecognised myocardial infarction differs from recognised infarction in the translation of resultant myocardial ischaemia into symptomatic discomfort. Another possibility is that interpretation of symptoms may differ between persons with unrecognised myocardial infarction and those with recognised infarction. The former patients may be less likely to conclude that their symptoms represent a significant health problem. Abnormalities in either of these steps may lead to a "defective anginal warning system" and consequently to a clinically unrecognised event.^(2,3)

The Perception of Myocardial Ischaemia- Proposed Mechanisms

The normal events that span the spectrum from myocardial ischaemia to the perception of discomfort begin with stimulation of free nerve endings in the myocardium. Potential stimuli include mechanical factors such as ischaemia-induced changes in the tone of the ventricular wall and chemical factors released by cardiac myocytes in response to hypoxia.^(4,5) One such mediator is adenosine, which has been shown to reproduce chest pain in patients with angina.⁽⁶⁾ In addition, evidence suggests that the size of the myocardial infarction is important; larger infarctions induce greater discomfort. This may relate to the number of activated receptors.⁽⁷⁾

Once nerve endings are stimulated, the impulses progress along the cardiac sympathetic nerves to the thoracic sympathetic ganglia and then to the dorsal horn spinal neurons. From there, they travel through the spin thalamic tract to the thalamus and then through the thalamocortical tract to the cerebral cortex. The cortex decodes the impulse, ultimately leading to the conscious perception of discomfort. Areas of the brain that have been shown to have augmented blood flow during angina include the thalamus, hypothalamus, periaqueductal gray area and prefrontal and cingulate cortex.⁽⁸⁾

Blunted Perception of Myocardial Infarction- Potential Causes

Several factors may modulate the generation, conduction and processing of the afferent impulse; any of these factors could lead to depressed perception of myocardial ischaemia. While it is yet to be determined whether the processes that underlie silent myocardial ischaemia also lead to unrecognised myocardial infarction, the two entities overlap significantly,

thus, are view of proposed mechanisms for silent ischaemia is relevant.

Receptor and Afferent Neuron Dysfunction

In the model described above, the anatomic and functional integrity of cardiac sensory receptors and afferent neurons is a major factor in the perception of myocardial ischaemia. Inadequate receptor stimulation or frank receptor dysfunction may block impulse initiation and pain perception. In addition, pathologic changes of the afferent fibers may hinder impulse conduction. Autonomic neuropathy is the suggested explanation for the relatively high incidence of painless ischaemia in diabetic patients.⁽⁹⁾

Gating Mechanisms

The conduction of the afferent impulse may also be affected by various "gating mechanisms." It has been proposed that "gates" exist both in the dorsal horn of the spinal cord and in the thalamus.⁽⁸⁾ At these sites, multiple stimuli from varying locations may converge and effectively cancel each other. Some researchers have postulated that many patients do not perceive pain with myocardial infarction because other stimuli, such as dyspnoea, saturate sensory mechanisms.⁽¹⁰⁾ Moreover, it appears that inhibitory inputs from peripheral nerves and higher centers are directed at these gates and that these too may modulate or abolish the afferent impulse.⁽⁸⁾

Neuropsychiatric Factors

The translation of ischaemia into discomfort may also be blunted at a supratentorial level. At least some patients with silent ischaemia have completely normal function of afferent neuronal pathways, this implies a defect in the central nervous system.⁽¹¹⁾ The patient's state of alertness as well as the endogenous opioid system, may affect pain perception. Several treadmill studies have indicated that elevated β -endorphin levels may delay or prevent the onset of angina.⁽¹²⁻¹⁴⁾ Other investigations, however, including efforts to "unmask" silent ischaemia with naloxone have contradicted this finding and at present the role of opioids in unrecognised ischaemia and myocardial infarction has not been clearly established.^(15,16)

Evidence from mental stress experiments also suggests that silent ischaemic events may be associated with distinct patterns of brain activity. These studies have shown that mental stress can induce both symptomatic and asymptomatic myocardial ischaemia.⁽¹⁷⁻²¹⁾ To investigate potential underlying mechanisms, Soufer and colleagues⁽²²⁾ performed simultaneous positron emission tomography brain imaging and transthoracic echocardiography during mental stress. In patients with known coronary artery disease, mental stress-induced silent ischaemia was associated with a unique pattern of hyperactivation of several left brain structures and concomitant deactivation of several right brain structures as well as the anterior cingulate bilaterally.⁽²²⁾ This result expands on the findings of previous pharmacologic stress studies, which suggested that dobutamine-induced silent ischaemia as compared with dobutamine-induced angina is associated with relatively low amounts of metabolic activity in the frontal cortex.⁽²³⁾ Taken together, these findings suggest that failure to perceive ischaemia maybe based on the pattern and sequence in which brain structures are activated.

The patient's psychosocial milieu also has a complex effect, but it too may influence the degree of discomfort accompanying a myocardial infarction.⁽²⁴⁻²⁶⁾ Characteristics such as stoicism and denial, which have personal, social and cultural groundings play a substantial role in this context. Patients with painless myocardial ischaemia have higher pain thresholds as defined by reports of pain in response to noxious stimuli.⁽²⁷⁻³⁰⁾ Similarly, a patient's threshold for somatic pain correlates with the reported pain level during myocardial infarction. Finally, clinical depression may also play a role. Depression has been associated with autonomic dysfunction, medical nonadherence and other motivational issues and each of these has been proposed as an explanation for the relatively poor prognosis of depressed patients with coronary artery disease.^(31,32) Hypothetically, each of these factors could also confound recognition of an acute infarction.

Frequency of Unrecognised Myocardial Infarction

The most comprehensive data available on the frequency of unrecognised myocardial infarction originate from large cohort studies. The best known is the Framingham Study, which was based on 34 years of follow-up of 5070 participants.⁽³³⁻³⁷⁾ The most recent analysis of this study was published in 1990. In this series, unrecognised myocardial infarction represented 26% and 34% of all myocardial infarctions in men and women, respectively. Approximately, half of the affected patients had no symptoms whatsoever, whereas the remainder experienced nonspecific symptoms that at the time were not perceived to be the consequence of myocardial infarction.^(38,39)

These data are reinforced by recent analyses of the Reykjavik and cardiovascular health study samples. In the Reykjavik study, 35% of infarctions in men and 33% of infarctions in women were initially unrecognised.^(40,41) In the cardiovascular health study, which is based in four U.S. field centers and is confined to persons 65 years of age or older, 22% of all prevalent Q-wave infarctions at study entry had previously gone undetected.⁽⁴²⁾

For several reasons, these data probably underestimate the frequency of unrecognised myocardial infarction.⁽⁴³⁾ First, the electrocardiographic diagnosis of a previous myocardial infarction is based primarily on the identification of Q waves, and thus previously unrecognised non-Q-wave infarctions will not be detected. Second, unrecognised myocardial infarctions resulting in sudden cardiac death will also be missed in the absence of autopsy evidence of a recent infarction. Finally, the diagnosis of myocardial infarction maybe missed if an electrocardiogram is not obtained shortly after the event. It has been estimated that the electrocardiographic features of myocardial infarction disappear within 2 years in 10% of patients with an anterior infarction and 25% of those with an inferior infarction.⁽³⁹⁾ Others have estimated that, overall, 20% of patients who have survived an infarction have normal electrocardiograms 4 years after their event.⁽⁴⁴⁾

Risk Factors for Unrecognised Myocardial Infarction

To better understand, diagnose, treat and ultimately prevent unrecognised myocardial infarction, identifying predisposing factors would be helpful. Several analyses have addressed this issue, but study methods have varied. In some studies, such as the Western collaborative group and Israeli heart

attack studies participants with unrecognised myocardial infarction were compared with persons drawn from the population at large.^(45,46) In others, patients with unrecognised myocardial infarction were directly compared with persons who had recognised infarctions.^(38,40,42,47) Furthermore, most studies comparing groups with recognised and unrecognised infarctions have been limited to univariate analyses and have not sought to identify factors that are independently associated with infarction recognition. To address this concern, the recent analysis of the cardiovascular health study used a multivariate model that tested several factors for associations with infarction recognition while controlling for potential confounding issues.⁽⁴²⁾

Hypertension

Previous research has suggested that hypertension is associated with alterations in pain perception. The baroreflex system has been shown to have the capacity to attenuate transmission of noxious stimuli and evidence indicates that endogenous opiates may affect blood pressure with possible depressor or pressor effects.⁽⁴⁸⁻⁵⁰⁾ Hypertensive patients have relatively high β -endorphin levels.⁽⁵¹⁾ Perhaps as a result, hypertensive patients with coronary artery disease report relatively little pain in response to somatic noxious stimuli.^(52,53)

Epidemiologic studies have supported these physiologic findings. In the Western Collaborative Group Study, mean systolic and diastolic blood pressures were higher in patients with "silent" infarctions than in those with no evidence of coronary disease.⁽⁴⁵⁾ In the Israeli Heart Attack Study, systolic blood pressure and left ventricular hypertrophy were clearly correlated with incidence of unrecognised myocardial infarction.⁽⁴⁶⁾ Similarly, in the Reykjavik cohort, when patients with unrecognised myocardial infarction were compared with all other participants, the use of antihypertensive diuretic therapy was significantly associated with the development of unrecognised myocardial infarction with an odds ratio of 6.2.⁽⁴⁰⁾

However, direct comparisons of patients with unrecognised myocardial infarction to those with recognised infarctions have failed to confirm a unique link between blood pressure and infarction recognition. The Reykjavik and Honolulu Heart studies as well as the most recent Framingham analysis suggested trends toward more hypertension in the unrecognised myocardial infarction group, but these trends were not statistically significant.^(38,40,47) Also, in the cardiovascular health study, systolic and diastolic blood pressures were univariate predictors of infarction recognition; in multivariate modeling, however, these associations lost significance.⁽⁴²⁾ Therefore, it remains uncertain whether hypertension and unrecognised myocardial infarction are specifically linked or whether the association simply reflects the fact that hypertension is a risk factor for coronary artery disease.

Age

During an evolving myocardial infarction, elderly patients appear prone to experience diminished or atypical symptoms and they are at increased risk for delayed presentation to the hospital.^(54,55) This suggests that they may also be at risk for unrecognised myocardial infarction. As with hypertension,

mechanisms linking age to unrecognised myocardial infarction have not been clearly established, but several possible explanations have been postulated. These include cognitive changes, such as dementia, the degree of comorbid illness and potential age-related decreases in sensory nerve function.^(56,57,58)

Most studies of unrecognised myocardial infarction have included few older patients, but the available data suggest that the incidence of unrecognised myocardial infarction increases with age. In the Reykjavik study, the risk for unrecognised myocardial infarction increased approximately 10% per year of life.⁽⁴⁰⁾ In the Israeli heart attack series, the proportion of unrecognised infarctions increased from 38% in participants 39 to 59 years of age to 49% in those 60 years of age or older.⁽⁴⁶⁾ Similarly, in the Bronx Aging Study, which followed 390 patients who were at least 75 years of age, the percentage of unrecognised incident myocardial infarctions was higher (44%).

As in the case for hypertension, only a few analyses have directly compared the ages of patients who had unrecognised myocardial infarction with the ages of those who had recognised infarction. The results are inconsistent. Unadjusted analyses in the Framingham cohort showed that among men, survivors of unrecognised myocardial infarction were significantly older than survivors of recognised infarction, but this was not the case for women.⁽³⁶⁾ In addition, in the cardiovascular health study, older age was a significant predictor of unrecognised myocardial infarction in unadjusted analysis; in multivariate analysis, however, the association lost statistical significance.⁽⁴²⁾ Consequently, as in the case of hypertension, it remains uncertain whether there is a specific link between age and unrecognised myocardial infarction or whether their association is due simply to the effects of ageing on the development of coronary atherosclerosis.

Diabetes Mellitus

Several basic sciences, clinical and epidemiologic studies have suggested an association between diabetes mellitus and unrecognised myocardial infarction. For example, diabetic patients have high rates of asymptomatic myocardial ischaemia.⁽⁵⁹⁻⁶²⁾ While the mechanisms have not been confirmed, evidence suggests that diabetic autonomic neuropathy plays a significant role by attenuating sensory inputs from ischaemic myocardium.⁽⁶³⁻⁶⁵⁾ In diabetic patients who had had a silent infarction, autopsy has shown pathologic changes in cardiac afferent neurons that are consistent with a neuropathy.⁽⁹⁾

Perhaps as a result of these neurologic issues, diabetic patients with suspected coronary artery disease pose a difficult challenge for clinicians. Among patients with recognised infarction, diabetic patients tend to report less pain and in fact diabetes mellitus is an independent predictor of "painless" myocardial infarction.^(66,67) Conversely, diabetic patients with myocardial infarction tend to have high rates of congestive heart failure and their evaluation and management maybe confounded by high rates of diabetic complications including renal failure and infections.⁽⁶⁸⁾

However, despite all these supporting evidence, none of the existing epidemiologic analyses have identified diabetes as an independent predictor of infarction recognition. The reasons for this are unclear.⁽⁶⁹⁾ Diabetic neuropathy may

certainly impair recognition, but significant neurologic dysfunction is typically a manifestation of relatively advanced diabetes. Thus, the impact of this diabetic complication maybe masked by the inclusion in epidemiologic databases of many diabetic patients with milder disease. Another possibility is that diabetic patients may receive more counseling and clinical attention for the presentations of coronary artery disease; thus, despite altered neuronal function, they may be less likely to have an infarction that escapes attention.

Finally, as suggested earlier, the pain suppression associated with diabetes mellitus maybe offset by other symptoms that often accompany myocardial infarction in patients with diabetes. Diabetic patients with acute infarctions not only have high rates of congestive heart failure, but also are more likely to present with shock or cardiac arrest.⁽⁷⁰⁾ Each of these conditions typically prompts emergency clinical attention and thus infarction recognition.

Sex

Relatively, few studies have evaluated potential associations between sex and infarction recognition, but the available data suggest that women are at relatively high risk for unrecognised myocardial infarction. As was seen with older age, female sex has been associated with delayed presentation to the hospital with a recognised myocardial infarction.⁽⁵⁵⁾ In the Framingham and cardiovascular health study analyses, the proportion of infarctions that were initially unrecognised was substantially higher in women than in men.^(40,41) In the Framingham study as discussed above, 34% of infarctions in women compared with only 26% in men were initially undetected.⁽³⁸⁾ In the cardiovascular health study, although sex was not independently associated with infarction recognition, the unadjusted odds of unrecognised myocardial infarction were 45% greater in women than in men ($P=0.02$).⁽⁴²⁾

Here again, the explanations are probably multifactorial and the cardiovascular health study analysis suggests that confounding factors are involved. Nonetheless, misperceptions of the prevalence and manifestations of coronary artery disease in women may play a significant role. Both physicians and the general public appear to mistakenly believe that coronary artery disease and myocardial infarction are relatively uncommon in women.^(71,72) Contributing factors include the under-representation of women in clinical trials and the resultant lack of data on the results of therapy in female patients. Consequently, many women may not appreciate the significance of cardiac symptoms. This problem is compounded by other factors that complicate the clinical evaluation of women with coronary syndromes. These include a relatively high prevalence of "atypical" symptoms, including abdominal and back pain that may inhibit infarct detection.⁽⁷³⁻⁷⁵⁾

Other Potential Risk Factors

Relatively, few data are available on other potential risk factors for unrecognised myocardial infarction, but the existing information provides valuable insights into the epidemiology of this entity. Many authors have argued that, in general, the other factors leading to unrecognised

myocardial infarction are probably identical to the other established risk factors for coronary artery disease. The data from the cardiovascular health study support this notion because they showed that none of the traditional coronary risk factors independently distinguished patients with prevalent unrecognised myocardial infarction from those with recognised infarction.⁽⁴²⁾

The more interesting finding of the cardiovascular health study was discovery of the factors that ultimately did distinguish these two groups. In multivariate analysis, the important factors were established cardiac conditions and diagnoses (or the lack thereof). The two independent predictors of unrecognised myocardial infarction were the absence of angina and the absence of congestive heart failure. There was also a trend toward an association with low FEV_1 .⁽⁴²⁾

The absence of angina predicted unrecognised myocardial infarction not only in the cardiovascular health study, but also in the Framingham and Reykjavik studies. In the Framingham study, 53% of patients with recognised infarction, but only 24% of those with unrecognised infarction reported a history of angina. In women, the percentages were 45% and 33%, respectively.⁽⁴⁰⁾ Similarly, in the Reykjavik study,⁽⁴⁰⁾ 58% of patients with recognised myocardial infarction, but only one third of those with unrecognised infarction reported a history of this condition ($P<0.001$).

This reproducible association with the absence of angina may at least partly explain the frequency and pathophysiology of unrecognised myocardial infarction. The influence of the absence of angina may simply reflect diagnosis bias. Physicians may more aggressively counsel and follow patients with angina and they maybe more likely to detect myocardial infarction in this population. Another possibility is that the central role of the absence of angina may relate to neurologic factors. More specifically, the association between the absence of angina and unrecognised myocardial infarction suggests that survivors of unrecognised infarction may have a generalised inability to perceive myocardial ischaemia. This theory has also been invoked to explain detected infarctions that are manifested by symptoms other than pain. Research has shown that patients with painless detected infarctions similar to patients with initially unrecognised infarctions have very low rates of antecedent angina.^(76,77)

The associations of congestive heart failure and FEV_1 with unrecognised myocardial infarction are speculative and have not been shown in other cohorts. In part, they too may relate to diagnosis bias. Patients with congestive heart failure may be followed more closely for new cardiovascular events and chest symptoms in patients with pulmonary disease maybe more likely to be attributed to respiratory processes. An alternative theory is that these associations may result from neurologic conditions. Patients with unrecognised myocardial infarction may have generalised sensory dysfunction that precludes the perception not only of infarction, but also of congestive heart failure.⁽⁷⁶⁾ Meanwhile, in patients with lung disease, the afferent nervous system maybe overloaded with respiratory signals and therefore block the perception of pain.

OBSERVATION

A total number of 22 patients were included in this study. While most of the patients were evaluated prospectively, few were evaluated retrospectively.

General Characteristics

Most of the patients belonged to the area in and around Guntur. The majority of the patients were engaged in agriculture or manual labour. The income range was between 500 to 1000 rupees per month. Patients presented directly or were referred to our hospital.

Those patients who did not develop serious complications were discharged after an average stay of 9.89 days and those patients who died had an average stay of 3.25 days.

Age

Patients above 40 yrs. were taken into study. Patients ranged from 40 yrs. to 78 yrs. Most patients were between age group 51 and 60, i.e. 10.

Age Groups	Number of Patients
40-49	8
50-59	10
60-69	2
70-79	2
Total	22

Gender

Female number was 12 and they dominated the study, compared to males, who were only 10 in number. M:F=5:6. Among females, 3 were premenopausal and 9 were postmenopausal.

Clinical History on Admission

Out of 22 patients, 11 presented with breathlessness, 10 with sweating, 8 with abdominal pain, 7 with cough and expectoration, 6 with fever, 5 with nausea and vomiting, 3 with oedema, 2 each with palpitation and hemiplegia and 1 each with giddiness, bleeding per rectum and coma.

Among 11 patients with breathlessness, 2 patients presented with palpitation; 2 with oedema; 1 with fever; 1 patient presented with abdominal pain, nausea and vomiting; 2 with sweating, cough and expectoration; 1 with sweating, cough and expectoration, nausea and vomiting; 1 with sweating, cough and expectoration, loose stools, fever; 1 with sweating, cough and expectoration, fever, abdominal pain.

Three patients presented with abdominal pain, sweating, cough and expectoration, loose stools, nausea and vomiting; 1 with sweating, cough and expectoration, nausea and vomiting, fever; 1 with sweating, nausea and vomiting.

Two patients presented with hemiplegia also had palpitation. 1 patient presented unconscious.

There exists a positive correlation between sweating and diabetes, which was statistically significant, i.e. $p < 0.001$ according to Pearson correlation coefficient.

Symptoms	Number of Patients
Breathlessness	11
Sweating	10
Abdominal pain	8
Cough and expectoration	7
Fever	6

Nausea and vomiting	5
Loose stools	4
Oedema	3
Hemiplegia	2
Palpitation	2
Giddiness	1
Unconsciousness	1

Risk Factors

Out of 22 patients, 9 were diabetic, 6 were hypertensive, 5 had family history of diabetes, 4 had family history of hypertension, 2 had family history of sudden death; 1 patient was diabetic and hypertensive; 3 had family history of diabetes and hypertension; none of the patient had history of coronary artery disease.

9 out of 10 male patients smoked and none of the female patients smoked. 6 out of 10 male patients consumed alcohol. Among smokers, 6 smoked more than one pack of beedies per day and 3 smoked more than one pack of cigarettes per day.

Out of 6 patients who consumed alcohol, 100-200 mL of arrack per day, 3 consumed 2 to 3 drinks of whisky occasionally, 1 patient consumed 1 pint of beer every month. None of the female patients smoked had consumed alcohol or oral contraceptive pills. All the 22 patients were married.

Sl. No.	Risk Factor	Number of Patients
1.	DM	9
2.	HTN	6
3.	Smoking	9
4.	Alcohol	6
5.	Family	5
6.	History of DM	4
7.	Family history of HTN	2

Lipid Profile

Serum cholesterol was elevated above 200 mg/dL in 14 patients. 16 had triglyceride levels above 200 mg/dL. All the 22 patients had HDL cholesterol levels below 50 mg/dL and 8 had LDL cholesterol levels above 130 mg/dL. Mean cholesterol was 198.2, mean triglyceride was 226.68, mean HDL cholesterol was 42.50 and mean LDL cholesterol was 127.46.

Sl. No.	Lipid Profile	Number of Patients
1.	Hypercholesterolaemia	14
2.	>200 mg/dL	16
3.	Hypertriglyceridaemia	22
4.	>200 mg/dL	8

Lipid Profile	Gender	No. of Pts.	Mean	S.D.	t' value	Level of Signi'
S. Chol	M	10	206.4	54.1	0.275	
	F	12	198.7	73.8		NS
S. Trigly	M	10	221.2	53.7	-0.712	
	F	12	239.7	65.2		NS
S. HDL	M	10	42.7	5.8	0.177	
	F	12	42.33	5.4		NS
S. LDL	M	10	126	40.6	-0.433	
	F	12	133.7	39		NS

The table reveals that males scored higher mean value of S. cholesterol and HDL levels, while females scored higher mean value of S. triglyceride and LDL levels.

On subjecting the data to Chi-square test, the t-value is <1.96, so it is inferred that, even though there exists a

difference in mean between males and females, it is not statistically significant.

General Examination

4 patients had pulse above 100 per minute, 6 were febrile, 3 had raised JVP, 7 were underweight (i.e., BMI <18.5), 1 was overweight (BMI=26.5), 9 were pale, 2 had bilateral pandigital clubbing, 3 had bilateral pitting pedal oedema, 4 had pansystolic murmur and 5 had bilateral basal crepitations.

Blood Pressure

8 patients had systolic BP in between 120-139 mmHg and 8 had <120 mmHg, 7 each had diastolic BP in between 80-89 mmHg and 90-99 mmHg, mean systolic BP was 121.82 mmHg and diastolic BP was 83.55 mmHg, 6 had systolic BP above 140 mmHg and 10 had diastolic BP above 90 mmHg.

JNC 7 Staging of HTN	Systolic BP (mmHg)	Number of Patients among 22
Normal	<120	8
Pre HTN	120-139	8
Stage I HTN	140-159	2
Stage II HTN	≥160	4

JNC 7 staging of HTN	Diastolic BP (mmHg)	Number of Patients
Normal	<80	5
Pre HTN	80-89	7
Stage I HTN	90-99	7
Stage II HTN	≥100	3

CPK-MB

Mean creatine phosphokinase-MB at admission 58.68, at 6 hrs. 60.50 and at 12 hrs. 30.7. CPK-MB is raised significantly in all patients at admission at 6 hrs. and at 12 hrs. There exists a positive correlation between these groups, which was statistically significant.

The table reveals that males scored higher mean value of CPK-MB at 6 hrs. and 12 hrs. while females scored higher mean value of CPK-MB at admission.

On subjecting the data to Chi-square test, the t-value is <1.96, so it is inferred that, even though there exists a difference in mean between males and females, it is not statistically significant.

CPK-MB	Gender	No. of Pts.	Mean	S.D.	t-value	Level of Significance
At Adm.	M	10	52.6	27.5	-0.37	NS
	F	12	59.1	51.6		
At 6 hrs.	M	10	65.3	54.6	0.38	NS
	F	12	56.08	54.2		
At 12 hrs.	M	10	31.6	22.8	0.88	NS
	F	12	23.8	15.8		

ECG

Out of 22 patients, 3 patient's ECG showed ASMI, 4 showed ALMI, 4 showed AAMI, 8 showed IWMI and 3 showed NQWMI.

Type of MI	Number of Patients
AAMI	4
ALMI	4
IWMI	8
ASMI	3
NQWMI	3

2D-Echo

Out of 22 patients, 9 had left ventricular dysfunction, 1 had ischaemic cardiomyopathy, 1 had pericardial effusion and 3 normal study. 2 of the 9 patients having LV dysfunction had mitral regurgitation.

Sl. No.	Clinical Diagnosis	No. of Patients among 22
1.	Pulmonary tuberculosis	4
2.	Cerebrovascular accident	3
3.	Acute gastroenteritis	3
4.	Hypothyroidism	3
5.	Iron deficiency anaemia	3
6.	Chronic alcoholism	1
7.	Leptospirosis	1
8.	Secondaries lung	1
9.	Fistula in ano	1
10.	Pneumonia	1

Mortality

4 patients expired among 22. Out of the 4, 2 were diagnosed acute gastroenteritis, 1 COPD and 1 CVA.

RESULTS

Of the 22 patients included in the study, 45.45% were in the age group of 50-59, 36.4% in the age group 40-49 and 9.09% each in the age group 60-69 and above 70 yrs. The age group 50-59 had 60% females and 40% males.

Out of 22 patients, 50% presented with breathlessness, 45.45% with sweating, 36.36% with abdominal pain, 31.82% with cough and expectoration, 27.27% with fever, 22.73% with nausea and vomiting, 13.64% with oedema, 18.18% with loose stools, 9.09% each with palpitation and hemiplegia, 4.55% each with giddiness, bleeding per rectum and coma.

Out of 22 patients, 40.9% were diabetic, 27.27% were hypertensive, 22.73% had family history of diabetes, 18.18% had family history of hypertension, 9.09% had family history of sudden death; 4.55% patient was diabetic and hypertensive; 13.64% had family history of diabetes and hypertension.

40.91% smoked and 27.27% consumed alcohol. Among smokers, 66.67% smoked more than one pack of beedies per day and 33.31% smoked more than one pack of cigarettes per day.

Serum cholesterol was elevated above 200 mg/dL in 63.64% patients. 72.73% had triglyceride levels above 200 mg/dL. 100% patients had HDL levels below 50 mg/dL and 36.36% had LDL levels above 130 mg/dL.

Out of 22 patients, 13.64% were ASMI, 18.18% were ALMI, 31.84% had AAMI and 36.36% had IWMI.

Clinical Diagnosis

18.18% were diagnosed as pulmonary tuberculosis, 13.64% as cerebrovascular accident, 13.64% as acute gastroenteritis, 13.64% as hypothyroidism, 4.55% each as COPD, chronic alcoholism, leptospirosis, secondaries lung, fistula in ano and pneumonia.

Mortality

9.09% of postmenopausal women expired and none of the premenopausal women expired.

18.18% patients expired among 22. Out of the 18.18%, 50% were diagnosed as acute gastroenteritis, 25% as COPD and 25% as CVA.

9.09% of the patients admitted with breathlessness, 9.09% with unconsciousness, 50% with loose stools, 37.5% with abdominal pain, 33.33% with nausea, 30% with sweating expired.

Patients admitted with abdominal pain, loose stools and sweating had a mortality rate of 50%. 33.33% of patients who smoked died and 33.33% who consumed alcohol died. None of the patients who were diabetic died.

50% of the patients who had history of hypertension died. 25% of the patients who had family history of hypertension died. 20% of the patients who had family history of diabetes died. 50% of the patients who had family history of sudden death died.

50% showed ASMI and 50% showed IWMI in patients who expired.

DISCUSSION

In this study of 22 patients during a period of 2 yrs., patients were included only above 40 yrs. The maximum number i.e. 10 of patients were in the age group 50-59 yrs.

The Reykjavik study done in 1995 showed that the incidence was almost zero for those younger than age 40 yrs. and increased steadily from age 40 yrs. to 60 yrs. After age 65 yrs., incidence decreased with age.^[40] Almost, a similar picture was seen in our study, i.e. the majority 18 (81.82%) were in age group 40 to 59 yrs. while only 4 (18.18%) in age group 60 to 79 yrs.

During an evolving myocardial infarction, elderly patients appear prone to experience diminished or atypical symptoms and they are at increased risk for delayed presentation to the hospital.^[54,55] This suggests that they may also be at risk for unrecognised myocardial infarction. As with hypertension, mechanisms linking age to unrecognised myocardial infarction have not been clearly established, but several possible explanations have been postulated. These include cognitive changes, such as dementia; the degree of comorbid illness; and potential age-related decreases in sensory nerve function.^[57,58]

Most studies of unrecognised myocardial infarction have included few older patients, but the available data suggest that the incidence of unrecognised myocardial infarction increases with age. In the Reykjavik study, the risk for

unrecognised myocardial infarction increased approximately 10% per year of life.^[40] In the Israeli Heart Attack Series, the proportion of unrecognised infarctions increased from 38% in participants 39 to 59 years of age to 49% in those 60 years of age or older.^[46] Similarly, in the Bronx Aging Study, which followed 390 patients who were at least 75 years of age, the percentage of unrecognised incident of myocardial infarction was higher (44%).

In addition, in the cardiovascular health study, older age was a significant predictor of unrecognised myocardial infarction in unadjusted analysis; in multivariate analysis, however, the association lost statistical significance.^[42] Consequently, as in the case of hypertension, it remains uncertain whether there is a specific link between age and unrecognised myocardial infarction or whether their association is due simply to the effects of ageing on the development of coronary atherosclerosis.

Females dominated the study compared to males, i.e. 6:5 relatively few studies have evaluated potential associations between sex and infarction recognition, but the available data suggest that women are at relatively high risk for unrecognised myocardial infarction. In the Framingham and Cardiovascular Health Study analyses, the proportion of infarctions that were initially unrecognised was substantially higher in women than in men.^[40,41] In the Framingham Study, 34% of infarctions in women compared with only 26% in men were initially undetected.^[38] In the cardiovascular health study, although sex was not independently associated with infarction recognition, the unadjusted odds of unrecognised myocardial infarction were 45% greater in women than in men ($P=0.02$).^[42]

Here again, the explanations are probably multifactorial and the cardiovascular health study analysis suggests that confounding factors are involved. Nonetheless, misperceptions of the prevalence and manifestations of coronary artery disease in women may play a significant role. Both physicians and the general public appear to mistakenly believe that coronary artery disease and myocardial infarction are relatively uncommon in women.^[71,72] Contributing factors include the under-representation of women in clinical trials and the resultant lack of data on the results of therapy in female patients. Consequently, many women may not appreciate the significance of cardiac symptoms. This problem is compounded by other factors that complicate the clinical evaluation of women with coronary syndromes. These include a relatively high prevalence of "atypical" symptoms, including abdominal and back pain that may inhibit infarct detection.^[73-75]

Mortality was 9.09% in postmenopausal women compared to nil in premenopausal women. A study done by C.B. Patil et al showed that complications and mortality were more common in postmenopausal women.

11 patients presented with breathlessness. It has been proposed that "gates" exist both in the dorsal horn of the spinal cord and in the thalamus.^[8] At these sites, multiple stimuli from varying locations may converge and effectively cancel each other. Some researchers have postulated that many patients do not perceive pain with myocardial infarction, because other stimuli, such as dyspnoea, saturate sensory mechanisms.^[10] Moreover, it appears that inhibitory inputs from peripheral nerves and higher centers are

directed at these gates and that these too may modulate or abolish the afferent impulse.⁽⁸⁾

9 presented with different gastrointestinal symptoms and 10 with sweating. This may be due to autonomic symptoms of diabetes. Several basic sciences, clinical and epidemiologic studies have suggested an association between diabetes mellitus and unrecognised myocardial infarction. For example, diabetic patients have high rates of asymptomatic myocardial ischaemia.⁽⁵⁹⁻⁶²⁾ While the mechanisms have not been confirmed, evidence suggests that diabetic autonomic neuropathy plays a significant role by attenuating sensory inputs from ischaemic myocardium.⁽⁶³⁻⁶⁵⁾ In diabetic patients who had had a silent infarction, autopsy has shown pathologic changes in cardiac afferent neurons that are consistent with a neuropathy.⁽⁹⁾

Among the risk factors associated with unrecognised myocardial infarction, 9 had diabetes, perhaps as a result of these neurologic issues, diabetic patients with suspected coronary artery disease pose a difficult challenge for clinicians. Among patients with recognised infarction, diabetic patients tend to report less pain and in fact diabetes mellitus is an independent predictor of "painless" myocardial infarction.^(66,67) Conversely, diabetic patients with myocardial infarction tend to have high rates of congestive heart failure and their evaluation and management maybe confounded by high rates of diabetic complications including renal failure and infections.⁽⁶⁸⁾

However, despite all this supporting evidence, none of the existing epidemiologic analyses have identified diabetes as an independent predictor of infarction recognition. The reasons for this are unclear.⁽⁶⁹⁾ Diabetic neuropathy may certainly impair recognition, but significant neurologic dysfunction is typically a manifestation of relatively advanced diabetes. Thus, the impact of this diabetic complication maybe masked by the inclusion in epidemiologic databases of many diabetic patients with milder disease. Another possibility is that diabetic patients may receive more counseling and clinical attention for the presentations of coronary artery disease; thus, despite altered neuronal function, they may be less likely to have an infarction that escapes attention.

Finally, as suggested earlier, the pain suppression associated with diabetes mellitus maybe offset by other symptoms that often accompany myocardial infarction in patients with diabetes. Diabetic patients with acute infarctions not only have high rates of congestive heart failure, but also are more likely to present with shock or cardiac arrest.⁽⁷¹⁾ Each of these conditions typically prompts emergency clinical attention and thus infarction recognition.

6 patients of the 22 were hypertensive. Previous research has suggested that hypertension is associated with alterations in pain perception. The baroreflex system has been shown to have the capacity to attenuate transmission of noxious stimuli and evidence indicates that endogenous opiates may affect blood pressure with possible depressor or pressor effects.⁽⁴⁸⁻⁵⁰⁾ Hypertensive patients have relatively high β -endorphin levels.⁽⁵¹⁾ Perhaps as a result, hypertensive patients with coronary artery disease report relatively little pain in response to somatic noxious stimuli.^(52,53)

Epidemiologic studies have supported these physiologic findings. In the Western Collaborative Group Study, mean systolic and diastolic blood pressures were higher in patients with "silent" infarctions than in those with no evidence of

coronary disease.⁽⁴⁵⁾ In the Israeli Heart Attack Study, systolic blood pressure and left ventricular hypertrophy were clearly correlated with incidence of unrecognised myocardial infarction.⁽⁴⁶⁾ Similarly, in the Reykjavik cohort, when patients with unrecognised myocardial infarction were compared with all other participants, the use of antihypertensive diuretic therapy was significantly associated with the development of unrecognised myocardial infarction with an odds ratio of 6.2.⁽⁴⁰⁾

However, direct comparisons of patients with unrecognised myocardial infarction to those with recognised infarctions have failed to confirm a unique link between blood pressure and infarction recognition. The Reykjavik and Honolulu Heart studies, as well as the most recent Framingham analysis, suggested trends toward more hypertension in the unrecognised myocardial infarction group, but these trends were not statistically significant.^(38,40,47) Also, in the cardiovascular health study, systolic and diastolic blood pressures were univariate predictors of infarction recognition; in multivariate modeling, however, these associations lost significance.⁽⁴²⁾

Therefore, it remains uncertain whether hypertension and unrecognised myocardial infarction are specifically linked or whether the association simply reflects the fact that hypertension is a risk factor for coronary artery disease.

The data from the cardiovascular health study showed that none of the traditional coronary risk factors independently distinguished patients with prevalent unrecognised myocardial infarction from those with recognised infarction.⁽⁴²⁾

Smoking is an individual risk factor for CAD. 90% of males included on the study smoked. Among the smokers, 6 smoked beedies and 3 smoked cigarettes. Smoking ≥ 10 beedies or cigarettes per day carries an independent four-fold increased risk of acute myocardial infarction.⁽⁷⁸⁾ There is evidence that the influence of smoking is not only independent, but also synergistic with other risk factors such as hypertension and elevated serum cholesterol.

60% of the males consumed alcohol in the study. High alcohol intake is an independent risk factor for CAD, hypertension and all cardiovascular diseases.

Hypercholesterolaemia was noticed in 14 of the 22 patients, hypertriglyceridaemia in 16, low HDL in all 22 and high LDL in 8. There was significantly high prevalence of dyslipidaemia in Indian population according to W. J. Wadhwani et al.⁽⁷⁹⁾

CPK-MB was elevated significantly in all patients. Currently, the most cost effective and valid method for detecting unrecognised myocardial infarction is ECG.⁽⁸⁰⁾ In our study, IWMi was found in 8 patients followed by AWMI and ALMI.

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